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A systematic review of the effectiveness and cost-effectiveness of neuroimaging assessments used to visualise the seizure focus in people with refractory epilepsy being considered for surgery

P Whiting, R Gupta, J Burch, RE Mujica Mota, K Wright, A Marson, U Weishmann, A Haycox, J Kleijnen and C Forbes

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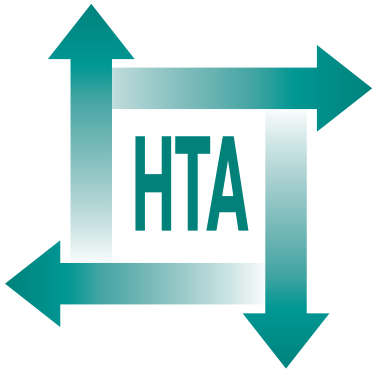

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The research reported in this monograph was commissioned by the HTA Programme as project number 02/05/01. The contractual start date was in June 2003. The draft report began editorial review in July 2004 and was accepted for publication in May 2005. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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Abstract

A systematic review of the effectiveness and cost-effectiveness of neuroimaging assessments used to visualise the seizure focus in people with refractory epilepsy being considered for surgery

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Objective: To review the effectiveness and/or accuracy, cost-effectiveness, and predictive value of neuroimaging of the cerebral cortex to visualise the seizure focus in people with refractory epilepsy being considered for surgery.
Data sources: Electronic databases, Internet searches, hand searching and consultation with experts.
Methods: A systematic review was undertaken according to published guidelines. Results of diagnostic accuracy studies were analysed according to the imaging test evaluated. For each study the proportion of patients who were correctly localised, not localised, partially localised or incorrectly localised by the index test was calculated. Due to the heterogeneity present between studies, statistical pooling was not performed. Instead, a narrative synthesis of results is presented. For studies using multivariate analysis to look at the association of neuroimaging findings and outcome following surgery, all factors considered in the analyses were presented. Studies were grouped according to the neuroimaging technique investigated and the findings discussed with reference to possible sources of heterogeneity between studies.
Results: No randomised controlled trials (RCTs) were identified, with the majority of studies evaluating the diagnostic accuracy of various imaging techniques in the localisation of epileptic seizure foci. There was significant heterogeneity ($p < 0.05$) between studies for at least one of the localisation categories (correctly localised, not localised, partially localised and incorrectly localised) for all imaging techniques. Possible explanations for this heterogeneity include differing study designs, index test characteristics, reference standards and population characteristics. Test performance was more promising in studies restricted to patients with temporal lobe epilepsy. Ictal single photon emission computed tomography (SPECT) generally had more correctly localising (70–100%) and fewer non-localising (0–7%) scans than other techniques evaluated in patients with temporal lobe epilepsy. Results for computed tomography and interictal SPECT suggest that these tests are relatively poor at localising the seizure focus. Volumeric magnetic resonance imaging (MRI) and position emission tomography (PET) appear promising, and subtraction ictal single photon emission computed tomography co-registered to magnetic resonance imaging (SISCOM) and magnetic resonance spectrosopy (MRS) less promising than ictal SPECT, but these technologies have been assessed in fewer studies. T2 relaxometry was reported in only one small study with inconclusive results. Seventeen studies (33 evaluations) provided sufficient data on the association of a localised scan with outcome following surgery to calculate a relative risk. The majority of evaluations (24/33) suggested that patients with a correctly or partially localised scan had a better outcome following surgery than those with an incorrectly localised or non-localised scan. However, this association was statistically significant in only three studies, two evaluating routine MRI [(relative risk (RR) 2.74, 95% confidence interval (CI): 1.32 to 5.67; RR 1.28, 95% CI: 1.00 to 1.63] and the other SISCOM (RR 2.12, 95% CI: 1.01, 4.44). Nine studies used multivariate analysis to investigate the association of MRI (7 studies), MRS and volumetric MRI (1 study), PET (3 studies), SPECT (1 study) and SISCOM (3

studies) with the outcome following surgery. There was a trend for localisation of abnormalities to be associated with a beneficial outcome.

Conclusions: Due to the limitations of the included studies, the results of this review do little to inform clinical practice, with insufficient evidence regarding effectiveness and cost-effectiveness of imaging techniques in the work-up for epilepsy surgery. Given the inadequacy of existing data, there is a pressing need for studies investigating the utility of imaging techniques in the work up for epilepsy surgery. The most reliable method to achieve this is the RCT, which could examine the single tests or combinations of tests on patient outcome. The authors suggest that it is important that clinicians, patient groups, policy makers and healthcare/research funders meet and debate the most appropriate way to investigate these technologies.

Contents

Glossary and list of abbreviations vii

Executive summary ix

1 Background 1
Epidemiology and cost of epilepsy 1
Classification of the epilepsies 1
Surgery for epilepsy 1
Work-up for epilepsy surgery 2
Evaluating diagnostic accuracy 4

2 Research questions 7

3 Review methods 9
Search strategy 9
Inclusion/exclusion criteria 9
Data extraction 11
Quality assessment 14
Statistical analysis 15
Sensitivity analyses 16

4 Details of studies included in the review .. 17
Diagnostic accuracy studies 17

5 Results of the review 23
Results of the literature searches 23
Study quality 23
Findings from diagnostic accuracy studies 31
Findings from outcome prediction studies 90

6 Sensitivity analysis 97

7 Economic analysis 101

8 Discussion 103
Key findings 103
Variability 103
Strengths and limitations of the review 105
Cost-effectiveness 106
Future directions 107

9 Conclusions 109
Implications for practice 109
Implications for research 109

Acknowledgements 111

References 113

Appendix 1 Advisory panel members 129

Appendix 2 Detailed search strategies 131

Appendix 3 Details of criteria for scoring studies 135

Appendix 4 Details of studies excluded from the review 139

Appendix 5 Study details 147

Appendix 6 Protocol changes 233

Health Technology Assessment reports published to date 235

Health Technology Assessment Programme 247

Glossary and list of abbreviations

Technical terms and abbreviations are used throughout this report. The meaning is usually clear from the context, but a glossary is provided for the non-specialist reader. In some cases, usage differs in the literature, but the term has a constant meaning throughout this review.

Glossary

BOLD signal localised decreases in blood oxygenation level

***F*-ratio** the ratio of the regression variance to the error variance [sums of squares regression/(number of estimated coefficients – 1)]/[sums of squares error/(sample size – number of estimated coefficients)]

ictal during a seizure

interictal during a period between seizures. Typically at least 24 hours have elapsed since the last seizure

postictal immediately after a seizure

QUOROM A checklist of items to improve the reporting of randomised controlled trials

Standardised regression coefficient regression coefficient that has been multiplied by the standard deviation; allows direct comparison between variables as to their relative power for predicting the response variable

STARD a checklist of items to improve the reporting of diagnostic studies

T1 imaging MRI images weighted with T1 signal

T2 imaging MRI images weighted with T2 signal

List of abbreviations

AED	antiepileptic drug
AH	amygdalohippocampectomy
AMT	α-methyl-L-tryptophan
ATL	anterior temporal lobectomy
CBF	cerebral blood flow
Cho	choline
CI	confidence interval
CPS	complex partial seizures
Cr	creatine
CRD	Centre for Reviews and Dissemination
CSAG	Clinical Standards Advisory Group
CSI	chemical shift imaging
CT	computed tomography
DTI	diffusion tensor imaging
ECD	^{99m}Tc-labelled ethyl cysteinate dimer
ECoG	electrocorticography
EEG	electroencephalogram
FDG	^{18}F-labelled fluorodeoxyglucose
FLAIR	fluid-attenuated inversion–recovery
fMRI	functional magnetic resonance imaging
FMZ	[^{11}C]flumazenil
FN	false negative
FP	false positive

continued

List of abbreviations *continued*

GRASS	gradient recalled acquistion in steady state
HIPDM	*N*,*N*,*N*′-trimethyl-*N*′-(2-hydroxy-3-methyl-5-[^{123}I]iodobenzyl)-1,3-propanediamine
HMPAO	^{99m}Tc-labelled hexamethylpropylenamine oxime
H-MRS	^{1}H (hydrogen) magnetic resonance spectroscopy
HS	hippocapmal sclerosis
IDEX	[^{123}I]iododexetimide
IMP	[^{123}I]isopropyliodoamphetamine
IMZ	[^{123}I]iomazenil
IQ	intelligence quotient
MAO	monoamine oxidase
MEG	magnetoencephalography
MR	magnetic resonance
MRI	magnetic resonance imaging
MRS	magnetic resonance spectroscopy
MRSI	magnetic resonance spectroscopic imaging
MTLE	mesial temporal lobe epilepsy
MTLS	mesial temporal lobe sclerosis
MTS	mesial temporal sclerosis
NAA	*N*-acetylaspartate
NIRS	near-infrared spectroscopy
Non-TL	non-temporal lobe extratemporal
OR	odds ratio
PET	positron emission tomography
QALY	quality-adjusted life-year
QUADAS	quality assessment of diagnostic accuracy studies
rCBF	regional cerebral blood flow
RCT	randomised controlled trial
ROI	region of interest
RR	relative risk
SISCOM	subtraction ictal single photon emission computed tomography co-registered to magnetic resonance imaging
SPECT	single photon emission computed tomography
SPGR	spoiled gradient-recalled echo
SPM	statistical parametric mapping
SR	systematic review
TLE	temporal lobe epilepsy
TL	temporal lobe
TN	true negative
TP	true positive

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Background

Epilepsy is the commonest serious neurological condition with a lifetime cumulative incidence of 2–3%. Although for the majority of people with epilepsy the outlook for seizure control is good, between 20 and 30% will continue to have seizures despite ongoing treatment with antiepileptic drugs (AEDs). Of these, the majority have a symptomatic or cryptogenic localisation-related epilepsy, which for some may be successfully treated with surgical resection of the focus (epilepsy surgery). The prime aim of epilepsy surgery is to remove the seizure focus and hence bring about seizure freedom without causing other disability.

Neuroimaging technologies can provide information about (1) structural abnormalities, hence information about the underlying aetiology of seizures, which in turn will suggest a potential focus, and (2) functional abnormalities (metabolism and/or blood flow) and hence the likely focus of seizures. If effective, these technologies could have a number of potential advantages. First, these tests are non-invasive and for certain patients the need for, and risk of, invasive seizure monitoring could be avoided. Second, they may influence the outcome of epilepsy surgery by influencing patient selection and the procedure undertaken. Third, where imaging results predict the outcome of surgery, patients could be better informed of the likely outcome of surgery.

Objectives

To review the following:

1. The effectiveness and/or accuracy of different methods of imaging the cerebral cortex to visualise the seizure focus in people with refractory epilepsy being considered for surgery.
2. The ability of different neuroimaging techniques to predict patient outcomes following surgery.
3. The effectiveness of imaging in the following subgroups:
   (a) People for whom a structural abnormality has been previously identified by other neuroimaging techniques.
   (b) People for whom no structural abnormality has been previously identified by other neuroimaging techniques.
   (c) People for whom surface or invasive EEG recording has isolated a seizure focus.
   (d) People for whom surface or invasive EEG recording has failed to isolate a seizure focus.
4. The cost-effectiveness of imaging the cerebral cortex to visualise the seizure focus in people with refractory epilepsy being considered for surgery.

Methods

A systematic review was undertaken according to published guidelines.

Data sources

Studies were identified through searches of electronic databases, Internet searches, handsearching, scanning reference lists of included papers and consultation with experts in the field.

Study selection

Two reviewers screened titles and abstracts for relevance. Full papers of potentially relevant studies were obtained and assessed for inclusion by one reviewer and checked by a second. Published and unpublished studies in any language were eligible for inclusion.

Data extraction

Data extraction and quality assessment were performed by one reviewer and checked by a second.

Data synthesis

For the diagnostic accuracy studies, results were analysed according to the imaging test evaluated. For each study the proportion of patients who were correctly localised, not localised, partially localised or incorrectly localised by the index test was calculated. Heterogeneity of these proportions was investigated using the χ^2 or Q statistic and through visual examination of forest plots of study results. Owing to the significant heterogeneity present between studies, statistical pooling was not performed. Instead, a narrative synthesis of results is presented.

For studies that used multivariate analysis to look at the association of neuroimaging findings and outcome following surgery, all factors considered in the analyses, whether related to the findings of neuroimaging assessments or not, were presented, whether statistically significant or not. The studies were grouped according to the neuroimaging technique investigated and the findings of the studies were discussed with reference to possible sources of heterogeneity between studies.

Sensitivity analyses were performed to investigate the usefulness of carrying out extensive literature searches and including studies published in languages other than English.

Results

No randomised controlled trials (RCTs) were identified, with the majority of studies being diagnostic accuracy studies, evaluating the diagnostic accuracy of various imaging techniques in the localisation of epileptic seizure foci.

Studies were heterogeneous with regard to study design, population characteristics, index test and characteristics, outcome measurements and reference standards. In addition, in the majority of studies, the data had been collected retrospectively or it was not reported whether data collection was prospective. The studies were generally of poor quality, largely owing to the inappropriate populations included in the studies. Only 4% of studies included an appropriate patient spectrum, defined as an unselected group of patients with refractory epilepsy being considered for surgery, prospectively enrolled in the study. The reference standards used varied, and included ictal EEG, a combination of tests, site of eventual surgery, magnetic resonance imaging (MRI), interictal EEG and a combination of ictal and interictal EEG.

The included studies investigated the following imaging techniques: single photon emission computed tomography (SPECT) (39 studies, 68 evaluations); MRI (30 studies, 40 evaluations); position emission tomography (PET) (18 studies, 25 evaluations); subtraction ictal single photon emission computed tomography co-registered to magnetic resonance imaging (SISCOM) (seven studies, 11 evaluations); magnetic resonance spectrosopy (MRS) (six studies); computed tomography (CT) (five studies); near-infrared spectroscopy (NIRS) (one study); combinations of more than one test (three studies). We found no studies evaluating functional magnetic resonance imaging (fMRI) or diffusion tensor imaging.

There was significant heterogeneity ($p < 0.05$) between studies for all imaging techniques for at least one of the localisation categories (proportions of patients who had a seizure focus correctly localised, not localised, partially localised and incorrectly localised). Statistical pooling was therefore not undertaken. It was difficult to draw any overall conclusions regarding the accuracy of any imaging technique owing to the differences between studies. Possible explanations for the heterogeneity of localisation categories between studies of the various imaging techniques include differing study designs, population characteristics, index test characteristics and reference standards.

One of the review objectives was to look at the accuracy of neuroimaging techniques to identify the seizure focus in the following four subgroups: people for whom a structural abnormality has/has not been previously identified by other neuroimaging techniques, and people for whom surface or invasive EEG recording has/has not isolated a seizure focus. These subgroups were considered as possible sources of heterogeneity but did not appear to account for any of the differences between studies for any of the imaging techniques evaluated.

Test performance was more promising in studies restricted to patients with temporal lobe epilepsy.

Ictal SPECT generally had more correctly localising and fewer non-localising scans than other techniques evaluated, with 70–100% correctly localising scans and 0–7% incorrectly localising scans in patients with temporal lobe epilepsy. Results for CT and interictal SPECT suggest that these tests are relatively poor at localising the seizure focus. Results for volumetric MRI and PET appear promising, but have been assessed in fewer studies than ictal SPECT. SISCOM and MRS have been assessed in fewer studies, but the results are less promising than those for ictal SPECT. T2 relaxometry was reported in only one small study, with inconclusive results.

A total of 32 studies (83 evaluations) provided data on the association of a localised scan with outcome following surgery. For 15 studies, it was not possible to calculate a relative risk (RR) and these were not included in the analysis. None of the studies included had an appropriate patient spectrum. The majority (24/33) of evaluations suggested that patients with a correctly or partially localised scan had a better outcome following surgery than those with an incorrectly localised or non-localised scan. However, only three studies

showed a significant association between having a localised scan and outcome following surgery, two evaluating routine MRI [RR 2.74, 95% confidence interval (CI) 1.32 to 5.67; RR 1.28, 95% CI: 1.00 to 1.63) and the other SISCOM (RR 2.12, 95% CI: 1.01 to 4.44). Both found that patients with a localised scan had a significantly better outcome following surgery than those with a non-localised or incorrectly localised scan.

Nine studies used multivariate analysis to investigate the association of various imaging techniques with the outcome following surgery. The imaging techniques evaluated included MRI (seven studies), MRS and volumetric MRI (one study), PET (three studies), SPECT (one study) and SISCOM (three studies). There was heterogeneity between studies of the ability of various imaging techniques to predict outcome. However, there was a trend for positive localisation of abnormalities to be associated with a beneficial outcome.

Conclusions

Owing to the limitations of the included studies, the results of this review do little to inform clinical practice. We are unable to provide evidence for effectiveness or cost-effectiveness of imaging techniques in the work-up for epilepsy surgery. Results of diagnostic accuracy studies are confounded by limitations in the reference standard used, and studies are subject to both clinical and statistical heterogeneity as outlined above.

Studies investigating the prognostic importance of imaging results for the outcome following epilepsy surgery suggest that abnormalities on imaging are associated with a better clinical outcome. However, the data do not allow an accurate prediction of patient outcome, possibly owing to small sample sizes, and therefore many studies may lack sufficient power to detect a significant association.

Given the inadequacy of existing data, there is a pressing need for studies investigating the utility of imaging techniques in the work-up for epilepsy surgery. The most reliable research methodology for evaluating the influence of imaging technologies on the outcome for patients being considered for surgery is the RCT. RCTs could examine the influence of single tests or combinations of tests on patient outcome. A study of a single test could evaluate the additional benefit that a particular test offers over other routinely offered tests. For example, in a study evaluating PET, all patients would receive routine tests such as MRI, EEG and Wada tests, with those in the experimental arm also receiving a PET scan. Similarly, studies could include a set of routine tests in both arms with an additional combination of tests being offered in the experimental arm. An alternative approach would be to compare different test combinations in different intervention arms. Health economic data could be collected in parallel, allowing a thorough examination of cost-effectiveness. We suggest that it is important that clinicians, patient groups, policy makers and healthcare/research funders meet and debate the most appropriate way to investigate these technologies.

Chapter 1
Background

Epidemiology and cost of epilepsy

Epilepsy is the commonest serious neurological condition with a prevalence of between 0.5 and 1% in developed countries and a lifetime cumulative incidence of 2–3%.[1] Although for the majority of people with epilepsy the outlook for seizure control is good, between 20 and 30% will continue to have seizures despite ongoing treatment with one or more antiepileptic drugs (AEDs).[2] Continuing to have seizures has a significant impact on education, employment, relationships, self-esteem and overall quality of life.[3] In a study published in 1998, the direct cost of epilepsy was estimated at £1568 per patient per annum.[4] When seizure frequency was taken into account, the total cost of care for patients having more than one seizure per month was eight times that of patients who were seizure free (£3508 versus £443). Drug cost accounted for 23% of the cost, 43% of which was spent on the new drugs vigabatrin and lamotrigine, which were prescribed for only 6% of patients. Given the increased number of new drugs and their greater use, it is likely that direct costs of treating refractory epilepsy in the UK are even higher.

Classification of the epilepsies

It is important to understand that epilepsy is not a single condition. The epilepsies are a large heterogeneous group of disorders ranging from those that are genetically determined to those that are symptomatic of a brain insult (e.g. stroke, tumour, head injury). The clinical history is most important when diagnosing and classifying epilepsy. The epilepsies are classified into syndromes according to seizure types, aetiology, age of onset, EEG changes and magnetic resonance imaging (MRI)/computed tomography (CT) findings.[5] One of the major categories in this classification is the localisation of related (focal) epilepsies. In these syndromes, seizures start at a single point (focus) in the cerebral cortex. These epilepsies are subclassified according to the site of the focus (frontal, temporal, parietal and occipital lobe epilepsies) and are further divided according to aetiology. The idiopathic localisation-related epilepsies are purely genetic and present primarily in childhood. The symptomatic localisation-related epilepsies are symptomatic of a lesion, such as mesial temporal lobe sclerosis, cortical dysplasia, tumour, vascular malformation, haemorrhage, infarct, infection and trauma. The cryptogenic localisation-related epilepsies are those thought to be symptomatic but for which the precise underlying aetiology has not been determined. Of the 20–30% of people who continue to have seizures despite drug treatment, the majority have a symptomatic or cryptogenic localisation-related epilepsy, which for some may be successfully treated with surgical resection of the focus (epilepsy surgery).

Surgery for epilepsy

The prime aim of epilepsy surgery is to remove the seizure focus and hence bring about seizure freedom without causing other disability. As already indicated, the focus may be located anywhere in the cerebral cortex and there are a number of potential aetiologies. Epilepsy surgery programmes focus mainly upon surgery of the temporal lobe owing to the high chance of success and a low chance of causing further harm (see below). Results of surgery for foci outside this area are less encouraging.[6] Hemispherectomy is another resective surgical procedure, sometimes used in the treatment of severe paediatric epilepsies. In addition, functional surgical procedures such as corpus callosotomy, multiple subpial transection and vagal nerve stimulation are sometimes performed to palliate rather than cure the epilepsy.

The modern era of epilepsy surgery began in 1886,[7] but it was not until 2001 that the first randomised controlled trial (RCT) was reported.[8] Eighty patients with drug-refractory temporal lobe epilepsy (TLE) were randomised to either surgery or continued AED treatment. The surgical group had a significantly better quality of life at 12 months, with 58% of the surgical group being free of seizures that affected awareness compared to 8% of the AED group, giving a number-needed-to-treat of 2 [95% confidence interval (CI) 1.3 to 3]. Uncontrolled surgical series provide longer follow-up and give higher estimates of the

proportion seizure free of approximately 70%.[9] To date, no health economic data derived from RCTs of epilepsy surgery have been reported. The direct costs of an anterior temporal lobectomy for a 30-year-old with refractory epilepsy have been estimated at $27,200 per quality-adjusted life-year (QALY).[10]

The 1999 Department of Health-commissioned report from the Clinical Standards Advisory Group (CSAG) on services for patients with epilepsy[11] uses a conservative estimate that between 5 and 10% of patients with refractory focal epilepsy might benefit from epilepsy surgery. Using this estimate, they highlight that between 5000 and 10,000 UK patients might benefit from epilepsy surgery and between 750 and 1500 cases are added to this cohort each year. Between April 1998 and March 1999, CSAG estimate that only 350 temporal lobectomies were undertaken in the UK, highlighting the disparity between need and service provision and a number of recommendations are made. A more recent study used the UK National General Practice Study of Epilepsy to estimate the number of patients with newly diagnosed epilepsy who may eventually require surgery.[12] This study estimated that the annual recurring need for surgery, based on an estimate of 30,000 incident cases in the UK, would be around 1.5% (95% CI: 0.5 to 2.5) or 450 patients per year.

Work-up for epilepsy surgery

The most important factor for the successful outcome of epilepsy surgery is appropriate patient selection. Hence the work-up of patients being considered for epilepsy surgery is crucial. The aim of the work-up is to isolate the seizure focus and the underlying aetiology.[13] The first step is to take a detailed history and examination. This should allow the selection of patients who have or may have seizures arising from the temporal lobe and those who do not. In the UK, all patients will have a routine (interictal) EEG and routine MRI, in an attempt to define the underlying aetiology. Following this, patients with temporal lobe (and some patients with extra-temporal lobe) epilepsy will undergo some or all of the investigations outlined below.

1. Neuroimaging (see below).
2. Simultaneous video and EEG seizure recording (ictal EEG) – patients are admitted to hospital for 1 week or more for continuous monitoring and usually have their medication reduced to increase the likelihood of seizures. EEG information may be acquired using:
   (a) Scalp EEG electrodes.
   (b) Depth electrodes – wires inserted into the brain via a small hole drilled into the skull.
   (c) Foramen ovale (FO) electrodes – wires passed through the foramen ovale to lie under the temporal lobe.
   (d) Subdural mats – a craniotomy is performed and a grid of electrodes is placed over an area of the cerebral cortex.
   (e) Sphenoidal electrodes – thin, sterilised, disposable wires inserted into the soft tissues anterior to the temporo-mandibular joint using a needle.

   Reducing AED medication is associated with a small risk of status epilepticus and even death. Invasive methods of EEG monitoring are associated with a small risk of infection and haemorrhage.
3. Psychometric testing – memory and IQ are tested to find evidence of focal cognitive dysfunction.
4. Neuropsychiatric evaluation is often conducted, particularly in children, to determine any behavioural psychiatric abnormalities and to determine the expectations that the patient and/or family have from the surgery.
5. Wada test – a short-acting barbiturate (sodium amytal) is injected into one carotid artery to anaesthetise part of one hemisphere, following which memory and language are tested in the opposite hemisphere. The procedure is repeated in the opposite hemisphere.

Neuroimaging

Neuroimaging technologies can provide information about (1) structural abnormalities and hence information about the underlying aetiology of seizures, which in turn will suggest a potential focus and (2) functional abnormalities (metabolism and/or blood flow) and hence the likely focus of seizures. If effective, these technologies could have a number of potential advantages. First, these tests are non-invasive and for certain patients the need for, and risk of, invasive seizure monitoring could be avoided. Second, these technologies may influence the outcome of epilepsy surgery by influencing patient selection and the procedure undertaken. Third, where imaging results predict the outcome of surgery, patients could be better informed of the likely outcome of surgery. The following imaging techniques will be assessed in this review.

Structural imaging

Routine magnetic resonance imaging (MRI) [T1, T2 and (FLAIR) imaging]

It is recommended that all patients with refractory focal epilepsy undergo routine MRI.[14,15] This may show features of mesial temporal sclerosis (MTS) and also pick up lesions such as tumours, vascular malformations, developmental malformation and the aftermath of trauma or infections.

Volumetric MRI examination

Here, stereological techniques[16] are used to estimate the volume of brain structures, most commonly the hippocampus, amygdala and temporal lobe.[17] Differences in volume (usually a reduction) when compared with normative data suggest focal pathology that may be the site of the seizure onset. Patients may have normal volumes, a unilateral abnormality or bilateral abnormalities, which should be taken into account when assessing this technology. In addition, volumetric information is usually interpreted in conjunction with quantitative T2 data.

Quantitative T2 measurements

This technique is usually applied to the hippocampus where mesial temporal lobe sclerosis (MTLS) is associated with high signal on T2 weighted images. This change can be measured quantitatively by measuring the T2 relaxation time[18] and making comparisons with normative data. As with volumetric examinations, abnormalities may be absent, unilateral or bilateral.

Computed tomography

Prior to the advent of MRI imaging, CT was the main tool for imaging the brain. Owing to the inferior resolution of this technique when imaging the brain, CT is no longer routinely used in the work-up for epilepsy surgery.

Functional imaging

These technologies measure blood flow and/or metabolism and can provide information about the site of seizure onset. The results must always be put in context with those of structural MRI imaging. Results may be used to guide the placement of intracranial electrodes for seizure recording or in combination with other investigations to inform the decision regarding surgery. The International League Against Epilepsy Commission on Diagnostic Strategies has recently published recommendations on the use of these technologies.[19] However, in the formulation of these recommendations, no attempt was made to appraise existing evidence critically. The following functional imaging technologies are available.

Single photon emission computed tomography (SPECT)

In this technique, the patient is given a radiolabelled compound, which, depending on the properties of the compound given, binds preferentially to certain areas of the brain. The brain is scanned using a SPECT camera, which provides information about the uptake of the tracer. Most commonly, the epilepsy surgery work-up uses ^{99m}Tc-labelled compounds [hexamethylpropylenamine oxime (HMPAO) or ethyl cysteinate dimer (ECD)] to provide information about cerebral blood flow. Once the tracer has been given, there is a maximum 6-hour window in which to do the scan. Interictal scans (not during a seizure) often show an area of reduced uptake at the site of seizure onset. More reliable information about the site of seizure onset is provided by injecting the radiolabelled compound at the start of a seizure (ictal) or just after it (postictal). Scans show an area of increased uptake at the site of seizure activity. This procedure is resource intensive, as patients require simultaneous video-EEG monitoring and the presence of a member of staff who can give the radiolabelled compound as soon as the seizure starts. In addition, 24-hour access to the radioactive isotope is required. Other tracers such as [^{123}I]iomazenil (IMZ), which binds to benzodiazepine receptors, and monamine oxidase (MAO)-B tracers have been assessed, but at present are largely used as research tools. Occasionally, both interictal and ictal/postictal studies are required to clarify questionable abnormalities.

Positron emission tomography (PET)

This technology also uses radiolabelled tracers, but provides better spatial resolution than SPECT, and can provide quantitative data as opposed to semi-quantitative data provided by SPECT. Information about blood flow is provided by using ^{15}O-labelled water, and information regarding glucose metabolism is provided using ^{18}F-labelled fluorodeoxyglucose (FDG). PET scanning using the latter is thought to provide more reliable results and provide better spatial resolution and is therefore more commonly used in selection for surgery. Interictal PET images are used for the purpose of the epilepsy surgery work-up. Ictal scans using ^{15}O-labelled water are not feasible owing to the 2.5-minute half-life of the isotope, whereas FDG uptake

occurs over more than 40 minutes and hence reflects a composite of both ictal and postictal metabolism.

Subtraction of ictal SPECT co-registered to MRI (SISCOM)
In this computer-aided technique, the interictal SPECT images are subtracted from the ictal SPECT images and the resultant functional image is superimposed over the individual's MRI to combine the functional and structural data. This enhances objectivity and the accuracy of data interpretation when compared with side-by-side interpretation of interictal and ictal/postictal images for seizure localisation in epilepsy patients. As already discussed, there are often practical difficulties in obtaining ictal or postictal SPECT scans. SISCOM represents a combination of two technologies, but is evaluated as a separate technology. This is because ictal SPECT looks at function only and MRI looks at structure only, whereas SISCOM uses structural and functional information and therefore provides additional information.

Functional MRI (fMRI)
Here, magnetic resonance (MR) technology is used to detect interictal epileptic activity, measuring the BOLD signal change (localised decreases in blood oxygenation level). This use of fMRI will be assessed in this review although it remains largely a research tool. fMRI can also be used to localise areas of the cortex responsible for language, motor activity or sensory perception. Although of potential importance in epilepsy surgery, this use of fMRI will not be assessed in this review.

Magnetic resonance spectroscopy (MRS)
Here, MR technology is used to provide information about the relative concentrations of certain molecules. Proton spectroscopy can provide information about *N*-acetylaspartate (NAA-), creatine-, lactate- and choline (Cho)-containing compounds. ^{31}P spectroscopy provides information about phosphorus-containing compounds such as adenosine triphosphate. MRS is used interictally to measure the relative concentration of these molecules in an attempt to find focal abnormalities consistent with the seizure focus. At present MRS is mainly used as a research tool.

Diffusion tensor imaging (DTI)
This is a new MR technique which provides quantitative measures of magnitude and directionality of diffusion in a three-dimensional space. The information can be used to detect microstructural abnormalities and to visualise tracts. This is a developing technique, which has not been widely used in the clinical setting. In epilepsy, DTI has been successfully used to demonstrate abnormalities where optimal standard MRI including volumetric measurements was normal. In addition, the technique has been applied to visualise nerve fibre tracts in patients with epilepsy.

Other MR techniques and postprocessing methods
Magnetisation transfer imaging is another MR contrast technique that has been successfully used to identify structural brain abnormalities in small studies. High-resolution imaging (with and without surface coils) has been used in epilepsy to visualise small abnormalities. Voxel-based morphometry, fractal analysis and curvilinear reconstruction of 3D magnetic resonance imaging are all postprocessing methods to detect subtle abnormalities in epilepsy. They are usually applied on T1-weighted images. In serial MR imaging, patients are scanned repeatedly and the images are compared using an automatic registration technique to detect subtle changes over time in epilepsy. Suppression techniques, such as double inversion recovery, to reveal occult neocortical abnormalities in patients with refractory epilepsy have also been developed.

Evaluating diagnostic accuracy

The diagnostic accuracy of an imaging technique is evaluated by comparing the results from the test being evaluated (index test) with those of a reference standard, established as the 'gold standard' technique. However, there is not an individual technique that can be considered a gold standard in the localisation of a seizure focus in people with epilepsy. In clinical practice, information may come from a number of sources. First, a careful description of the seizure semiology is required, and should be obtained by interviewing the patient and also eye witnesses to seizures. Investigations that may provide further information on the location of the seizures focus include interictal EEG, ictal EEG, neuroimaging, neuropsychological testing and Wada testing. In clinical practice, information from a number of these sources may be used to localise the seizure focus. Evaluating the diagnostic accuracy of neuroimaging techniques, when there is no accepted gold standard, is therefore difficult.

There are several potential reference standards that may be used as comparison techniques for the index test being evaluated.

EEG

The use of continuous EEG and video monitoring for a number of days to record ictal activity directly assesses the seizure onset. However, ictal EEG using surface electrodes may fail to find a seizure focus, or may localise it inaccurately, particularly when the seizure activity arises from parts of the cerebral cortex some distance from the scalp. Ictal EEG using depth electrodes and/or grids directly assesses seizure onset from cerebral grey matter, but requires electrodes to be accurately placed in or adjacent to the site of the seizure focus. Interictal EEG cannot be considered as an appropriate gold standard, as by definition this technique does not directly record seizure onset.

Combination of tests

Results from a combination of tests may be used as a reference standard, for example a combination of results from video EEG monitoring, MR imaging and Wada test results. The use of a combination of tests as a reference standard would best reflect the methods used to localise a seizure focus in clinical practice.

Surgery

Once a seizure focus has been identified, a decision as to whether to undertake surgery or not can be made. If surgery is undertaken, the site of surgery can also be considered as a reference standard. However, using site of surgery as the gold standard has limitations, as only patients proceeding to surgery can be included, and results of the index test may have been used in making the decision to proceed with surgery. These factors would tend to increase the estimated diagnostic accuracy of the index test.

Chapter 2

Research questions

The objectives of this review are to investigate the following:

1. *The effectiveness and/or accuracy of different methods of imaging the cerebral cortex to visualise the seizure focus in people with refractory epilepsy being considered for surgery*.
   Studies comparing the effects of employing versus not employing a particular imaging technique, or that compare the effects of different imaging techniques upon patient outcomes, will be preferred to answer this question as these give information on effectiveness. However, if studies of this design are not available, studies that look at the diagnostic accuracy of the tests will be evaluated.

2. *The ability of different neuroimaging techniques to predict patient outcomes following surgery*.
   Studies should examine how the findings of imaging techniques predict patient outcomes following surgery.

3. *The effectiveness and/or accuracy of neuroimaging techniques in people with refractory epilepsy in the following subgroups: (i) people for whom a structural abnormality has been previously identified by other neuroimaging techniques; (ii) people for whom no structural abnormality has been previously identified by other neuroimaging techniques; (iii) people for whom surface or invasive EEG recording has isolated a seizure focus; (iv) people for whom surface or invasive EEG recording has failed to isolate a seizure focus*.
   Studies comparing the effects of imaging with no imaging, or that compare the effects of different imaging techniques, using patient outcomes, will be preferred to answer these questions in these subgroups of patients. However, if studies of this design are not available, studies that look at the diagnostic accuracy of imaging techniques will be evaluated.

4. *The cost-effectiveness of imaging the cerebral cortex to visualise the seizure focus in people with refractory epilepsy being considered for surgery*.
   Studies should assess the cost-effectiveness of employing versus not employing a particular imaging technique, or compare the cost-effectiveness of different imaging techniques.

Chapter 3
Review methods

An advisory panel was established. In addition to providing subject-specific input during the review, members of the panel were invited to offer comment on the protocol and draft report. Details of advisory panel members can be found in Appendix 1. The systematic review was undertaken in accordance with the Centre for Reviews and Dissemination (CRD) guidelines for undertaking systematic reviews[20] and published guidelines on the meta-analysis of diagnostic tests.[21,22]

Search strategy

An Endnote database of published and unpublished literature was created from systematic searches of electronic sources, handsearching and consultation with experts in the field. Studies were identified by searching the major medical databases such as MEDLINE, EMBASE, BIOSIS, Pascal, Science Citation Index and LILACS, with no language restriction. In addition, information on studies in progress, unpublished research or research reported in the grey literature was sought by searching a range of relevant databases, including Inside Conferences, SIGLE, Dissertation Abstracts, metaRegister of Controlled Trials, NTIS and the GrayLit network. The search strategy, and dates the searches were undertaken, can be found in Appendix 2.

Key journals, including *Neurology* (1986–December 2003), *Epilepsia* (1986–December 2003), *Epilepsy Research* (1987–December 2003), *Seizure* (1992–December 2003) and *Brain* (1989–December 2003) were handsearched. Internet searches were also carried out using specialist search engines (for example OMNI: http://www.omni.ac.uk/), general search engines (for example Google: http://www.google.co.uk/) and meta-search engines (for example Copernic: http://www.copernic.com/). Attempts to identify further studies were made by contacting clinical experts and examining the reference lists of all retrieved articles.

Searches for economic evaluations were undertaken in the databases listed above. In addition searches of NHS EED and HEED were and resources such as the Economics Working Paper Archive were searched. Full details of the search dates, database coverage, numbers of records retrieved and the search strategies used are given in Appendix 2.

Inclusion/exclusion criteria

Two reviewers screened titles and abstracts for relevance independently and any disagreements were resolved by consensus. Full papers of potentially relevant studies were obtained and assessed for inclusion by one reviewer and checked by a second. Separate criteria for each section of the review were used to assess the inclusion of primary studies, as follows.

1. *The effectiveness and/or accuracy of different methods of imaging the cerebral cortex to visualise the seizure focus in people with refractory epilepsy being considered for surgery.*
   (a) Population(s)
   All adults and children with refractory epilepsy being considered for surgery. Where possible the following subgroups of participants were studied: those with definite TLE, possible TLE, extra-temporal lobe epilepsy or other underlying pathology. Children with syndromes such as infantile spasms, tuberose sclerosis, Sturge–Weber syndrome and hemimegalencephaly were eligible for inclusion. Studies had to include at least 20 patients. For the types of study included in the review it was difficult to determine when to classify a study as a 'case series' and when to classify it as a 'diagnostic accuracy study'. Case series represent a lower level of evidence and to include them would dramatically increase the number of included studies without strengthening the evidence. Given the time and resources available, case series were not included in this review. We chose a cut-off point of 20 patients to make the distinction between diagnostic accuracy studies and case series.
   (b) Intervention(s)
   Any form of neuroimaging technique, including MRI, PET and SPECT, used to image the cerebral cortex.

(c) Study design(s)
Study designs were ranked according to the following hierarchy:

Level 1 (Randomised) controlled trials in which patients are randomised/allocated to different tests or combinations of tests.
Level 2 Cohort studies which compare patients who received different tests or combination of tests.
Level 3 Diagnostic accuracy studies in which tests or combinations of tests are compared with any reported reference standard.

As no level 1 or 2 studies were identified, level 3 studies were also included in the review.

(d) Outcome(s)
For level 1 and 2 studies, any patient-related outcome was considered, including Engel's classification[23] of seizure outcome, and outcomes related to seizure activity, functional capacity, patient-related quality of life and adverse events. Level 3 studies had to report sufficient information to extract data on the number of patients with correctly localised, not localised, partially localised and incorrectly localised scans.

2. *The ability of different neuroimaging techniques to predict patient outcomes.*
(a) Population(s)
All adults and children with refractory epilepsy (see item 1) being considered for surgery. Studies with less than 20 patients were excluded.
(b) Intervention(s)
Any form of neuroimaging technique, including MRI, PET and SPECT, used to image the cerebral cortex.
(c) Study design(s)
Prospective cohort studies. If insufficient numbers of prospective cohort studies were available, then other study designs were considered according to the following hierarchy of design:

Level 1 Prospective cohort studies in which outcome following surgery was compared between patients with and without findings on neuroimaging investigation.
Level 2 Retrospective cohort studies in which outcome following surgery was compared between patients with and without findings on neuroimaging investigation.
Level 3 Uncontrolled studies

(d) Outcome(s)
Any patient-related outcome was considered, including Engel's classification of seizure outcome, and outcomes related to seizure activity, functional capacity, patient-related quality of life and adverse events. Studies had to use multivariate analyses of potential prognostic factors.

3. *The effectiveness and/or accuracy of imaging for people with refractory epilepsy in the following subgroups: (i) people for whom a structural abnormality has been previously identified by other neuroimaging techniques; (ii) people for whom no structural abnormality has been previously identified by other neuroimaging techniques; (iii) people for whom surface or invasive EEG recording has isolated a seizure focus (iv) people for whom surface or invasive EEG recording has failed to isolate a seizure focus.*
(a) Population(s)
All adults and children with refractory epilepsy (see item 1) in whom either a structural abnormality has been previously identified/ruled out during neuroimaging assessments, or a seizure focus had/had not been identified on EEG. Studies with less than 20 patients were excluded.
(b) Intervention(s)
All imaging techniques including SPECT, PET, MRS and fMRI used both during (ictally) and after (postictally) seizures.
(c) Study design(s)
Study designs were ranked according to the following hierarchy:

Level 1 (Randomised) controlled trials in which patients are randomised/allocated to different tests or to a test compared with no test.
Level 2 Cohort studies which compare patients who received different tests or a test compared with no test.
Level 3 Diagnostic accuracy studies in which tests or combinations of tests are compared with any reference standard.

As no level 1 or 2 studies were identified, level 3 studies were included in the review.

(d) Outcome(s)
For level 1 and 2 studies, any patient-related outcome was considered, including Engel's classification[23] of seizure outcome, and outcomes related to seizure activity, functional capacity, patient-related quality of life and adverse events. Level 3 studies had to report sufficient information to extract data on the number of patients with correctly localised, not localised, partially localised and incorrectly localised scans.

4. *The cost-effectiveness of imaging the cerebral cortex to visualise the seizure focus in people with refractory epilepsy being considered for surgery.*
   (a) Population(s)
   All adults and children with refractory epilepsy (see item 1) being considered for surgery.
   (b) Intervention(s)
   Any form of neuroimaging technique, including MRI, PET and SPECT, used to image the cerebral cortex.
   (c) Study design(s)
   Full economic evaluations that compare two or more options and consider both costs and consequences, including cost-effectiveness, cost–utility and cost–benefit analyses.
   (d) Outcome(s)
   Costs and any patient-related outcome will be considered, including Engel's classification of seizure outcome, and outcomes related to seizure activity, functional capacity, patient-related quality of life and adverse events.

Data extraction

Data extraction forms were developed using Microsoft Access. These were piloted on a small selection of studies. Data extraction was performed by one reviewer and checked by a second. Foreign language papers were extracted by one reviewer, accompanied by a speaker of that language, and the data entered directly into the Access database. A second reviewer did not check foreign language studies. The following information was extracted for all studies:

- Study details: author, year, study design (retrospective/prospective/unclear diagnostic accuracy or cohort study), details of any duplicate reports of the study, study objective, country of study, language of publication and whether the study report was only available as an abstract.
- Patient details: number of patients, number male/female, age, duration of epilepsy, type of epilepsy (temporal lobe, MTLS, non-temporal lobe epilepsy (non-TL), other focal lesions), epilepsy syndromes, general inclusion criteria, whether any inclusion criteria relating to outcome were specified (e.g. restriction of study to patients who underwent surgery or who had a good postsurgical outcome).
- Surgery details: number of patients who underwent surgery, type of surgery (anterial temporal lobectomy (ATL), amygdalo-hippocampectomy (AH), lesionotomy, non-temporal lobe surgery or other).
- Outcome following surgery details: duration of follow-up postsurgery, patient outcome (Engel's classification[23] if reported; if not, classification as reported in the paper).

Study design was poorly reported in the diagnostic accuracy studies and it was often impossible to tell whether studies were prospective or retrospective. Studies that clearly stated that they were prospective or retrospective were classified as such and other studies were classified as 'unclear'. Studies in which patients were clearly reported as being recruited to the study were classed as prospective.

Separate forms were developed from which to extract additional data for the different study designs, as follows.

Diagnostic accuracy studies

Additional data were extracted on:

1. Reference standard details: reference standard, details of reference standard execution, definition of a positive result.
2. Test details: imaging type (PET, SPECT, MRI, etc.), test specific details as summarised in *Table 1*, definition of a positive test result.
3. Results: two separate sets of results were extracted where possible. The accuracy of the test in localising the seizure focus, using the reference standard; and the accuracy of the test using patient outcome following surgery as the reference standard.
4. For seizure localisation, the following data were extracted:
   (a) This classification is illustrated in *Box 1*.
   (b) Patients were divided into three groups: (1) patients in whom the reference standard identified a seizure focus; (2) patients in whom the reference standard failed to

TABLE 1 *Data extracted on each of the different imaging techniques*

Test	Data extracted						
MRI	Was the imaging routine MR, volumetric, T2 relaxation	Contrast agent	Magnet strength	Weighting (T1/T2/ FLAIR, etc.)	Slice orientation (axial, coronal, sagittal)	Slice thickness	Areas imaged
MRS			Magnet strength	H_MRS or P_MRS	Metabolites (e.g. NAA/ choline, creatine)	How partial volume effects were excluded	ROI or CSI
SPECT and PET	Ictal/interictal	Radiopharmaceutical/ tracer	Gamma camera strength	Timing from seizure onset to injection	Timing from injection to scan		ROI: hippocampus, temporal lobe or other
CT		Contrast agent			Slice orientation	Slice thickness	
SISCOM	Details as for SPECT and MRI						

CSI, chemical shift imaging; NAA, *N*-acetylaspartate; ROI, region of interest.

BOX 1 *Classification of study results using seizure localisation as the reference standard*

		Reference standard		
		Localised (+)	**Not localised (–)**	**Multifocal**
Index test	+	A	B	I
	–	C	D	J
	P1	E		K
	P2	F		
	P3	G		
	Incorrectly localised	H		L

localise the seizure focus; and (3) patients in whom the reference standard identified the patient as having a multifocal seizure origin.

(c) Within the first group, patients were further categorised according to whether the index test correctly identified the seizure focus (A), failed to identify a seizure focus (C), incorrectly identified a seizure focus (H) or partially identified the seizure focus (E, F, G). Patients in whom the seizure focus was classed as partially localised were those in whom the index test either correctly identified part of the seizure focus but failed to identify all of the seizure focus (P1), identified the seizure focus but also showed it as covering an additional area not found on the reference standard (P2) or identified the seizure focus, failed to identify all of the seizure focus identified by the reference standard, but showed it as covering an additional area not found on the reference standard (P3).

(d) Within the second group, patients were classified according to whether they were localised (B) or not localised (D) on the index test.

(e) Within the third group, patients were classed as a true positive if they were correctly identified as having a multifocal seizure origin (I) and a true negative if they failed to identify a seizure focus (J). Where they identified the patient as having a single seizure focus, if this was specified as being concordant with one of the foci on the reference standard they were classed as P1 (K), otherwise they were classed as incorrectly localised (L).

TABLE 2 *Engel's classification[23] and our interpretation of the categories*

Class	Engel's definition	Our interpretation
I	**Free of disabling seizures** (a) Completely seizure-free since surgery (b) Non-disabling simple partial seizures only since surgery (c) Some disabling seizures after surgery but completely seizure-free for at least 2 years, convulsions only when medications are withdrawn	Seizure free
II	**Almost seizure-free** (a) Initially seizure-free but now has disabling seizures (b) Rare disabling seizures since surgery (c) More than rare seizures after surgery but now rare seizures for at least 2 years, nocturnal seizures only	>90% reduction in seizure frequency
III	**Worthwhile improvement** (a) Worthwhile seizure reduction (b) Prolonged seizure-free intervals amounting to half the follow-up period, but not less than 2 years	>50% reduction in seizure frequency
IV	**No worthwhile improvement** (a) No significant seizure reduction (b) No appreciable change (c) Seizures getting worse	<50% reduction in seizure frequency

5. For *patient outcome* the following data were extracted:
   (a) Patients were divided into two groups: patients with a class I or II Engel outcome following surgery (regarded as positive), and patients with a class III or IV Engel outcome following surgery (regarded as negative). Engel III outcome was classified as a negative result of surgery, as it includes patients who have not been rendered seizure free or have minimal seizures, which are the desired outcomes after surgery. This was supported by included studies, which also classified Engel III as a poor outcome. Where studies either did not report outcome according to Engel's classification or only provided data grouped according to Engel class I or class II–IV, then the closest approximation to Engel I and II and Engel III and IV was extracted. As the Engel classification can be interpreted in different ways, we aimed to extract data as closely as possible to the interpretation of Engel's criteria given in *Table 2*. We also extracted the authors' definitions of each of the categories.
   (b) Within these two groups, the number of patients in the following groups were extracted: index test positive and concordant with reference standard (A, B); index test negative (C, D); index test positive but not concordant with reference standard (K, L); index test concordant with reference standard but failed to identify all of the seizure focus (P1); index test concordant with reference standard but also showed it as covering an additional area not removed by surgery (P2); index test concordant with reference standard but also showed it as covering an additional area not identified by the reference standard, and also missed an area identified by the reference standard (P3). This is illustrated in *Box 2*.
6. Further details: drop-outs, adverse events and subgroup analyses performed were also extracted.

Studies to predict patient outcomes

Additional data were extracted on the statistical methods used for both the univariate and multivariate analysis performed and the dependent variable (i.e. the outcome measure used to assess outcome following surgery). For each dependent variable, the following details were extracted (separately for both the univariate and multivariate analysis):

- Independent variables assessed (i.e. those factors that may be associated with the outcome variable). For example, the concordance of the index test result with site of surgery, presence or absence of lesions, type of resection and patient

BOX 2 *Classification of study results using outcome following surgery as the reference*

		Engel's classification	
		I & II (+)	**III & IV (–)**
Index test	+ Concordant with reference standard	A	B
	–	C	D
	P1	E	F
	P2	G	H
	P3	I	J
	+ Not concordant with reference standard	K	L

characteristics. All variables assessed by the studies were extracted for the univariate analyses. For the multivariate analyses, only variables included in the final multivariate model were extracted.

- The measure of association used to assess the association between the independent variable and outcome following surgery. Where possible, odds ratios were extracted. Where these were either not reported, or insufficient information was available to calculate them, any alternative measure reported by the authors was extracted.
- *p*-Values for the significance of the association of each independent variable with outcome following surgery.
- For the multivariate analysis, the *p*-values for the significance of the final model were extracted and, where available, r^2 (as this provides an indication of how well the final model fitted the data).

Quality assessment

Quality assessment forms were developed using Microsoft Access for the each of the different study designs included in the review. Quality assessment was carried out by one reviewer and checked by a second.

Diagnostic accuracy studies

Diagnostic accuracy studies included in the review were assessed for methodological quality using QUADAS.[24] This covers the following sources of bias: spectrum bias, description of inclusion criteria, appropriateness of reference standard, verification bias, disease progression bias, description of index test and reference standard execution, review bias, clinical review bias and handling of uninterpretable results and reporting of withdrawals. Disease progression bias was not assessed, as we felt this would not be a problem for this topic area. Patients included in the review are already known to have epilepsy and it is very unlikely that the seizure focus will change between tests, even if there was a considerable delay between tests. The majority of these items were assessed at the study level. However, five items (incorporation bias, description of index test execution, test and diagnostic review bias and clinical review bias) were assessed separately for the each evaluation included in a study. This was because these items could be scored differently for the individual techniques evaluated. Full details of each of the items included in QUADAS, and on how these items were scored, are provided in Appendix 3.

Studies to predict patient outcomes

Included cohort studies were assessed for methodological quality using the checklist for cohort studies in the CRD guidelines for undertaking systematic reviews.[20] This checklist covers distribution of prognostic factors, stage of groups in disease progression, measurement of the exposure of interest, comparability of groups with respect to confounding factors, adjustment for the effect of confounding variables, dose–response between exposure and outcome, outcome assessment blind to exposure status, appropriateness of follow-up period, proportion of the cohort followed up and details of study withdrawals. Two of the variables were not assessed – stage of groups in disease progression and the dose–response between exposure and outcome. We did not consider that these items were relevant to this topic area. As with the item on disease progression bias for diagnostic accuracy studies, patients included in the review are already known to have epilepsy and it is very unlikely that the seizure focus will change between tests, even if there was a considerable delay between tests. We would also not expect to see a dose–response between an imaging evaluation and outcome following surgery. Full details of the quality tool used and how items were scored are provided in Appendix 3.

Statistical analysis

The effectiveness and/or accuracy of different methods of imaging the cerebral cortex to visualise the seizure focus in people with refractory epilepsy being considered for surgery

Seizure focus localisation

Each of the neuroimaging techniques was evaluated separately. Where studies provided more than one evaluation for the same imaging technique, only one was included in the main analysis. The evaluation judged to be most similar to those from other studies in the same category was retained for the analysis. The differences between the evaluations from the same study were discussed in a narrative synthesis.

For each study, we calculated the proportion of scans which (1) correctly identified the seizure focus, (2) failed to localise the seizure focus, (3) partially localised the seizure focus and (4) incorrectly identified the seizure focus. The partially localised categories P1, P2 and P3 were combined for the analysis. The exact confidence intervals for the binomial proportions were calculated using the *F* distribution method.[25] Forest plots were produced for each of the four proportions to provide a visual indication of the heterogeneity between studies. This was formally investigated using the likelihood ratio test.[25] If studies were homogeneous for all four categories (i.e. proportion correctly localised, not localised, partially localised and incorrectly localised), standard methods for pooling sensitivity and specificity were used to pool studies.[26] The following equation was used to pool studies:

$$\text{pooled proportion} = \frac{\sum_i (\text{number of patients in index test category, e.g. number correctly localised})}{\sum_i (\text{total number of patients localised by reference standard})}$$

The Meta-DiSc program, designed specifically for the meta-analysis of diagnostic accuracy studies, was used to produce forest plots of study results.[26] It was originally planned that Meta-DiSc would also be used to pool study results in a meta-analysis. This program weights studies according to sample size, during a meta-analysis, which it may be argued is not the most appropriate characteristic to weight studies. However, owing to the heterogeneity of the included studies, pooling of results was not considered appropriate, and the program was only used to produce forest plots for graphical presentation of the results. Therefore, the weighting of studies was not required.

As very few studies provided data on patients with a non-localising or multifocal reference standard, and the clinical value of this information is questionable, analysis was not carried out on these data. This is because a non-localising reference standard cannot be interpreted to mean that the patient did not have a seizure focus. Similarly, a non-localising index test need not mean that the index test was correct in not identifying a seizure focus. It may be that the seizure focus was simply missed in either of these scenarios. Furthermore, if the index test localised a seizure focus in patients with a non-localised reference standard, it would not be possible to deduce which was correct.

Meta-regression was not carried out on the study results. The problem with carrying out a meta-regression analysis would be what to use as the dependent variable. We are unaware of methods to carry out meta-regression on data of the type presented in the review, which has four possible outcomes (correctly localised, partially localised, wrongly localised, not localised). In addition, most sections do not have enough studies to carry out meta-regression.

Association of seizure focus localisation with surgical outcome

Studies were analysed separately for each of the neuroimaging techniques evaluated. Relative risks for the association of a localised neuroimaging scan with outcome following surgery were calculated for each study. The correctly localised and partially localised results were combined to indicate a localised scan, and the incorrectly localised and non-localised scans were combined to indicate a non-localised scan. Within these two groups the risk of having a good outcome was calculated and this was then used to calculate the relative risk (RR) as follows:

	Good outcome	**Bad outcome**
Localised scan	*a*	*b*
Non-localised scan	*c*	*d*

$$\text{RR} = \frac{(a/a + b)}{(c/c + d)}$$

A forest plot of individual study results together with their CIs was produced to provide a visual summary of heterogeneity between studies. The *Q* statistic and I^2 was used formally to test for heterogeneity.[27] If studies were homogeneous,

random effects models were used to pool studies using the methods described by DerSimonian and Laird.[28] The Meta-DiSc program was used to pool study results and to produce the forest plot.[26] If studies were statistically or clinically heterogeneous, studies were not pooled.

The ability of different neuroimaging techniques to predict patient outcomes

Results are presented as a narrative synthesis owing to the limited number of studies included in this section, and the differences between studies in terms of neuroimaging techniques investigated, definitions of a good outcome following surgery and methods of analysis used. All factors considered in the analyses, whether related to the findings of neuroimaging assessments or not, were presented, whether statistically significant or not. The studies were grouped according to the neuroimaging technique investigated and the findings of the studies were discussed with reference to possible sources of heterogeneity between studies, in particular in terms of study quality.

The effectiveness of functional imaging for people with refractory epilepsy for whom a structural abnormality has/has not been previously identified by other neuroimaging techniques or where a seizure focus has/has not been identified on EEG

Owing to the poor quality of the included studies, no formal statistical analysis was carried out for this section. Instead, the following patient subgroups were considered as potential sources of heterogeneity in the main analysis for the diagnostic accuracy section of the review:

- people for whom a structural abnormality had been previously been identified by other neuroimaging techniques
- people for whom no structural abnormality had been previously identified by other neuroimaging techniques
- people for whom surface or invasive EEG recording had isolated a seizure focus
- people for whom surface or invasive EEG recording had failed to isolate a seizure focus.

Sensitivity analyses

Sensitivity analyses were performed to investigate the usefulness of carrying out extensive literature searches and including studies published in languages other than English. We compared the results obtained using all studies identified by the extensive searches carried out for this review with the results that would have been obtained if we had included studies identified by a search of MEDLINE only. Similarly, the results using all studies regardless of language of publication were compared with the results that would have been obtained if only studies published in English had been included in the review.

Chapter 4

Details of studies included in the review

This chapter summarises the studies included in the review. Full details of these studies are given in Appendix 5.

Diagnostic accuracy studies

Study (duplicate report reference numbers in parentheses)	Index test	Reference standard	Restricted to surgery patients?	Restricted to patients with good outcome following surgery?
Achten, 1998[29]	MRI MRS PET: FDG	Combination	No	No
Adams, 1992[30]	CT MRI SPECT: HMPAO	Site of surgery/ pathology site	Yes	No
Assadi, 1997[31]	MRI SPECT: HMPAO	Unclear EEG	No	No
Boundy, 1996[32]	MRI SPECT: HMPAO SPECT: IDEX	Site of surgery	No	No
Brooks, 1990[33]	CT MRI	Site of surgery	Yes	No
Cendes, 1995[34]	MRS and MRI	Unclear EEG	No	No
Cendes, 1997[35]	MRI MRS	Combination	No	No
Chee, 1993[36(37)]	PET: FDG	Ictal EEG	Yes	No
Chugani, 1993[38]	PET: FDG Combination: CT and MRI	Site of surgery	Yes	No
Cross, 1996[39]	MRI MRS	Combination	No	No
Debets, 1997[40]	PET: FDG PET: FMZ SPECT: IMZ	Site of surgery	No	No
Doi, 1995[41]	MRI SPECT: IMZ SPECT: rCBF with IMP, HMPAO and ECD	Combination	No	No
Duncan, 1993[42]	SPECT: HMPAO	Combination	No	No
Engel, 1990[43]	PET: FDG	Ictal EEG	Yes	No
Gilliam, 2000[44(45)]	MRI	Site of surgery	No	No
Gram, 1988[46]	CT MRI SPECT: HMPAO	Interictal EEG	No	No

continued

Study (duplicate report reference numbers in parentheses)	Index test	Reference standard	Restricted to surgery patients?	Restricted to patients with good outcome following surgery?
Grunwald, 1991[47(48)]	SPECT: HMPAO	Combination	Yes	No
Hajek, 1991[49]	MRI SPECT: HMPAO	Site of surgery	No	No
Harvey, 1993[50]	SPECT: HMPAO	Ictal EEG	No	No
Ho, 1995[51]	PET: FDG SPECT: HMPAO	Combination	No	No
Hong, 2002[52]	SPECT: HMPAO PET: FDG	Site of surgery	Yes	No
Hwang, 2001[53]	MRI PET: FDG SPECT: HMPAO	Pathology at site of surgery	Yes	No
Jabbari, 1991[54]	CT MRI SPECT: IMP	Ictal EEG in some patients, interictal EEG in others	No	No
Jack, 1994[55]	MRI	Combination	Yes	No
Jack, 1990[56]	MRI	Site of surgery	Yes	No
Jackson, 1990[57]	MRI	Site of surgery	No	No
Juhasz, 2003[58]	MRI PET: AMT PET: FDG	Site of surgery	No	No
Kaiboriboon, 2002[59]	SISCOM SPECT: ECD	Site of surgery	No	No
Kaminska, 2003[60]	MRI SISCOM	Site of surgery	No	No
Kang, 1997[61]	SPECT: ECD	Site of surgery	Yes	Yes (Engel I)
Kilpatrick, 1997[62]	MRI PET SPECT	Site of surgery	No	No
Kim, 2000[63]	MRI PET: FDG SPECT: HMPAO	Ictal EEG	Yes	No
Kim, 2002[64]	MRI PET: FDG	Site of surgery	Yes	Yes (Engel I or II)
Knowlton, 1997[65(66)]	MRI MRS PET: FDG	Ictal EEG	No	No
Kuzniecky, 1991[67]	MRI	Ictal EEG	Unclear	No
Kuzniecky, 1998[68,69]	MRI MRS	Site of surgery	Yes	No
Kuzniecky, 1993[70]	MRI	Site of surgery	Yes	No
Lee, 2001[71(72)]	SPECT: ECD SPECT: HMPAO	Combination	No	No
Lee, 2002[73(74)]	SPECT: HMPAO	Combination	No	No
Lee, 2000[75(76)]	SPECT: HMPAO	Combination	Yes	Yes (seizure free)
Lewis, 1998[77]	MRI SPECT: HMPAO or ECD	Ictal EEG	No	No

continued

Study (duplicate report reference numbers in parentheses)	Index test	Reference standard	Restricted to surgery patients?	Restricted to patients with good outcome following surgery?
Li, 2000[78]	MRI MRS	Site of surgery	Yes	No
Markand, 1997[79]	MRI PET: FDG SPECT: HMPAO, HIPDM or ECD SPECT: HMPAO	Combination	Yes	No
Markand, 1994[80]	SPECT: HIPDM, HMPAO or IMP	Site of surgery	No	No
Mastin, 1996[81]	PET: FDG SPECT: HMPAO	Site of surgery	Yes	No
Newton, 1995[82]	SPECT: HMPAO	Combination	No	No
Newton, 1994[83(84)]	SPECT: HMPAO	Combination	No	No
Ng, 1994[85]	MRS	Ictal EEG	No	No
O'Brien, 2001[86]	PET: FDG	Site of surgery	No	No
O'Brien, 2000[87]	SISCOM	Site of surgery	Yes	No
O'Brien, 1998[88(89,90)]	MRI SISCOM SPECT: HMPAO	Site of surgery	No	No
O'Brien, 2001[91]	SISCOM	Ictal EEG	No	No
Oliveira, 1999[92]	SPECT: ECD	Combination	No	No
Oommen, in progress[93(94)]	SPECT: ECD	Site of surgery	Yes	No
Otsubo, 1995[95]	SPECT: HMPAO	Ictal EEG	Yes	No
Park, 2001[96]	MRS PET: FDG	MRI	Yes	Yes (Engel I or II)
Rowe, 1989[97(98,99)]	SPECT: HMPAO	Ictal EEG	No	No
Rowe, 1991[100]	SPECT: HMPAO	Combination	No	No
Runge, 1997[101]	MRI SPECT: ECD	Ictal EEG/ECoG	No	No
Ryvlin, 1998[102]	MRI PET: FMZ	EEG Combination	No	No
Seki, 1998[103]	MRI SPECT: HMPAO or ECD	Site of surgery	Yes	Yes (Engel I or II)
Shen, 1990[104]	SPECT: HIPDM	Site of surgery	Yes	No
Siegel, 2001[105]	SISCOM: HMPAO or ECD	Ictal EEG	No	No
Sperling, 1986[106]	MRI PET: FDG	Combination	No	No
Tatlidil, 2000[107]	PET: [^{15}O]water	Site of surgery	Yes	No
Tatum, 1995[108]	SPECT: HMPAO	Combination	No	No
Theodore, 1990[109]	CT MRI PET: FDG	Ictal EEG	Yes	No
Venz, 1994[110]	MRI SPECT: HMPAO SPECT: IMZ	Ictal EEG	No	No
Vera, 1999[111]	SISCOM	Combination	No	No

continued

Study (duplicate report reference numbers in parentheses)	Index test	Reference standard	Restricted to surgery patients?	Restricted to patients with good outcome following surgery?
Watanabe, 2002[112]	NIRS SPECT: HMPAO or ECD	Ictal EEG	No	No
Weil, 2001[113]	SPECT: ECD	Combination	Yes	Yes (Engel I)
Weis, 1997[114]	SPECT: HMPAO or ECD	Site of surgery	Yes	No
Wheless, 1999[115]	MRI	Site of surgery	Yes	No
Zhou, 1994[116]	SPECT: ECD	Combination	No	No
Yu, 1995[117]	SPECT: HMPAO	Combination	Yes	No

AMT, α-methyl-L-tryptophan; ECoG, electrocorticography; FMZ, [^{11}C]flumazenil; HIPDM, *N*,*N*,*N*′-trimethyl-*N*′-(2-hydroxy-3-methyl-5-[^{123}I]iodobenzyl)-1,3-propanediamine; IDEX, [^{123}I]iododexetimide; IMP, [^{123}I]isopropyliodoamphetamine; IMZ, [^{123}I]iomazenil; NIRS, near-infrared spectroscopy; rCBF, regional cerebral blood flow.

Outcome prediction studies

Study	Dependent variable	Variables investigated
Antel, 2002[118]	1. Seizure free 2. Worthwhile improvement (>90% reduction in seizures)	Ipsilateral, contralateral (to site of surgery) and asymmetry *Z* scores for each of the following: hippocampal volume, amygdaloid volume, NAA/Cr in the midtemporal lobe and NAA/Cr in the posterior temporal lobe.
Dupont, 2000[119]	Outcome class A compared with class C	FDG PET scans positive in the following temporal regions: 1. Temporal region: medial 2. Temporal region: pole 3. Temporal region: anterolateral 4. Temporal region: medium lateral 5. Temporal region: posterolateral
O'Brien, 2000[87]	1. Excellent outcome 2. Favourable outcome (>75% reduction in seizure frequency)	1. SISCOM (concordant vs non-concordant/non-localising) 2. Pre-operative MRI (lesional vs non-lesional) 3. Ictal scalp EEG (localisation vs non-localising) and separate analysis for: 1. Extent of excision of SISCOM focus (complete excision vs non-complete or non-excision) 2. Preoperative MRI findings (focal structural lesions vs no lesion) 3. Ictal scalp EEG findings (localisation vs non-localising)
O'Brien, 1998[88]	1. Postoperative seizure frequency 2. Improvement in seizure frequency score	1. SISCOM (concordant vs non-concordant or non-localising) 2. MRI (lesions vs no-lesion) 3. Type of surgery (temporal vs non-temporal)
O'Brien, 2001[86]	Engel categories I–IV	1. MRI (definite focal lesions vs no focal lesion) 2. FDG–PET (localising vs non-localising)
O'Brien, 2001[91]	Postoperative seizure frequency score	1. SISCOM results (no further details) 2. MRI results (no further details)
Paolicchi, 2000[120]	Good outcome (Engel I and II) and seizure free	1. Age at epilepsy onset 2. Duration of epilepsy before surgery 3. Presence of cognitive impairment 4. Temporal vs extra-temporal resection 5. Lesional vs non-lesional resection on MRI 6. Developmental vs acquired pathology 7. Complete vs incomplete resection

continued

Study	Dependent variable	Variables investigated
Radhakrishnan, 1998[121]	Excellent outcome (seizure free or non-disabling seizures)	1. Age at unprovoked seizure onset 2. Symptomatic epilepsy aetiology 3. Duration of epilepsy history 4. History of febrile seizures 5. Unilateral hippocampal formation atrophy on MRI 6. Other lesions on neuroimaging 7. Concordant interictal epileptiform discharge (scalp EEG) 8. Age at surgery 9. Postsurgery: no epileptiform discharge on corticogram 10. Postsurgery: no epileptiform discharge at 1 week 11. Postsurgery: no epileptiform discharge at 3 months 12. Postsurgery: seizure free during 1st year 13. Postsurgery: only non-disabling seizures during 1st year 14. Postsurgery: length of follow-up
Son, 1999[122]	Engel I following surgery	1. Interictal EEG (localisation results, details unclear) 2. Video-EEG (localisation results, details unclear) 3. MRI (localisation results, details unclear) 4. PET (localisation results, details unclear) 5. Ictal SPECT (localisation results, details unclear) 6. Interictal SPECT (localisation results, details unclear) 7. Neuropsychological test (localisation results, details unclear) 8. Wada test (localisation results, details unclear)

Chapter 5

Results of the review

Results of the literature searches

The literature searches identified 9266 references. These were screened and 341 references were considered to be potentially relevant. *Figure 1* shows the flow of studies through the review process and the number of studies excluded according to each of the inclusion criteria. Appendix 4 summarises the studies excluded from the review. Searches for economic studies identified an additional nine references.

A total of 94 studies met inclusion criteria. Of these, 75 were primary diagnostic accuracy studies, 14 were duplicate reports and five were cohort studies. No full economic evaluation studies that met the inclusion criteria were identified. Four of the diagnostic accuracy studies, all by the same author,[86–88,91] and the five cohort studies[118–122] used regression analysis to assess the value of imaging findings in the prediction of outcome following surgery. The 75 studies on the diagnostic accuracy of imaging for the localisation of seizure focus included a total of 179 test evaluations. The majority of studies were published in English. However, one study published in Danish,[46] one in German[110] and two in Japanese[41,103] were included. No studies were excluded based on language of publication. Five studies reported only as abstracts contained sufficient data to be included.[31,34,61,91,117]

Where studies were published only as abstracts, or where studies did not provide adequate data on the number of patients with correctly localised, non-localised, partially localised and incorrectly localised scans, the authors were contacted for further information (33 studies). Replies were received from 15, six of whom provided full reports of the study. A further three had full papers in preparation. The author of one of these sent an unpublished report, which was included in the review.[93] A further author provided sufficient additional data to enable their abstract to be included in the review.[31] Seven authors were contacted to confirm whether reports that appeared to relate to the same study were duplicates or not. Replies were received from five, four of whom confirmed that the reports identified related to the same study.

Study quality is referred to throughout the results chapter but readers requiring more information on the quality of an individual study should refer to the section 'Study quality' (below), where study quality is discussed in detail and tables of study quality for each study are presented.

Study quality

Diagnostic accuracy studies

The studies were generally of poor quality, largely owing to the inappropriate patient spectra included in the studies. *Table 3* presents the results of the quality assessment for each study. As most studies included more than one evaluation, and different evaluations fulfilled different quality criteria, the quality assessment for each evaluation is given.

The proportion of studies (evaluations for items 6, 7, 9, 10 and 11) scoring 'yes', 'no' or 'unclear' for each of the QUADAS items is summarised in *Figure 2*. The median number of the 13 QUADAS items assessed in this review fulfilled by these studies was 7.5 (range 6–11).

A particular feature of these studies was the failure to include an appropriate patient spectrum. Only 4% of studies included an appropriate patient spectrum, defined as an unselected group of patients with refractory epilepsy being considered for surgery, prospectively enrolled in the study. We consider an unselected group of patients to be either a consecutive or random sample of referrals, selected for surgical work-up, but not selected on the basis of test results carried out as part of the work-up for surgery. This was deemed an appropriate patient spectrum as it reflected the patient group that would receive the tests in practice, and eliminate selection bias. Eighteen of the 75 studies were retrospective in design, 46 had unclear study design and 11 used a prospective design. Three of the 11 prospective studies were restricted to patients who underwent surgery and a further five studies included selected patient populations or did not provide sufficient details on the population to determine whether the patients were unselected. Hence only three studies included an appropriate patient spectrum.[29,54,106]

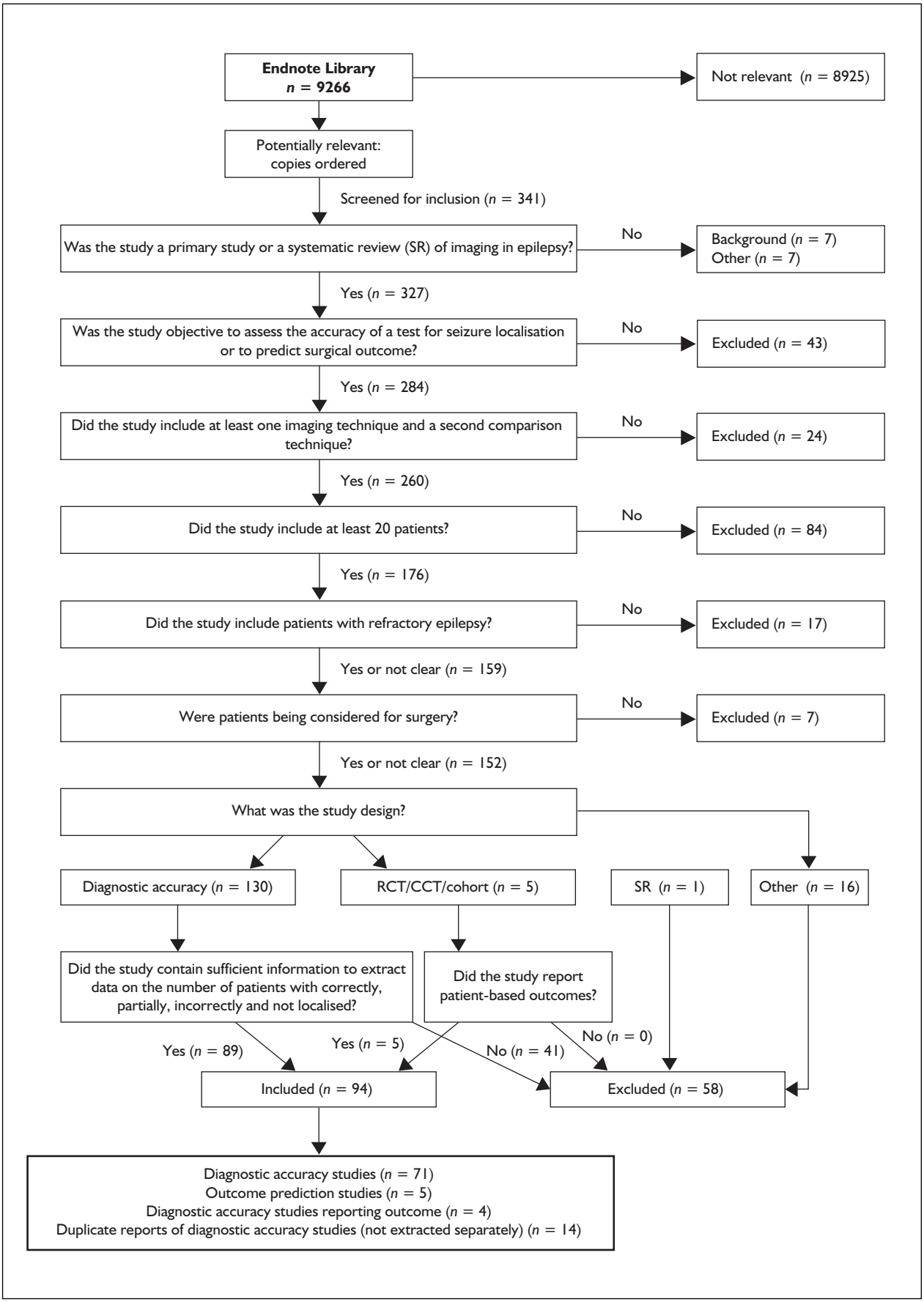

FIGURE 1 *Flow chart of studies through review process*

TABLE 3 *Summary of quality assessment results: diagnostic accuracy studies*

Study	Index test	Spectrum composition	Selection criteria	Appropriate reference standard	Partial verification bias	Differential verification bias	Incorporation bias	Test execution details	Reference execution details	Test review bias	Diagnostic review bias	Clinical review bias	Uninterpretable results	Withdrawals
Achten, 1998[29]	MRI						+	+		?	?	?		
	MRS	+	+	+	+	+	+	+	+	?	?	?	+	+
	PET: FDG						+	+		?	?	?		
Adams, 1992[30]	CT						–	+		?	?	–		
	MRI	–	+	+	+	+	–	+	–	?	?	–	+	–
	SPECT: HMPAO						–	+		?	?	–		
Assadi, 1997[31]	MRI	–	–	?	+	+	+	+	–	+	+	–	+	–
	SPECT: HMPAO						+	–		+	+	–		
Boundy, 1996[32]	MRI						–	+		+	?	–		
	SPECT: HMPAO	?	+	+	+	+	–	–	+	+	?	–	+	+
	SPECT: IDEX						–	+		+	?	–		
Brooks, 1990[33]	CT	–	–	+	+	+	?	–	–	+	?	–	+	–
	MRI						?	–		+	?	–		
Cendes, 1995[34]	MRS and MRI	?	+	?	+	+	+	–	–	?	?	?	?	+
Cendes, 1997[35]	MRI	–	+	+	+	+	–	+	+	?	?	?	+	–
	MRS													
Chee, 1993[36]	PET: FDG	–	+	+	+	+	+	–	+	?	?	?	+	+
Chugani, 1993[38]	PET: FDG	–	+	+	+	+	–	–	+	?	–	?	+	+
	CT/MRI combined						–	–		?	–	?		
Cross, 1996[39]	MRI	?	–	–	+	+	+	+	+	?	?	?	+	+
	MRS						+	+		?	?	?		
Debets, 1997[40]	PET: FDG						+	+		?	?	?		
	PET: FMZ	?	–	+	+	+	+	+	+	?	?	?	+	+
	SPECT: IMZ						+	–		?	?	?		
Doi, 1995[41]	MRI						–	–		?	–	?		
	SPECT: IMZ	?	–	+	+	+	+	–	–	?	?	?	+	+
	SPECT: rCBF						–	–		?	?	?		
Duncan, 1993[42]	SPECT: HMPAO	?	+	+	+	+	+	+	–	+	?	–	+	+
Engel, 1990[43]	PET: FDG	–	+	+	+	+	+	+	+	+	?	–	+	+
Gilliam, 2000[44]	MRI	?	+	+	+	+	–	+	+	?	–	?	+	–
Gram, 1988[46]	CT						+	–		+	?	–		
	MRI	?	–	–	+	+	+	–	–	+	?	–	+	+
	SPECT: HMPAO						+	–		+	?	–		
Grunwald, 1991[47]	SPECT: HMPAO	–	+	+	+	+	?	+	–	+	?	–	?	+
Hajek, 1991[49]	MRI	–	+	+	+	+	?	–	–	+	?	–	+	+
	SPECT: HMPAO						?	+		+	?	–		
Harvey, 1993[50]	SPECT: HMPAO	?	+	+	+	+	+	+	+	+	+	–	+	+

continued

TABLE 3 *Summary of quality assessment results: diagnostic accuracy studies (cont'd)*

Study	Index test	Spectrum composition	Selection criteria	Appropriate reference standard	Partial verification bias	Differential verification bias	Incorporation bias	Test execution details	Reference execution details	Test review bias	Diagnostic review bias	Clinical review bias	Uninterpretable results	Withdrawals
Ho, 1995[51]	PET: FDG	–	+	+	+	+	+	+	+	+	?	–	+	+
	SPECT: HMPAO						+	+		+	?	–		
Hong, 2002[52]	PET: FDG	–	–	+	+	+	+	–	–	?	?	?	+	+
	SPECT: HMPAO						+	–		?	?	?		
Hwang, 2001[53]	MRI						–	+		+	–	–		
	PET: FDG	–	+	+	+	+	+	+	+	+	?	–	+	+
	SPECT: HMPAO						+	+		+	?	–		
Jabbari, 1991[54]	CT						+	–		–	?	?		
	MRI	+	+	–	+	+	+	–	+	+	?	?	+	+
	SPECT: IMP						+	+		+	?	?		
Jack, 1994[55]	MRI	–	+	+	+	+	+	+	+	?	–	?	+	+
Jack, 1990[56]	MRI	–	+	+	+	+	+	+	+	+	+	–	+	+
Jackson, 1990[57]	MRI	–	+	+	+	+	+	–	+	+	–	+	+	+
Juhasz, 2003[58]	MRI						?	–		?	?	?		
	PET: AMT	?	–	+	+	+	?	+	+	?	?	?	+	+
	PET: FDG						?	+		?	?	?		
Kaiboriboon, 2002[59]	SISCOM	–	+	+	+	+	+	–	+	+	?	–	+	+
	SPECT: ECD						+	+		+	?	–		
Kaminska, 2003[60]	MRI	–	+	+	+	+	?	+	+	?	?	?	+	+
	SISCOM						?	–		?	?	?		
Kang, 1997[61]	SPECT: ECD	–	–	?	+	+	?	–	–	+	?	–	+	+
Kilpatrick, 1997[62]	MRI						–	–		?	–	?		
	PET	?	+	+	–	+	–	–	+	?	–	?	+	+
	SPECT						–	–		?	–	?		
Kim, 2000[63]	MRI						+	–		?	?	?		
	PET: FDG	–	+	+	+	+	+	–	–	?	?	?	+	+
	SPECT: HMPAO						+	–		?	?	?		
Kim, 2002[64]	MRI	–	+	+	+	+	–	–	+	?	?	–	+	+
	PET: FDG						–	+		+	?	–		
Knowlton, 1997[65]	MRI						+	+		+	?	–		
	MRS	?	+	+	+	+	+	+	+	+	?	–	+	+
	PET: FDG						+	+		+	?	–		
Kuzniecky, 1991[67]	MRI	–	–	+	+	+	+	+	+	+	+	–	+	+
Kuzniecky, 1998[68]	MRI	–	+	+	+	+	+	+	+	?	?	?	+	+
	MRS						+	+		+	?	–		
Kuzniecky, 1993[70]	MRI	–	+	+	+	+	+	+	+	+	?	–	+	+
Lee, 2001[71]	SPECT: ECD	?	–	+	+	+	+	–	–	+	+	–	+	+
	SPECT: HMPAO						+	–		+	+	–		

continued

TABLE 3 *Summary of quality assessment results: diagnostic accuracy studies (cont'd)*

Study	Index test	Spectrum composition	Selection criteria	Appropriate reference standard	Partial verification bias	Differential verification bias	Incorporation bias	Test execution details	Reference execution details	Test review bias	Diagnostic review bias	Clinical review bias	Uninterpretable results	Withdrawals
Lee, 2002[73]	SPECT: HMPAO	–	+	+	+	+	+	+	–	+	?	?	+	+
Lee, 2000[75]	SPECT: HMPAO	–	+	+	+	+	?	+	–	+	?	–	+	+
Lewis, 1998[77]	MRI SPECT: HMPAO or ECD	?	–	+	+	+	+ +	+ +	+	+ +	? ?	– –	+	+
Li, 2000[78]	MRI MRS	–	–	+	+	+	? ?	+ +	+	? ?	? ?	? ?	+	+
Markand, 1997[79]	MRI PET: FDG SPECT: HMPAO, HIPDM or ECD SPECT: HMPAO	–	+	+	+	+	– – – –	– – – –	+ +	+ + + +	– – – –	– – – –	+	–
Markand, 1994[80]	SPECT: HIPDM, HMPAO or IMP	–	+	+	+	+	–	–	+	+	?	–	+	–
Mastin, 1996[81]	PET: FDG SPECT: HMPAO	–	–	+	+	+	– –	+ +	–	+ +	– –	+ +	+	–
Newton, 1995[82]	SPECT: HMPAO	?	+	+	+	+	+	+	+	?	+	?	+	–
Newton, 1994[83]	SPECT: HMPAO	–	+	+	+	+	–	–	–	+	?	–	+	+
Ng, 1994[85]	MRS	–	+	+	+	+	+	+	+	+	+	–	+	+
O'Brien, 2001[86]	PET: FDG	?	+	+	–	+	–	+	–	+	–	–	+	+
O'Brien, 2000[87]	SISCOM	–	+	+	+	+	?	–	–	+	?	–	+	+
O'Brien, 1998[88]	MRI SISCOM SPECT: HMPAO	?	+	+	–	+	– – –	– – –	–	+ + +	– – –	– – –	+	+
O'Brien, 2001[91]	SISCOM	?	–	+	+	+	+	–	–	+	?	–	?	+
Oliveira, 1999[92]	SPECT: ECD	?	+	+	+	+	+	+	+	+	?	–	+	–
Oommen, in progress[93]	SPECT: ECD	–	–	+	+	+	+	–	+	+	?	–	+	+
Otsubo, 1995[95]	SPECT: HMPAO	–	+	+	+	+	+	+	+	+	?	–	+	+
Park, 2001[96]	MRS: PET: FDG	–	+	–	+	+	+ +	+ +	+	? ?	? ?	? ?	+	+
Rowe, 1989[97]	SPECT: HMPAO	?	+	+	+	+	+	+	+	+	?	–	+	+
Rowe,1991[100]	SPECT: HMPAO	–	+	+	+	+	+	–	+	+	+	–	+	+
Runge, 1997[101]	MRI SPECT: ECD	?	–	+	+	+	+ +	+ +	+	? +	+ +	– –	+	+
Ryvlin, 1998[102]	MRI PET	–	+	–	+	+	– +	–	–	+	+	–	+	+

continued

TABLE 3 *Summary of quality assessment results: diagnostic accuracy studies (cont'd)*

Study	Index test	Spectrum composition	Selection criteria	Appropriate reference standard	Partial verification bias	Differential verification bias	Incorporation bias	Test execution details	Reference execution details	Test review bias	Diagnostic review bias	Clinical review bias	Uninterpretable results	Withdrawals
Seki, 1998[103]	MRI	–	+	+	+	+	–	–	–	?	–	?	+	+
	SPECT: HMPAO or ECD						–	–		?	–	?		
Shen, 1990[104]	SPECT: HIPDM	–	+	+	+	+	–	+	–	?	–	–	+	+
Siegel, 2001[105]	SISCOM: HMPAO or ECD	?	+	+	+	+	+	–	+	?	–	?	+	+
Sperling, 1986[106]	MRI	+	+	+	+	+	+	–	–	?	?	?	+	–
	PET: FDG						+	–		?	?	?		
Tatlidil, 2000[107]	PET: [^{15}O]water	–	–	+	+	+	–	–	–	?	–	+	+	+
Tatum, 1995[108]	SPECT: HMPAO	–	–	+	+	+	+	+	+	+	?	–	+	+
Theodore, 1990[109]	CT	–	+	+	+	+	+	–	+	+	+	–	+	+
	MRI						+	–		+	–	–		
	PET: FDG						+	+		–	+	–		
Venz, 1994[110]	MRI	?	–	+	+	+	+	+	+	–	?	?	+	+
	SPECT: HMPAO						+	+		+	?	–		
	SPECT: IMZ						+	+		+	?	–		
Vera, 1999[111]	SISCOM	?	–	+	+	+	+	+	+	?	?	?	+	+
Watanabe, 2002[112]	NIRS	?	+	+	+	+	+	–	+	?	?	?	+	+
	SPECT: HMPAO or ECD						+	–		?	?	?		
Weil, 2001[113]	SPECT: ECD	–	–	+	+	+	+	+	+	?	?	?	+	+
Weis, 1997[114]	SPECT: HMPAO or ECD	–	+	+	+	+	+	+	+	+	?	–	+	+
Wheless, 1999[115]	MRI	–	+	+	+	+	–	+	–	?	–	?	+	+
Zhou, 1994[116]	SPECT: ECD	–	–	+	+	+	–	–	+	?	–	?	+	+
Yu, 1995[117]	SPECT: HMPAO	–	–	+	+	+	?	–	–	?	?	?	+	+

+, Yes; –, no; ?, not clear.

Of the 46 studies for which the study design was unclear, 16 were restricted to patients who underwent surgery, and five of these were restricted to patients who had a good outcome following surgery. Twelve of the retrospective diagnostic cohort studies were also restricted to patients who underwent surgery, and one of these was restricted to patients with a good outcome following surgery.

Studies generally scored well on the use of an appropriate reference standard, avoidance of partial verification bias, avoidance of differential verification bias, reporting of uninterpretable results and providing details of study withdrawals. Three studies failed to use an appropriate reference standard: one used MRI,[96] one used surface (interictal) EEG[46] and one used video (ictal) EEG in selected patients and surface (interictal) EEG in the remaining patients.[54] In a further four studies, it was unclear whether an appropriate reference standard had been used for all patients.[31,34,61,102] Two reported the use of EEG,[31,34] but did not state whether this was ictal or interictal. One stated the use of intercranial EEG or video EEG in a proportion of patients, but

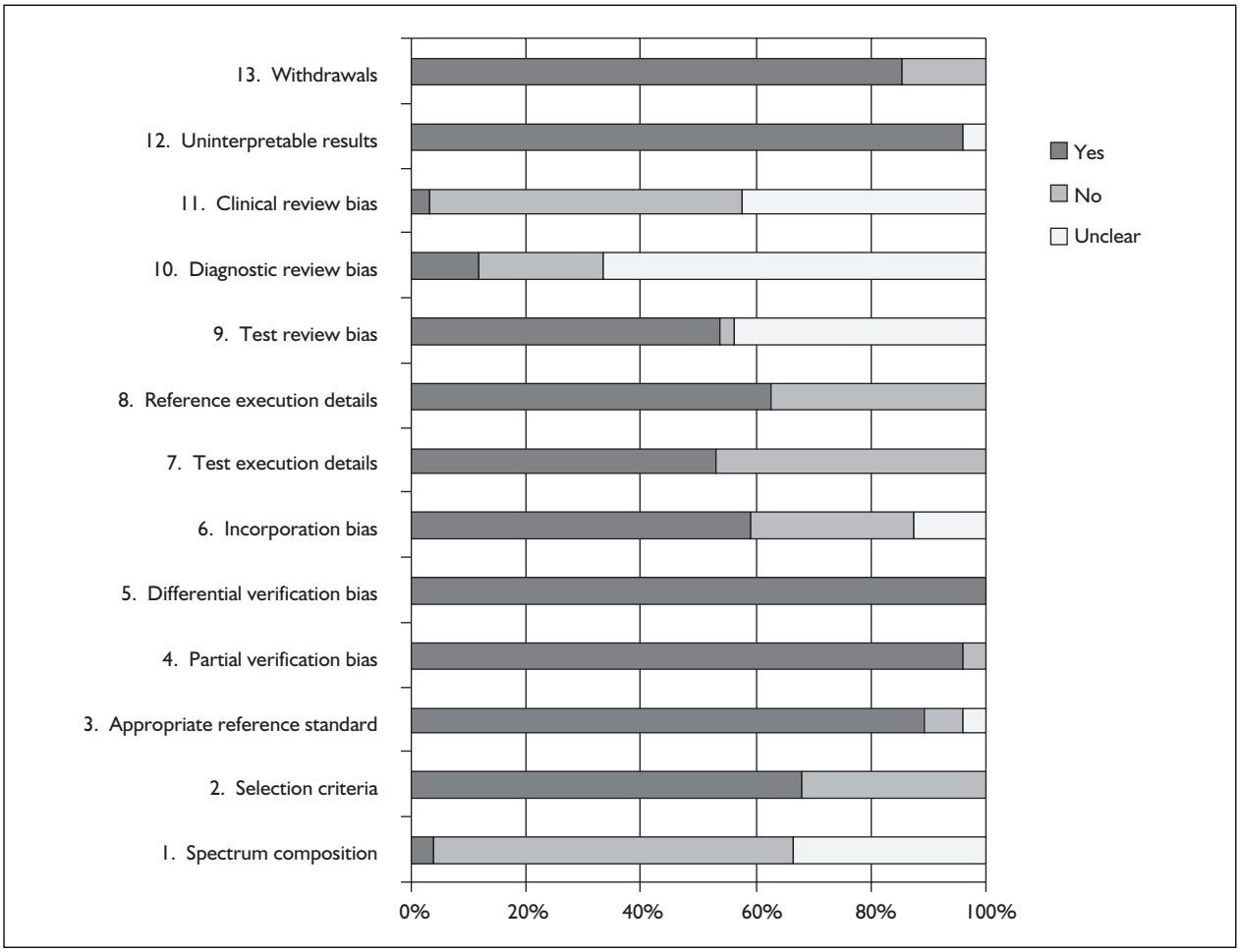

FIGURE 2 *Proportion of studies scoring 'yes', 'no' or 'unclear' for each of the QUADAS items*

did not specify the type of EEG used in all patients.[102] A combination reference standard where patients received a variety of reference tests was considered acceptable. All studies avoided differential verification bias, but partial verification bias was a potential problem in three studies.[62,86,88] These three studies included patients being considered for surgery in the study but only reported results for patients who underwent surgery, with site of surgery being the reference standard. These have a similar problem in terms of applicability to studies restricted to patients who underwent surgery, and were therefore considered to include an inappropriate patient spectrum. Almost all studies reported data for test results that were uninterpretable. However, in three studies it was unclear whether or not uninterpretable results were included in the results.[34,47,91] Withdrawals were also generally well reported, with only 14% of studies failing to account for all the patients who were reported to have been included.

Blinding was generally poorly reported. Only 12% of evaluations reported that diagnostic review bias had been avoided, i.e. that the reference standard was interpreted without knowledge of the results of the index test. In 66% of evaluations this information was not reported and in the remaining 22% investigators knew the results of the index test when interpreting the results for the reference standard. In all but six of the evaluations where diagnostic review bias may have been present, incorporation bias was also a problem, that is, the index test formed part of the reference standard. Clinical review bias may have been a particular problem in these studies. Only 3% of evaluations reported that clinical review bias had been avoided and a further 42% did not provide any details on the information available to the person interpreting the test results. In practice, when the results of imaging tests for the localisation of the seizure focus are evaluated, information from a wide range of sources would be available to the person interpreting the scans.

This information would include patient details, such as seizure history, and also the results of other imaging evaluations and tests such as EEG. These studies therefore have the slightly unusual feature in that it is not possible for a study to avoid both clinical review bias and test review bias. Test review bias was poorly reported by the studies, but those that did report this tended to report that the results of the reference standard were not available to those interpreting the results of the index test. Only 2% of evaluations reported that the results of the reference standard were available to those interpreting the index test, 54% that test review bias was avoided and in the remaining 44% this information was not provided.

Details of index test and reference standard execution were relatively poorly reported, with only 53 and 63% reporting sufficient details of test execution, respectively. Reporting of selection criteria was slightly better, with 68% of studies providing sufficient details on how patients were selected for inclusion in the study.

Outcome prediction studies

The quality of the cohort studies reporting the prediction of outcome following surgery is summarised in *Table 4*. *Figure 3* summarises the proportion of studies scoring 'yes', 'no' or 'unclear' for each of the quality items. Generally the studies were all of relatively poor quality. The median number of the eight quality items fulfilled by these studies was four (range 0–5).

All studies failed to control for all factors identified by a previous review as being predictive of outcome following surgery.[123] All studies also failed to provide any details of the distribution of these confounding factors between the different exposure groups and also failed to report on whether assessment of outcome following surgery was performed blind to the results of the imaging techniques under evaluation. All but one of the studies reported on participant withdrawals.[91] There were no withdrawals in these studies, therefore all fulfilled the criteria of comparability of withdrawals between groups. The study that did not report on withdrawals was published as an abstract and therefore limited details were available.[91] This was also the only study that failed to provide sufficient details on selection criteria. Less than half of the studies provided sufficient details on the neuroimaging techniques being investigated. Three studies failed to include sufficient details of test execution and/or the definition of a positive result.[91,120,121] In a further two studies, it was unclear whether the results of the index test were interpreted without knowledge of the outcome following surgery.[119,122] Six studies had a follow-up period >12 months in all

TABLE 4 *Summary of quality assessment results: outcome prediction studies*

Study	Selection criteria	Test details	Comparability on confounding factors	Control for confounding	Blinded outcome assessment	Follow-up > 12 months	Reporting of withdrawals	Comparability of withdrawals between groups
Antel, 2002[118]	+	+	?	–	?	–	+	+
Dupont, 2000[119]	+	?	?	–	?	+	+	+
O'Brien, 2001[86]	+	+	?	–	?	+	+	+
O'Brien, 2000[87]	+	+	?	–	?	–	+	+
O'Brien, 1998[88]	+	+	?	–	?	+	+	+
O'Brien, 2001[91]	–	–	?	–	?	?	?	?
Paolicchi, 2000[120]	+	–	?	–	?	+	+	+
Radhakrishnan, 1998[121]	+	–	?	–	?	+	+	+
Son, 1998[122]	+	?	?	–	?	+	+	+

+, yes; –, no; ?, not clear.

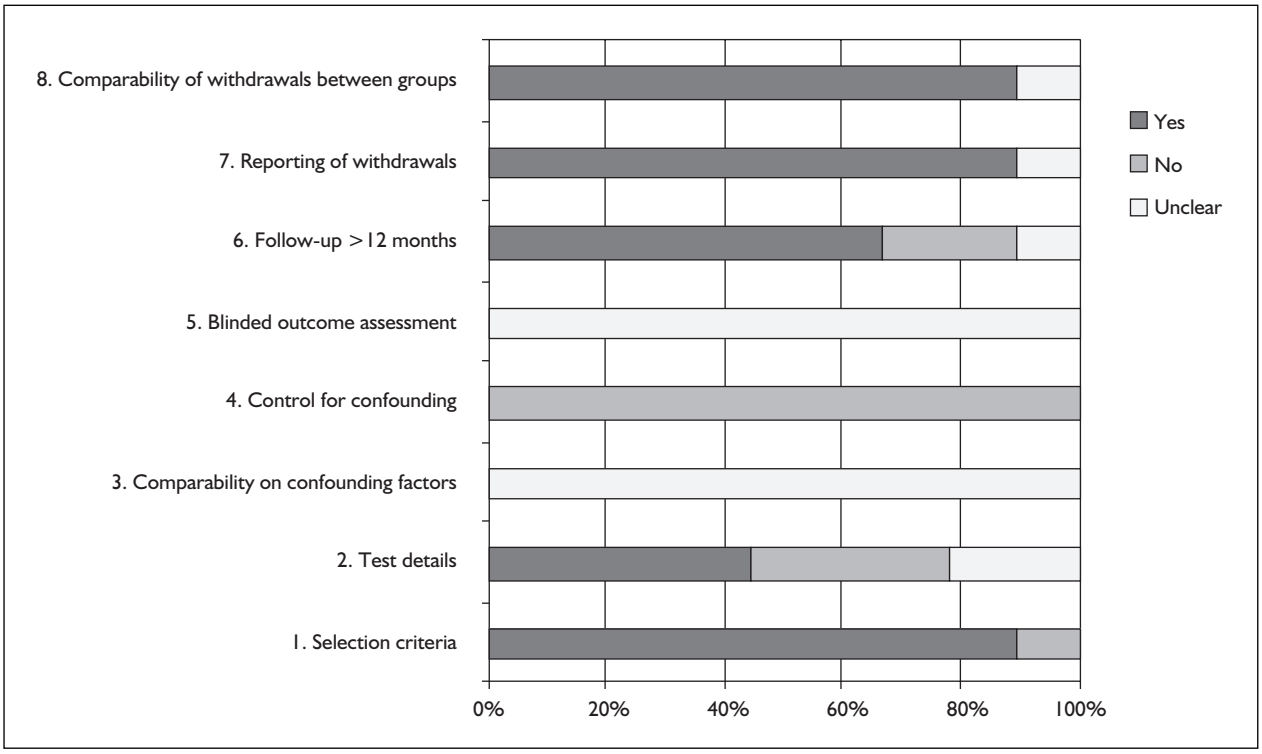

FIGURE 3 *Proportion of studies scoring 'yes', 'no' or 'unclear' for each of the quality items*

patients,[86,88,119–122] one study did not report duration of follow-up[91] and two studies included some patients with follow-up <12 months.[86,119]

Findings from diagnostic accuracy studies

A total of 72 studies looked at the diagnostic accuracy of various imaging tests for the localisation of the seizure focus. The majority of included studies were carried out in the USA (30). The remaining studies were carried out in a wide range of countries: Australia (nine), Korea (nine), Germany (six), Canada (four), Japan (three), France (two), Belgium (one), Brazil (one), China (one), Denmark (one), The Netherlands (one), Switzerland (one), Taiwan (one) and the UK (two). All studies used a diagnostic cohort (or single sample) design. Forty-seven studies looked at the accuracy of imaging tests for the localisation of the seizure focus, 24 at the accuracy of tests in lateralising the seizure focus in patients with TLE and one at the ability of tests to lateralise the epileptic focus in patients with all types of epilepsy.

The number of patients included in the studies ranged from 20 to 177 (studies with <20 patients were excluded). The total number of patients included in the 72 studies was 3156 (mean 44 per study). Nine studies were carried out in adults only, ten in children only, 42 in both adults and children and the remaining 11 studies did not report on age range. The age of included patients ranged from 3 months to 72 years, with the mean age ranging from 6 to 38 years. All studies included both men and women and on average included equal numbers of men and women. Forty-six studies did not report on the duration of epilepsy. In those that did, duration ranged from <1 to 52 years.

The included studies investigated the following imaging techniques: SPECT (39 studies, 68 evaluations); MRI (30 studies, 40 evaluations); PET (18 studies, 25 evaluations); SISCOM (seven studies, 11 evaluations); MRS (six studies); CT (five studies); near-infrared spectroscopy (NIRS) (one study); and combinations of more than one test (three studies).

Localisation of the seizure focus

SPECT

SPECT was assessed in 39 studies (68 evaluations). Seven studies assessed the accuracy of SPECT in the lateralisation of the seizure focus in patients with TLE,[32,47,51,79,80,83,93] and 30 studies reported on the accuracy of SPECT in the localisation of the seizure focus in patients with epilepsy being

considered for surgery. The results of these studies are presented in *Table 5*. Reference standards used were combination (14 studies), site of surgery (12 studies), combination of site of surgery and pathology site (two studies), ictal EEG (seven studies), interictal EEG (one study), unclear EEG (one study), interictal EEG in some patients ictal EEG in others (one study) and EEG/electrocorticography (ECoG) (one study). Studies reporting more than one evaluation reported either results for both ictal and interictal SPECT, more than one tracer, different subgroups (EEG focus or previous neuroimaging findings), separate scans on the same patients or different timings from seizure onset to injection or from injection to scanning.

Ictal SPECT

Twenty-two studies (28 evaluations) assessed ictal SPECT.[30,41,51–53,62,63,71,73,79–83,92,93,97,101,104,112,114,117] Sixteen studies looked at the accuracy of ictal SPECT in the localisation of the seizure focus,[30,41,52,53,62,63,71,73,81,82,92,97,101,104,114,117] five at the accuracy of SPECT in the lateralisation of the seizure focus in patients with TLE,[51,79,80,83,93] and one at the accuracy of SPECT in the lateralisation of the seizure focus in patients with all types of epilepsy.[112] Ten studies only included patients with TLE,[51,62,79,80,83,93,97,101,104,117] 11 included patients with both temporal and non-temporal epilepsy[41,52,53,63,71,73,81,82,92,112,114] and one study was unclear as to the type of epilepsy patients included.[30] None of the studies included an appropriate patient spectrum.

One study used two tracers (HMPAO and ECD) and reported results separately for these.[71] For this study the evaluation for HMPAO was included in the main analysis below. One study scanned patients twice and reported results for the first and second scans and a consensus from the two scans.[73] For this study the evaluation for the first scan is included in the main analysis. Three studies reported results separately according to the timing from seizure onset to injection of tracer, for which results were extracted separately. Two studies, by the same author, reported results separately for patients who received the tracer <30 seconds after seizure onset and >30 seconds after seizure onset.[82,83] For these studies the evaluation for within 30 seconds of seizure onset is included in the main analysis. A further study reported results separately for patients who received the tracer immediately after seizure onset, within 30 minutes of seizure onset and over 30 minutes after seizure onset.[117] For this study the results immediately after onset were included in the main analysis.

Nine studies used a combination reference standard,[41,51,71,73,79,82,83,92,117] seven used site of surgery,[52,62,80,81,93,104,114] two used a combination of site of surgery/pathology,[30,53] three used ictal EEG[63,97,112] and one used a combination of EEG and ECoG.[101] The reference standard was considered appropriate in all studies. Partial verification bias may have been a problem in one study which only reported results on patients who underwent surgery, which was also the reference standard.[62] The tracers varied: 13 used HMPAO,[30,51–53,63,71,73,81–83,97,114,117] four ECD,[71,92,93,101] one *N*,*N*,*N*′-trimethyl-*N*′-(2-hydroxy-3-methyl-5-[^{123}I]iodobenzyl)-1,3-propanediamine (HIPDM),[124] one HMPAO/ECD,[112] one HMPAO/HIPDM/IMP,[80] one HMPAO/ECD/[^{123}I]isopropyliodoamphetamine (IMP)[41] and one HMPAO/HIPDM/ECD.[79] One study did not report the tracer used.[62]

The results of studies of ictal SPECT are summarised in *Figures 4* and *5*. These studies generally reported relatively high proportions of correctly localised scans and low rates of non-localised, partially localised and incorrectly localised scans. However, there was considerable heterogeneity between studies. The proportion of correctly localised scans ranged from 25 to 100%, with all but five of the 22 studies reporting proportions of 70% or more.[52,71,73,81,112] These five studies all included patients with both temporal and non-temporal lobe epilepsy. There were no other apparent differences between this subset of studies and studies which reported higher proportions of correctly localised scans with regard to tracers, subgroups, study quality, year of publication or reference standard.

The proportion of patients with non-localised scans also showed considerable heterogeneity, ranging from 0 to 60%, although only one study reported more than 30% non-localised scans.[73] This study also reported the second lowest rate of correctly localised scans and was restricted to patients who had ambiguous or unexpected findings on their first ictal SPECT scan. It would therefore be expected to show less favourable results than studies conducted in less selected patients. Six studies reported that SPECT localised the seizure focus in all patients,[30,51,101,92,93,117] and in three of these studies all patients had correctly localised scans.[30,83,117] Two of these three studies were restricted to patients with TLE.[83,117] All three studies used HMPAO as the tracer, but so did several other studies, including three of the four studies with the lowest proportions of correctly localised patients.[71,73,81] Tracer therefore appears

TABLE 5 *Results of studies that assessed SPECT for seizure focus localisation*

Study	Subgroup	Tracer and additional details	Reference standard	Reference standard	Results: No. (%)						
					Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Combination of ictal and interictal											
Duncan, 1993[42]	No subgroup	HMPAO: combined scans	Combination	Localised Not localised	25 (89.3) 0	0 0	0	3 (10.7)	0	0	28 0
Jabbari, 1991[54]	EEG focus	IMP: 6 ictal, 18 interictal	Ictal EEG in some, interictal in others	Localised Not localised	20 (46.5) 3 (21.4)	23 (53.5) 11 (78.6)	0	0	0	0	43 14
Kaiboriboon, 2002[59]	No subgroup	ECD: combined scans	Site of surgery	Localised Not localised	15 (39.5) 0	20 (52.6) 0	1 (2.6)	0	0	2 (5.3)	38 0
O'Brien, 1998[88]	No subgroup			Localised Not localised	5 (19.2) 0	15 (57.7) 0	1 (3.9)	2 (7.7)	0	3 (11.5)	26 0
	EEG focus	HMPAO and ECD	Site of surgery	Localised Not localised	5 (23.8) 0	12 (57.2) 0	0	2 (9.5)	0	2 (9.5)	21 0
	No EEG focus			Localised Not localised	0 0	3 (60.0) 0	1 (20.0)	0	0	1 (20.0)	5 0
Otsubo, 1995[95]	EEG focus	HMPAO: combined scans	Ictal EEG	Localised Not localised	15 (88.2) 0	2 (11.8) 0	0	0	0	0	17 0
Ictal											
Adams, 1992[30]	EEG focus	HMPAO	Site of surgery/ pathology	Localised Not localised	4 (100) 0	0 0	0	0	0	0	4 0
Doi, 1995[41]	EEG focus	HMPAO, IMP and ECD	Combination	Localised Not localised	16 (84.2) 1 (50.0)	1 (5.3) 1 (50.0)	0	2 (10.5)	0	0	19 2
Ho, 1995[51]	No subgroup	HMPAO	Combination	Localised Not localised	33 (94.3) 0	0 0	0	0 0	0	2 (5.7)	35
Hong, 2002[52]	No subgroup	HMPAO	Site of surgery	Localised Not localised	9 (33)	5 (19)	0	6 (22)	0	7 (26)	27
Hwang, 2001[53]	No subgroup	HMPAO	Site of surgery/ pathology	Localised Not localised	64 (70)	7 (8)	0	0	0	20 (22)	91
Kim, 2000[63]	No subgroup	HMPAO	Ictal EEG	Localised Not localised	21 (70.0) 0	5 (16.7) 0	0	0	0	4 (13.3)	30 0

continued

TABLE 5 *Results of studies that assessed SPECT for seizure focus localisation (cont'd)*

Study	Subgroup	Tracer and additional details	Reference standard	Reference standard	Results: No. (%)						
					Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Lee, 2001[71]	No subgroup	HMPAO	Combination	Localised	21 (52.5)	10 (25.0)	0	8 (20.0)	0	1 (2.5)	40
				Not localised	0	0					0
		ECD		Localised	7 (50.0)	7 (50.0)	0	0	0	0	14
				Not localised	0	0		0			
Lee, 2002[73]	No structural abnormality	HMPAO: first scan	Combination	Localised	5 (25.0)	12 (60.0)	1 (5.0)	1 (5.0)	0	1 (5.0)	20
				Not localised	0	0					0
				Multifocal	1 (33.3)	0	0			2 (66.7)	3
		HMPAO: second scan		Localised	6 (30.0)	4 (20.0)	1 (5.0)	3 (15.0)	0	6 (30.0)	20
				Not localised	0	0					0
				Multifocal	0	0	0			3 (100)	3
		HMPAO: first + second scans combined		Localised	6 (28.6)	4 (19.0)	1 (4.8)	6 (28.6)	0	4 (19.0)	21
				Not localised	0	0		0			
				Multifocal	3 (100)	0	0			0	3
Markand, 1997[79]	EEG focus	HMPAO, HIPDM or ECD	Combination	Localised	38 (86.4)	5 (11.3)	0	0	0	1 (2.3)	44
				Not localised	0	0					0
Markand, 1994[80]	EEG focus	HMPAO, HIPDM or IMP	Site of surgery	Localised	65 (79.3)	11 (13.4)	2 (2.4)	1 (1.2)	0	3 (3.7)	82
				Not localised	0	0					0
Kilpatrick, 1997[62]	EEG focus	Not reported	Site of surgery	Localised	13 (92.9)	1 (7.1)	0	0	0	0	14
				Not localised	0	0					0
Mastin, 1996[81]	No subgroup	HMPAO	Site of surgery	Localised	12 (52.2)	1 (4.3)	0	0	0	10 (43.5)	23
				Not localised	0	0					0
Newton, 1994[83]	No subgroup	HMPAO: >30 s from seizure to injection	Combination	Localised	22 (71.0)	7 (22.6)	0	0	0	2 (6.4)	31
				Not localised	0	0					0
		HMPAO: <30 s from seizure to injection		Localised	50 (100)	0	0	0	0	0	50
				Not localised	0	0					0
Newton, 1995[82]	No subgroup	HMPAO: <30 s from seizure to injection	Combination	Localised	64 (95.5)	3 (4.5)	0	0	0	0	67
				Not localised	8 (88. 9)	1 (11.1)					9
		HMPAO: >30 s from seizure to injection		Localised	62 (70.5)	23 (26.1)	0	0	0	3 (3.4)	88
				Not localised	10 (38. 5)	16 (61.5)		26 (100)			
Oliveira, 1999[92]	EEG focus	ECD	Combination	Localised	20 (87.0)	0	0	1 (4.3)	0	2 (8.7)	23
				Not localised	0	0					0

continued

TABLE 5 *Results of studies that assessed SPECT for seizure focus localisation (cont'd)*

Study	Subgroup	Tracer and additional details	Reference standard	Reference standard	Results: No. (%)						
					Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Oommen, in progress[93]	EEG focus	ECD	Site of surgery	Localised Not localised	27 (93.1) 0	0 0	0	0	0	2 (6.9)	29 0
Rowe, 1989[97]	EEG focus	HMPAO	Ictal EEG	Localised Not localised	21 (70.0) 0	7 (23.4) 2 (100)	1 (3.3)	0	0	1 (3.3)	30 2
Runge, 1997[101]	EEG focus	ECD	EEG/ECoG	Localised Not localised	17 (80.9) 0	0 0	3 (14.3)	1 (4.8)	0	0	21 0
Shen, 1990[104]	EEG focus	HIPDM	Site of surgery	Localised Not localised	26 (83.9) 0	1 (3.2) 0	1 (3.2)	3 (9.7)	0	0	31 0
Watanabe,2002[112]	EEG focus	HMPAO or ECD	Ictal EEG	Localised Not localised	19 (65.5) 0	8 (27.6) 0	0	0	0	2 (6.9)	29 0
Weis, 1997[114]	No subgroup	HMPAO or ECD	Site of surgery	Localised Not localised	66 (75.9) 0	5 (5.7) 0	0	15 (17.2)	0	1 (1.2)	87 0
Yu, 1995[117]	No subgroup	HMPAO: immediately after seizure	Combination	Localised Not localised	3 (100) 0	0 0	0	0	0	0	3 0
		HMPAO: >30 minutes after		Localised Not localised	21 (67.7) 0	4 (12.9) 0	0	0	0	6 (19.4)	31 0
		HMPAO: within 30 minutes after seizure		Localised Not localised	16 (80.0) 0	2 (10.0) 0	0	0	0	2 (10.0)	20 0
Interictal											
Adams, 1992[30]	EEG focus	HMPAO	Site of surgery/ pathology	Localised Not localised	9 (47.4) 1 (100)	3 (15.8) 0	4 (21.0)	0	0	3 (15.8)	19 1
Assadi, 1997[31]	EEG focus	HMPAO	Unclear EEG	Localised Not localised	8 (42.1) 0	5 (26.3) 0	0	3 (15.8)	0	3 (15.8)	19 0
Boundy, 1996[32]	No structural abnormality	HMPAO	Site of surgery	Localised Not localised	9 (50.0) 3 (60.0)	5 (27.8) 2 (40.0)	0	0	0	4 (22.2)	18 5
		IDEX		Localised Not localised	14 (77.8) 3 (60.0)	3 (16.7) 2 (40.0)	0	0	0	1 (5.5)	18 5
Debets, 1997[40]	No subgroup	IMZ	Site of surgery	Localised Not localised	6 (31.6) 0	1 (5.2) 0	0	6 (31.6)	0	6 (31.6)	19 0
	EEG focus			Localised Not localised	6 (33.3) 0	1 (5.6) 0	0	5 (27.8)	0	6 (33.3)	18 0

continued

TABLE 5 *Results of studies that assessed SPECT for seizure focus localisation (cont'd)*

Study	Subgroup	Tracer and additional details	Reference standard	Reference standard	Results: No. (%)						
					Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Doi, 1995[41]	EEG focus	HMPAO, IMP & ECD	Combination	Localised	12 (52.2)	6 (26.1)	0	4 (17.4)	0	1 (4.3)	23
				Not localised	2 (100)	0					2
Gram, 1988[46]	EEG focus	HMPAO	Interictal EEG	Localised	8 (53.3)	4 (26.7)	0	0	0	3 (20.0)	15
				Not localised	5 (55. 6)	4 (44.4)					9
Grunwald, 1991[47]	EEG focus	HMPAO	Combination	Localised	27 (67.5)	7 (17.5)	0	3 (7.5)	0	3 (7.5)	40
				Not localised	0	0					0
Hajek, 1991[49]	EEG focus	HMPAO	Site of surgery	Localised	9 (29.0)	13 (41.9)	0	6 (19.4)	0	3 (97)	31
				Not localised	0	0					0
Harvey, 1993[50]	EEG focus	HMPAO	Ictal EEG	Localised	5 (22.7)	8 (36.4)	0	8 (36.4)	0	1 (4.5)	22
				Not localised	0	0					0
Kilpatrick, 1997[62]	EEG focus	Not reported	Site of surgery	Localised	20 (69.0)	5 (17.2)	0	1 (3.4)	0	3 (10.4)	29
				Not localised	0	0					0
Kim, 2000[63]	No subgroup	HMPAO	Ictal EEG	Localised	6 (31.6)	12 (63.1)	0	0	0	1 (5.3)	19
				Not localised	0	0					0
Lewis, 1998[77]	EEG focus	HMPAO or ECD	Ictal EEG	Localised	25 (75.8)	1 (3.0)	0	0	0	7 (21.2)	33
				Not localised	0	0					0
Markand, 1994[80]	EEG focus	HMPAO, HIPDM or IMP	Site of surgery	Localised	56 (59.6)	32 (34.0)	0	0	0	6 (6.4)	94
				Not localised	0	0					0
Markand, 1997[79]	EEG focus	HMPAO	Combination	Localised	37 (69.8)	11 (20.8)	0	0	0	5 (9.4)	53
				Not localised	0	0					0
Mastin, 1996[81]	No subgroup	HMPAO	Site of surgery	Localised	20 (60.6)	5 (15.2)	0	0	0	8 (24.2)	33
				Not localised	0	0					0
Newton, 1994[83]	No subgroup	HMPAO	Combination	Localised	36 (49.3)	28 (38.4)	0	0	0	9 (12.3)	73
				Not localised	0	0					0
Newton, 1995[82]	No subgroup	HMPAO	Combination	Localised	64 (45.7)	64 (45.7)	0	0	0	12 (8.6)	140
				Not localised	10 (33.3)	20 (66.7)					30
Oliveira, 1999[92]	EEG focus	ECD	Combination	Localised	41 (60.3)	3 (4.4)	0	2 (2.9)	0	22 (32.4)	68
				Not localised	0	0					0
Oommen, in progress[93]	EEG focus	ECD	Site of surgery	Localised	32 (80.0)	4 (10.0)	0	0	0	4 (10.0)	40
				Not localised	0	0					0

continued

TABLE 5 *Results of studies that assessed SPECT for seizure focus localisation (cont'd)*

Study	Subgroup	Tracer and additional details	Reference standard	Reference standard	Results: No. (%)						
					Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Otsubo, 1995[95]	EEG focus	HMPAO	Ictal EEG	Localised	15 (27.2)	9 (16.4)	16 (29.1)	9 (16.4)	0	6 (10.9)	55
				Not localised	0	0					0
Rowe, 1989[97]	EEG focus	HMPAO	Ictal EEG	Localised	17 (56.7)	9 (30.0)	1 (3.3)	0	0	3 (10.0)	30
				Not localised	0	2 (100)					2
Rowe, 1991[100]	EEG focus	HMPAO	Combination	Localised	18 (39.1)	23 (50.0)	2 (4.4)	0	0	3 (6.5)	46
				Not localised	0	0					0
Runge, 1997[101]	EEG focus	ECD	EEG/ECoG	Localised	13 (56.5)	6 (26.1)	1 (4.4)	3 (13.0)	0	0	23
				Not localised	0	0					0
Shen, 1990[104]	EEG focus	HIPDM	Site of surgery	Localised	20 (60.6)	8 (24.3)	0	4 (12.1)	0	1 (3.0)	33
				Not localised	0	0					0
Tatum, 1995[108]	No subgroup	HMPAO	Combination	Localised	8 (47.1)	4 (23.5)	0	3 (17.6)	0	2 (11.8)	17
				Not localised	1 (33.3)	2 (66.7)					3
Timing not reported											
Doi, 1995[41]	EEG focus	IMZ: early scanning (5–10 minutes postinjection)	Combination	Localised	10 (43.5)	5 (21.7)	0	8 (34.8)	0	0	23
				Not localised	1 (50.0)	1 (50.0)					2
		IMZ: late scanning (165–195 minutes postinjection)		Localised	11 (47.8)	3 (13.1)	0	9 (39.1)	0	0	23
				Not localised	1 (50.0)	1 (50.0)					2
Venz, 1994[110]	EEG focus	IMZ	Ictal EEG	Localised	18 (72.0)	2 (8.0)	0	0	0	5 (20.0)	25
				Not localised	0	0					0
		HMPAO		Localised	12 (48.0)	9 (36.0)	0	0	0	4 (16.0)	25
				Not localised	0	0					0
Zhou, 1994[116]	EEG focus	ECD	Combination	Localised	46 (90.2)	1 (2.0)	0	0	0	4 (7.8)	51
				Not localised	0	0					0

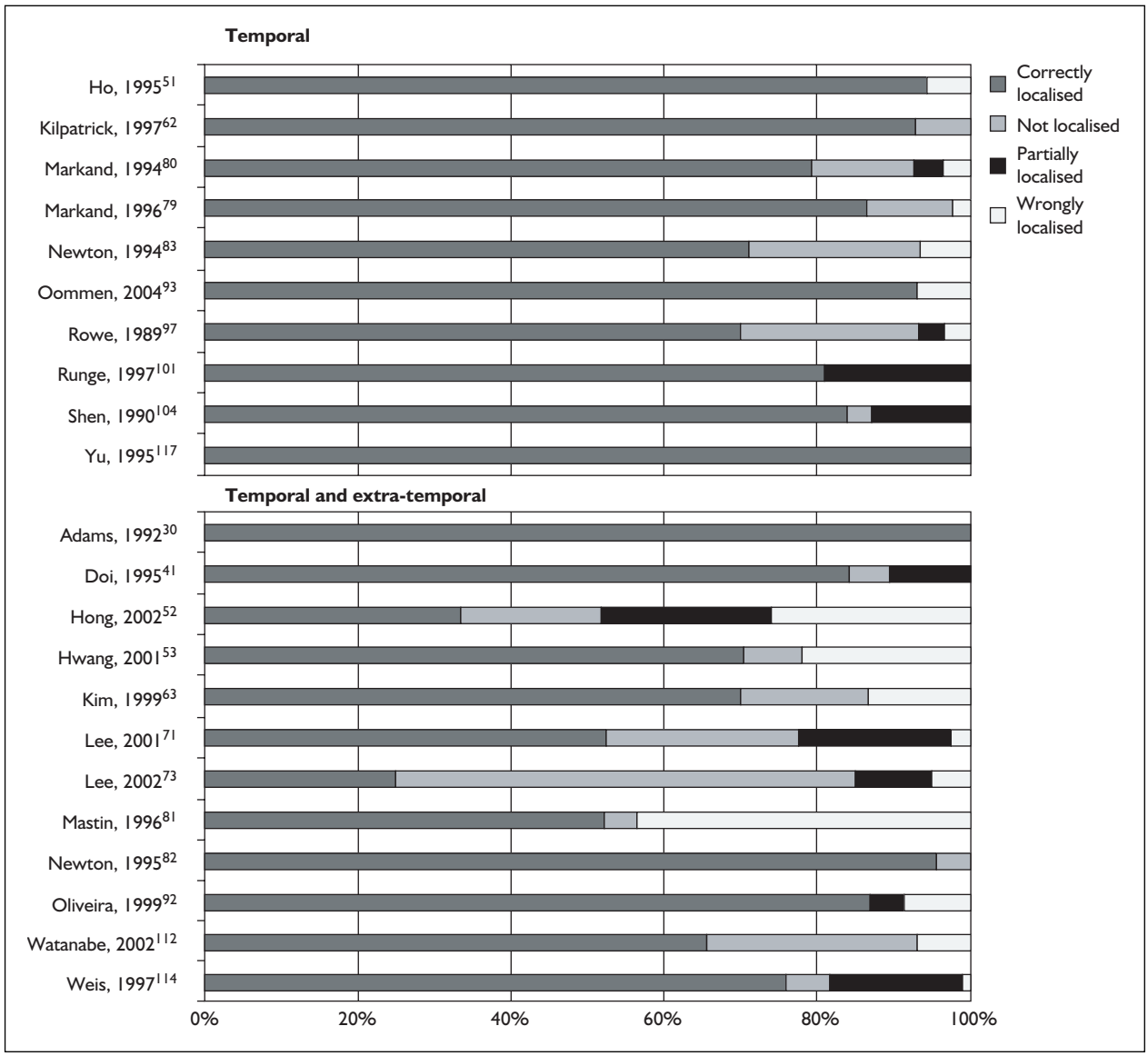

FIGURE 4 *Ictal SPECT: proportion of scans in each localisation category*

to be an unlikely explanation for the observed excellent performance of ictal SPECT in these studies. There were also no other apparent differences between these studies and the other studies included in this section that could explain this increased performance of ictal SPECT.

The proportion of partially localised scans was relatively low, ranging from 0 (in 12 studies) to 22%. The proportion of incorrectly localised scans was low in all but three studies, ranging from 0 (in seven studies) to 13%. Two studies reported 22%[53] and 26%[52] incorrectly localised, and the third reported a much higher rate of incorrectly localised scans of 43%.[81] All three studies included patients with both temporal and non-temporal lobe epilepsy but did not show any unique features compared with the other studies of ictal SPECT that could account for the higher proportions of incorrectly localised scans.

Generally the performance of ictal SPECT did not appear to show an association with subgroup (EEG focus or previous neuroimaging findings), tracer, reference standard, study quality or year of publication. One study reported results separately for different tracers, ECD and HMPAO.[71] This study found that the proportion of patients with a correctly localised scan was similar using the two tracers, although patients who received ECD had more non-localised scans and no partially or incorrectly localised scans, whereas those who received HMPAO had some partially and incorrectly localised scans.[71]

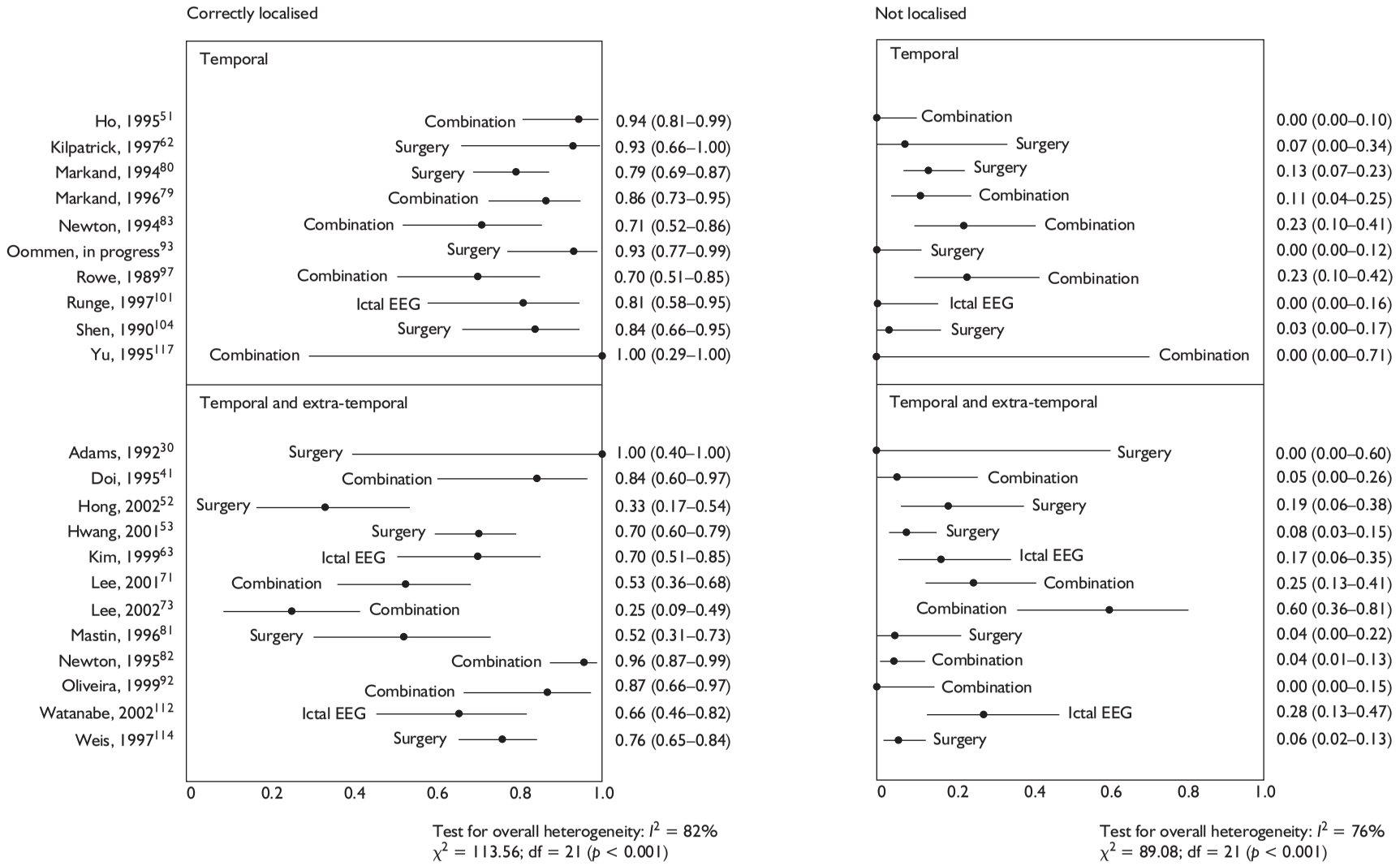

FIGURE 5 *Ictal SPECT: forest plots for each localisation category*

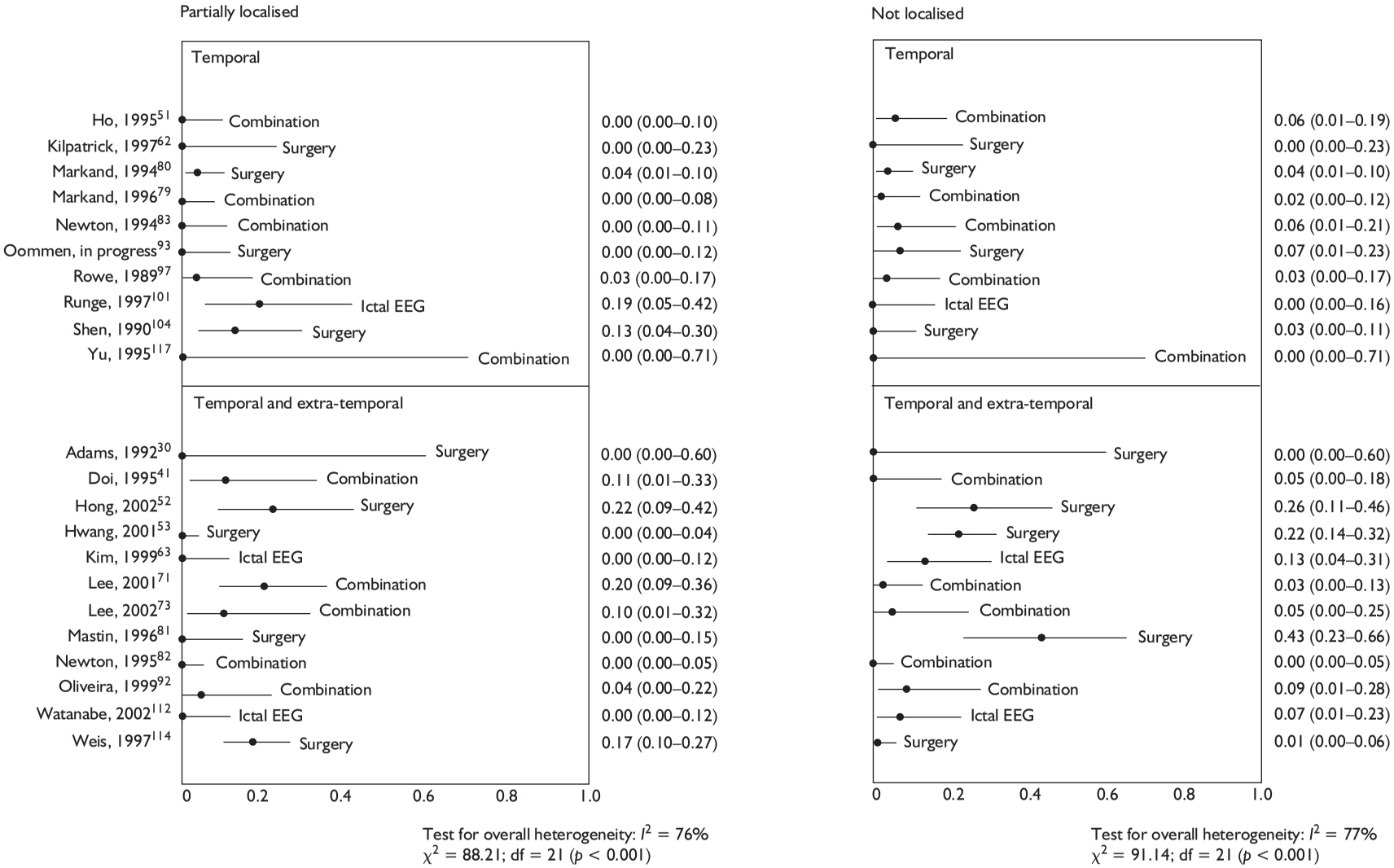

FIGURE 5 (cont'd) *Ictal SPECT: forest plots for each localisation category*

Three studies reported results separately for tracer injections carried out at different time points following seizure onset. Two studies reported results separately for a timing of <30 seconds from seizure onset to injection and >30 seconds from seizure onset to injection.[82,83] Both studies reported a greater proportion of correctly localised scans for the patients who received the tracer <30 seconds after seizure onset. A third study reported results separately for patients who received the tracer immediately after seizure onset, within 30 minutes of seizure onset and >30 minutes after seizure onset.[117] This study reported a greater proportion of correctly localised scans in patients who received the tracer immediately after onset, although this applied to only three patients, all of whom had their seizure focus correctly localised. Patients who received the tracer within 30 minutes were found to have a greater proportion of correctly localised scans than those who received the tracer more than 30 minutes after seizure onset. These studies therefore suggest that ictal SPECT performs better the earlier tracer is given to the patient.

A further study reported results for patients scanned twice, reporting results separately for each of the two scans and also for a combination of the two scans.[73] This study reported very low rates of correctly localised patients for all scan combinations, but found that the second and combined scans correctly localised one more patient than the first scan.

Interictal SPECT

Twenty-five studies (27 evaluations) assessed the accuracy of interictal SPECT.[30–32,40,41,46,47,49,50,62,63,77,79–83,92,93,95,97,100,101,104,108] Six studies evaluated the accuracy of interictal SPECT in the lateralisation of the epileptogenic focus in patients with temporal lobe epilepsy[32,47,79,80,83,93] and 19 studies looked at the accuracy of interictal SPECT in the localisation of the epileptic focus.[30,31,40,41,46,49,50,62,63,77,81,82,92,95,97,100,101,104,108] Thirteen studies were restricted to patients with TLE,[32,40,47,49,62,79,80,83,93,97,100,101,104] seven included patients with both temporal and non-temporal epilepsy,[41,63,81,82,92,95,108] one was restricted to patients with frontal lobe epilepsy,[50] and the remaining four studies did not report on type of epilepsy.[30,31,46,77] One study allowed results for all patients and for those in whom EEG had localised the seizure focus to be extracted separately.[40] The results for all patients were included in the main analysis below. One study provided results separately for two tracers, HMPAO and [^{123}I]iododexetimide (IDEX).[32] The results for the scans using HMPAO were included in the analysis below. None of these studies included an appropriate patient spectrum.

Eight studies used site of surgery as the reference standard,[32,40,49,62,80,81,93,104] one used a combination of site of surgery and pathology,[30] eight used a combination,[41,47,79,82,83,92,100,108] five used ictal EEG[50,63,77,95,97] one used interictal EEG,[46] one did not state whether EEG was ictal or interictal[31] and one used a combination of EEG and ECoG.[101] Interictal EEG was considered an inappropriate reference standard.[46] Partial verification bias may have been a problem in one of these studies which only reported results of patients who underwent surgery, surgery being the reference standard.[62] The most commonly used tracer was HMPAO, used in 16 studies,[30–32,46,47,49,50,63,79,81–83,95,97,100,108] and a further three studies used a combination of tracers including HMPAO.[41,77,80] Three studies used ECD,[92,93,101] one IDEX,[32] one IMZ[40] and one HIPDM.[104] One study did not report the tracer used.[62]

Figure 6 shows the proportion of studies with correctly localised, non-localised, partially localised or incorrectly localised scans. *Figure 7* presents forest plots for each of the localisation categories. There was significant statistical heterogeneity between studies in all localisation categories. The proportion of correctly localised scans ranged from 23 to 80%. None of the studies stood out as particular outliers, for being either better or worse, than the other studies in terms of their localising ability. The proportion of patient with non-localised scans ranged from 3 to 63%, partially localised scans from 0 to 45% and incorrectly localised scans from 0 to 32%. Differences in tracer, reference standard, type of epilepsy (temporal versus extra-temporal), year of publication or subgroup did not appear to show any association with the accuracy of interictal SPECT in the localisation of the epileptic focus. Studies of the lateralisation of the seizure focus in patients with TLE tended to show slightly better proportions (range 49–80%) of correctly localised scans than the other studies.[32,47,79,80,83,93] These studies also showed slightly lower rates of non-localised (range 10–38%) and incorrectly localising scans (range 6–12%). Only one reported partially localised scans.[47] One study reported results for all patients included in the study and also allowed results to be extracted separately for patients in whom EEG localised the seizure focus.[40] This study reported very similar results for both sets of data. A second study reported data for two different tracers: IDEX and HMPAO.[32] This study

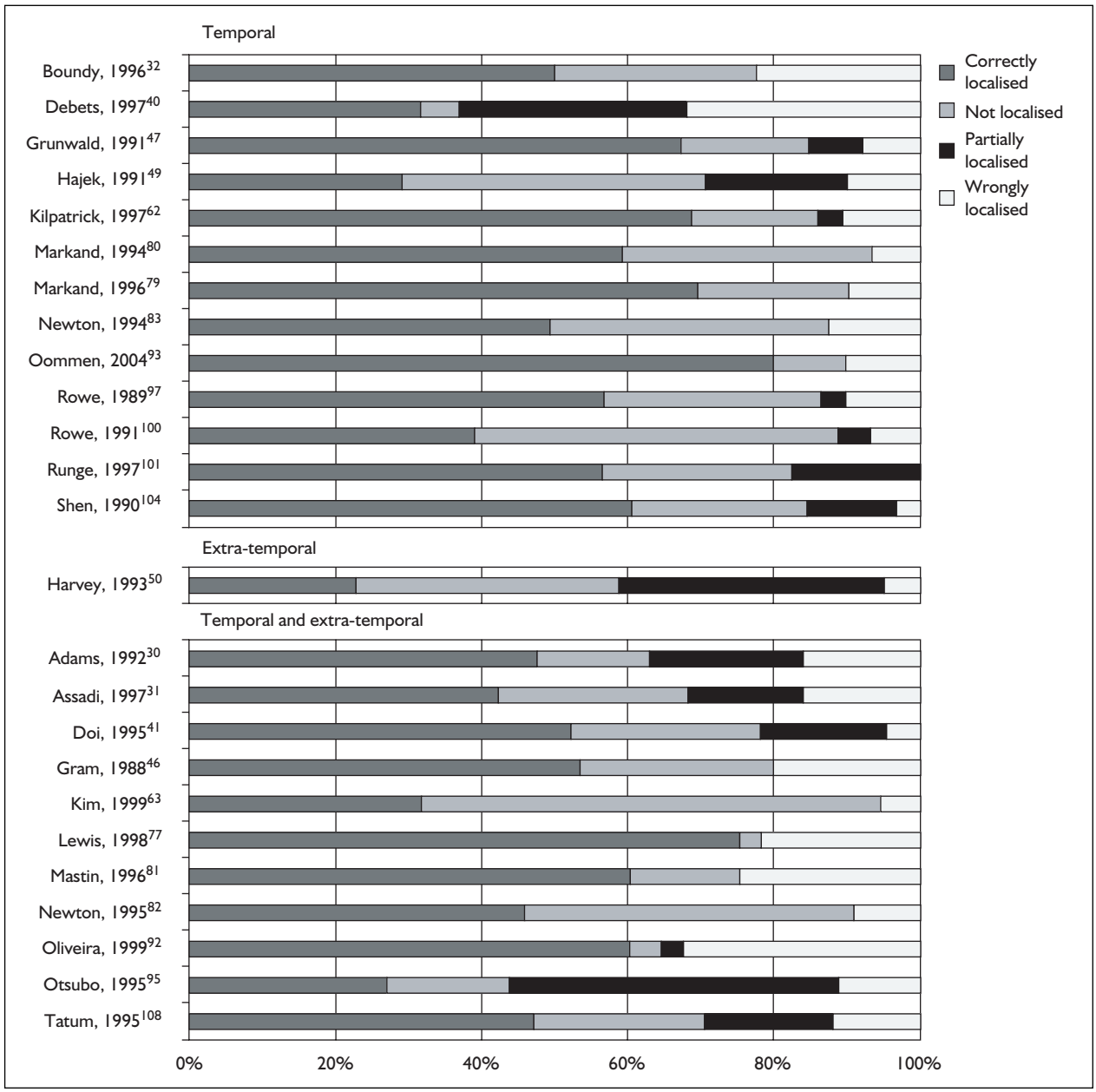

FIGURE 6 *Interictal SPECT: proportion of scans in each localisation category*

found a greater proportion of correctly localised scans when patients were scanned using IDEX (78%) compared with HMPAO (50%) This study also reported a greater proportion of non-localised and incorrectly localised scans using HMPAO.

Combination of ictal and interictal SPECT

Five studies (seven evaluations) assessed the combination of ictal and interictal SPECT.[42,54,59,88,95] All studies assessed the accuracy of SPECT in the localisation of the seizure focus. Three studies included patients with both temporal and non-temporal lobe epilepsy,[59,88,95] one was restricted to patients with TLE[42] and one study did not report the type of epilepsy.[54] Four studies used both ictal and interictal SPECT in all patients, one reported on ictal scans in six patients and interictal scans in 18 patients.[54] One study reported data for the total study population, but allowed data to be extracted separately for those in whom EEG localised the seizure focus and those in whom it did not.[88] Only one study included an appropriate patient spectrum.[54]

Two studies used site of surgery as the reference standard.[59,88] one used ictal EEG[95] and one study used a combination reference standard.[42] One

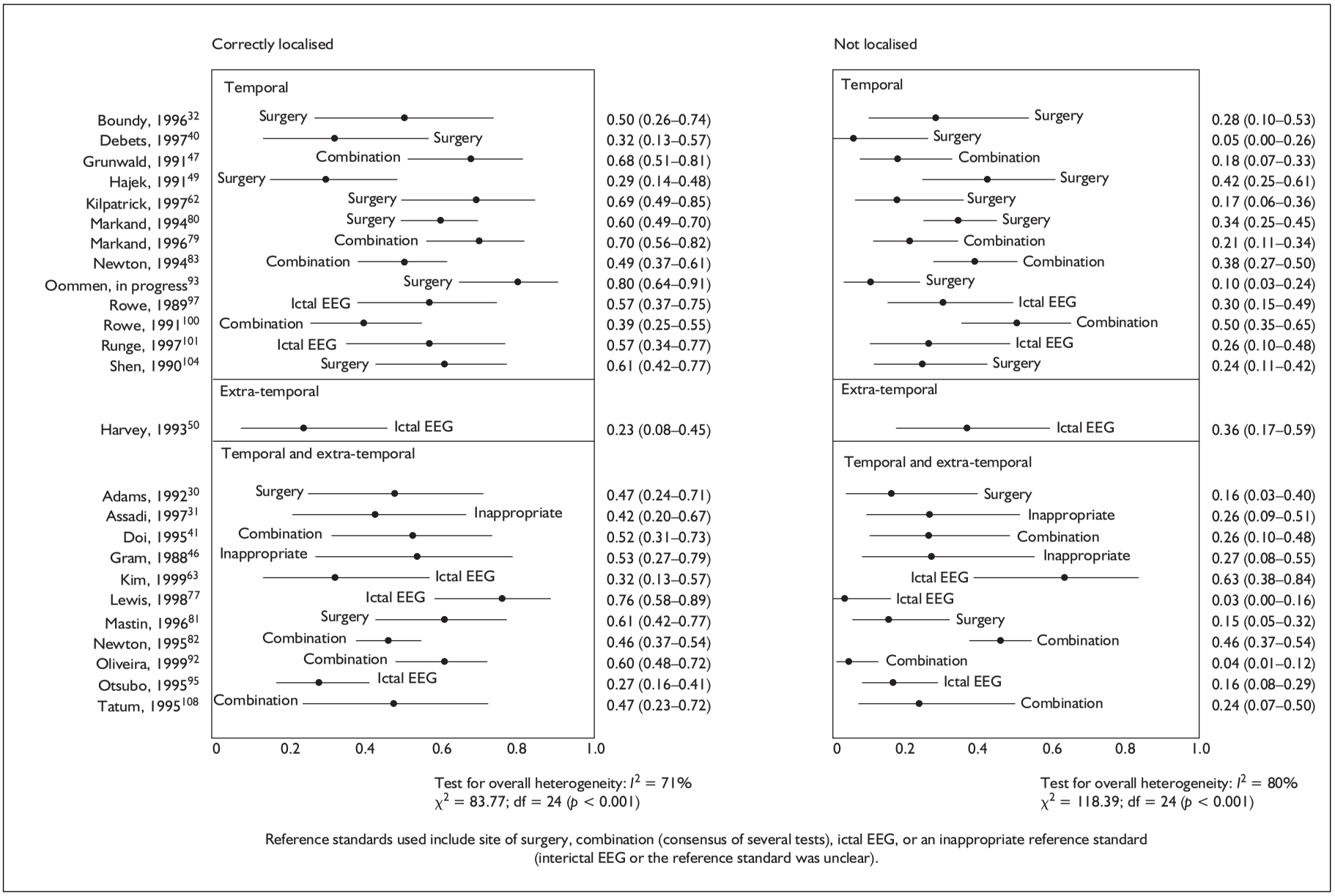

FIGURE 7 *Interictal SPECT: forest plots for each localisation category*

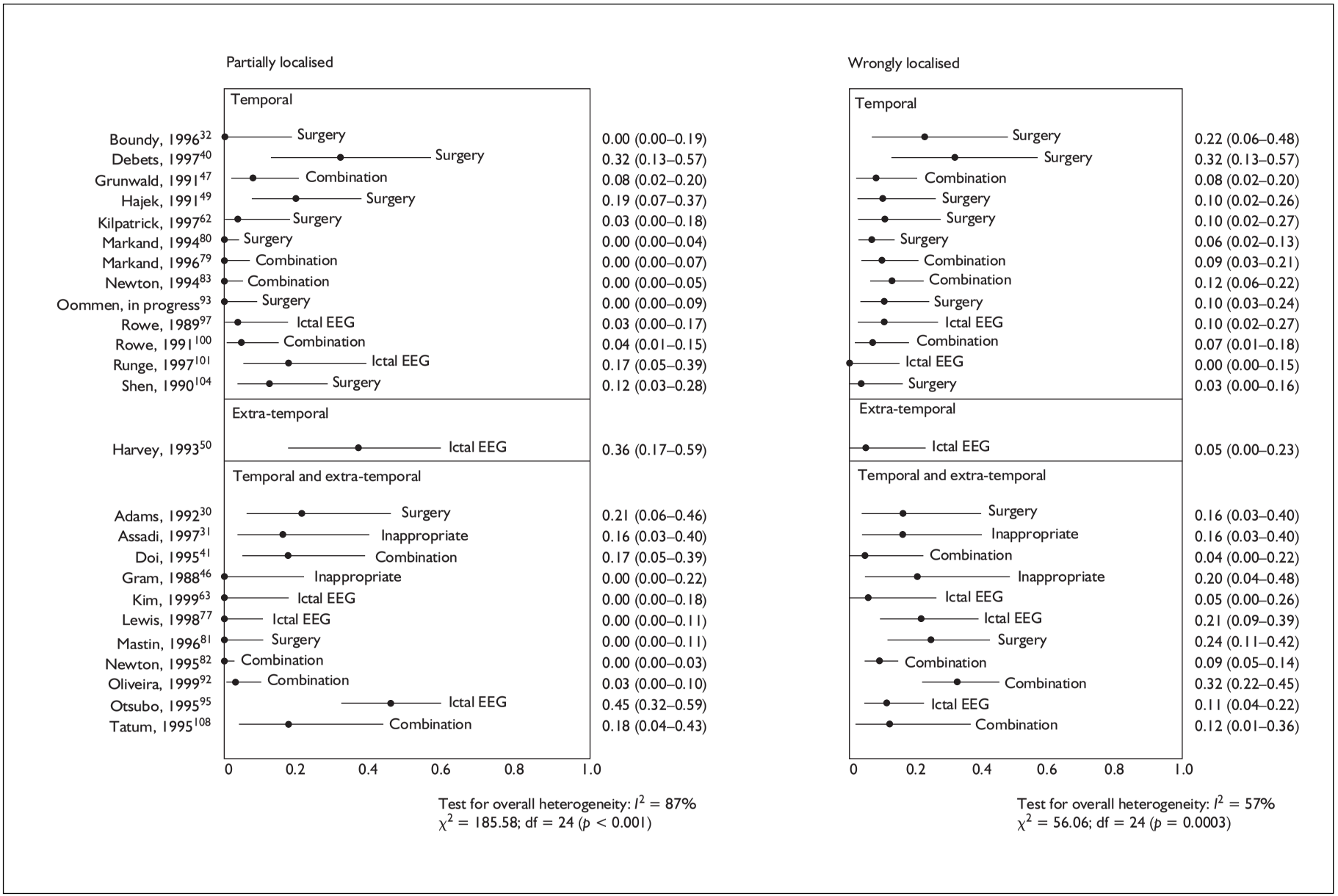

FIGURE 7 (cont'd) *Interictal SPECT: forest plots for each localisation category*

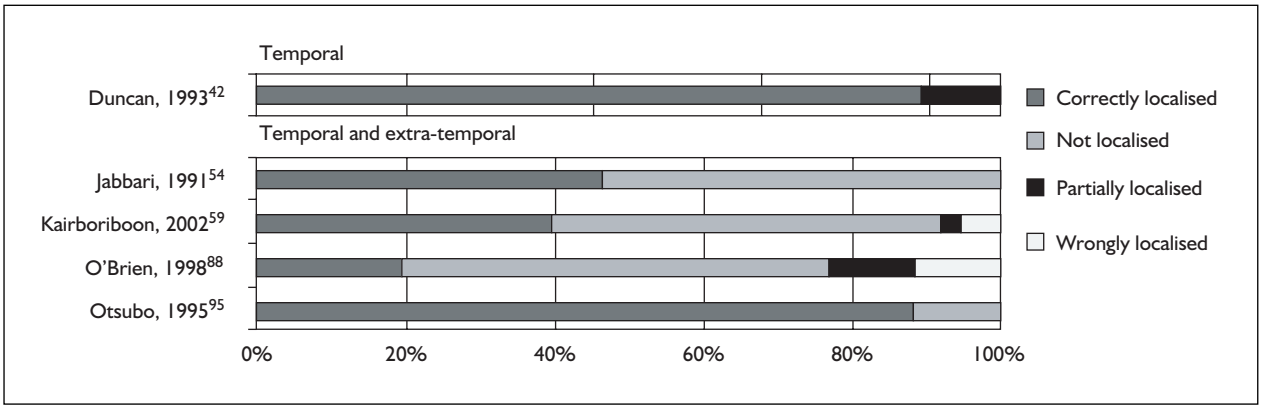

FIGURE 8 *Combination of ictal and interictal SPECT: proportion of scans in each localisation category*

study used ictal EEG in some patients and interictal in others,[54] therefore this reference standard was considered inappropriate.[54] One study had the potential for partial verification bias as the reference standard was site of surgery and results were only reported for patients who underwent surgery.[88] Another study was restricted to patients who underwent surgery.[95] A variety of tracers were used: two used HMPAO,[42,95] one ECD,[59] one IMP[54] and one a combination of HMPAO and ECD.[88]

Figure 8 shows the proportion of correctly localised, non-localised, partially localised or incorrectly localised scans for each study. *Figure 9* presents forest plots for each of the localisation categories. There was significant heterogeneity for all localisation categories ($p < 0.05$). The proportion of patients with correctly localised scans showed particular heterogeneity, with estimates ranging from 19 to 89%. Two studies reported high proportions of correctly localising scans of 88 and 89%.[42,95] Both of these studies used ictal EEG as the reference standard, whereas other studies used site of surgery or a combination reference standard. These two studies also only included patients with an EEG focus, whereas the other studies included patients with and without an EEG focus. One study allowed data to be extracted separately for patients with and without an EEG focus.[88] This study found that 19% of the total population were correctly localised, increasing slightly to 24% when the patients had an EEG focus. One study with a high proportion of correctly localised scans was the only study to have been carried out exclusively in children.[95] This study used a combination of ictal and interictal scans, whereas the other study with a high proportion of correctly localised scans reported ictal scans in six patients and interictal scans in 18 patients.[42]

The proportion of not localised scans ranged from 0 to 58% with the two studies that reported the highest proportion of correctly localised scans reporting the lowest rates of non-localised scans (0 or 12%). The remaining studies reported similar rates of non-localised scans ranging from 53 to 58%. The proportion of partially localised patients was similar across studies, ranging from 0 to 12%, although significant heterogeneity was present ($p = 0.043$). Two studies found no partially localised scans.[54,95] One of these also reported a very high rate of correctly localised scans.[95] Only two studies reported incorrectly localised scans, with 5 and 12% of patients incorrectly localised.[59,88] Both studies also reported the lowest rates of correctly localised scans, used site of surgery as the reference standard and were not restricted to any specific subgroups. One used ECD as the tracer[59] and the other used a combination of HMPAO and ECD.[88] The other studies in this section used HMPAO or IMP as the tracer. The only study to include an appropriate patient spectrum reported 47% correctly localised scans and no partially or incorrectly localised scans.[54]

Timing not reported

Three studies (five evaluations) did not report the timing from seizure onset to injection of tracer. It is therefore unclear whether the SPECT scans reported were ictal or interictal.[41,110,116] All studies assessed the accuracy of SPECT in the localisation of the seizure focus. Two studies included patients with both temporal and non-temporal epilepsy.[41,110] The type of epilepsy was unclear in the remaining study.[116] One study scanned all patients twice and reported results separately for early (5–10 minutes postinjection) and late

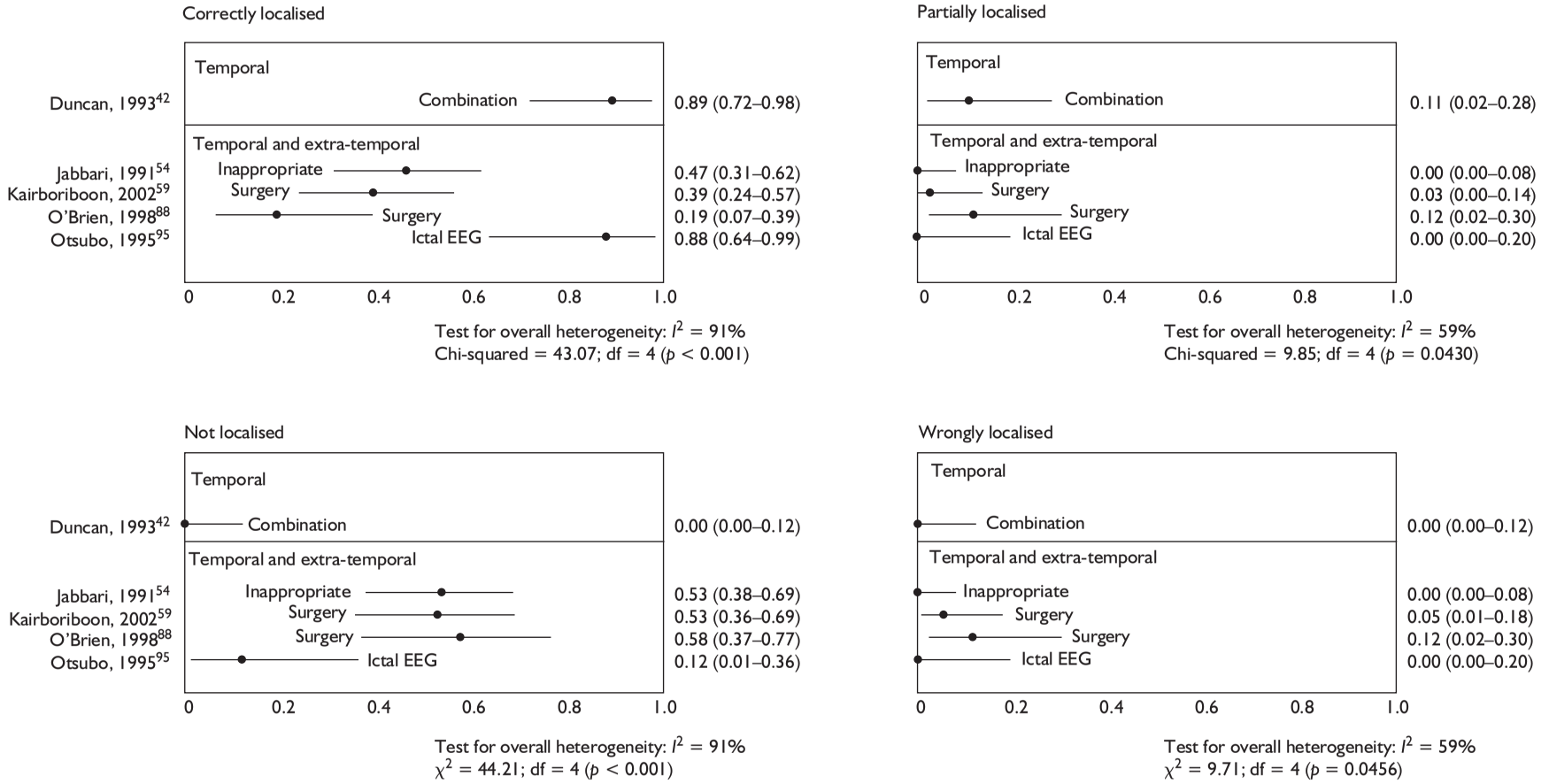

FIGURE 9 *Combination of ictal and interictal SPECT: forest plots for each localisation category*

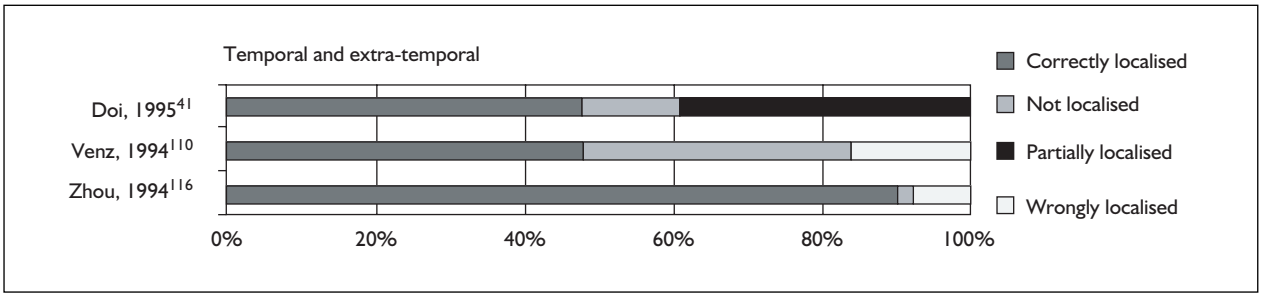

FIGURE 10 *Unclear timing SPECT: proportion of scans in each localisation category*

(165–195 minutes postinjection) scanning.[41] Another study reported results separately for two tracers, HMPAO and IMZ.[110] None of these studies included an appropriate patient spectrum.

All three studies used an appropriate reference standard and appeared to avoid partial verification bias. Two used a combination reference standard[41,116] and one used ictal EEG.[110] Two studies used IMZ as the tracer,[41,110] one used ECD[116] and one used HMPAO.[110] None of the studies were restricted to patients who underwent surgery. All studies included patients in whom EEG had identified a seizure focus.

Figure 10 presents a summary of the proportion of correctly localised, not localised, partially localised and incorrectly localised scans for each study. *Figure 11* presents forest plots for each of the localisation categories. The studies of unclear timing SPECT were heterogeneous for the proportion of patients correctly localised, not localised and partially localised. The test for heterogeneity failed to reach statistical significance for the proportion of patients incorrectly localised ($p = 0.06$); however, with so few studies, statistical power to detect heterogeneity was limited. Two studies reported that 48% of patients were correctly localised by SPECT.[41,110] The third study reported 90% correctly localised scans.[116] This study used ECD as the tracer whereas the other two used IMZ and HMPAO. This was the only apparent difference that may explain the higher proportion of patients with correctly localised scans.

The proportion of patients with non-localised scans also showed great variation between studies, ranging from 2 to 36%. The proportion of non-localised scans was smallest in the study with the greatest proportion of correctly localised scans.[116] Only one study reported partially localised scans (29%), but did not report any incorrectly localised scans.[41] The other two studies reported 8 and 16% of patients with incorrectly localised scans. One study reported results for early scanning (5–10 minutes postinjection) and late scanning (165–195 minutes postinjection) separately.[41] This study found that two patients who were not localised from the early scan were localised on the later scan, one correctly and the other partially. One study reported a greater proportion of correctly localised scans when patients were injected with IMZ compared with HMPAO.[110]

MRI

MRI was assessed in 36 studies (42 evaluations). These included 33 evaluations of routine MRI, eight of volumetric MRI and one of T2-relaxometry. Two studies reported the results of more than one MRI technique separately.[56,65] Eighteen studies looked at the accuracy of MRI in the localisation of the seizure focus,[30,31,33,41,46,49,53,54,58,60,62,63,77,101,102,109,110,115] and 14 studies at the lateralisation of the seizure focus in patients with TLE.[11,29,30,32,35,39,44,56,65,67,68,70,79,106] Two studies allowed data for subgroups with EEG focus and no EEG focus to be extracted separately,[60,88] and 16 studies provided additional data on the association of MRI localisation with outcome following surgery. Reference standards included: combination (six studies), site of surgery (13 studies), combination of site of surgery and pathology site (two studies), ictal EEG (six studies), interictal EEG (one study), unclear EEG (one study), ictal EEG in some patients and either interictal, or did not specify the type of EEG, EEG in others (two studies) and EEG/ECoG (one study). The results of these studies are summarised in *Table 6*.

Routine MRI

Twenty-eight studies (33 evaluations) assessed routine MRI.[30–33,39,41,44,46,49,53,54,56–58,60,63,65,67,70,77,79,88,101,102,106,109,110,115] Three used gadolinium enhancement, one in all patients,[110] one in only six patients,[70] and the third in the last 28 patients to enter the study.[54] Nineteen studies looked at the

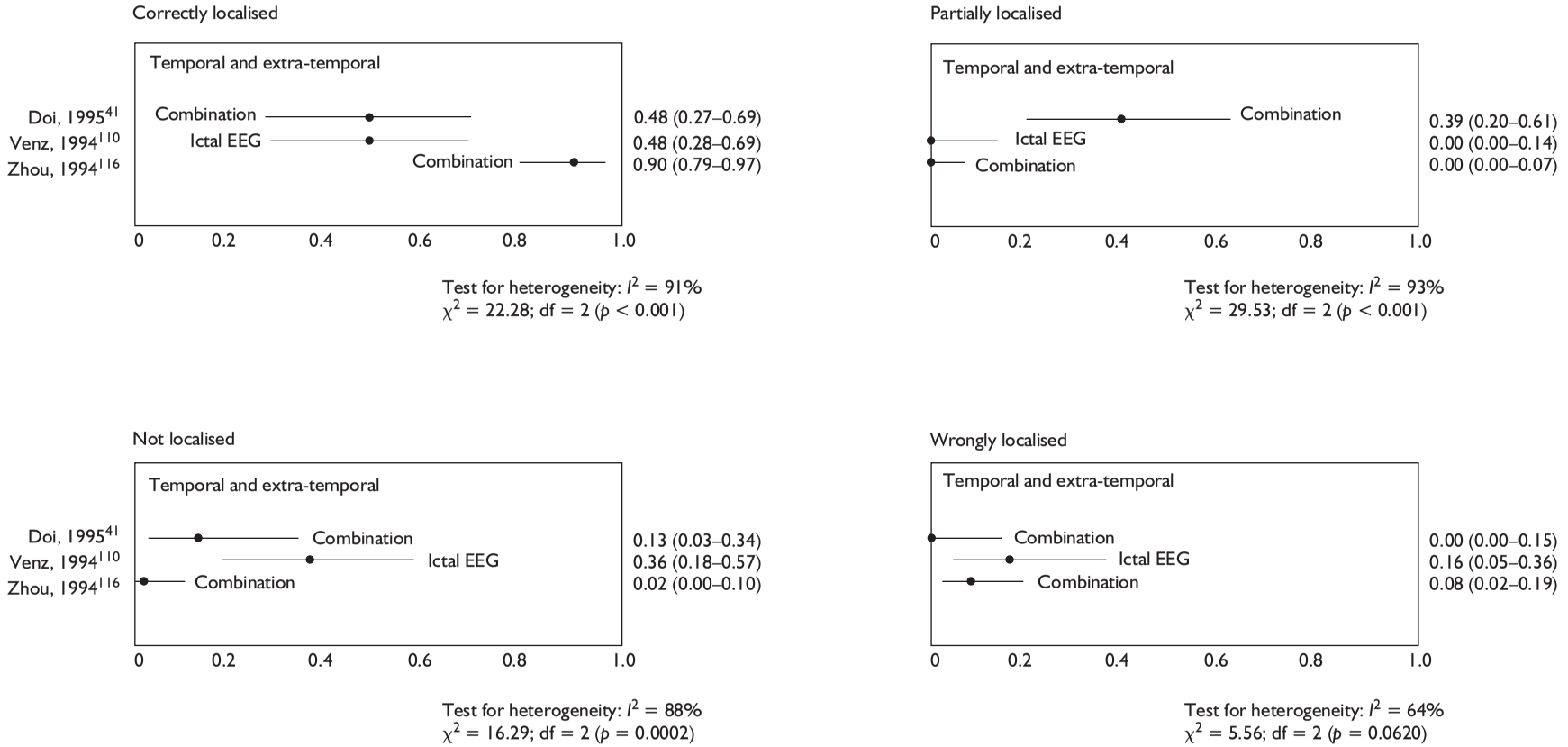

FIGURE 11 *Unclear timing SPECT: forest plots for each localisation category*

TABLE 6 *Results of studies that assessed MRI for seizure focus localisation*

Study	Subgroup	Additional details	Reference standard	Reference standard	Results: No. (%)					
					Correctly localised	Not localised	P1	P2	Incorrectly localised	Total
Adams, 1992[30]	EEG focus	Routine	Site of surgery/ pathology site	Localised Not localised	13 (92.9) 0	1 (7.1) 0	0	0	0	14 0
Assadi, 1997[31]	EEG focus	Routine	Unclear EEG	Localised Not localised	9 (37.4) 0	13 (54.2) 0	0	1 (4.2)	1 (4.2)	24 0
Boundy, 1996[32]	No structural abnormality	Routine	Site of surgery	Localised Not localised	13 (72.2) 4 (80.0)	5 (27.8) 1 (20.0)	0	0	0	18 5
Brooks, 1990[33]	No subgroup	Routine	Site of surgery	Localised Not localised	20 (39.2) 0	30 (58.8) 0	0	0	1 (2.0)	51 0
Cross, 1996[39]	No subgroup	Routine	Combination	Localised Not localised	17 (85) 0	3 (15) 0	0	0	0	20 0
Doi, 1995[41]	EEG focus	Routine	Combination	Localised Not localised	15 (65.1) 1 (50.0)	6 (26.1) 1 (50.0)	0	1 (4.4)	1 (4.4)	23 2
Gilliam, 2000[44]	No structural abnormality and EEG focus	Routine	Site of surgery	Localised Not localised	52 (77.6) 6 (46.2)	15 (22.4) 7 (53.8)	0	0	0	67 13
Gram, 1988[46]	EEG focus	Routine	Interictal EEG	Localised Not localised	5 (35.7) 2 (22.2)	6 (42.9) 7 (77.8)	0	0	3 (21.4)	14 9
Hajek, 1991[49]	EEG focus	Routine	Site of surgery	Localised Not localised	20 (64.5) 0	11 (35.5) 0	0	0	0	31 0
Hwang, 2001[53]	No subgroup	Routine	Site of surgery/ pathology	Localised Not localised	70 (60) 0	36 (31) 0	0	0	11 (9)	117 0
Jabbari, 1991[54]	EEG focus	Routine: gadolinium enhanced in last 28 patients	Ictal EEG in some patients, interictal in others	Localised Not localised	28 (65.1) 1 (6.7)	15 (34.9) 14 (93.3)	0	0 15 (100)	0	43
Jack, 1990[56]	No structural abnormality and EEG focus	Routine (anterior temporal lobe)		Localised Not localised	15 (36.6) 0	23 (56.1) 0	0	0	3 (7.3)	41 0
		Routine (hippocampus)	Site of surgery	Localised Not localised	28 (68.3) 0	12 (29.3) 0	0	0	1 (2.4)	41 0
		Routine (medial temporal parenchyma)		Localised Not localised	5 (12.2) 0	36 (87.8) 0	0	0	0	41 0
Jackson, 1990[57]	EEG focus	Routine	Site of surgery	Localised Not localised	72 (89.0) 0	7 (9.0) 0	0	0	2 (2.0)	81 0

continued

TABLE 6 *Results of studies that assessed MRI for seizure focus localisation (cont'd)*

Study	Subgroup	Additional details	Reference standard	Reference standard	Results: No. (%)					
					Correctly localised	Not localised	P1	P2	Incorrectly localised	Total
Juhasz, 2003[58]	EEG focus	Routine	Site of surgery	Localised Not localised	1 (4.8) 1 (16.7)	14 (66.7) 5 (83.3)	2 (9.5)	2 (9.5)	2 (9.5)	21 6
Kaminska, 2003[60]	No subgroup			Localised Not localised	15 (78.9) 0	1 (5.3) 1 (100)	1 (5.3)	2 (10.5)	0	19 1
	EEG focus	Routine	Site of surgery	Localised Not localised	12 (79.9) 0	1 (6.7) 1 (100)	1 (6.7)	1 (6.7)	0	15 1
	No EEG focus			Localised Not localised	3 (75.0) 0	0 0	0	1 (25.0)	0	4 0
Kim, 2000[63]	No subgroup	Routine	Ictal EEG	Localised Not localised	23 (60.5) 0	14 (36.9) 0	0	0	1 (2.6)	38 0
Knowlton, 1997[65]	No structural abnormality and EEG focus	Routine	Ictal EEG	Localised Not localised	25 (100) 0	0 0	0	0	0	25 0
Kuzniecky, 1991[67]	Structural abnormality and EEG focus	Routine	Ictal EEG	Localised Not localised	29 (78.4) 0	6 (16.2) 0	0	0	2 (5.4)	37 0
Kuzniecky, 1993[70]	EEG focus	Routine: gadolinium enhanced in 6 patients	Site of surgery	Localised Not localised	25 (73.5) 0	9 (26.5) 0	0	0	0	34 0
Lewis, 1998[77]	EEG focus	Routine	Ictal EEG	Localised Not localised	16 (48.5) 0	13 (39.4) 0	0	0	4 (12.1)	33 0
Markand, 1997[79]	EEG focus	Routine	Combination	Localised Not localised	43 (65.2) 0	23 (34.8) 0	0	0	0	66 0
O'Brien, 1998[88]	No subgroup			Localised Not localised	15 (57.7) 0	8 (30.8) 0	0	3 (11.5)	0	26 0
	No EEG focus	Routine	Site of surgery	Localised Not localised	3 (60.0) 0	1 (20.0) 0	0	1 (20.0)	0	5 0
	EEG focus			Localised Not localised	12 (57.1) 0	7 (33.3) 0	0	2 (9.6)	0	21 0
Runge, 1997[101]	EEG focus	Routine	EEG/ECoG	Localised Not localised	11 (50.0) 0	6 (27.3) 0	2 (9.1)	3 (13.6)	0	22 0

continued

TABLE 6 *Results of studies that assessed MRI for seizure focus localisation (cont'd)*

Study	Subgroup	Additional details	Reference standard	Reference standard	Results: No. (%)					
					Correctly localised	Not localised	P1	P2	Incorrectly localised	Total
Ryvlin, 1998[102]	EEG focus	Routine	EEG	Localised	53 (65.0)	28 (35.0)	0	0	0	81
				Not localised	0	0				0
				Multifocal	13 (100)	0	0		0	13
Sperling, 1986[106]	No structural abnormality	Routine	Combination	Localised	6 (19.4)	23 (74.2)	1 (3.2)	0	1 (3.2)	31
				Not localised	0	4 (100)				4
Theodore, 1990[109]	EEG focus	Routine	Ictal EEG	Localised	7 (26.9)	18 (69.2)	0	0	1 (3.9)	26
				Not localised	0	0				0
Venz, 1994[110]	EEG focus	Routine Gadolinium enhanced	Ictal EEG	Localised	12 (48.0)	10 (40.0)	0	1 (4.0)	2 (8.0)	25
				Not localised	0	0				0
Wheless, 1999[115]	No subgroup	Routine	Site of surgery	Localised	21 (47.7)	20 (45.5)	0	0	3 (6.8)	44
				Not localised	0	0				0
Knowlton, 1997[65]	No structural abnormality and EEG focus	T2	Ictal EEG	Localised	9 (69.2)	4 (30.8)	0	0	0	13
				Not localised	0	0				0
Achten, 1998[29]	No structural abnormality	Volumetric (temporal lobes and hippocampal structures)	Combination	Localised	22 (95.6)	0	0	1 (4.4)	0	23
				Not localised	5 (83.3)	1 (16.7)				6
Cendes, 1997[35]	No structural abnormality	Volumetric (amygdala and hippocampus)	Combination	Localised	97 (97.0)	0	0	0	3 (3.0)	100
				Not localised	0	0				0
Jack, 1990[56]	No structural abnormality and EEG focus	Volumetric (hippocampus)	Site of surgery	Localised	31 (75.6)	10 (24.4)	0	0	0	41
				Not localised	0	0				0
		Volumetric (anterior temporal lobe)		Localised	9 (22.0)	31 (75.6)	0	0	1 (2.4)	41
				Not localised	0	0				0
Kilpatrick, 1997[62]	EEG focus	Volumetric (hippocampus)	Site of surgery	Localised	49 (98.0)	0	0	0	1 (2.0)	50
				Not localised	0	0				0
Knowlton, 1997[65]	No structural abnormality and EEG focus	Volumetric (hippocampus)	Ictal EEG	Localised	17 (68.0)	8 (32.0)	0	0	0	25
				Not localised	0	0				0
Kuzniecky, 1998[68]	No subgroup	Volumetric (whole brain)	Site of surgery	Localised	28 (93.3)	0	0	0	2 (6.7)	30
				Not localised	0	0				0
Li, 2000[78]	EEG focus	Volumetric (hippocampus)	Site of surgery	Localised	16 (76.2)	2 (9.5)	0	0	3 (14.3)	21
				Not localised	0	0				0

accuracy of routine MRI in the localisation of the seizure focus,[30,31,33,41,46,49,53,54,57,58,60,63,77,88,101,102,109,110,115] and nine the lateralisation of the seizure focus in patients with TLE.[32,39,44,56,65,67,70,79,106] Eleven studies were restricted to patients with TLE,[32,39,44,49,56,65,67,70,79,101,109] 12 studies included patients with both temporal and non-temporal lobe epilepsy[31,41,53,57,58,60,63,88,102,106,110,115] and five studies did not report on type of epilepsy.[30,33,46,54,77] For the purpose of further analysis, these studies were considered to have included patients with both temporal and non-temporal lobe epilepsy as we assumed that they would have made it clear if they had been restricted to patients with a particular type of epilepsy. Only two studies included an appropriate patient spectrum.[54,106]

The majority of studies used an appropriate reference standard: nine used site of surgery,[32,33,44,49,56,60,70,88,115] seven ictal EEG,[58,63,65,67,77,109,110] four a combination of tests,[13,29,41,106] one EEG/ECoG,[101] two surgery/pathology site,[30,53] and one pathological findings.[57] Three studies used an inappropriate reference standard, either interictal EEG,[46] or ictal EEG in some patients and either interictal EEG,[54] or did not specify the type of EEG, in others.[102] The final study reported that EEG was used as the reference standard without providing further details; therefore, it was unclear whether an appropriate reference standard had been used.[31] Partial verification bias did not appear to be a problem in any of these studies. One study reported three evaluations of routine MRI, each scan of a different area of the temporal lobe.[56] Two studies allowed data for all patients to be extracted but also allowed data for subgroups with EEG focus and no EEG focus to be extracted separately.[60,88]

Figure 12 shows the proportion of correctly localised, non-localised, partially localised or incorrectly localised scans in each study. There was considerable heterogeneity between studies in all localisation categories, particularly in correctly localising and non-localising scans. This was apparent from visual inspection of the forest plots (*Figure 13*) and confirmed by statistical tests for heterogeneity ($p < 0.05$).

The proportion of patients in whom routine MRI correctly identified the seizure focus ranged from 5 to 100%. Those scans that did not correctly localise a focus were usually non-localising, with the proportion of partially or incorrectly localising scans being small in comparison. One factor that may account for some of the observed heterogeneity in the proportion of correctly localised scans was magnet strength. Of the six studies reporting fewer than 40% correctly localising scans,[31,33,46,58,106,109] three used a low magnet strength machine. One used either 0.3 or 0.35 T[106] and two used 0.5 T.[31,109] Two studies used 1.5 T, which was the most common magnet strength employed,[33,46] and one did not report on the magnet strength.[58] Another study used a low magnet strength camera of 0.5 T and reported 78% correctly localising scans.[67] The study that reported the lowest proportion of correctly localised scans, only 5%, was the only one which specified that the scans were undertaken in those with neocortical involvement.[58]

The proportion of non-localising scans ranged from 0 to 74%. The proportion of partially localised scans ranged from 0 to 23%. Only four studies had more than 10% partially localising scans.[58,60,88,101] Three of these were the only studies in which patients had a SPECT scan prior to the MRI scan. Individual patient data were available for all four studies, facilitating the identification of partially localising scans. Studies restricted to patients with TLE reported fewer patients with partially localised scans than studies that included patients with both temporal and non-temporal lobe epilepsy. This may be explained by the fact that nine of the 11 studies restricted to patients with TLE only looked at lateralisation of the seizure focus. These studies would not have provided data on partially localised scans (they identified the seizure focus as being either the left or right temporal lobe).

The proportion of incorrectly localised scans ranged from 0 to 21%, with 12 studies reporting no patients with incorrectly localised scans. Studies of patients with TLE tended to report fewer patients with incorrectly localised scans (range 0–5% compared with 0–21% for studies that also included patients with non-temporal lobe epilepsy). Eight of the 11 studies restricted to patients with TLE reported no incorrectly localised scans (compared with four of the 14 studies that included patients with non-temporal lobe epilepsy). The study reporting the highest proportion of incorrectly localised scans[46] used the inappropriate reference standard of interictal EEG only. One other study used EEG as the reference standard and did not report whether this was ictal or interictal; this study reported 4% incorrectly localised scans.[31] Five other studies reporting incorrectly localising scans also used EEG as the reference standard.[63,67,77,109,110]

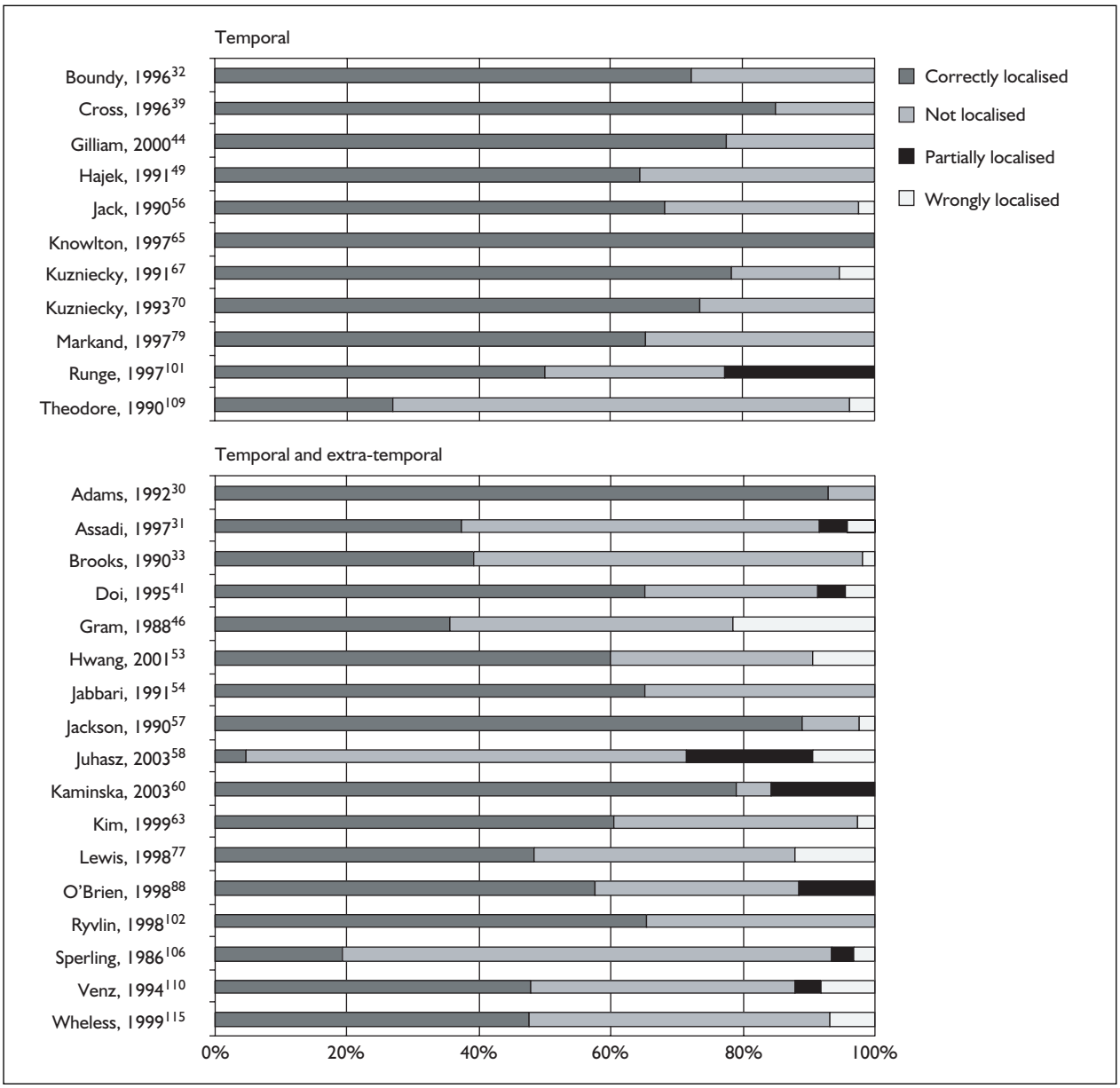

FIGURE 12 *Routine MRI: proportion of scans in each localisation category*

However, all these studies used ictal EEG. Another study used ictal EEG as the reference standard and reported no incorrectly localising scans.[65] A further five studies reported incorrectly localised scans, ranging from 2 to 7%.[33,41,56,106,115] Three used site of surgery as the reference standard,[33,56,115] and the remaining two a combination of tests.[41,106]

The observed heterogeneity in the localisation categories could not be explained by variation in reference standard used, weighting of scan (T1 or T2), slice orientation, number of patients, patient spectrum (adults and/or children), proportion of male to female, year of publication (a surrogate for improved technology) or the subgroup investigated. One study reported results separately for scans of three different regions of the brain.[56] This found that scans of the hippocampus correctly localised the seizure focus in a greater proportion of patients (68%) than scans of the anterial temporal lobe (37%) or the medial temporal parenchyma (12%). Scans of the hippocampus also resulted in a lower proportion of non-localised scans. Another study reported results for no subgroup and for patients with and without a seizure focus identified by EEG,[56] and reported similar localisation rates for the each subgroup.

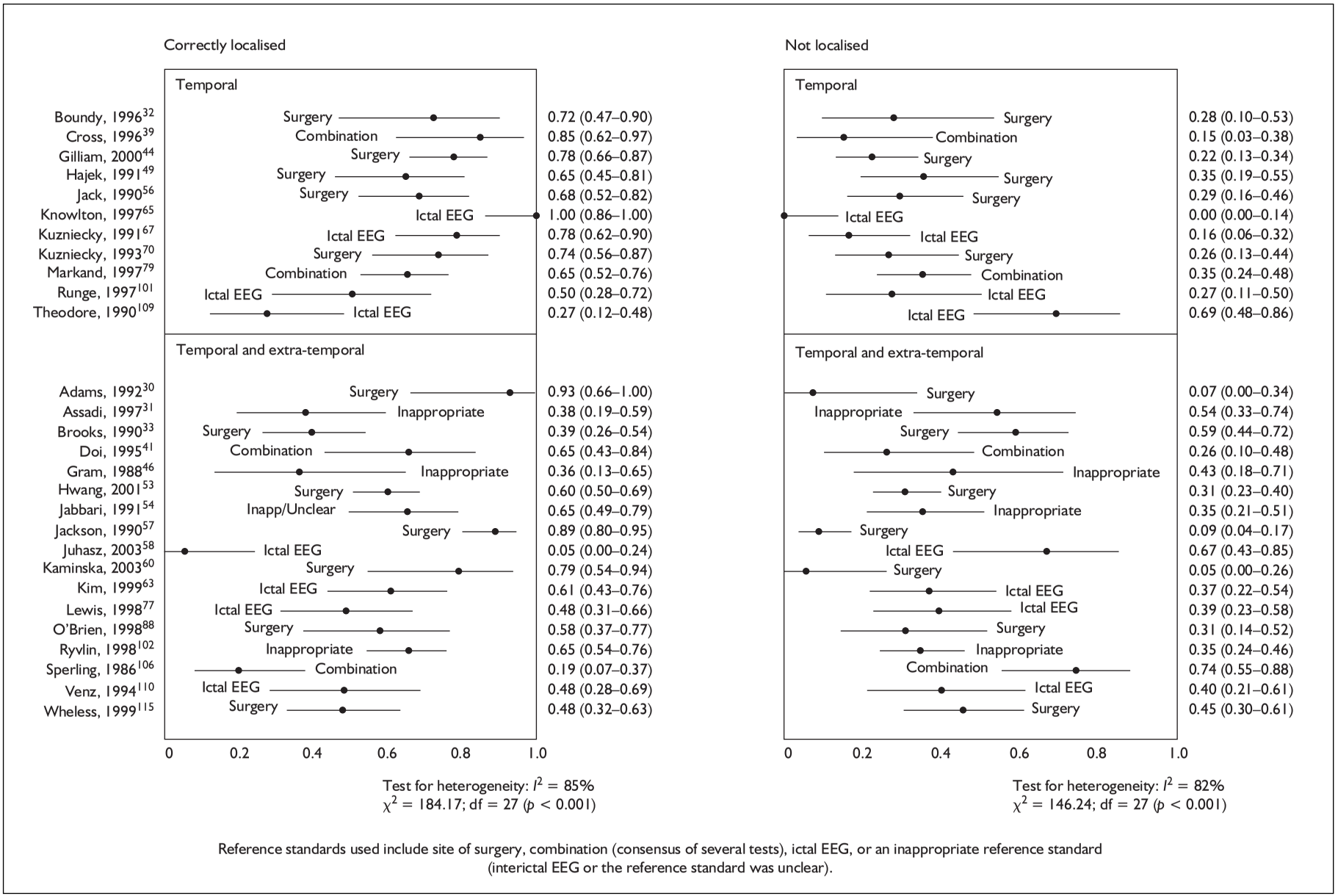

FIGURE 13 *Routine MRI: forest plots for each localisation category*

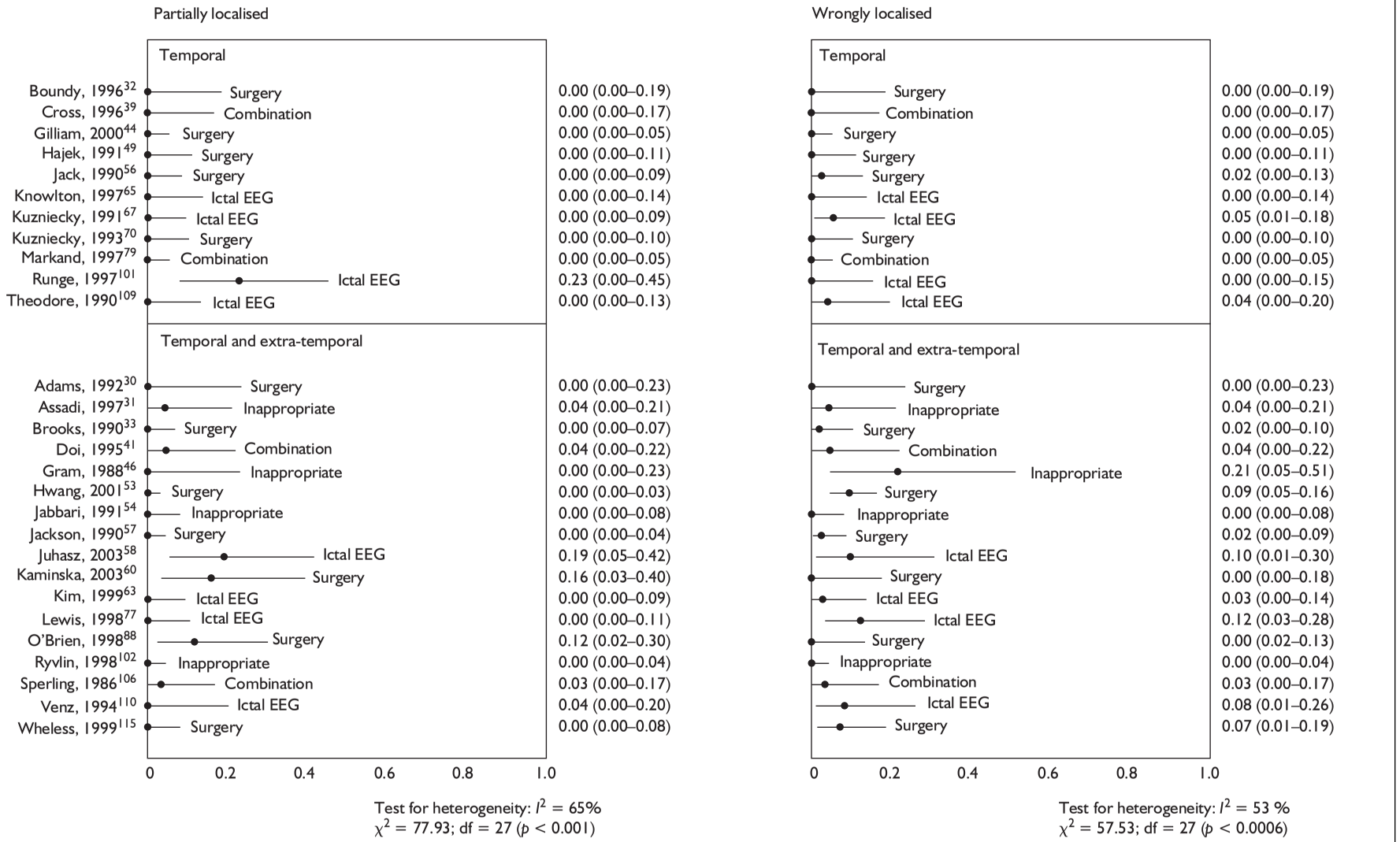

FIGURE 13 (cont'd) *Routine MRI: forest plots for each localisation category*

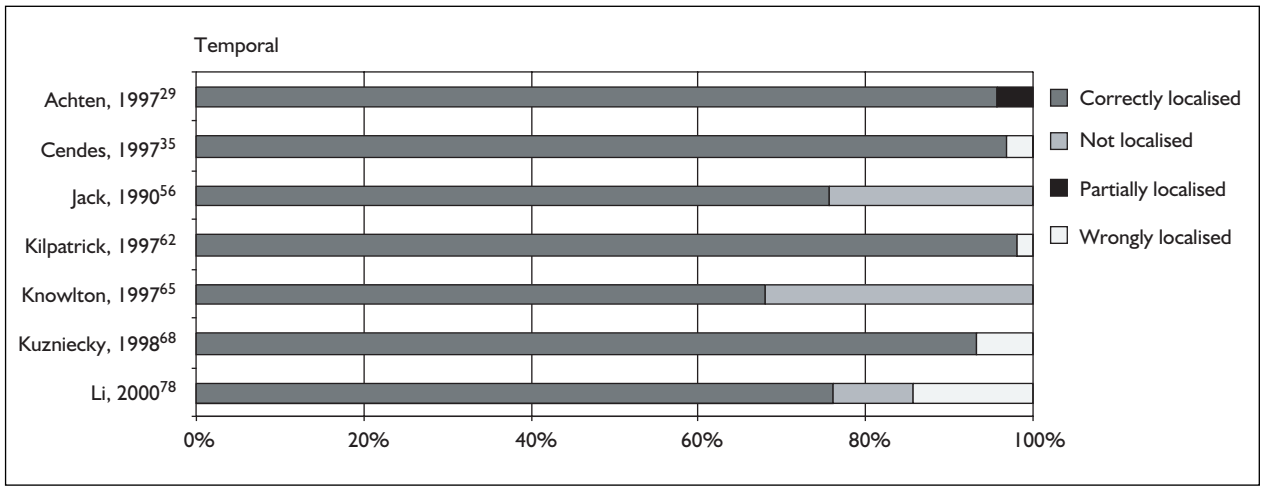

FIGURE 14 *Volumetric MRI: proportion of scans in each localisation category*

Volumetric MRI

Seven studies (eight evaluations) assessed volumetric MRI.[29,35,56,62,65,68,78] All studies were restricted to patients with TLE, and looked at lateralisation of the seizure focus. Only one study included an appropriate patient spectrum.[29] Four studies looked at hippocampal volumes,[56,65,68,78] two at temporal lobe and hippocampal volume[29,56] and one at amygdal and hippocampal volumes.[35]

Four of the studies used site of surgery as the reference standard,[56,62,68,78] one ictal EEG[65] and two a combination of tests.[29,35] These were all considered to be appropriate reference standards. Partial verification bias may have been a problem in one study, which only reported results on patients who underwent surgery, which was also the reference standard.[62]

Figure 14 summarises the proportion of scans that correctly localised, did not localise, partially localised or incorrectly localised the seizure focus for each study. There was considerable heterogeneity between studies in all localisation categories, particularly in correctly localising and non-localising scans. This was apparent from visual inspection of the forest plots (*Figure 15*) and confirmed by statistical tests for heterogeneity ($p < 0.05$ for correctly localised and non-localised). Volumetric MRI appears to be a reasonably accurate test for the lateralisation of the epileptic focus in those with TLE. The proportion of patients in whom volumetric MRI correctly identified the seizure focus ranged from 68 to 98%. Only one study reported any partially localised scans. This study reported that all patients had localised scans with 96% correctly localised and 4% partially localised. Four studies reported incorrectly localised scans, with the proportion ranging from 2 to 14%. Three studies reported non-localised scans, with the proportion ranging from 9 to 32%. The observed heterogeneity could not be explained by variation in reference standard used, weighting of scan (T1 or T2), magnet strength, slice orientation, year of publication, number of patients, patient spectrum, proportion female or the subgroup investigated.

T2-relaxometry MRI

One study assessed T2-relaxometry MRI.[65] This study looked at the accuracy of T2-relaxometry of the hippocampus in the lateralisation of the seizure focus in patients with temporal lobe epilepsy.[65] The reference standard used was ictal EEG, and did not include an appropriate patient spectrum. The study was restricted to patients with an EEG focus and no structural abnormality. All patients with a localised scan (69%) were correctly localised, with the remainder having non-localised scans. The results of this study are summarised in *Figure 16*.

PET

Nineteen studies (26 evaluations) assessed PET.[29,36,38,40,43,51–53,58,62,63,65,79,81,86,102,106,107,109]

Five studies assessed the accuracy of PET in the lateralisation of the seizure focus in patients with TLE[29,51,65,79,107] and 14 the localisation of the seizure focus.[36,38,40,43,52,53,58,62,63,81,86,102,107,109]

Nine studies were restricted to patients with TLE,[29,36,40,51,62,65,79,107,109] nine included patients with both temporal and non-temporal lobe epilepsy[38,43,52,53,63,81,86,102,106] and one study did not report on the type of epilepsy.[58] One study reported four separate evaluations: two different tracers [FDG and [^{11}C]flumazenil (FMZ)] and two

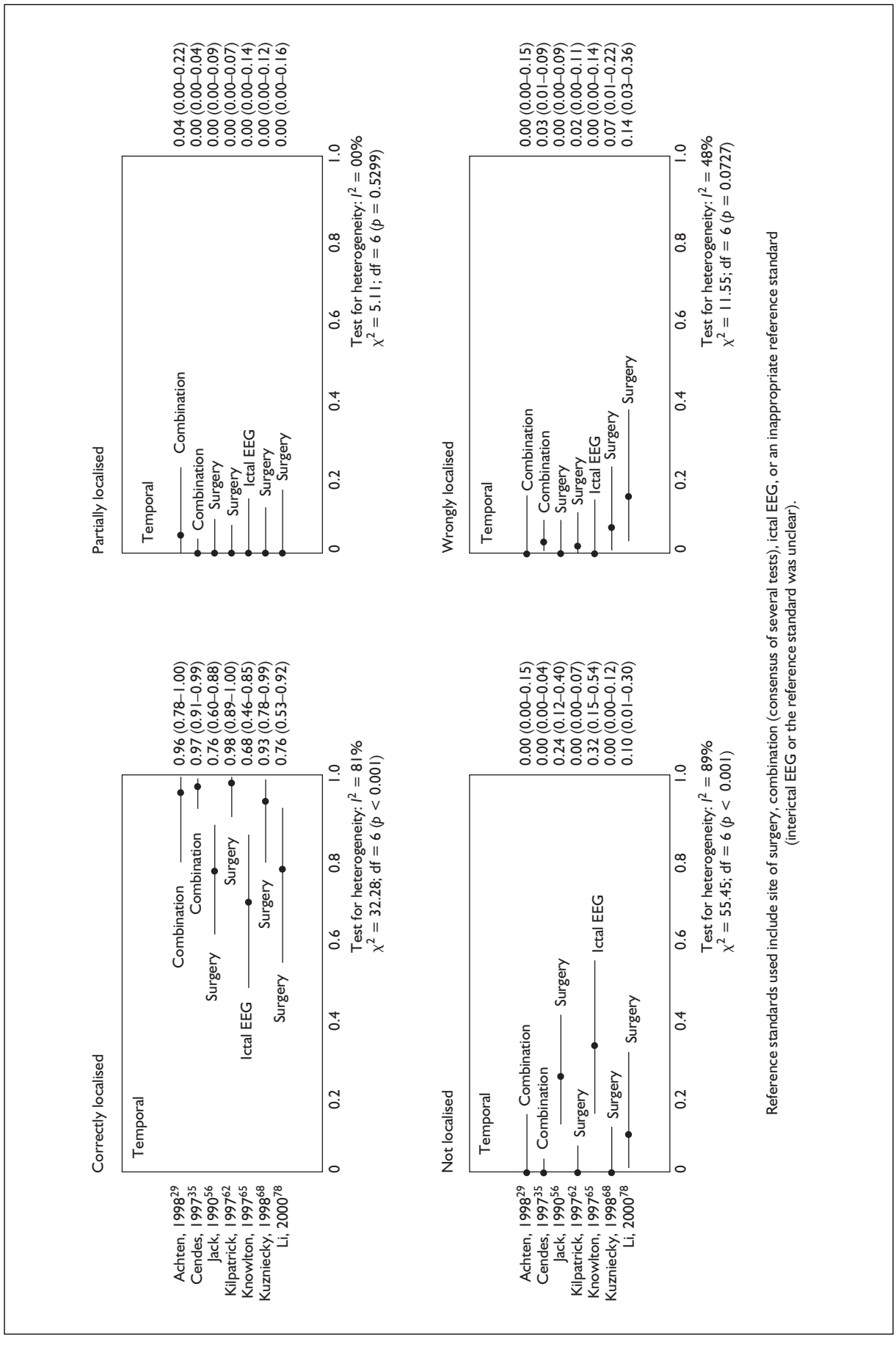

FIGURE 15 *Volumetric MRI: forest plots for each localisation category*

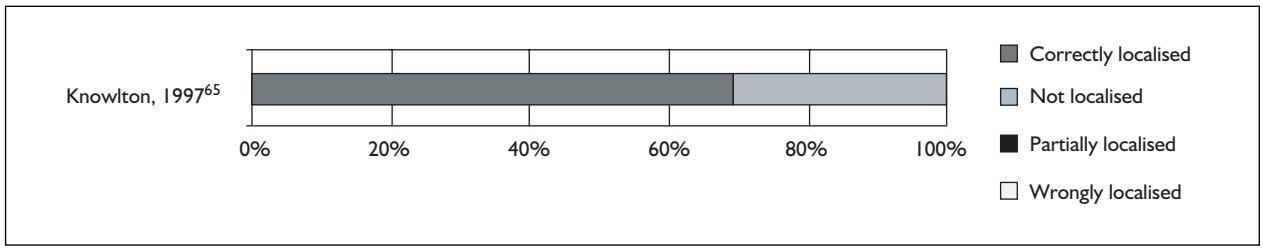

FIGURE 16 *T2-Relaxometry MRI: proportion of scans in each localisation category*

subgroups (patients in whom EEG identified a seizure focus and patients in whom it did not).[40] Another study also reported results separately for two different tracers [α-methyl-L-tryptophan (AMT) and FDG].[58] A further study reported results for two methods of interpretation of the PET scans: visual and statistical parameter mapping (SPM) analysis.[64] Two studies included an appropriate patient spectrum.[29,106] The results of these studies are presented in *Table 7*.

The tracer used in all but five evaluations was FDG. Other tracers used were [^{15}O]water,[107] FMZ[40,102] and AMT.[58] One study did not report on the tracer used.[62] Twelve studies reported that PET scans were performed interictally,[29,36,38,51–53,58,79,81,86,102,109] six studies did not report on the timing of PET scans,[40,43,62,63,65,106] and one study reported that 22 scans were carried out interictally and two ictally.[107] Eight studies used site of surgery as the reference standard,[38,40,52,58,62,81,86,107] five ictal EEG,[36,43,63,65,109] five a combination reference standard[29,51,79,102,106] and one pathology at the site of surgery.[53] Partial verification bias may have been a problem in two studies which only reported results on patients who underwent surgery, which was also the reference standard.[62,86]

Figure 17 summarises the proportion of correctly localised, non-localised, partially localised or incorrectly localised scans for each study. There was considerable heterogeneity between studies in all localisation categories. This was apparent from visual inspection of the forest plots (*Figure 18*) and confirmed by statistical tests for heterogeneity ($p < 0.05$). The proportion of patients in whom PET correctly identified the seizure focus ranged from 29 to 92%, with three studies reporting <50% correctly localised.[52,58,106] These studies included both patients with temporal and non-temporal lobe epilepsy. The study which correctly localised only 29% of patients, partially localised a further 62% but also incorrectly localised 5%.[58] The study correctly localising 43% of scans, did not localise 18%, partially localised 14% and incorrectly localised 25%.[52] The study correctly localising in 44% of scans did not localise a seizure focus in the remaining 56% of patients.[106] All three studies used FDG PET. Two included only children,[39,58] with one restricted to children in whom EEG identified the seizure focus.[58] The third study was restricted to patients with no focal lesion on prior CT scanning.[106] Another study, restricted to children, found that PET correctly localised the seizure focus in 87%. Other studies restricted to patients with no structural abnormalities on previous neuroimaging scans reported rates of correct localisation ranging from 56–88%.

The proportion of patients in whom PET failed to localise a seizure focus ranged from 0 to 56%, although all but three studies reported <25% non-localised.[43,81,106] These three studies all included patients with both temporal and non-temporal lobe epilepsy. PET localised a seizure focus in all patients in two studies, although some were partially or incorrectly localised.[40,63] The proportion of patients in whom PET partially localised the seizure focus ranged from 0 to 62%, with all but two studies having <25% partially localised.[40,58] Eight studies did not report any patients with partially localised scans; however, one of these did not report data in a format that would allow extraction of data on partially localised scans.[81] Nine studies reported incorrectly localised scans,[36,43,52,53,58,63,65,81,102] with the proportion ranging from 3 to 25%. Four of these studies had ≤5% incorrectly localised scans.[36,43,58,65] The study with the greatest proportion of incorrectly localised scans (25%) did not appear to differ from the other studies in any way that may explain this difference.[52]

The difference in tracers (FDG, FMZ and [^{15}O]water), reference standard, year of publication or patient subgroups (EEG focus or previous structural abnormality) did not appear to explain the observed heterogeneity. Two studies reported results for more than one tracer.[40,58] One used

TABLE 7 *Results of studies that assessed PET for seizure focus localisation*

Study	Subgroup	Tracer	Reference standard	Reference standard	Results: No. (%)						
					Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Ictal and interictal combined: 22 scanned interictally, 2 scanned ictally											
Tatlidil, 2000[107]	No subgroup	[^{15}O]water	Site of surgery	Localised	19 (79.2)	5 (20.8)	0	0	0	0	24
				Not localised	0	0					0
Interictal											
Achten, 1998[29]	No structural abnormality	FDG	Combination	Localised	16 (69.6)	5 (21.7)	0	2 (8.7)	0	0	23
				Not localised	5 (83.3)	1 (16.7)					6
Chee, 1993[36]	No structural abnormality and EEG focus	FDG	Ictal EEG	Localised	22 (56.4)	7 (17.9)	1 (2.6)	8 (20.5)	0	1 (2.6)	39
				Not localised	1 (100)	0					1
Chugani, 1993[38]	No subgroup	FDG	Site of surgery	Localised	17 (73.9)	0	0	5 (21.7)	1 (4.3)	0	23
				Not localised	0	0					0
Debets, 1997[40]	No subgroup	FDG		Localised	14 (60.9)	0	0	9 (39.1)	0	0	23
				Not localised	0	0					0
	EEG focus			Localised	13 (59.1)	0	0	9 (40.9)	0	0	22
				Not localised	0	0					0
	No subgroup	FMZ	Site of surgery	Localised	20 (87.0)	0	1 (4.3)	2 (8.7)	0	0	23
				Not localised	0	0					0
	EEG focus			Localised	19 (86.4)	0	1 (4.5)	2 (9.1)	0	0	22
				Not localised	0	0					0
Engel, 1990[43]	EEG focus	FDG	Ictal EEG	Localised	67 (56.3)	41 (34.4)	0	7 (5.9)	0	4 (3.4)	119
				Not localised	6 (21.4)	22 (78.6)					28
Ho, 1995[51]	No subgroup	FDG	Combination	Localised	33 (94.3)	2 (5.7)	0	0	0	0	35
				Not localised	0	0					0
Hong, 2002[52]	No subgroup	FDG	Site of surgery	Localised	12 (43)	5 (18)	0	4 (14)	0	7 (25)	28
				Not localised	0	0				0	0
Hwang, 2001[53]	No subgroup	FDG	Site of surgery/ pathology	Localised	80 (78)	10 (10)	0	0	0	13 (12)	103
				Not localised	0	0	0			0	0
Juhasz, 2003[58]	EEG focus	AMT	Site of surgery	Localised	4 (19.0)	9 (42.9)	8 (38.1)	0	0	0	21
				Not localised	3 (50)	3 (50)					6
		FDG		Localised	6 (28.6)	1 (4.8)	5 (23.8)	6 (28.6)	2 (9.5)	1 (4.7)	21
				Not localised	6 (100)	0					6

continued

TABLE 7 *Results of studies that assessed PET for seizure focus localisation (cont'd)*

Study	Subgroup	Tracer	Reference standard	Reference standard	Results: No. (%)						
					Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Kilpatrick, 1997[62]	EEG focus	Not reported	Site of surgery	Localised	22 (91.7)	2 (8.3)	0	0	0	0	24
				Not localised	0	0					0
Kim, 2000[63]	No subgroup	FDG	Ictal EEG	Localised	26 (86.7)	0	0	0	0	4 (13.3)	30
				Not localised	0	0					0
Knowlton, 1997[65]	No structural abnormality and EEG focus	FDG	Ictal EEG	Localised	21 (84.0)	3 (12.0)	0	0	0	1 (4)	25
				Not localised	0	0					0
Markand, 1997[79]	EEG focus	FDG	Combination	Localised	44 (80.0)	8 (14.5)	3 (5.5)	0	0	0	55
				Not localised	0	0					0
Mastin, 1996[81]	No subgroup	FDG	Site of surgery	Localised	15 (60.0)	7 (28.0)	0	0	0	3 (12.0)	25
				Not localised	0	0					0
O'Brien, 2001[86]	No structural abnormality	FDG	Site of surgery	Localised	21 (87.5)	3 (12.5)	0	0	0	0	24
				Not localised	0	0					0
Ryvlin, 1998[102]	EEG focus	FMZ	Combination	Localised	47 (59.0)	18 (22.0)	9 (11.0)	2 (2.0)	0	5 (6.0)	81
				Not localised	0	0					
				Multifocal	2 (11.0)	5 (28.0)	6 (33.0)			5 (28.0)	18
Sperling, 1986[106]	No structural abnormality	FDG	Combination	Localised	12 (44.4)	15 (55.6)	0	0	0	0	27
				Not localised	0	3 (100)					3
Theodore, 1990[109]	EEG focus	FDG	Ictal EEG	Localised	17 (65.4)	4 (15.4)	1 (3.8)	4 (15.4)	0	0	26
				Not localised	0	0					0

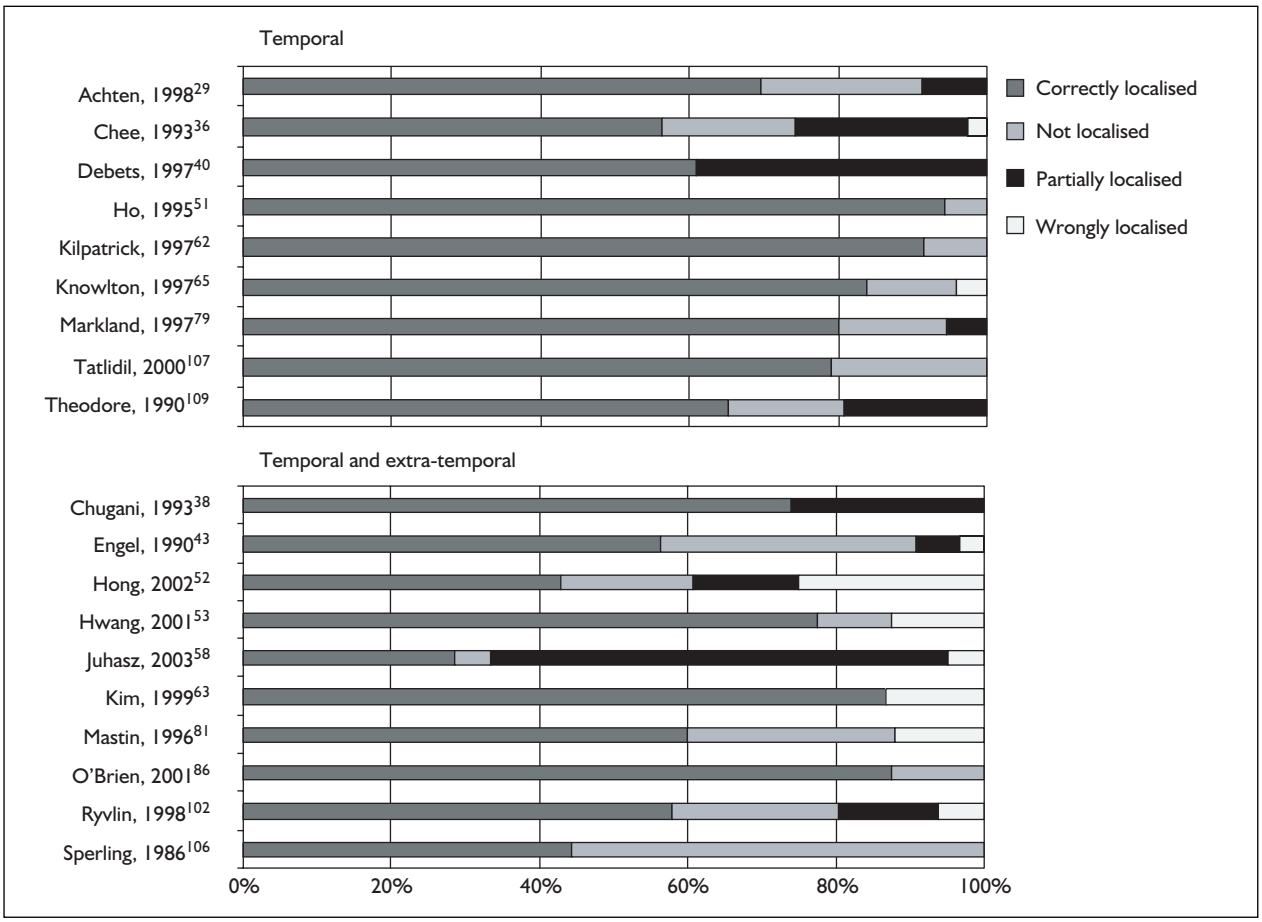

FIGURE 17 *PET: proportion of scans in each localisation category*

AMT and FDG, and found that FDG was more sensitive (i.e. greater proportion correctly localised) but less specific (more incorrectly localised and partially localised) than AMT.[58] The second used FDG and FMZ, and found that PET identified a seizure focus in all patients (correctly or partially) regardless of tracer. However, FMZ correctly identified the seizure focus in a greater proportion of patients than FDG (87 and 61%, respectively), with all other scans partially identifying the seizure focus.

SISCOM

Seven studies (11 evaluations) assessed the accuracy of SISCOM in the localisation of the seizure focus.[60,70,87,88,91,105,111] Four studies included patients with both temporal and non-temporal lobe epilepsy,[59,60,88,105] one was restricted to patients with non-temporal lobe epilepsy[87] and two studies did not report on the type of epilepsy.[91,111] Three of these studies were by the same authors.[87,88,91] Two studies reported results for all the patients included in the study combined, but also allowed results to be extracted separately for patients in whom EEG was able to localise the seizure focus and patients in whom EEG could not localise the seizure focus.[60,88] None of these studies included an appropriate patient spectrum. The results of these studies are presented in *Table 8*.

All studies used an appropriate reference standard. Four used site of surgery,[59,60,87,88] two ictal EEG[91,105] and one a combination reference standard.[111] Partial verification bias may have been a problem in one of these studies, which only reported results on patients who underwent surgery, which was also the reference standard.[88] Three studies used ECD as the tracer,[59,60,111] one used HMPAO,[105] one used HMPAO in some patients and [^{99m}Tc]bicistate in others[87] and two used HMPAO in some patients and ECD in others.[88,105] The remaining study did not report on the tracer used.[91]

Figure 19 summarises the proportion of correctly localised, non-localised, partially localised or incorrectly localised scans for each study. There was considerable heterogeneity between studies, apparent from visual inspection of the forest plots

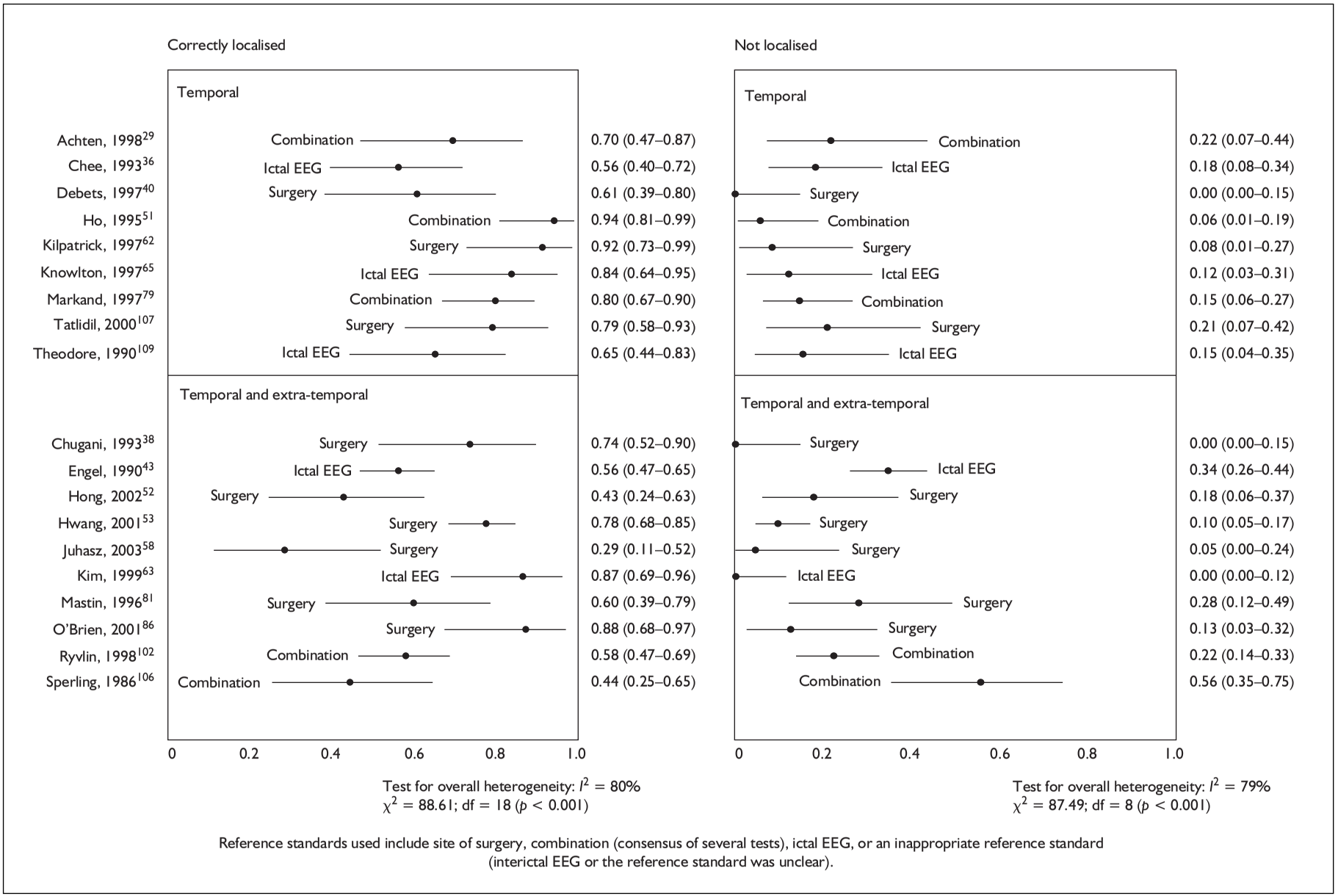

FIGURE 18 *PET: forest plots for each localisation category*

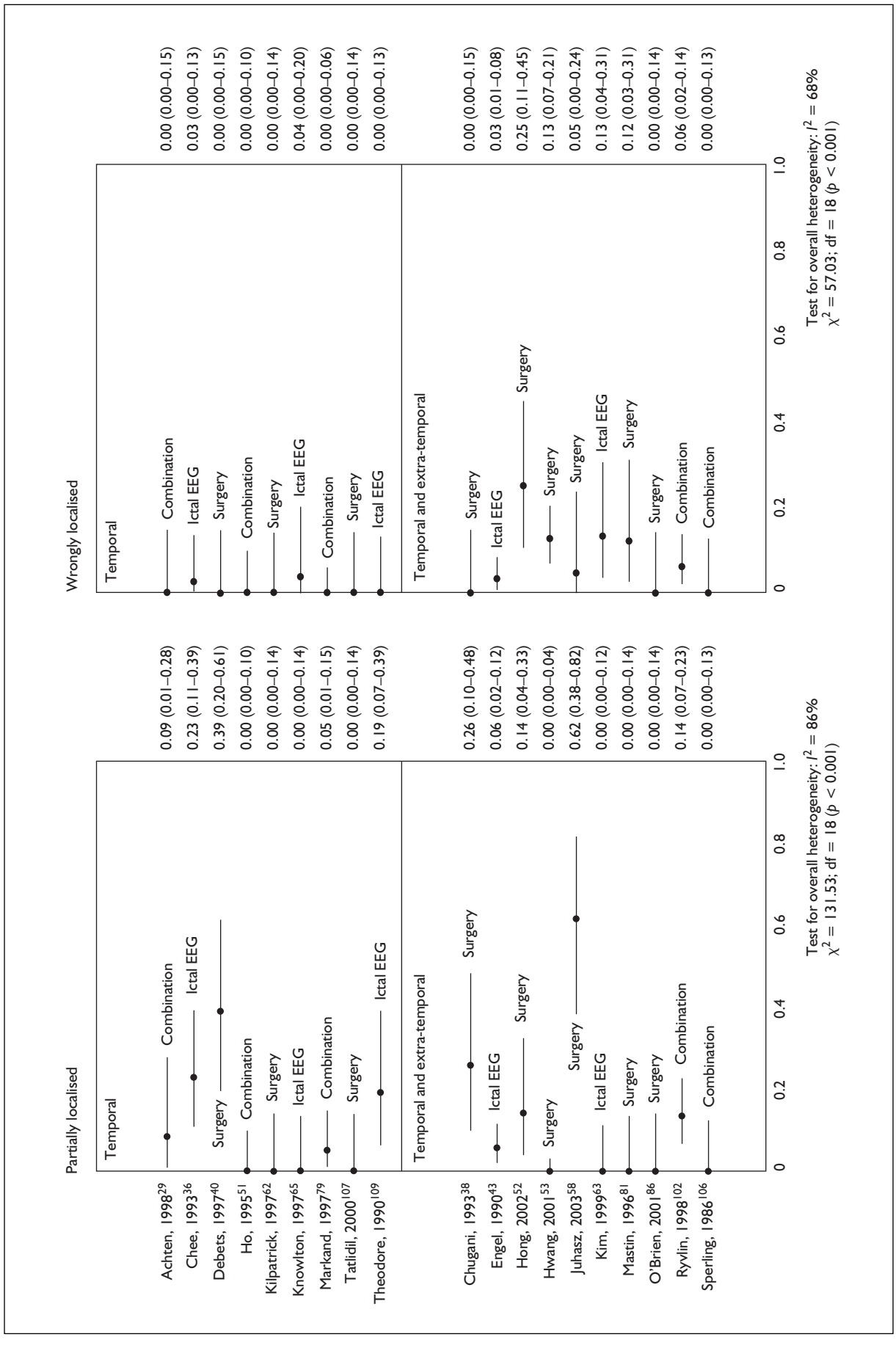

FIGURE 18 (cont'd) *PET: forest plots for each localisation category*

TABLE 8 *Results of studies that assessed SISCOM for seizure focus localisation*

Study	Subgroup	Tracer	Reference standard	Reference standard	Results: No. (%)						
					Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Kaiboriboon, 2002[59]	No subgroup	ECD	Site of surgery	Localised	24 (63.2)	11 (28.9)	0	0	0	3 (7.9)	38
				Not localised	0	0					0
Kaminska, 2003[60]	No subgroup	ECD		Localised	8 (42.1)	1 (5.26)	2 (10.53)	5 (26.32)	1 (5.26)	2 (10.53)	19
				Not localised	1 (100)	0					1
	EEG focus		Site of surgery	Localised	6 (40.0)	1 (6.7)	2 (13.3)	3 (20.0)	1 (6.7)	2 (13.3)	15
				Not localised	1 (100)	0					1
	No EEG focus			Localised	2 (50.0)	0	0	2 (50.0)	0	0	4
				Not localised	0	0					0
O'Brien, 2000[87]	No subgroup	HMPAO or [^{99m}Tc]bicisate	Site of surgery	Localised	19 (52.8)	12 (33.3)	0	0	0	5 (13.9)	36
				Not localised	0	0					0
O'Brien, 1998[88]	No subgroup			Localised	14 (53.8)	5 (19.2)	1 (3.9)	2 (7.7)	0	4 (15.4)	26
				Not localised	0	0					0
	EEG focus	HMPAO or ECD	Site of surgery	Localised	12 (57.1)	4 (19.1)	1 (4.8)	2 (9.5)	0	2 (9.5)	21
				Not localised	0	0					0
	No EEG focus			Localised	2 (40.0)	1 (20.0)	0	0	0	2 (40)	5
				Not localised	0	0					0
O'Brien, 2001[91]	No subgroup	Not reported	Ictal EEG	Localised	19 (86.4)	3 (13.6)	0	0	0	0	22
				Not localised	0	0					0
Siegel, 2001[105]	No structural abnormality	HMPAO	Ictal EEG	Localised	13 (76.5)	1 (5.9)	0	3 (17.6)	0	0	17
				Not localised	4 (100)	0					4
				Multifocal	0	2 (20)	8 (80)			0	10
Vera, 1999[111]	No subgroup	ECD	Combination	Localised	11 (55.0)	1 (5.0)	0	7 (35.0)	0	1 (5.0)	20
				Not localised	6 (85.7)	1 (14.3)					7

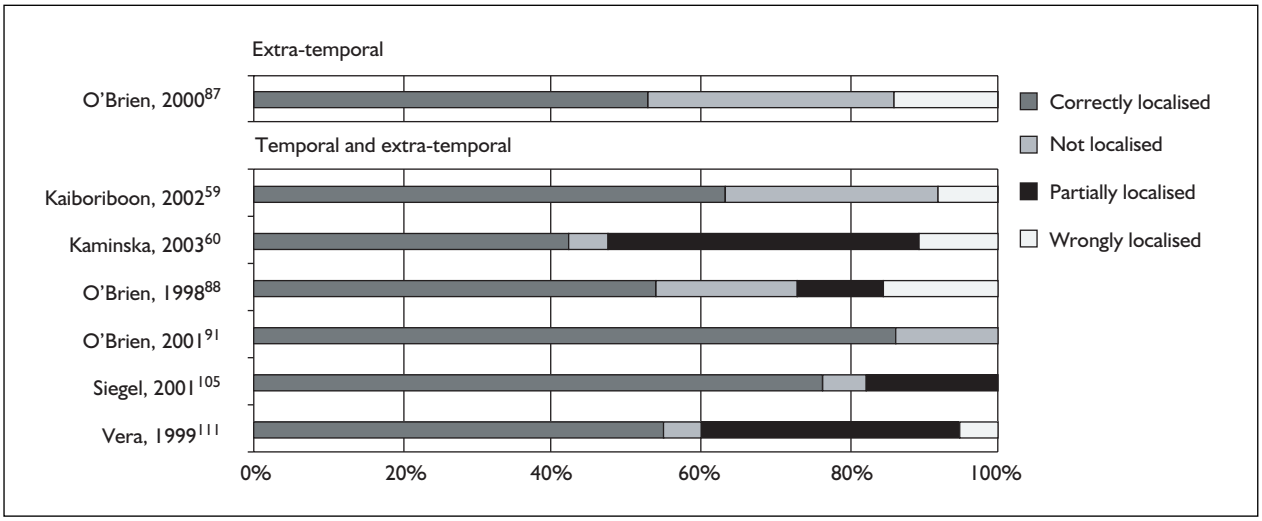

FIGURE 19 *SISCOM: proportion of scans in each localisation category*

(*Figure 20*) and formal statistical tests ($p < 0.05$). The proportion of patients with correctly localised scans ranged from 42 to 86%. The two studies with the greatest proportion of correctly localised scans (86 and 76%) were the only two studies to use ictal EEG as the reference standard.[91,105] The other studies used site of surgery[59,60,87,88] or a combination reference standard.[111]

The proportion of non-localised scans ranged from 5 to 33%. Three studies each reported very low rates of non-localised scans of 5–6%.[60,105,111] These studies did not show any particular similarities to one another, or differences from other studies in this section with higher rates of non-localised scans. They used different reference standards, two different tracers and two were not restricted to any particular patient subgroups whereas the other included only patients in whom previous MRI scans were normal.

The proportion of patients with partially localised scans also showed significant heterogeneity ranging from 0 to 42%. Three studies reported no patients with partially localised scans.[59,87,91] These studies also did not show any particular similarities to one another or differences from other studies in this section that reported patients with partially localised scans. The proportion of patients with incorrectly localised scans was relatively low and statistically homogeneous across studies. It ranged from 0 to 15% with two studies reporting no incorrectly localised scans.[91,105] These two studies were also the two with the greatest proportion of correctly localised scans and were the only two to use ictal EEG as the reference standard. The study which suggested the best performance of SISCOM (greatest proportion of correctly localised scans and no incorrectly or partially localised scans) was available only as an abstract.[91] Factors such as study population (adults, children, both), type of epilepsy, tracer used, subgroup (EEG focus or previous structural abnormality) or year of publication did not appear to explain the observed heterogeneity for any of the localisation categories.

MRS

Seven studies evaluated MRS in the lateralisation of the seizure focus in patients with TLE.[29,35,39,65,68,78,85] Only one study included an appropriate patient spectrum.[29] Two studies used site of surgery as the reference standard,[68,78] two ictal EEG[65,85] and three a combination reference standard.[29,35,39] Partial verification bias did not appear to be a problem in any of the studies. The metabolites used in these studies were various combinations of NAA, creatine (Cr), and choline (Cho). The results of these studies are presented in *Table 9*.

Figure 21 summarises the proportion of correctly localised, non-localised, partially localised or incorrectly localised scans for each study. There was considerable heterogeneity between studies across the localisation categories with the exception of the incorrectly localised category, which was statistically homogeneous ($p = 0.58$). This can be seen by visual inspection of the forest plots (*Figure 22*). The proportion of correctly localised scans ranged from 52 to 97%. Four studies did not report any non-localised patients.[29,35,68,85] Two of these reported that all patients had their seizure focus either correctly

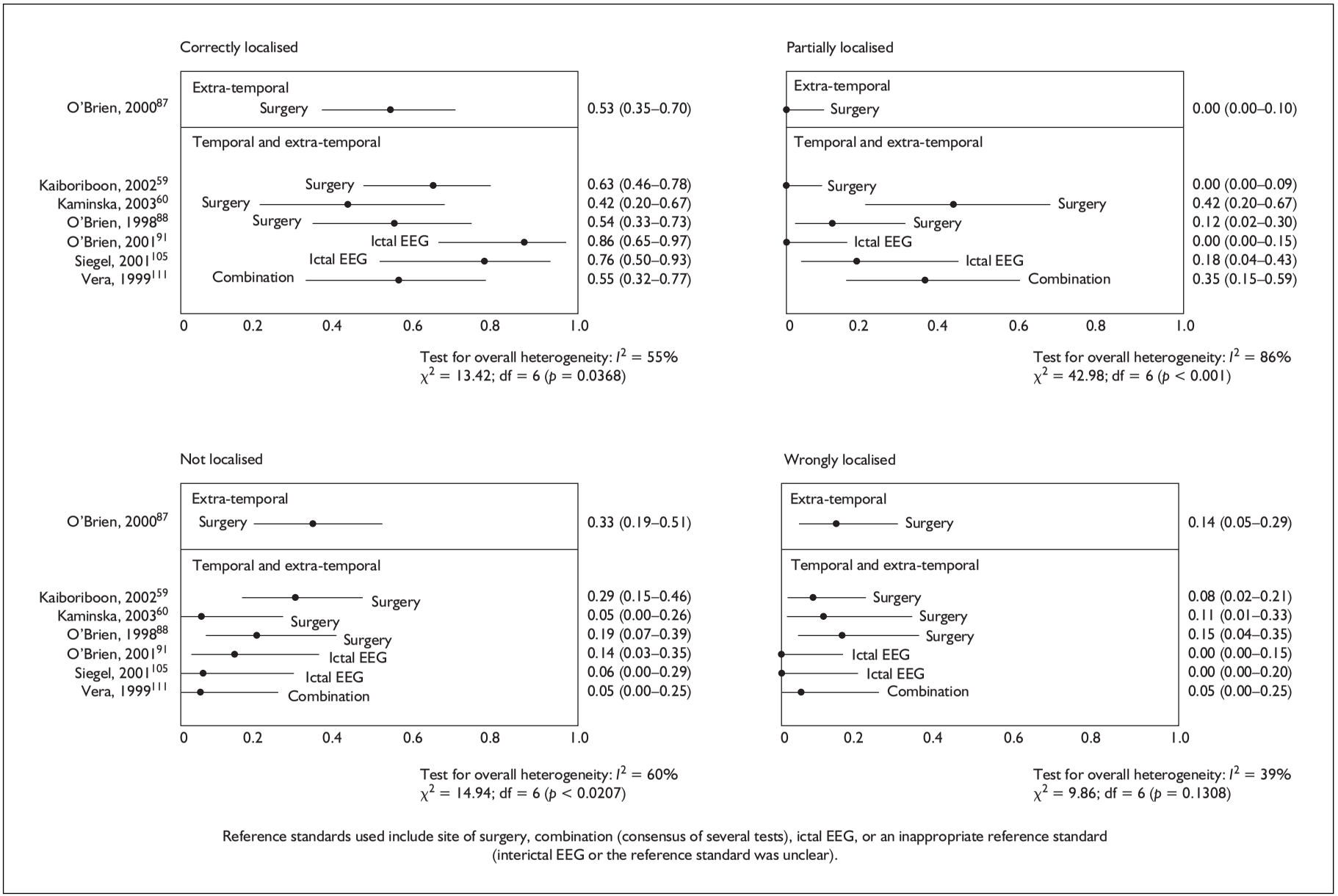

FIGURE 20 *SISCOM: forest plots for each localisation category*

TABLE 9 *Results of studies that assessed MRS for seizure focus localisation*

Study	Subgroup	Metabolites (ratios used)	Reference standard	Reference standard	Results: No. (%)					
					Correctly localised	Not localised	P1	P2	Incorrectly localised	Total
Achten, 1998[29]	No structural abnormality	NAA, Cr and Cho [NAA/(Cho + Cr)]	Combination	Localised Not localised	12 (52.2) 5 (83.3)	0 1 (16.7)	0	11 (47.8)	0	23 6
Cendes, 1997[35]	No structural abnormality	NAA, Cr and Cho (NAA/Cr)	Combination	Localised Not localised	98 (98.0) 0	0 0	0	0	2 (2.0)	100 0
Cross, 1996[39]	No subgroup	NAA, Cr and Cho [NAA/(Cho+Cr)]	Combination	Localised Not localised	11 (55) 0	9 (45) 0	0	0	0	20 0
Knowlton, 1997[65]	No structural abnormality and EEG focus	NAA, Cr and Cho (not reported)	Ictal EEG	Localised Not localised	14 (58.3) 0	9 (37.5) 0	0	0	1 (4.2)	24 0
Kuzniecky, 1998[68]	No subgroup	NAA and Cr (Cr/NAA)	Site of surgery	Localised Not localised	29 (96.7) 0	0 0	0	0	1 (3.3)	30 0
Li, 2000[78]	EEG focus	NAA and Cho (NAA/Cho)	Site of surgery	Localised Not localised	16 (76.2) 0	4 (19.1) 0	0	0	1 (4.7)	21 0
Ng, 1994[85]	No structural abnormality and EEG focus	NAA and Cho (NAA/Cho)	Ictal EEG	Localised Not localised	16 (76.2) 0	0 0	2 (9.5)	3 (14.3)	0	21 0

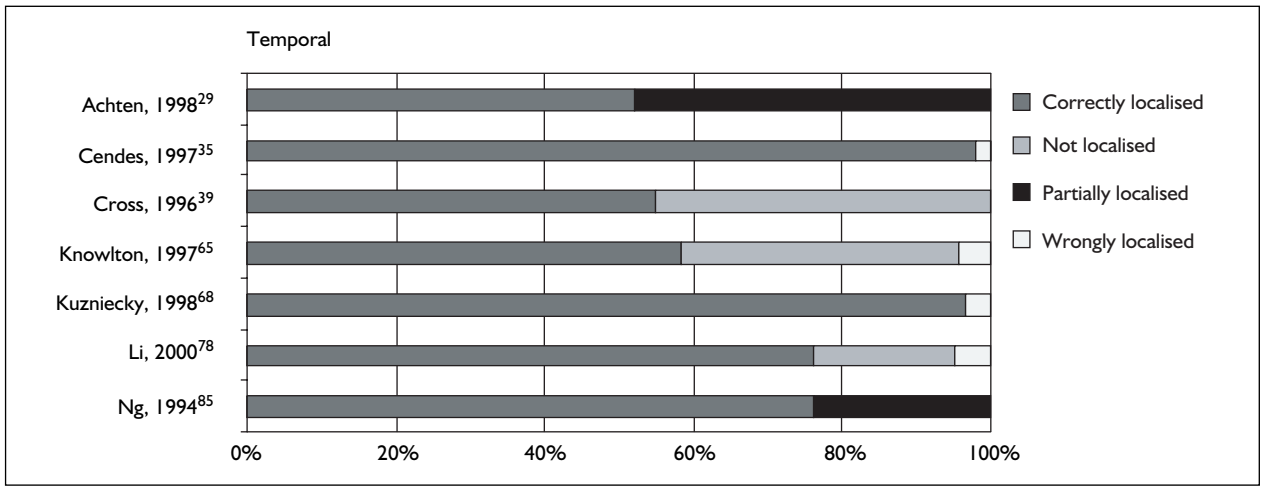

FIGURE 21 *MRS: proportion of scans in each localisation category*

localised or partially localised.[29,85] The other two reported the highest proportions of correctly localised scans, and only 2–3% incorrectly localised scan, with no partially or non-localising scans.[35,68] One of these studies was restricted to patients who also had MTLS, used a more powerful magnet than most of the other studies (4.1 compared with 1.5 T in all other studies) and was the only study to use the metabolite ratio of Cr to NAA.[68] The other included only those with no structural abnormality on MRI and used a 1.5 T magnet.[35] Three studies reported patients with non-localised scans, with 19, 38 and 45% non-localising.[39,65,78] These studies did not appear to differ from the studies that did not report non-localised scans. Only two studies reported patients with partially localised scans;[29,85] these studies reported localised scans in all patients. The proportion of incorrectly localised scans was low in all studies, ranging from 0 to 5%.

CT

Five studies looked at the accuracy of CT in the localisation of the seizure focus.[30,33,46,54,109] Four studies did not report on type of epilepsy and one study was restricted to patients with temporal lobe epilepsy.[109] Only one study included an appropriate patient spectrum.[54] The results of these studies are summarised in *Table 10*.

One study used ictal EEG as the reference standard,[109] one interictal EEG,[46] one ictal EEG in some patients and interictal in others,[54] one site of surgery[33] and one a combination of site of surgery and pathology.[30] The reference standard was considered inappropriate in the two studies that used interictal EEG as the reference standard in some or all patients.[46,54] Partial verification bias did not appear to be a problem in any of the studies. Three studies reported that CT scans were carried out with and without contrast agent but did not report on the contrast agent used.[33,46,109] One study used meglumine diatrizoate sodium as the contrast agent[54] and one did not provide any information on whether a contrast agent was used.[30]

Figure 23 summarises the proportion of correctly localised, non-localised, partially localised or incorrectly localised scans for each study. Visual inspection of the forest plots (*Figure 24*) showed that the studies evaluating CT showed considerable heterogeneity. This was statistically significant for the proportion of correctly localised, not localised and incorrectly localised scans ($p < 0.001$). Only one study reported any partially localised scans.[33]

The proportion of correctly localised scans was low in four studies, ranging from 12 to 26%.[33,46,54,109] The remaining study reported 75% correctly localised scans.[30] The proportion of non-localised scans was high in four studies (range 67–88%),[33,46,54,109] with the study that reported a high proportion of correctly localised scans reporting a low proportion of non-localised scans and no partially or incorrectly localised scans.[30] This study was also the only one to be restricted to children and used the site of pathology as the reference standard, whereas the other studies used site of surgery[33] or EEG.[46,54,109] This study provided very few details on how CT was performed, so it is not possible to determine whether CT methodology may have accounted for the better performance of CT in this study. Only one study reported any partially localised scans,

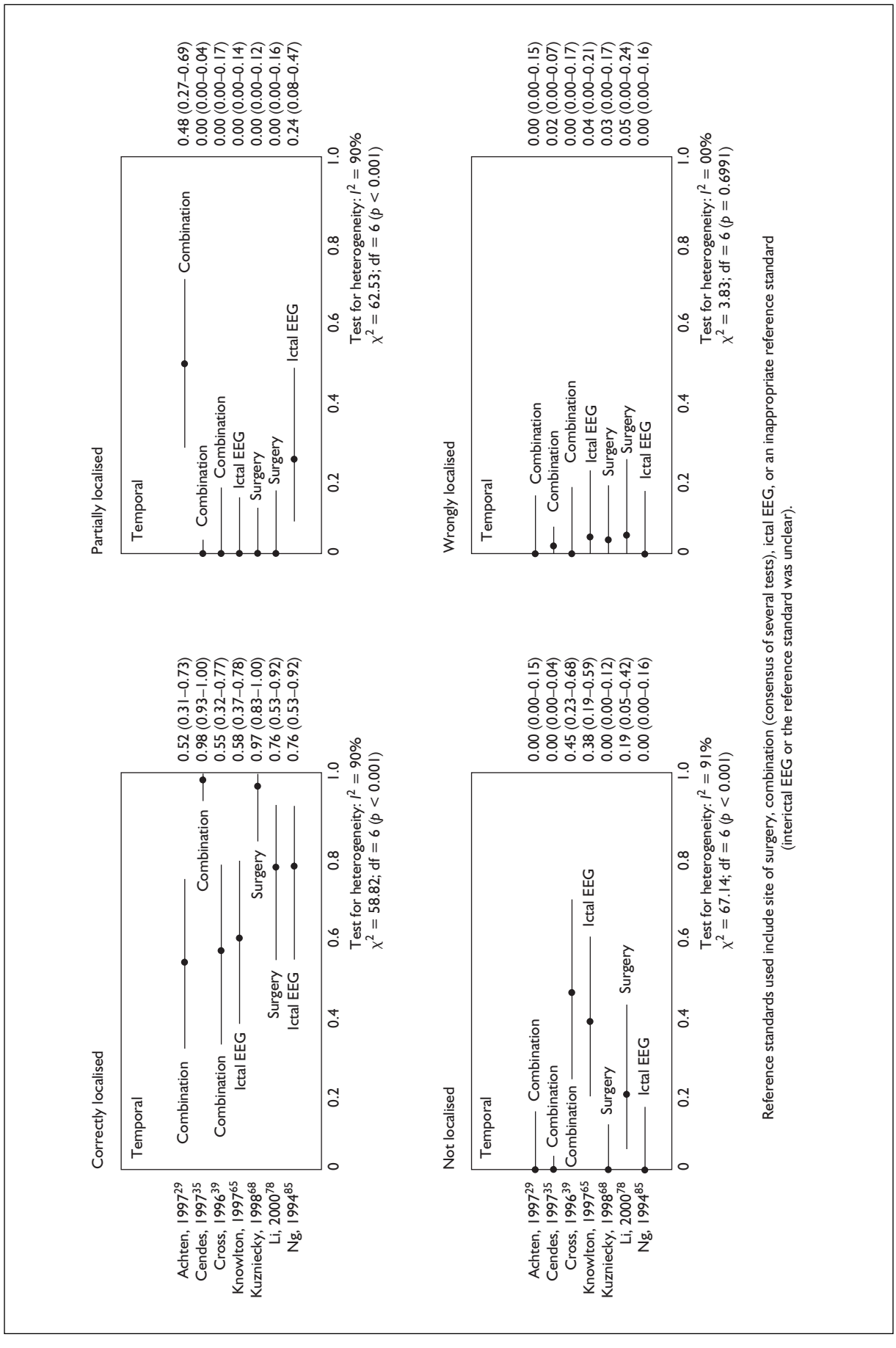

FIGURE 22 *MRS: forest plots for each localisation category*

TABLE 10 *Results of studies that assessed CT for seizure focus localisation*

Study	Subgroup	Contrast agent	Reference standard	Reference standard	Results: No. (%)				
					Correctly localised	Not localised	PI	Incorrectly localised	Total
Adams, 1992[30]	EEG focus	Not reported	Site of surgery/pathology	Localised Not localised	15 (75) 0	5 (25) 0	0	0	20 0
Brooks, 1990[33]	No subgroup	With and without contrast agent (agent not reported)	Site of surgery	Localised Not localised	6 (13.0) 0	35 (76.1) 0	1 (2.2)	4 (8.7)	46 0
Gram, 1988[46]	EEG focus	With and without contrast agent (agent not reported)	Interictal EEG	Localised Not localised	3 (20) 4 (44.4)	10 (66.7) 5 (55.6)	0	2 (13.3)	15 9
Jabbari, 1991[54]	EEG focus	Diatrizoate meglumine–diatrizoate sodium	Ictal EEG in some patients, interictal in others	Localised Not localised	11 (25.6) 1 (6.7)	32 (74.4) 14 (93.3)	0	0	43 15
Theodore, 1990[109]	EEG focus	With and without contrast agent (agent not reported)	Ictal EEG	Localised Not localised	3 (11.5) 0	23 (88.5) 0	0	0	26 0

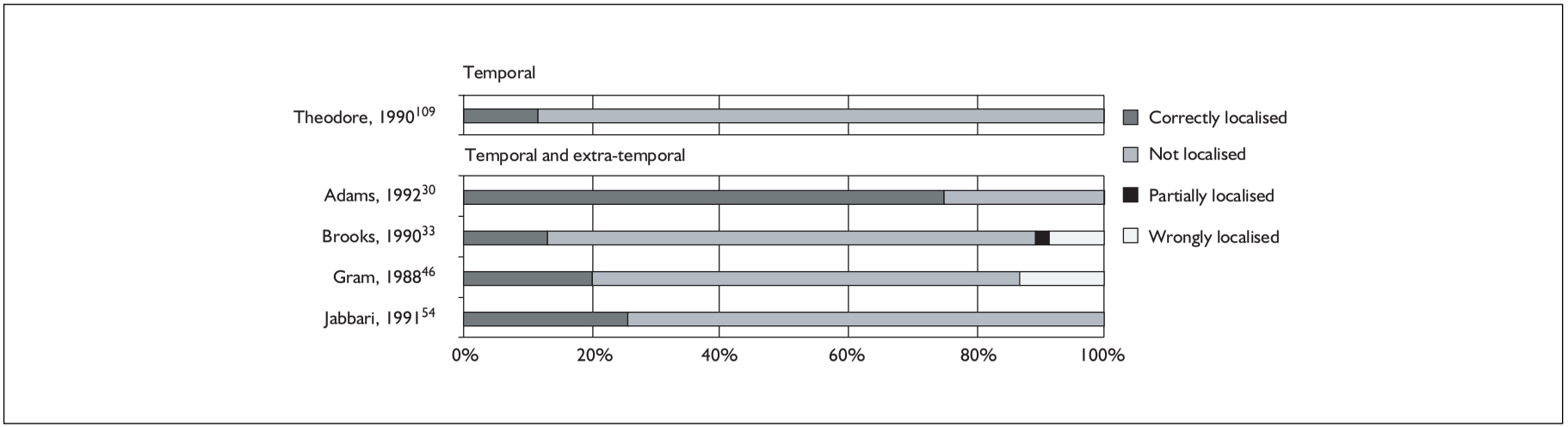

FIGURE 23 *CT: proportion of scans in each localisation category*

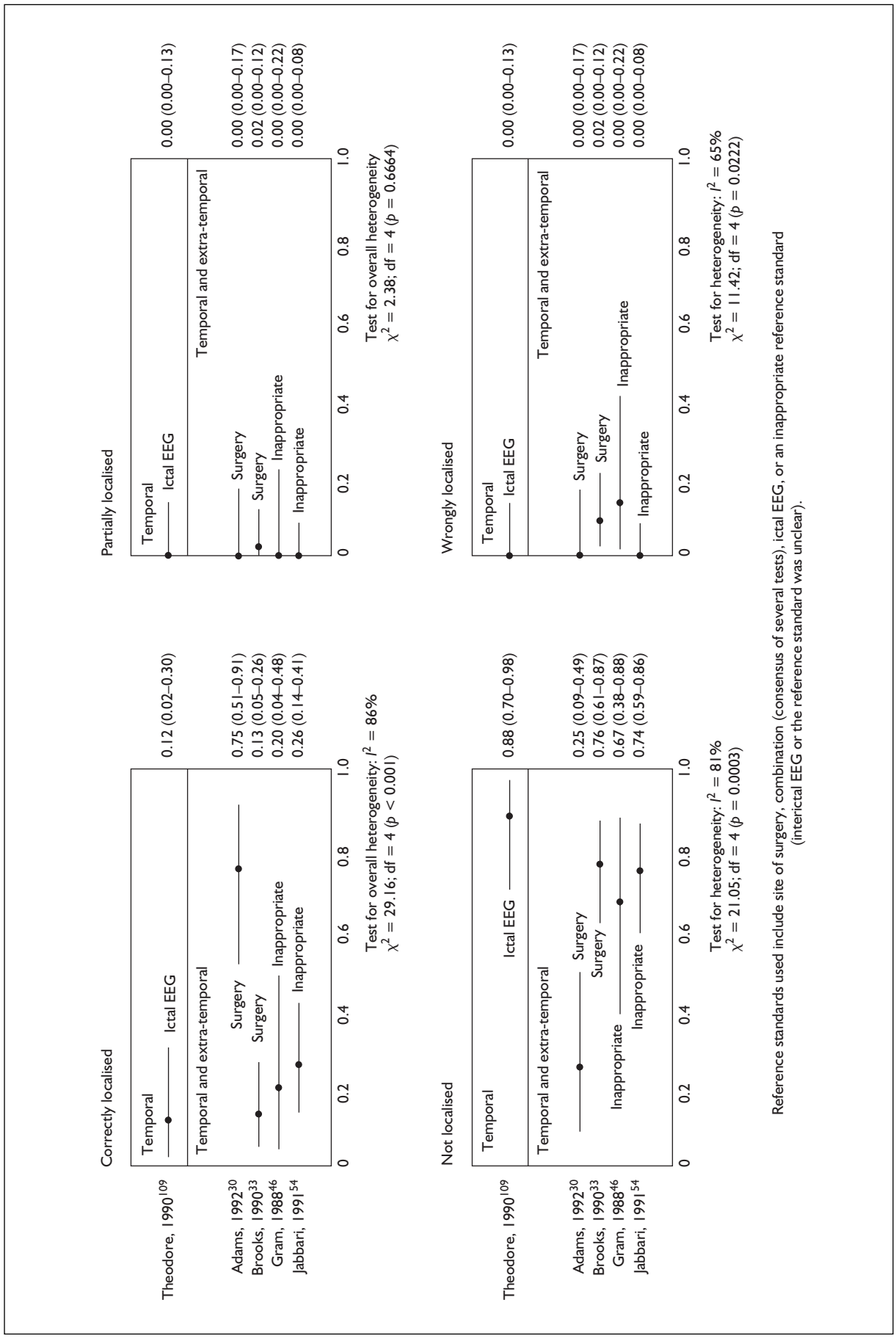

FIGURE 24 *CT: forest plots for each localisation category*

with only one patient having a partially localised scan (the scan identified part but not all of the seizure focus).[33] Only two studies reported incorrectly localising CT scans,[33,46] with 9 and 13% incorrectly localised. These two studies did not show any apparent differences from the other studies that could have explained why CT incorrectly localised the seizure focus in some patients in these studies but did not in other studies.

Other

Four studies evaluated other tests.[34,38,54,112] Three evaluated combinations of different tests: one a combination of MRI, CT and SPECT for the localisation of the epileptic focus,[54] the second a combination of MRS and MRI for the lateralisation of the epileptic focus in patients with TLE[34] and the third a combination of MRI and CT in the localisation of the epileptic focus in children with a recent history of infantile spasms.[38] The final study evaluated NIRS in the lateralisation of the epileptic focus.[112] Only the study evaluating the combination of MRI and CT looked at the association of the imaging tests evaluated with outcome following surgery. Only one study included an appropriate patient spectrum.[54] Three studies used EEG as the reference standard. This was ictal in one study,[112] ictal in some patients and interictal in others[54] and in one study it was unclear whether patients underwent only interictal EEG or whether they also received ictal EEG.[34] The fourth study used site of surgery as the reference standard.[38] Interictal EEG was considered an inappropriate reference standard. Partial verification bias did not appear to be a problem in any of these studies. The results of these studies are summarised in *Table 11*.

Two of the studies that looked at combinations of tests showed good accuracy. The combination of MRI, CT and SPECT correctly localised the seizure focus in 79% of patients. This study defined a localised scan as at least one focally abnormal scan.[54] The combination of MRS and MRI correctly localised a seizure focus in all patients.[34] This study was restricted to patients with temporal lobe epilepsy. The combination of MRI and CT, however, correctly localised only 17% of patients; the majority of scans were non-localising with 21% partially localised and no incorrectly localised scans.[38] NIRS localised a seizure focus in all patients, with 28 of the 29 scans being correctly localised and one incorrectly localised.[112]

Comparisons between different tests

Forty-one studies investigated the accuracy of more than one imaging technique on the same patients.

Table 12 summarises the number of studies that evaluated the different test combinations. *Tables 13–16* present the results for each imaging test evaluated from studies that reported more than one imaging evaluation. *Table 13* presents the proportion of correctly localised scans, *Table 14* the proportion of non-localised scans, *Table 15* the proportion of partially localised scans and *Table 16* the proportion of incorrectly localised scans. SPECT evaluations where the timing of the scan was not clear were omitted, because the results of the individual studies have shown that timing of injection for SPECT scans has an impact on the localisation ability of SPECT and so it is not sensible to compare the results of SPECT when timing is not known with other techniques. Where studies provided more than one evaluation for the same imaging technique, only the evaluation judged to be most similar to the evaluations from other studies was included.

Ictal SPECT compared with interictal SPECT, routine MRI and CT

All studies that compared ictal SPECT with interictal SPECT (n = 13), routine MRI (n = 6) and CT (n = 1) reported a greater proportion of correctly localised scans and fewer non-localised scans for ictal SPECT. The difference in the proportion of partially and incorrectly localised scans was less marked.

Ictal SPECT compared with PET (n = 7)

The proportion of scans in each of the localisation categories was similar in those studies evaluating both techniques.

Ictal SPECT compared with volumetric MRI (n = 1)

One study evaluated both ictal SPECT and volumetric MRI and reported similar rates of correctly localised scans (93 and 98%, respectively).[62] Ictal SPECT failed to localise 7% of scans, with no incorrectly localised scans, whereas volumetric MRI localised all scans, with 2% incorrectly localised.

Ictal SPECT compared with others (n = 1)

One study reported more correctly localised and fewer incorrectly localised scans using NIRS compared with ictal SPECT.[112] There were no non-localised NIRS scans, whereas 28% of scans were non-localised. There were no partially localised scans for either technique.

Interictal SPECT compared with combination SPECT (n = 1)

One study reported that a combination SPECT (ictal and interictal SPECT in all patients)

TABLE 11 *Results of studies that assessed other imaging evaluations for seizure focus localisation*

Study	Subgroup	Reference standard	Reference standard	Results: No. (%)						
				Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Combination: MRI, CT and SPECT										
Jabbari, 1991[54]	EEG focus	Ictal EEG in some patients, interictal in others	Localised	34 (79.1)	9 (20.9)	0	0	0	0	43
			Not localised	4 (26.7)	11 (73.3)	0			0	15
Combination: MRS and MRI										
Cendes, 1995[34]	EEG focus	Unclear EEG	Localised	55 (100)	0	0	0	0	0	55
			Not localised	0	0	0			0	0
			Multifocal	5 (100)	0	0			0	5
Combination: MRI and CT										
Chugani, 1993[38]	No subgroup	Site of surgery	Localised	4 (17)	14 (61)	2 (9)	2 (9)	1 (4)	0	23
			Not localised	0	0	0			0	0
NIRS										
Watanabe, 2002[112]	EEG focus	Ictal EEG	Localised	28 (96.6)	0	0	0	0	1 (3.4)	29
			Not localised	0	0	0			0	0

TABLE 12 *Number of studies that evaluated the different combinations of tests*

	Interictal SPECT	Combination SPECT	Routine MRI	Volumetric MRI	PET	SISCOM	MRS	CT	NIRS
Ictal SPECT	13	0	6	1	7	0	0	1	1
Interictal SPECT		1	10	1	4	0	0	2	0
Combination SPECT			2	0	0	2	0	1	0
Routine MRI				1	7	2	2	5	0
Volumetric MRI					4	0	5	0	0
PET						0	2	1	0
SISCOM							0	0	0
MRS								0	0
CT									0

TABLE 13 *Proportion of correctly localised scans for studies that evaluated more than one test*

Study	Proportion (95% CI) of correctly localised scans									
	Ictal SPECT	**Interictal SPECT**	**Combination SPECT**	**Routine MRI**	**Volumetric MRI**	**PET**	**SISCOM**	**MRS**	**CT**	**NIRS**
Markand, 1997[79]	86 (73 to 95)	61 (42 to 77)		65 (52 to 76)		80 (67 to 90)				
Kim, 2000[63]	70 (51 to 85)	70 (56 to 82)		61 (43 to 76)		87 (69 to 96)				
Doi, 1995[41]	84 (60 to 97)	52 (31 to 73)		65 (43 to 84)						
Adams, 1992[30]	100 (40 to 100)	47 (24 to 71)		93 (66 to 100)					75 (51 to 91)	
Runge, 1997[101]	81 (58 to 95)	57 (34 to 77)		50 (28 to 72)						
Newton, 1995[82]	70 (60 to 80)	46 (37 to 54)								
Newton, 1994[83]	100 (93 to 100)	49 (37 to 61)								
Rowe, 1989[97]	70 (51 to 85)	57 (37 to 75)								
Oliveira, 1999[92]	87 (66 to 97)	60 (48 to 72)								
Markand, 1994[80]	79 (69 to 87)	60 (49 to 70)								
Shen, 1990[104]	84 (66 to 95)	61 (42 to 77)								
Kilpatrick, 1997[62]	93 (66 to 100)	69 (49 to 85)			98 (89 to 100)	92 (73 to 99)				
Oommen, in progress[93]	93 (77 to 99)	80 (64 to 91)								
Hwang, 2001[53]	70 (60 to 79)			60 (50-69)		78 (69 to 85)				
Hong, 2002[52]	33 (17 to 54)					43 (24 to 63)				
Mastin, 1996[81]	52 (31 to 73)					60 (39 to 79)				
Watanabe, 2002[112]	66 (46 to 82)									98 (82 to 100)
Ho, 1995[51]	94 (81 to 99)					94 (81 to 99)				
Gram, 1988[46]		68 (51 to 81)		36 (13 to 65)					20 (4 to 48)	
Assadi, 1997[31]		42 (20 to 67)		38 (19 to 59)						
Hajek, 1991[49]		23 (8 to 45)		65 (45 to 81)						
Boundy, 1996[32]		50 (26 to 74)		72 (47 to 90)						
Lewis, 1998[77]		76 (58 to 89)		48 (31 to 66)						
Otsubo, 1995[95]		27 (16 to 41)	88 (64 to 99)							
Debets, 1997[40]		32 (13 to 57)				61 (39 to 80)				
Cross, 1996[39]				85 (62 to 97)				55 (32 to 77)		
Knowlton, 1997[65]				100 (86 to 100)	68 (46 to 85)	84 (64 to 95)		76 (53 to 92)		
Ryvlin, 1998[102]				65 (54 to 76)		58 (47 to 69)				

continued

TABLE 13 *Proportion of correctly localised scans for studies that evaluated more than one test (cont'd)*

Study	Proportion (95% CI) of correctly localised scans									
	Ictal SPECT	Interictal SPECT	Combination SPECT	Routine MRI	Volumetric MRI	PET	SISCOM	MRS	CT	NIRS
Sperling, 1987[106]				19 (7 to 37)		44 (25 to 65)				
Theodore, 1990[109]				27 (12 to 48)		65 (44 to 83)			12 (2 to 30)	
Kaminska, 2003[60]				79 (54 to 94)			42 (20 to 67)			
O'Brien, 1998[88]			19 (7 to 39)	58 (37 to 77)			54 (33 to 73)			
Brooks, 1990[33]				39 (26 to 54)					13 (5 to 26)	
Juhasz, 2003[58]				5 (0 to 24)		29 (11 to 52)				
Achten, 1998[29]					96 (78 to 100)	70 (47 to 87)		76 (53 to 92)		
Cendes, 1997[35]					97 (91 to 99)			98 (93 to 100)		
Li, 2000[78]					76 (53 to 92)			58 (37 to 78)		
Kuzniecky, 1998[68]					93 (78 to 99)			97 (83 to 100)		
Jabbari, 1991[54]			47 (31 to 62)	65 (49-79)					26 (14 to 41)	
Kaiboriboon, 2002[59]			39 (24 to 57)				63 (46 to 78)			

TABLE 14 *Proportion of non-localised scans for studies that evaluated more than one test*

Study	Proportion (95% CI) of non-localised scans									
	Ictal SPECT	Interictal SPECT	Combination SPECT	Routine MRI	Volumetric MRI	PET	SISCOM	MRS	CT	NIRS
Markand, 1997[79]	11 (4 to 25)	15 (5 to 32)		35 (24 to 48)		15 (6 to 27)				
Kim, 2000[63]	17 (6 to 35)	21 (11 to 34)		37 (22 to 54)		0 (0 to 12)				
Doi, 1995[41]	5 (0 to 26)	26 (10 to 48)		26 (10 to 48)						
Adams, 1992[30]	0 (0 to 60)	16 (3 to 40)		7 (0 to 34)					25 (9 to 49)	
Runge, 1997[101]	0 (0 to 16)	26 (10 to 48)		27 (11 to 50)						
Newton, 1995[82]	26 (17 to 37)	46 (37 to 54)								
Newton, 1994[83]	0 (0 to 7)	38 (27 to 50)								
Rowe, 1989[97]	23 (10 to 42)	30 (15 to 49)								
Oliveira, 1999[92]	0 (0 to 15)	4 (1 to 12)								
Markand, 1994[80]	13 (7 to 23)	34 (25 to 45)								
Shen, 1990[104]	3 (0 to 17)	24 (11 to 42)								

continued

TABLE 14 *Proportion of non-localised scans for studies that evaluated more than one test (cont'd)*

Study	Proportion (95% CI) of non-localised scans									
	Ictal SPECT	**Interictal SPECT**	**Combination SPECT**	**Routine MRI**	**Volumetric MRI**	**PET**	**SISCOM**	**MRS**	**CT**	**NIRS**
Kilpatrick, 1997[62]	7 (0 to 34)	17 (6 to 36)			0 (0 to 7)	8 (1 to 27)				
Oommen, in progress[93]	0 (0 to 12)	10 (3 to 24)								
Hwang, 2001[53]	8 (3 to 15)			31 (23 to 40)		10 (5 to 17)				
Hong, 2002[52]	19 (6 to 38)					18 (6 to 37)				
Mastin, 1996[81]	4 (0 to 22)					28 (12 to 49)				
Watanabe, 2002[112]	28 (13 to 47)									0 (0 to 10)
Ho, 1995[51]	0 (0 to 10)					6 (1 to 19)				
Gram, 1988[46]		27 (8 to 55)		43 (18 to 71)					67 (38 to 88)	
Assadi, 1997[31]		26 (9 to 51)		54 (33 to 74)						
Hajek, 1991[49]		36 (17 to 59)		35 (19 to 55)						
Boundy, 1996[32]		28 (10 to 53)		28 (10 to 53)						
Lewis, 1998[77]		3 (0 to 16)		39 (23 to 58)						
Otsubo, 1995[95]		16 (8 to 29)	12 (1 to 36)							
Debets, 1997[40]		5 (0 to 26)				0 (0 to 15)				
Cross, 1996[39]				15 (3 to 38)				45 (23 to 68)		
Knowlton, 1997[65]				0 (0 to 14)	32 (15 to 54)	12 (3 to 31)		19 (5 to 42)		
Ryvlin, 1998[102]				35 (24 to 46)		22 (14 to 33)				
Sperling, 1986[106]				74 (55 to 88)		56 (35 to 75)				
Theodore, 1990[109]				69 (48 to 86)		15 (4 to 35)			88 (70 to 98)	
Kaminska, 2003[60]				5 (0 to 26)			5 (0-26)			
O'Brien, 1998[88]			58 (37 to 77)	31 (14 to 52)			19 (7-39)			
Brooks, 1990[33]				59 (44 to 72)					76 (61 to 87)	
Juhasz, 2003[58]				67 (43 to 85)		5 (0 to 24)				
Achten, 1998[29]					0 (0 to 15)	22 (7 to 44)		0 (0 to 16)		
Cendes, 1997[35]					0 (0 to 4)			0 (0 to 4)		
Li, 2000[78]					10 (1 to 30)			38 (19 to 59)		
Kuzniecky, 1998[68]					0 (0 to 12)			0 (0 to 12)		
Jabbari, 1991[54]			53 (38 to 69)	35 (21 to 51)					74 (59 to 86)	
Kaiboriboon, 2002[59]			53 (36 to 69)				29 (15 to 46)			

TABLE 15 *Proportion of partially localised scans for studies that evaluated more than one test*

Study	Proportion (95% CI) of partially localised scans										
	Ictal SPECT	**Interictal SPECT**	**Combination SPECT**	**Routine MRI**	**Volumetric MRI**	**T2-relaxometry MRI**	**PET**	**SISCOM**	**MRS**	**CT**	**NIRS**
Markand, 1997[79]	0 (0 to 8)	0 (0 to 7)		0 (0 to 5)			5 (1 to 15)				
Kim, 2000[63]	0 (0 to 12)	0 (0 to 18)		0 (0 to 9)			0 (0 to 12)				
Doi, 1995[41]	11 (1 to 33)	17 (5 to 39)		4 (0 to 22)							
Adams, 1992[30]	0 (0 to 60)	21 (6 to 46)		0 (0 to 23)						0 (0 to 17)	
Runge, 1997[101]	19 (5 to 42)	17 (5 to 39)		23 (8 to 45)							
Newton, 1995[82]	0 (0 to 6)	0 (0 to 3)									
Newton, 1994[83]	0 (0 to 7)	0 (0 to 5)									
Rowe, 1989[97]	3 (0 to 17	3 (0 to 17)									
Oliveira, 1999[92]	4 (0 to 22)	0 (0 to 10)									
Markand, 1994[80]	4 (1 to 10)	0 (0 to 4)									
Shen, 1990[104]	13 (4 to 30)	12 (3 to 28)									
Kilpatrick, 1997[62]	0 (0 to 23)	3 (0 to 18)			0 (0 to 7)		0 (0 to 14)				
Oommen, in progress[93]	0 (0 to 12)	0 (0 to 9)									
Hwang, 2001[53]	0 (0 to 4)			0 (0 to 3)		0 (0 to 4)					
Hong, 2002[52]	22 (9 to 42)					14 (4 to 33)					
Mastin, 1996[31]	0 (0 to 15)	0 (0 to 11)					0 (0 to 14)				
Watanabe, 2002[112]	0 (0 to 12)										0 (0 to 12)
Ho, 1995[51]	0 (0 to 10)						0 (0 to 10)				
Gram, 1988[46]		0 (0 to 22)		0 (0 to 23)						0 (0 to 22)	
Assadi, 1997[31]		16 (3 to 40)		4 (0 to 21)							
Hajek, 1991[49]		19 (7 to 37)		0 (0 to 11)							
Boundy, 1996[32]		0 (0 to 19)		0 (0 to 19)							
Lewis, 1998[77]		0 (0 to 11)		0 (0 to 11)							
Otsubo, 1995[95]		45 (32 to 59)	0 (0 to 20)								
Debets, 1997[40]		32 (13 to 57)					39 (20 to 61)				
Cross, 1996[39]				0 (0 to 17)					0 (0 to 17)		
Knowlton, 1997[65]				0 (0 to 14)	0 (0 to 14)		0 (0 to 14)		0 (0 to 16)		
Ryvlin, 1998[102]				0 (0 to 4)			14 (7 to 23)				
Sperling, 1986[106]				3 (0 to 17)			0 (0 to 13)				

continued

TABLE 15 *Proportion of partially localised scans for studies that evaluated more than one test (cont'd)*

Study	Proportion (95% CI) of partially localised scans										
	Ictal SPECT	**Interictal SPECT**	**Combination SPECT**	**Routine MRI**	**Volumetric MRI**	**T2-relaxometry MRI**	**PET**	**SISCOM**	**MRS**	**CT**	**NIRS**
Theodore, 1990[109]				0 (0 to 13)			19 (7 to 39)			0 (0 to 13)	
Kaminska, 2003[60]				16 (3 to 40)				42 (20 to 67)			
O'Brien, 1998[88]			12 (2 to 30)	12 (2 to 30)				12 (2 to 30)			
Brooks, 1990[33]				0 (0 to 7)						2 (0 to 12)	
Juhasz, 2003[58]				19 (5 to 42)			62 (38 to 82)				
Achten, 1998[29]					4 (0 to 22)		9 (1 to 28)		24 (8 to 47)		
Cendes, 1997[35]					0 (0 to 4)				0 (0 to 4)		
Li, 2000[78]					0 (0 to 16)				0 (0 to 14)		
Kuzniecky, 1998[68]					0 (0 to 12)				0 (0 to 12)		
Jabbari, 1991[54]			0 (0 to 8)	0 (0 to 8)						0 (0 to 8)	
Kaiboriboon, 2002[59]			3 (0 to 14)					0 (0 to 9)			

TABLE 16 *Proportion of incorrectly localised scans for studies that evaluated more than one test*

Study	Proportion (95% CI) of incorrectly localised scans										
	Ictal SPECT	**Interictal SPECT**	**Combination SPECT**	**Routine MRI**	**Volumetric MRI**	**T2-relaxometry MRI**	**PET**	**SISCOM**	**MRS**	**CT**	**NIRS**
Markand, 1997[79]	2 (0 to 12)	9 (3 to 21)		0 (0 to 5)			0 (0 to 6)				
Kim, 2000[63]	13 (4 to 31)	5 (0 to 26)		3 (0 to 14)			13 (4 to 31)				
Doi, 1995[41]	0 (0 to 18)	4 (0 to 22)		4 (0 to 22)							
Adams, 1992[30]	0 (0 to 60)	16 (3 to 40)		0 (0 to 23)						0 (0 to 17)	
Runge, 1997[101]	0 (0 to 16)	0 (0 to 15)		0 (0 to 15)							
Newton, 1995[82]	3 (1 to 10)	9 (5 to 14)									
Newton, 1994[83]	0 (0 to 7)	12 (6 to 22)									
Rowe, 1989[97]	3 (0 to 17)	10 (2 to 27)									
Oliveira, 1999[92]	9 (1 to 28)	32 (22 to 45)									
Markand, 1994[80]	4 (1 to 10)	6 (2 to 13)									

continued

TABLE 16 *Proportion of incorrectly localised scans for studies that evaluated more than one test (cont'd)*

Study	Proportion (95% CI) of incorrectly localised scans										
	Ictal SPECT	**Interictal SPECT**	**Combination SPECT**	**Routine MRI**	**Volumetric MRI**	**T2-relaxometry MRI**	**PET**	**SISCOM**	**MRS**	**CT**	**NIRS**
Shen, 1990[104]	0 (0 to 11)	3 (0 to 16)									
Kilpatrick, 1997[62]	0 (0 to 23)	10 (2 to 27)			2 (0 to 11)		0 (0 to 14)				
Oommen, in progress[93]	7 (1 to 23)	10 (3 to 24)									
Hwang, 2001[53]	22 (14 to 32)			9 (5 to 16)		13 (7 to 21)					
Hong, 2002[52]	26 (11 to 46)					25 (11 to 45)					
Mastin, 1996[81]	43 (23 to 66)	24 (11 to 42)					12 (3-31)				
Watanabe, 2002[112]	7 (1 to 23)										3 (0 to 18)
Ho, 1995[51]	6 (1 to 19)						0 (0 to 10)				
Gram, 1988[46]		20 (4 to 48)		21 (5 to 51)						13 (2 to 40)	
Assadi, 1997[31]		16 (3 to 40)		4 (0 to 21)							
Hajek, 1991[49]		10 (2 to 26)		0 (0 to 11)							
Boundy, 1996[32]		22 (6 to 48)		0 (0 to 19)							
Lewis, 1998[77]		21 (9 to 39)		12 (3 to 28)							
Otsubo, 1995[95]		11 (4 to 22)	0 (0 to 20)								
Debets, 1997[40]		32 (13 to 57)					0 (0 to 15)				
Cross, 1996[39]				0 (0 to 17)					0 (0 to 17)		
Knowlton, 1997[65]				0 (0 to 14)	0 (0 to 14)		4 (0 to 20)		5 (0 to 24)		
Ryvlin, 1998[102]				0 (0 to 4)			6 (2 to 14)				
Sperling, 1986[106]				3 (0 to 17)			0 (0 to 13)				
Theodore, 1990[109]				4 (0 to 20)			0 (0 to 13)			0 (0 to 13)	
Kaminska, 2003[60]				0 (0 to 18)				11 (1 to 33)			
O'Brien, 1998[88]			12 (2 to 30)	0 (0 to 13)				15 (4 to 35)			
Brooks, 1990[33]				2 (0 to 10)						9 (2 to 21)	
Juhasz, 2003[58]				10 (1 to 30)			5 (0 to 24)				
Achten, 1998[29]					0 (0 to 15)		0 (0 to 15)		0 (0 to 16)		
Cendes, 1997[35]					3 (1 to 9)				2 (0 to 7)		
Li, 2000[78]					14 (3 to 36)				4 (0 to 21)		
Kuzniecky, 1998[68]					7 (1 to 22)				3 (0 to 17)		
Jabbari, 1991[54]			0 (0 to 8)	0 (0 to 8)						0 (0 to 8)	
Kaiboriboon, 2002[59]			5 (1 to 18)					8 (2 to 21)			

correctly localised more scans than interictal SPECT alone.[95] The combination SPECT also had fewer partially and incorrectly localised scans and a similar proportion of non-localised scans compared to interictal SPECT.

Interictal SPECT compared with routine MRI (n = 10)

Five studies reported that interictal SPECT correctly localised a greater proportion of scans than routine MRI[31,46,63,77,101] and the remaining five correctly localised fewer.[30,32,41,49,79] Interictal SPECT tended to show a lower proportion of non-localised scans, with five studies reporting fewer non-localised scans for interictal SPECT,[31,46,63,77,79] four reporting similar numbers of localised scans for the two techniques[32,41,49,101] and one reporting a higher proportion of non-localised scans than MRI.[30] There were a greater proportion of partially and incorrectly localised scans for interictal SPECT than for routine MRI.

Interictal SPECT compared with volumetric MRI (n = 1)

One study reported that interictal SPECT showed a lower proportion of correctly localised scans and a greater proportion of non-localised, partially localised and incorrectly localised scans compared with volumetric MRI.[62]

Interictal SPECT compared with PET (n = 4)

All four studies reported more correctly localised PET scans than interictal SPECT scans.[40,62,63,79] Three studies also reported lower rates of non-localised PET scans and the fourth reported similar rates of non-localised scans for the two techniques.[79] Three studies reported lower rates of incorrectly localised PET scans and one a higher rate for PET.[63] Three studies reported on partially localised scans, one had a higher rate for PET,[79] one had a higher rate for interictal SPECT[62] and the other reported similar high rates for both techniques.[40]

Interictal SPECT compared with CT (n = 2)

These two studies showed conflicting results, with one reporting much higher rates of localised scans for CT[30] and the other for interictal SPECT.[46] Both reported higher rates of non-localised scans for CT and higher rates of incorrectly localised scans for interictal SPECT.

Combination SPECT compared with routine MRI (n = 2)

Both studies reported a higher proportion of correctly localised scans and a lower proportion of non-localised scans for routine MRI.[54,88] One study also reported fewer incorrectly localised scans for MRI and the same proportion of partially localised scans[88] and the other reported no incorrectly or partially localised scans for either technique.[54]

Combination SPECT compared with SISCOM (n = 2)

Both studies reported higher rates of correctly localised scans and lower rates of non-localised scans for SISCOM than for combination SPECT.[59,88] Both studies reported similar rates of incorrectly localised scans for both techniques, although these proportions were slightly higher for SISCOM. The proportion of partially localised scans was similar.

Routine MRI compared with volumetric MRI (n = 1)

This study reported a higher proportion of correctly localised scans and fewer non-localised for routine MRI.[65] There were no partially or incorrectly localised scans for either technique.

Routine MRI compared with PET (n = 7)

Five studies reported that PET correctly localised a greater proportion of scans than MRI and had fewer non-localising scans.[53,63,79,106,109] Two reported that MRI correctly localised a greater proportion of scans,[65,102] with one of these also reporting that MRI had fewer non-localising scans[65] and the other fewer incorrectly localised scans.[102] Neither technique appeared consistently better than the other in any of the localisation categories.

Routine MRI compared with SISCOM (n = 2)

Both studies reported higher proportions of correctly localised scans for routine MRI.[60,88] The proportion of non-localised scans was the same for both techniques in one study[60] and higher for routine MRI in the other.[88] The proportion of partially localised scans was higher for SISCOM in one study[60] and was the same for both techniques in the other.[88] Both studies reported no incorrectly localised scans for routine MRI but around 15% incorrectly localised for SISCOM.

Routine MRI compared with MRS (n = 2)

One study reported 100% correctly localised scans for MRI but only 76% for MRS.[65] The other study reported 85% correctly localising and 15% non-localising for MRI, compared with 55% correctly localising and 45% non-localising for MRS.

Routine MRI compared with CT (n = 5)

All five studies suggested that MRI was a more accurate test than CT in the localisation of the seizure focus.[30,33,46,54,109] All reported that MRI correctly localised a greater proportion of scans and failed to localise fewer scans than CT. Only one study reported any partially localised scans and this was for CT.[33] The proportion of incorrectly localised scans varied: two studies reported no incorrectly localised scans for both techniques,[30,54] two reported more incorrectly localised scans for MRI than for CT[46,109] and one reported more incorrectly localised scans for CT.[33]

Volumetric MRI compared with PET (n = 4)

Neither technique appeared to be superior to the other. Some studies reported that volumetric MRI was better than PET and others that PET was better.[29,58,62,65]

Volumetric MRI compared with MRS (n = 5)

Neither technique appeared to be superior to the other,[29,35,65,68,78] with some studies reporting volumetric MRI as being better than MRS and others MRS better than MRI. One study reported very similar results for both techniques in all localisation categories.[35]

PET compared with MRS (n = 2)

Neither technique appeared to be superior to the other, with one study reporting a higher proportion of correctly localised scans for PET[29] and the other for MRS.[65]

PET compared with CT (n = 1)

One study reported a greater proportion of correctly and partially localised scans and fewer non-localised for PET than for CT.[109] There were no incorrectly localised scans for either technique.

Association of seizure focus localisation with outcome following surgery

A total of 32 studies (83 evaluations) provided data on the association of a localised scan with outcome following surgery. These studies reported data on the number of correctly localised, non-localised, partially localised and incorrectly localised scans separately for patients with a good and bad outcome following surgery. We used these data to calculate the RR of having a good outcome in patients with a localised scan (correctly localised and partially localised combined) compared with those with a non-localised scan (non-localised and incorrectly localised combined). The results from these studies are summarised in *Table 17*.

Ten studies only reported results for patients with a good outcome following surgery[32,55,59,61,64,75,96,103,108,113] and one only reported results for patients with a bad outcome following surgery.[30] For these 11 studies, it was not possible to calculate an RR and these were not included in the analysis. A number of other studies reported one or more evaluations for which it was not possible to calculate an RR, but other evaluations that were included.[29,38,40,62] None of the studies included in this section included an appropriate patient spectrum. Twenty-four studies defined a good outcome following surgery as Engel class I or II and the remaining eight studies defined a good outcome as being seizure free following surgery.[30,44,47,56,59,61,75,113] The imaging techniques evaluated by these studies are summarised in *Table 18*.

A forest plot showing the RRs for each of the individual studies is presented in *Figure 25*. Owing to the heterogeneity between studies, statistical pooling was not performed. The majority (24/33) of evaluations suggested that patients with a correctly or partially localised scan had a better outcome following surgery than those with an incorrectly localised or non-localised scan. However, only three studies showed a significant association between having a localised scan and outcome following surgery, two evaluating routine MRI[53,63] and the other SISCOM.[88] Both found that patients with a localised scan had a significantly better outcome following surgery than those with a non-localised or incorrectly localised scan.

One study of MRI reported an RR of 2.74 (95% CI: 1.32 to 5.67).[62] The other only just reached statistical significance with a pooled RR of 1.28 (95% CI: 1.00 to 1.63).[53] These studies did not appear to differ significantly from other studies of MRI: one did not use a contrast agent,[62] the other used a contrast agent in only selected individuals[53] and both defined a good outcome following surgery as Engel class I or II. The sample size for one study was 38[62] and for the other 117,[53] which are two of the highest for the MRI studies, suggesting that the other studies may have lacked power to detect a significant association. The RR for the evaluation of SISCOM only just reached statistical significance with a pooled RR of 2.12 (95% CI: 1.01 to 4.44). There were no significant differences between this study and other SISCOM studies that may have explained the significant association in this study.

TABLE 17 *Results of studies that looked at the association of scans with surgical outcome*

Study	Subgroup	Contrast agent/tracer	Definition of a good outcome	Index test and site of surgery No. (%)							
				Outcome following surgery	Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Combination of ictal and interictal SPECT											
Kaiboriboon, 2002[59]	No subgroup	ECD	Seizure free	Good	8 (38.1)	12 (57.1)	0	0	0	1 (4.8)	21
				Poor	0	0	0	0	0	0	0
O'Brien, 1998[88]	No subgroup	HMPAO or ECD	Engel I and II	Good	5 (25)	10 (50)	1 (5)	1 (5)	0	3 (15)	20
				Poor	0	5 (83.3)	0	1 (16.7)	0	0	6
	EEG focus			Good	5 (27.8)	10 (55.6)	0	1 (5.6)	0	2 (11.1)	18
				Poor	0	2 (66.7)	0	1 (33.3)	0	0	3
	No EEG focus			Good	0	0	1 (50)	0	0	1 (50)	2
				Poor	0	3 (100)	0	0	0	0	3
Ictal SPECT											
Kang, 1997[61]	No subgroup	ECD	Seizure free	Good	22 (95.7)	1 (4.3)	0	0	0	0	23
				Bad	0	0					0
Weil, 2001[113]	No subgroup	ECD	Seizure free	Good	24 (80)	2 (6.7)	0	0	1 (3.3)	3 (10)	30
				Poor	0	0	0	0	0	0	0
Shen, 1990[104]	EEG focus	HIPDM	Engel I and II	Good	22 (81.5)	1 (3.7)	1 (3.7)	3 (11.1)	0	0	27
				Poor	3 (100)	0	0	0	0	0	3
Adams, 1992[30]	EEG focus	HMPAO	Seizure free	Good	0	0	0	0	0	0	0
				Poor	4 (100)	0	0	0	0	0	4
Lee, 2000[75]	No subgroup	HMPAO	Seizure free	Good	61 (89.7)	2 (3.0)	0	0	0	5 (7.3)	68
				Bad	0	0					0
Lee, 2002[73]	No structural abnormality	HMPAO: first scan	Engel I and II	Good	1 (10)	7 (70)	1 (10)	0	0	1 (10)	10
				Poor	2 (28.6)	4 (57.1)	0	1 (14.3)	0	0	7
		HMPAO: second scan		Good	2 (20)	2 (20)	1 (10)	1 (10)	0	4 (40)	10
				Poor	2 (28.6)	2 (28.6)	0	1 (14.3)	0	2 (28.6)	7
		HMPAO: first + second scans combined		Good	2 (20)	2 (20)	1 (10)	2 (20)	0	3 (30)	10
				Poor	2 (25.0)	2 (25.0)	0	3 (37.5)	0	1 (12.5)	8
Kilpatrick, 1997[62]	EEG focus	Not reported	Engel I and II	Good	12 (92.3)	1 (7.7)	0	0	0	0	13
				Poor	1 (100)	0	0	0	0	0	2

continued

TABLE 17 *Results of studies that looked at the association of scans with surgical outcome (cont'd)*

Study	Subgroup	Contrast agent/tracer	Definition of a good outcome	Index test and site of surgery No. (%)							
				Outcome following surgery	Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Interictal SPECT											
Shen, 1990[104]	EEG focus	HIPDM	Engel I and II	Good	18 (64.3)	8 (28.6)	0	1 (3.6)	0	1 (3.6)	28
				Poor	0	0	0	3 (100)	0	0	3
Tatum, 1995[108]	No subgroup	HMPAO	Engel I and II	Good	7 (50)	4 (28.6)	0	2 (14.3)	0	1 (7.1)	14
				Poor	0	0	0	0	0	0	0
Grunwald, 1991[47]	EEG focus	HMPAO	Seizure free	Good	19 (67.9)	5 (17.9)	0	2 (7.1)	0	2 (7.1)	28
				Poor	8 (66.7)	2 (16.7)	0	1 (8.3)	0	1 (8.3)	12
Hajek, 1991[49]	EEG focus	HMPAO	Engel I and II	Good	8 (29.6)	12 (44.4)	0	5 (18.5)	0	2 (7.4)	22
				Poor	1 (25.0)	1 (25.0)	0	1 (25.0)	0	1 (25.0)	4
Boundy, 1996[32]	No structural abnormality	HMPAO	Engel I and II	Good	7 (58.3)	4 (33.3)	0	0	0	1 (8.3)	12
				Poor	0	0	0	0	0	0	0
		IDEX		Good	11 (91.7)	1 (8.3)	0	0	0	0	12
				Poor	0	0	0	0	0	0	0
Debets, 1997[40]	No subgroup	IMZ	Engel I and II	Good	5 (31.3)	0	0	6 (37.5)	0	5 (31.3)	16
				Poor	1 (33.3)	1 (33.3)	0	0	0	1 (33.3)	3
	EEG focus			Good	5 (33.3)	0	0	5 (33.3)	0	5 (33.3)	15
				Poor	1 (33.3)	1 (33.3)	0	0	0	1 (33.3)	3
Seki, 1998[103]	No subgroup	HMPAO or ECD	Engel I and II	Good	12 (46.2)	6 (23.1)	0	6 (23.1)	0	2 (7.7)	26
				Poor	0	0	0	0	0	0	0
	EEG focus			Good	11 (47.8)	5 (21.7)	0	5 (21.7)	0	2 (8.7)	23
				Poor	0	0	0	0	0	0	0
	No EEG focus			Good	1 (33.3)	1 (33.3)	0	1 (33.3)	0	0	3
				Poor	0	0	0	0	0	0	0
Kilpatrick, 1997[62]	EEG focus	Not reported	Engel I and II	Good	18 (66.7)	5 (18.5)	0	1 (3.7)	0	3 (11.1)	27
				Poor	2 (100)	0	0	0	0	0	2
MRI: routine											
Boundy, 1996[32]	No structural abnormality	N/A	Engel I and II	Good	9 (75)	3 (25)	0	0		0	12
				Poor	0	0	0	0		0	0
Cross, 1996[39]	No subgroup	Routine	Engel I and II	Good	8 (89)	1 (11)	0	0	0	0	9
				Poor	1 (100)	0	0	0	0	0	1

continued

TABLE 17 *Results of studies that looked at the association of scans with surgical outcome (cont'd)*

Study	Subgroup	Contrast agent/tracer	Definition of a good outcome	Index test and site of surgery No. (%)							
				Outcome following surgery	Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Hwang, 2001[53]	No subgroup	Routine	Engel I and II	Good	57 (66)	22 (25)	0	0	0	8 (9)	87
				Poor	13 (43)	14 (47)	0	0	0	3 (10)	30
Gilliam, 2000[44]	No structural abnormality and EEG focus	N/A	Seizure free	Good	36 (81.8)	8 (18.2)	0	0		0	44
				Poor	16 (69.6)	7 (30.4)	0	0		0	23
Hajek, 1991[49]	EEG focus	N/A	Engel I and II	Good	18 (66.7)	9 (33.3)	0	0		0	27
				Poor	2 (50)	2 (50)	0	0		0	4
Jack, 1994[55]	No structural abnormality	N/A	Engel I and II	Good	37 (86.0)	6 (14.0)	0	0		0	43
				Poor	0	0	0	0		0	0
Juhasz, 2003[58]	EEG focus	N/A	Engel I and II	Good	1 (7.1)	8 (57.1)	2 (14.3)	1 (7.1)		2 (14.3)	14
				Poor	0	4 (100)	0	0		0	4
Kaminska, 2003[60]	No subgroup	N/A	Engel I and II	Good	10 (100)	0	0	0		0	10
				Poor	5 (55.6)	1 (11.1)	1 (11.1)	2 (22.2)		0	9
	EEG focus			Good	7 (100)	0	0	0		0	7
				Poor	5 (62.5)	1 (12.5)	1 (12.5)	1 (12.5)		0	8
	No EEG focus			Good	3 (100)	0	0	0		0	3
				Poor	0	0	0	1 (100)		0	1
Kim, 2000[63]	No subgroup	N/A	Engel I and II	Good	21 (80.7)	4 (15.4)	0	0		1 (3.8)	26
				Poor	2 (16.7)	10 (83.3)	0	0		0	12
Kim, 2002[64]	No subgroup	N/A	Engel I and II	Good	12 (42.9)	14 (50)	0	1 (3.6)		1 (3.6)	28
				Poor	0	0	0	0		0	0
Kuzniecky, 1993[70]	EEG focus	Gadolinium enhanced in 6 patients	Engel I and II	Good	19 (82.6)	4 (17.4)	0	0		0	23
				Poor	6 (54.5)	5 (45.5)	0	0		0	11
O'Brien, 1998[88]	No subgroup	Routine and volumetric	Engel I and II	Good	14 (70)	5 (25)	0	1 (5)		0	20
				Poor	1 (16.7)	3 (50)	0	2 (33.3)		0	6
	EEG focus			Good	12 (66.7)	5 (27.8)	0	1 (5.6)		0	18
				Poor	0	2 (66.7)	0	1 (33.3)		0	3
	No EEG focus			Good	2 (100)	0	0	0		0	2
				Poor	1 (33.3)	1 (33.3)	0	1 (33.3)		0	3
Theodore, 1990[109]	EEG focus	N/A	Engel I and II	Good	6 (27.3)	15 (68.2)	0	0		1 (4.5)	22
				Poor	1 (25)	3 (75)	0	0		0	4

continued

TABLE 17 *Results of studies that looked at the association of scans with surgical outcome (cont'd)*

Study	Subgroup	Contrast agent/tracer	Definition of a good outcome	Index test and site of surgery No. (%)							
				Outcome following surgery	Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
MRI: volumetric											
Achten, 1998[29]	No structural abnormality	N/A	Engel I and II	Good	10 (90.9)	0	0	1 (9.1)		0	11
				Poor	2 (100)	0	0	0		0	2
Jack, 1994[55]	No structural abnormality	Volumetric (hippocampus)	Engel I and II	Good	37 (86.0)	6 (14.0)	0	0	0	0	43
				Poor	0	0	0	0		0	0
Jack, 1990[56]	No structural abnormality and EEG focus	N/A	Seizure free	Good	28 (75.7)	9 (24.3)	0	0		0	37
				Poor	3 (75)	1 (25)	0	0		0	4
Kilpatrick, 1997[62]	EEG focus	N/A	Engel I and II	Good	46 (97.9)	0	0	0		1 (2.1)	47
				Poor	3 (100)	0	0	0		0	3
Li, 2000[78]	EEG focus	N/A	Engel I and II	Good	12 (92.3)	0	0	0		1 (7.7)	13
				Poor	4 (50)	2 (25)	0	0		2 (25)	8
Seki, 1998[103]	No subgroup	Volumetric and T2-relaxometry in patients with TLE	Engel I and II	Good	29 (87.9)	1 (3.0)	0	0		3 (9.1)	33
				Poor	0	0	0	0		0	0
	EEG focus			Good	26 (86.7)	1 (3.3)	0	0		3 (10.0)	30
				Poor	0	0	0	0		0	0
	No EEG focus			Good	3 (100)	0	0	0		0	3
				Poor	0	0	0	0		0	0
PET: 22 scanned interictally, 2 scanned ictally											
Tatlidil, 2000[107]	No subgroup	[^{15}O]water	Engel I and II	Good	18 (81.8)	4 (18.2)	0	0	0	0	22
				Poor	1 (50)	1 (50)	0	0	0	0	2
PET: interictal											
Achten, 1998[29]	No structural abnormality	FDG	Engel I and II	Good	9 (81.8)	1 (9.1)	0	1 (9.1)	0	0	11
				Poor	2 (100)	0	0	0	0	0	2
Chugani, 1993[38]	No subgroup	FDG	Engel I and II	Good	16 (89)	0	0	2 (11)	0	0	18
				Poor	1 (20)	0	0	3 (60)	1 (20)	0	5
Juhasz, 2003[58]	EEG focus	AMT	Engel I and II	Good	3 (21.4)	6 (42.9)	5 (35.7)	0	0	0	14
				Poor	1 (25.0)	1 (25.0)	2 (50.0)	0	0	0	4
		FDG		Good	3 (21.4)	1 (7.1)	4 (28.7)	3 (21.4)	2 (14.3)	1 (7.1)	14
				Poor	3 (75)	0	1 (25)	0	0	0	4

continued

TABLE 17 *Results of studies that looked at the association of scans with surgical outcome (cont'd)*

Study	Subgroup	Contrast agent/tracer	Definition of a good outcome	Index test and site of surgery No. (%)							
				Outcome following surgery	Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
Kim, 2002[64]	No subgroup	FDG (SPM analysis)	Engel I and II	Good	19 (70.4)	0	0	4 (14.8)	0	4 (14.8)	27
				Poor	0	0	0	0	0	0	0
		FDG (visual assessment)		Good	16 (55.2)	9 (31.0)	0	4 (13.8)	0	0	29
				Poor	0	0	0	0	0	0	0
O'Brien, 2001[86]	No structural abnormality	FDG	Engel I and II	Good	20 (90.9)	2 (9.1)	0	0	0	0	22
				Poor	1 (50)	1 (50)	0	0	0	0	2
Park, 2001[96]	Structural abnormality	FDG	Engel I and II	Good	28 (84.9)	3 (9.1)	0	0	0	2 (6.0)	33
				Poor	0	0	0	0	0	0	0
Theodore, 1990[109]	EEG focus	FDG	Engel I and II	Good	14 (63.6)	4 (18.2)	0	4 (18.2)	0	0	22
				Poor	3 (75)	0	1 (25)	0	0	0	4
PET: unclear timing											
Debets, 1997[40]	No subgroup	FDG	Engel I and II	Good	12 (60.0)	0	0	8 (40.0)	0	0	20
				Poor	2 (66.7)	0	0	1 (33.3)	0	0	3
	EEG focus			Good	11 (57.9)	0	0	8 (42.1)	0	0	19
				Poor	2 (66.7)	0	0	1 (33.3)	0	0	3
	No subgroup	FMZ		Good	18 (90)	0	0	2 (10)	0	0	20
				Poor	2 (66.7)	0	1 (33.3)	0	0	0	3
	EEG focus			Good	17 (89.5)	0	0	2 (10.5)	0	0	19
				Poor	2 (66.7)	0	1 (33.3)	0	0	0	3
Kilpatrick, 1997[62]	EEG focus	Not reported	Engel I and II	Good	22 (91.7)	2 (8.3)	0	0	0	0	24
				Poor	0	0	0	0	0	0	0
SISCOM											
Kaiboriboon, 2002[59]	No subgroup	ECD	Seizure free	Good	12 (57.1)	7 (33.3)	0	0	0	2 (9.6)	21
				Poor	0	0	0	0	0	0	0
Kaminska, 2003[60]	No subgroup	ECD	Engel I and II	Good	5 (50.0)	0	1 (10.0)	3 (30.0)	0	1 (10.0)	10
				Poor	3 (33.4)	1 (11.1)	1 (11.1)	2 (22.2)	1 (11.1)	1 (11.1)	9
	EEG focus			Good	3 (42.9)	0	1 (14.3)	2 (28.6)	0	1 (14.3)	7
				Poor	3 (37.5)	1 (12.5)	1 (12.5)	1 (12.5)	1 (12.5)	1 (12.5)	8
	No EEG focus			Good	2 (66.7)	0	0	1 (33.3)	0	0	3
				Poor	0	0	0	1 (100)	0	0	1

continued

TABLE 17 *Results of studies that looked at the association of scans with surgical outcome (cont'd)*

Study	Subgroup	Contrast agent/tracer	Definition of a good outcome	Index test and site of surgery No. (%)							
				Outcome following surgery	Correctly localised	Not localised	P1	P2	P3	Incorrectly localised	Total
O'Brien, 1998[88]	No subgroup	HMPAO or ECD	Engel I and II	Good	14 (70.0)	3 (15.0)	1 (5.0)	1 (5.0)	0	1 (5.0)	20
				Poor	0	2 (33.3)	0	1 (16.7)	0	3 (50)	6
	EEG focus			Good	12 (66.6)	3 (16.6)	1 (5.6)	1 (5.6)	0	1 (5.6)	18
				Poor	0	1 (33.3)	0	1 (33.3)	0	1 (33.3)	3
	No EEG focus			Good	2 (100)	0	0	0	0	0	2
				Poor	0	1 (33.3)	0	0	0	2 (66.7)	3
MRS											
Achten, 1998[29]	No structural abnormality	NAA, Cr and Cho (NAA/(Cho + Cr)	Engel I and II	Good	5 (45.5)	0	0	6 (54.5)	0	0	11
				Poor	1 (50.0)	0	0	1 (50.0)	0	0	2
Cross, 1996[39]	No subgroup	NAA/(Cho + Cr)	Engel I and II	Good	6 (67)	3 (33)	0	0	0	0	9
				Poor	1 (100)	0	0	0	0	0	1
Li, 2000[78]	EEG focus	NAA and Cho (NAA/Cho)	Engel I and II	Good	13 (100)	0	0	0	0	0	13
				Poor	3 (37.5)	4 (50.0)	0	0	0	1 (12.5)	8
Park, 2001[96]	Structural abnormality	NAA, Cr and Cho (NAA/Cho and NAA/Cr)	Engel I and II	Good	18 (54.6)	4 (12.1)	0	10 (30.3)	0	1 (3.0)	33
				Poor	0	0	0	0	0	0	0
CT											
Theodore, 1990[109]	EEG focus	With and without contrast agent (agent not reported)	Engel I and II	Good	3 (13.6)	19 (86.4)					22
				Poor	0	4 (100)					4
MRI/CT combined											
Chugani, 1993[38]	No subgroup	Not reported	Engel I and II	Good	2 (11)	12 (67)	2 (11)	2 (11)	0	0	18
				Poor	2 (40)	2 (40)	0	0	1 (20)	0	5

N/A, not applicable; TLE, temporal lobe epilepsy.

TABLE 18 *Summary of imaging techniques evaluated by studies looking at the association of localised scans with outcome following surgery*

Imaging technique	No. of studies	No. with good outcome only	No. with bad outcome only	No. with localised scans only	No. included in analysis
Combination SPECT	2	1	0	0	1
Ictal SPECT	7	3	1	0	3
Interictal SPECT	8	3	0	0	5
Routine MRI	11	1	0	0	10
Volumetric MRI	5	1	1	0	3
PET	8	2	0	1	5
SISCOM	3	1	0	0	2
MRS	4	1	0	1	2
CT	1	0	0	0	1
Combination: CT/MRI	1	0	0	0	1

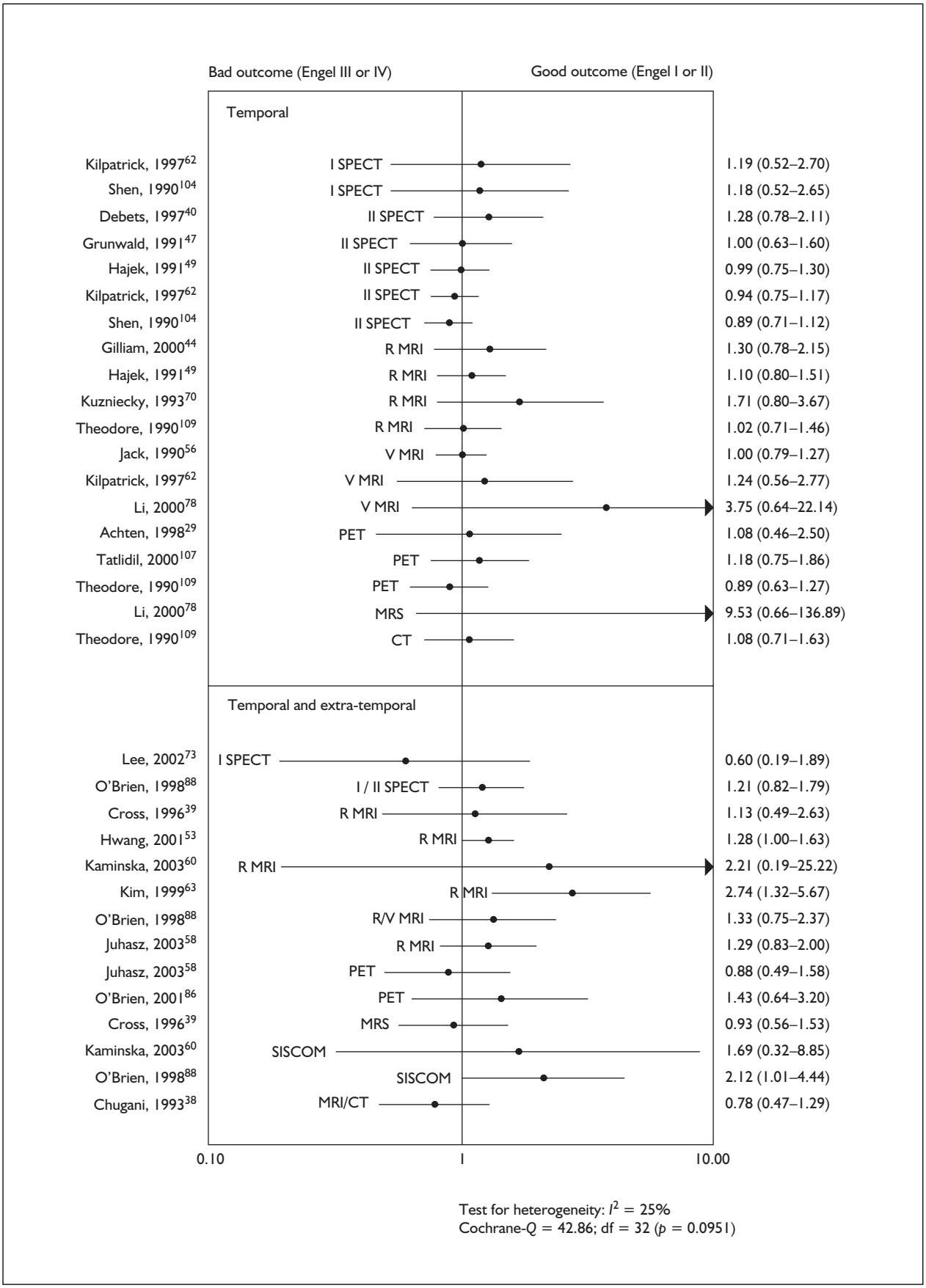

FIGURE 25 *Forest plot showing RRs for studies evaluating the association of localised scans with outcome following surgery. Index test evaluated: local (I) SPECT, Interictal (II) SPECT, routine (R) MRI, volumetric (V) MRI, PET, MRS, SISCOM and CT.*

Findings from outcome prediction studies

Nine studies used a multivariate analysis to investigate the association of various imaging techniques with outcome following surgery.[86–88,91,118–122] The results of these studies are summarised in *Table 19*. The studies used several different methods of analysis. Three studies used multiple regression analysis to investigate the association of various factors with outcome following surgery.[86,88,91] Two of these used Fisher's exact test to carry out univariate analysis for the association of categorical data with outcome following surgery[86,88] and one also included continuous data and used the Mann–Whitney test for these data.[88] Three studies used logistic regression analysis,[87,120,121] using χ^2 tests for the univariate analysis for categorical data, and one study also used the rank sum test for continuous data.[121] One study used Bayesian classifiers to predict outcome following surgery based on conditional probability distributions,[118] one used discriminant analysis,[119] and the final study used a log-linear model to compare the predictive value of MRI with those of other test combinations.[122] One study was only reported as an abstract and so limited details were available.[91] The imaging techniques evaluated in these studies included MRI, MRS, PET, SPECT and SISCOM.

SPECT

Only one study included SPECT results in the analysis.[122] This study compared outcome following surgery (whether or not patients were seizure free) between patients with and without findings on SPECT scans. This study found no association between ictal or interictal SPECT localisation (details were not clearly reported in the paper) and outcome following surgery on univariate χ^2 analysis. The multivariate analysis used a log-linear model to compare the predictive abilities of EEG, PET, SPECT, neuropsychological tests and the Wada test for outcome following surgery with that of MRI. This analysis found that ictal SPECT and interictal SPECT had significantly less predictive value than MRI ($p < 0.05$), whereas PET had a comparable predictive value ($p > 0.05$) to MRI.

MRI

Seven studies assessed the association of routine MRI with outcome following surgery.[86–88,91,120–122] Two of these studies found an association between MRI results and outcome following surgery.[86,121] The first included both MRI and PET results in a multivariate model, PET showed a significant association with having a good outcome (Engel class I or II) following surgery (standardised regression coefficient = 0.32, $p = 0.007$), but MRI showed only a borderline association in the final model (standardised regression coefficient = 0.51, $p = 0.07$).[86] The second investigated a variety of variables and found that the presence of unilateral hippocampal atrophy on MRI [odds ratio (OR) = 3.7], epileptiform discharge on scalp EEG concordant with the site of surgery (OR = 3.5), being seizure free during the first year (OR = 55.9) and having non-disabling seizure only during the first year (OR = 22.7) were all predictive of being seizure free after surgery ($p < 0.05$).[121] A further study investigated a wide range of factors, including lesional and non-lesional MRI, but the only item to show a significant association with a good outcome following surgery (Engel I and II) was complete resection (OR = 11, $p < 0.05$).[120] One study that used a log-linear model to compare the predictive values of EEG, PET, SPECT and neuropsychological testing with MRI reported that MRI, EEG and PET have comparable predictive values for Engel class I, and SPECT, neuropsychological testing and the WADA test have lower predictive values.[122] However, this study failed to find a significant association between MRI localisation and being seizure free following surgery on univariate χ^2 analysis (measure of association not reported, $p = 0.723$). Three further studies, all by the same authors, which assessed models including SISCOM and MRI found no significant association between MRI results and outcome following surgery in the multivariate analysis.[87,88,91] One of these studies also included type of surgery in the model[88] and another included EEG results.[87] Neither of these variables showed a significant association with outcome following surgery. One found a borderline association between both MRI ($p = 0.066$) and SISCOM ($p = 0.097$) and seizure frequency following surgery (measure of association not reported).[91]

PET

Three studies looked at the association of PET with outcome following surgery.[86,119,122] The first used discriminant analysis to investigate the association of PET scans positive in various regions and outcome following surgery.[119] Univariate analysis of the association of the individual PET scan regions and outcome found that only a positive PET scan of the temporal pole region showed a significant association with outcome (F-ratio = 10.2, $p = 0.005$). Multivariate

TABLE 19 *Results of outcome prediction studies*

Study	Dependent variable	Independent variables	Multivariate analysis
Antel, 2002[118] **Analysis type: Multivariate** Bayesian classifiers used to predict outcome based on conditional probability distributions	Seizure free Worthwhile improvement (>90% reduction in seizures)	Ipsilateral, contralateral (to site of surgery), and asymmetry *Z*-scores for each of the following: hippocampal volume, amygdaloid volume, NAA/Cr in the midtemporal lobe and NAA/Cr in the posterior temporal lobe	The following combination of variables had the highest classification accuracy for predicting seizure free following surgery: NAA/Cr in mid-temporal region ipsilateral to site of surgery (MRS), NAA/Cr in contralateral posterior temporal region (MRSI), and hippocampal asymmetry (MRI volumetric). With this combination of features, 39/52 patients who were seizure free and 21/29 who were not seizure free were correctly classified The following combination of variables had the highest classification accuracy for predicting worthwhile improvement: NAA/Cr in mid-temporal region ipsilateral to site of surgery (MRS), ipsilateral hippocampal volume (MRI volumetric) and hippocampal asymmetry (MRI volumetric). With this combination of features, 60/65 patients who had worthwhile improvement and 10/16 with no worthwhile improvement were correctly classified

			Univariate analysis		Multivariate analysis
			Measure of association: *F*-ratio	*p*-Value	
Dupont, 2000[119] **Analysis type: Univariate** Discriminant analysis **Multivariate** Discriminant analysis using as multiple dependent variables the regional metabolic asymmetries	Class A (totally seizure free) compared with class C (rare but disabling seizures after surgery)	Temporal region: medial Temporal region: pole Temporal region: anterolateral Temporal region: medium lateral Temporal region: posterolateral	0.0031 10.2 0.053 0.064 0.0004	0.95 0.005 0.82 0.80 0.98	The equation combining the metabolism of the temporal pole, the basofrontal cortex, the anterior part of the lateral temporal neocortex and the medial temporal cortex was highly significant [$F(4,15) = 7.21$, $p = 0.02$]. The multivariate equation correctly classified 14/14 category A patients and 6/6 category C patients. The mean normalised *Z*-score for category A patients was 1.43 (SD = 1.10) and for category C patients 1.43 (SD = 0.65). This equation was tested on the 10 patients in category B and the equation generated individual normalised *Z*-scores ranging from 1.99 to –1.89. The difference between the groups was highly significant ($F = 15.4$, $p < 0.001$)

continued

TABLE 19 *Results of outcome prediction studies (cont'd)*

Study	Dependent variable	Independent variables	Univariate analysis		Multivariate analysis	
			Measure of association: OR	***p*-Value**	**Measure of association: standardised regression coefficient**	***p*-Value**
O'Brien, 2001[86] **Analysis type: Univariate** Fisher's exact test **Multivariate** Multiple regression	Good outcome (Engel I and II combined) for univariate Engel categories I–IV for multivariate	MRI (definite focal lesions vs no focal lesion) FDG–PET (localising vs non-localising)	Not reported 10.0	Not reported 0.099	0.32 0.51 $r^2 = 0.40$ ($p = 0.004$)	0.07 0.007

Study	Dependent variable	Independent variables	Univariate analysis		Multivariate analysis	
			Measure of association: OR	***p*-Value**	**Measure of association: OR**	***p*-Value**
O'Brien, 2000[87] **Analysis type: Univariate** χ^2 **Multivariate** Logistic regression	Excellent outcome (seizure free or non-disabling seizures)	SISCOM (concordant vs non-concordant/non-localising)	6.4	0.019	7.2	0.03
		Preoperative MRI (lesional vs non-lesional)	Not reported	Not reported	2.3	0.32
		Ictal scalp EEG (localisation vs non-localising)	Not reported	Not reported	2.6	0.27
		Extent of excision of SISCOM focus (complete vs non-complete)	19.3	0.018	201.0	0.03
		Preoperative MRI findings (focal structural lesions vs no lesion)	Not reported	Not reported	4.7	0.28
		Ictal scalp EEG findings (localisation vs non-localising)	Not reported	Not reported	2.1	0.60
	Favourable outcome (>75% reduction in seizure frequency)	SISCOM (concordant vs non-concordant/non-localising)	7.6	0.025	11.2	0.03
		Preoperative MRI (lesional vs non-lesional)	Not reported	Not reported	4.5	0.14
		Ictal scalp EEG (localisation vs non-localising)	Not reported	Not reported	2.1	0.42
		Extent of excision of SISCOM focus (complete vs non-complete)	4.2	0.018	17.3	0.08
		Preoperative MRI findings (focal structural lesions vs no lesion)	Not reported	Not reported	3.7	0.37
		Ictal scalp EEG findings (localisation vs non-localising)	Not reported	Not reported	0.1	0.76

continued

TABLE 19 *Results of outcome prediction studies (cont'd)*

Study	Dependent variable	Independent variables	Univariate analysis		Multivariate analysis	
			Measure of association: Not reported	***p*-Value**	**Measure of association: standardised regression coefficient**	***p*-Value**
O'Brien, 1998[88]	Postoperative seizure frequency	SISCOM (concordant vs non-concordant or non-localising)	Median 2.5 in concordant, 6 in others	<0.01	0.54	0.004
Analysis type:		MRI (lesions vs no lesion)	Not reported	Not reported	0.10	0.59
Univariate		Type of surgery (temporal vs non-temporal)	Not reported	Not reported	0.24	0.19
Mann–Whitney *U*-test for continuous, Fisher's exact test for categorical	Improvement in seizure frequency score (no further details)	SISCOM (concordant vs non-concordant or non-localising)	47.7 (Fisher's exact)	<0.001	–0.66	<0.001
		MRI (lesions vs no lesion)	Not reported	Not reported	–0.19	0.25
Multivariate		Type of surgery (temporal vs non-temporal)	Not reported	Not reported	–0.09	0.60
Multiple regression						

O'Brien, 2001[91]			**Multivariate analysis**	
			Measure of association: partial correlation coefficients	***p*-Value**
Analysis type:				
Multivariate (no univariate reported)	Postoperative seizure frequency score	SISCOM results (no further details)	Not reported	0.097
Multiple regression		MRI results (no further details)		0.066
				$r^2 = 0.47$, $p = 0.03$

			Univariate analysis		**Multivariate analysis**	
			Measure of association: OR	***p*-Value**	**Measure of association: OR**	***p*-Value**
Paolicchi, 2000[120]	Good outcome (Engel I and II), repeated for seizure free – models the same	Age at epilepsy onset	Not reported	>0.05	Not reported	>0.05
		Duration of epilepsy before surgery	Not reported	>0.05	Not reported	>0.05
Analysis type:		Presence of cognitive impairment	Not reported	>0.05	Not reported	>0.05
Univariate		Temporal vs extra-temporal resection	Not reported	>0.05	Not reported	>0.05
χ^2		Lesional vs non-lesional resection on MRI	Not reported	>0.05	Not reported	>0.05
		Developmental vs acquired pathology	Not reported	>0.05	Not reported	>0.05
Multivariate		Complete vs incomplete resection	11 for good outcome, 7.8 for seizure free	<0.05	11 for good outcome, 7.8 for seizure free	<0.05
Logistic regression						

continued

TABLE 19 *Results of outcome prediction studies (cont'd)*

Study	Dependent variable	Independent variables	Univariate analysis		Multivariate analysis	
			Measure of association: Not reported	***p*-Value**	**Measure of association: OR**	***p*-Value**
Radhakrishnan, 1998[121] **Analysis type:** **Univariate** χ^2 for categorical and rank sum test for continuous variables. **Multivariate** Logistic regression analysis	Seizure free	Age at unprovoked seizure onset	Not reported	0.465	Not in model	N/A
		Symptomatic epilepsy aetiology		0.215	Not in model	N/A
		Duration of epilepsy history		0.566	Not in model	N/A
		History of febrile seizures		0.606	Not in model	N/A
		Unilateral hippocampal formation atrophy on MRI		0.016	3.7	0.024
		Other lesions on neuroimaging		0.152	Not in model	N/A
		Concordant interictal epileptiform discharge (scalp EEG)		<0.001	3.5	0.019
		Age at surgery		0.196	Not in model	N/A
		Postsurgery: no epileptiform discharge on corticogram		0.118	Not in model	N/A
		Postsurgery: no epileptiform discharge at 1 week		0.163	Not in model	N/A
		Postsurgery: no epileptiform discharge at 3 months		0.005	Not in model	N/A
		Postsurgery: seizure free during 1st year		<0.001	55.9	<0.001
		Postsurgery: only non-disabling seizures during 1st year		<0.001	22.7	<0.001
		Postsurgery: length of follow-up		0.705	Not in model	N/A
			Univariate analysis		**Multivariate analysis**	
			Measure of association: Not reported	***p*-Value**	**Measure of association: Not reported**	***p*-Value**
Son, 1999[122] **Analysis type:** **Univariate** χ^2 **Multivariate** Logit log-linear model used to compare MRI with other diagnostic tests – *p*-values presented refer to comparison with MRI	Seizure free	Interictal EEG (localisation results, details unclear)	Not reported	0.987	Not reported	0.492
		Video EEG (localisation results, details unclear)		0.079		0.203
		MRI (localisation results, details unclear)		0.723		Comparison
		PET (localisation results, details unclear)		0.561		0.268
		Ictal SPECT (localisation results, details unclear)		0.978		0.024
		Interictal SPECT (localisation results, details unclear)		0.502		<0.001
		Neuropsychological test (localisation results, details unclear)		0.863		<0.001
		Wada test (localisation results, details unclear)		0.738		<0.001

N/A, not applicable; SD, standard deviation.

analysis combining the different regions produced an equation that correctly classified all patients in whom the model was developed. A second study used multiple regression analysis to investigate the association of PET and MRI with outcome following surgery, classified according to Engel.[86] This study found that PET showed a significant association with outcome in the multivariate analysis (standardised regression coefficient = 0.51, $p = 0.007$), whereas MRI showed only a borderline significant association (standardised regression coefficient = 0.32, $p = 0.07$). The final study used χ^2 analysis to investigate the association of PET localisation (details not clearly reported in the paper) and outcome following surgery and found no significant association.[122] The multivariate analysis used a log-linear model to compare the predictive abilities of EEG, PET, SPECT, neuropsychological tests and the Wada test with that of MRI for outcome following surgery. This found that PET did not differ significantly from MRI in the prediction of surgical outcome.

SISCOM

Three studies, all by the same authors, evaluated the association of SISCOM with outcome following surgery.[87,88,91] One study, which also looked at MRI and EEG, found a significant association between SISCOM results (concordant with site of surgery versus non-concordant/non-localising) and having an excellent (OR = 7.2, $p = 0.03$) or a favourable (OR = 11.2, $p = 0.03$) outcome following surgery. The other two variables were not significant in the multivariate model.[87] This study also investigated the association of the extent of excision of the SISCOM focus (complete versus non-complete) and outcome following surgery and found a significant association with having an excellent outcome following surgery (OR = 201.0, $p = 0.03$) but only a borderline association with having a favourable outcome (OR = 17.3, $p = 0.08$). The second study, which included MRI and type of surgery in the model, also found a significant association between SISCOM result (concordant with site of surgery versus non-concordant/non-localising) and both postoperative seizure frequency (standardised regression coefficient = 0.54, $p = 0.004$) and improvement in seizure frequency score ($p < 0.001$).[88] The other two variables were not significant in the multivariate model. The third study included only SISCOM and MRI results (no further details) and reported only a borderline association between both variables and postoperative seizure frequency score (measure of association not reported, $p = 0.097$ for MRI and 0.066 for SISCOM).[91]

MRS and volumetric MRI

One study assessed the association of volumetric MRI and MRS with outcome following surgery.[118] This study used two definitions of success of surgery: being seizure free following surgery and having a worthwhile improvement (>90% reduction in seizure frequency) following surgery. It investigated various volumetric and MRS factors using Bayesian classifiers to predict outcome. It found that models containing the following combination of variables had the highest classification accuracy for predicting seizure-free outcome following surgery: NAA/Cr in the mid-temporal region ipsilateral to site of surgery (MRS), NAA/CR in contralateral posterior temporal region (MRS) and hippocampal asymmetry (volumetric MRI). The following combination of variables had the highest classification accuracy for predicting worthwhile improvement: NAA/Cr in the mid-temporal region ipsilateral to site of surgery (MRS), ipsilateral hippocampal volume (volumetric MRI) and hippocampal asymmetry (volumetric MRI).

Chapter 6

Sensitivity analysis

The following electronic databases were searched to identify papers for inclusion in the review: MEDLINE, EMBASE, Science Citation Index, BIOSIS Previews, Pascal, SIGLE, LILACS, NTIS, Dissertation Abstracts, Inside Conferences, NHS EED and HEED. In addition, Internet searching, contacting experts, handsearching and reference screening were carried out. Of the included studies, 57 were identified via MEDLINE,[30,32,36–40,42,44–48,50,52–55,60,62,64,67–70,73–90,92,95,100,101,104–106,108–111,113,115,116] 12 via EMBASE,[29,33,41,49,51,56,58,65,66,96,103,112] nine via BIOSIS,[31,59,61,93,94,97–99,117] six via Science Citation Index,[34,63,71,72,91,107] one via handsearching[114] and one via reference screening.[43] (See *Table 20*.) Searching the following databases therefore failed to identify any additional studies: Pascal, SIGLE, LILACS, NTIS, Dissertation Abstracts, Inside Conferences, NHS EED and HEED. Internet searching and contacting experts also failed to identify any additional studies.

Of the 12 studies found in EMBASE, 10 were also available via MEDLINE.[29,33,51,56,58,65,66,96,103,112] Of the nine studies found in BIOSIS, four were also available via MEDLINE[59,97–99] Of the six studies found in Science Citation Index, two were also available via MEDLINE.[63,107] If the searches had been limited to MEDLINE, without any additional searching or reference screening, 11 studies included in the diagnostic accuracy section[31,34,41,43,49,61,71,91,93,114,117] and one study included in the outcome prediction section would have been missed.[91] Of these diagnostic accuracy studies, eight looked at SPECT,[31,41,49,61,71,93,114,117] three at MRI,[31,41,49] one at PET,[43] one at SISCOM[91] and one at a combination of MRS and MRI.[34]

Four studies in a language other than English met the inclusion criteria. One was in Danish,[46] one in German[110] and two in Japanese.[41,103] Three studies were included in the section 'Localisation of the seizure focus' (p. 31) and evaluated ictal SPECT,[41] interictal SPECT,[41,46] unclear timing SPECT[110] and routine MRI.[41,46,110] The last study was included in the section 'Association of localised scans with outcome following surgery' (p. 81) and evaluated MRI and SPECT.[103] This study was restricted to patients who had a good outcome following surgery and so was not included in the analysis.

Owing to the poor quality of the studies included in this review and the fact that pooling was not carried out, it is unlikely that the overall findings of the review would have been different if the searches had been limited to MEDLINE or if foreign language papers were not included.

TABLE 20 *Databases from which included studies were identified*

(a) Diagnostic accuracy studies

Study	Index test	Database	In MEDLINE?
Achten, 1998[29]	MRI MRS PET: FDG	EMBASE	Yes
Adams, 1992[30]	CT MRI SPECT: HMPAO	MEDLINE	Yes
Assadi, 1997[31]	MRI SPECT: HMPAO	BIOSIS	No
Boundy, 1996[32]	MRI SPECT: HMPAO SPECT: IDEX	MEDLINE	Yes

continued

TABLE 20 *Details of which databases included studies were identified from (cont'd)*

(a) Diagnostic accuracy studies

Study	Index test	Database	In MEDLINE?
Brooks, 1990[33]	CT MRI	EMBASE	Yes
Cendes, 1995[34]	MRS and MRI	Science Citation Index	No
Chee, 1993[36(37)]	PET: FDG	MEDLINE	Yes
Chugani, 1993[38]	PET: FDG MRI and CT	MEDLINE	Yes
Cross, 1996[39]	MRI MRS	MEDLINE	Yes
Debets, 1997[40]	PET: FDG PET: FMZ SPECT: IMZ	MEDLINE	Yes
Doi, 1995[41]	MRI SPECT: IMZ SPECT: rCBF with: IMP, HMPAO and ECD	EMBASE	No
Duncan, 1993[42]	SPECT: HMPAO	MEDLINE	Yes
Engel, 1990[43]	PET: FDG	Reference screening	No
Gilliam, 2000[44]	MRI	MEDLINE	Yes
Gram, 1988[46]	CT MRI SPECT: HMPAO	MEDLINE	Yes
Grunwald, 1991[47(48)]	SPECT: HMPAO	MEDLINE	Yes
Hajek, 1991[49]	MRI SPECT: HMPAO	EMBASE	No
Harvey, 1993[50]	SPECT: HMPAO	MEDLINE	Yes
Ho, 1995[51]	PET: FDG SPECT: HMPAO	EMBASE	Yes
Hong, 2002[52]	PET: FDG SPECT: HMPAO	MEDLINE	Yes
Hwang, 2001[53]	MRI PET: FDG SPECT: HMPAO	MEDLINE	Yes
Jabbari, 1991[54]	CT MRI SPECT: IMP	MEDLINE	Yes
Jack, 1994[55]	MRI	MEDLINE	Yes
Jack, 1990[56]	MRI	EMBASE	Yes
Juhasz, 2003[58]	MRI PET: AMT PET: FDG	EMBASE	Yes
Kaiboriboon, 2002[59]	SISCOM SPECT: ECD	BIOSIS	Yes
Kaminska, 2003[60]	MRI SISCOM	MEDLINE	Yes
Kang, 1997[61]	SPECT: ECD	BIOSIS	No
Kilpatrick, 1997[62]	MRI PET SPECT	MEDLINE	Yes
Kim, 2000[63]	MRI PET: FDG SPECT: HMPAO	Science Citation Index	Yes

continued

TABLE 20 *Details of which databases included studies were identified from (cont'd)*

(a) Diagnostic accuracy studies

Study	Index test	Database	In MEDLINE?
Kim, 2002[64]	MRI PET: FDG	MEDLINE	Yes
Knowlton, 1997[65]	MRI MRS PET: FDG	EMBASE	Yes
Kuzniecky, 1991[67]	MRI	MEDLINE	Yes
Kuzniecky, 1998[68]	MRI MRS	MEDLINE	
Kuzniecky, 1993[70]	MRI	MEDLINE	Yes
Lee, 2001[71]	SPECT: ECD SPECT: HMPAO	Science Citation Index	No
Lee, 2002[73]	SPECT: HMPAO	MEDLINE	Yes
Lee, 2000[75]	SPECT: HMPAO	MEDLINE	Yes
Lewis, 1998[77]	MRI SPECT: HMPAO or ECD	MEDLINE	Yes
Li, 2000[78]	MRI MRS	MEDLINE	Yes
Markand, 1997[79]	MRI PET: FDG SPECT: HMPAO, HIPDM or ECD SPECT: HMPAO	MEDLINE	Yes
Markand, 1994[80]	SPECT: HIPDM, HMPAO or IMP	MEDLINE	Yes
Mastin, 1996[81]	PET: FDG SPECT: HMPAO	MEDLINE	Yes
Newton, 1995[82]	SPECT: HMPAO	MEDLINE	Yes
Newton, 1994[83]	SPECT: HMPAO	MEDLINE	Yes
Ng, 1994[85]	MRS	MEDLINE	Yes
O'Brien, 2001[86]	PET: FDG	MEDLINE	Yes
O'Brien, 2000[87]	SISCOM	MEDLINE	Yes
O'Brien, 1998[88]	MRI SISCOM SPECT: HMPAO	MEDLINE	Yes
O'Brien, 2001[91]	SISCOM	Science Citation Index	No
Oliveira, 1999[92]	SPECT: ECD	MEDLINE	Yes
Oommen, in progress[93]	SPECT: ECD	BIOSIS	No
Otsubo, 1995[95]	SPECT: HMPAO	MEDLINE	Yes
Park, 2001[96]	MRS: PET: FDG	EMBASE	Yes
Rowe, 1989[97]	SPECT: HMPAO	BIOSIS	Yes
Rowe, 1991[100]	SPECT: HMPAO	MEDLINE	Yes
Runge, 1997[101]	MRI SPECT: ECD	MEDLINE	Yes
Seki, 1998[103]	MRI SPECT: HMPAO or ECD	EMBASE	Yes
Shen, 1990[104]	SPECT: HIPDM	MEDLINE	Yes
Siegel, 2001[105]	SISCOM: HMPAO or ECD	MEDLINE	Yes
Sperling, 1986[106]	MRI PET: FDG	MEDLINE	Yes

continued

TABLE 20 *Details of which databases included studies were identified from (cont'd)*

(a) Diagnostic accuracy studies

Study	Index test	Database	In MEDLINE?
Tatlidil, 2000[107]	PET: [^{15}O]water	Science Citation Index	Yes
Tatum, 1995[108]	SPECT: HMPAO	MEDLINE	Yes
Theodore, 1990[109]	CT MRI PET: FDG	MEDLINE	Yes
Venz, 1994[110]	MRI SPECT: HMPAO SPECT: IMZ	MEDLINE	Yes
Vera, 1999[111]	SISCOM	MEDLINE	Yes
Watanabe, 2002[112]	NIRS SPECT: HMPAO or ECD	EMBASE	Yes
Weil, 2001[113]	SPECT: ECD	MEDLINE	Yes
Weis, 1997[114]	SPECT: HMPAO or ECD	Handsearch	No
Wheless, 1999[115]	MRI	MEDLINE	Yes
Zhou, 1994[116]	SPECT: ECD	MEDLINE	Yes
Yu, 1995[117]	SPECT: HMPAO	BIOSIS	No

rCBF, regional cerebral blood flow.

(b) Outcome prediction studies

Study	Database	In MEDLINE?
Antel, 2002[118]	MEDLINE	Yes
Dupont, 2000[119]	MEDLINE	Yes
O'Brien, 2000[87]	MEDLINE	Yes
O'Brien, 1998[88]	MEDLINE	Yes
O'Brien, 2001[86]	MEDLINE	Yes
O'Brien, 2001[91]	Science Citation Index	No
Radhakrishnan, 1998[121]	MEDLINE	Yes
Son, 1999[122]	MEDLINE	Yes

Chapter 7
Economic analysis

Given the lack of data on patient outcomes associated with neuro-imaging tests for visualising the seizure focus in patients with refractory epilepsy being considered for surgery, and the limited quality of the data on the accuracy of such tests, both individually and in combination, an economic model could not be developed. Although data on medium-term resource use implications and quality of life exist for patients following temporal lobectomy, there is insufficient evidence to determine what tests or combination of tests would be most accurate in the selection of patients who are able to benefit from surgery and, consequently, be most effective. Chapter 9 includes a discussion about the type of evidence-based questions that need to be addressed before the cost-effectiveness of neuro-imaging assessment in the patient population of interest may be assessed.

Chapter 8
Discussion

Key findings

Although we identified over 9000 studies, of which 94 met inclusion criteria, neither effectiveness nor cost-effectiveness were assessed in these studies, with the majority assessing diagnostic accuracy. Of the investigations assessed in this systematic review, test performance was more promising in studies restricted to patients with TLE, where the proportion of correctly localising scans tended to be higher and the proportion of incorrectly localising scans tended to be lower compared with studies with more heterogeneous patient groups. Results for ictal SPECT were the most promising, with the proportion of correctly localising scans ranging from 79 to 100% and incorrectly localising scans from 0 to 7% for patients with TLE. Results for CT and interictal SPECT suggest that these tests are poor localisers of the site of a seizure focus. Results for volumetric MRI and PET appear promising, but have been assessed in fewer studies than ictal SPECT. SISCOM and MRS have also been assessed in fewer studies, but results are less promising than ictal SPECT. T2-relaxometry was reported in only one small study with inconclusive results.

The results of this review show that, generally, outcome following surgery is better in those patients with a correctly or partially localised scan, compared with those with an incorrectly or non-localising scan. When evaluating the accuracy of imaging tests to predict the outcome following surgery, MRI seemed to be the most consistent predictor of surgical outcome, with significant or borderline associations in several studies. This consistency may be due to MRI being effective in the localisation of lesions, such as tumours, and vascular malformations. If a tumour is the cause of the epilepsy, its dimensions can be defined more precisely and the affected tissue removed more completely than with other epileptogenic foci, leading to improved seizure control after surgery. SISCOM and PET also seem promising, with either significant or borderline associations with outcome following surgery in the studies evaluating these techniques. One study evaluated SPECT, and the results were not encouraging, with no association between a positive SPECT scan and surgical outcome, and SPECT being a worse predictor of outcome than MRI.

In clinical practice, tests are used in combination; however, neither the effectiveness nor diagnostic accuracy of combinations of tests was assessed in the studies included in this review.

Variability

There were a number of potential sources of variability among studies, which are outlined below.

Patient population

The quality of included studies was poor in terms of patient spectrum. There were a number of selection processes likely to have resulted in heterogeneity of results.

Some studies were restricted to patients thought to have TLE, whereas others recruited a broader spectrum of patients including those with foci outside the temporal lobe. Extra-temporal foci can prove more difficult to localise, which could have two effects. First, this could result in fewer correctly localising and more partially and incorrectly localising scans in studies recruiting a patient population with a range of seizure foci. Second, differences in the spectrum of patients in terms of the site of seizure focus (e.g. some studies recruiting a greater proportion of patients with TLE but others a greater proportion of patients with a frontal lobe epilepsy) could result in greater heterogeneity in the 'temporal and extra-temporal' populations. These effects are evident when the results for studies including patients with either 'temporal' or 'temporal and extra-temporal' epilepsy are examined for ictal SPECT and routine MRI. It would also be expected that the association between a correctly localising scan and a good outcome following surgery would be better in studies restricted to patients with TLE. However, of the studies providing such information, the two reporting a significant association between a positive scan and surgical outcome included patients with epilepsy of both temporal and extra-temporal origin.

Some studies restricted selection to patients undergoing surgery or with a good outcome following surgery. These represent a selected population who have already had the seizure focus localised. These studies would be likely to exclude patients in whom it is more difficult to localise the seizure focus and in whom new imaging techniques could potentially be most useful.

Other clinical factors that may have similar effects include age and selection processes which may have resulted in differing patient populations among studies, such as referral patterns to centres and differences in screening procedures for patients prior to entering an epilepsy surgery programme. Our results do not allow a comment on the magnitude of effect that these factors may have had.

Reference standard

A range of reference standards were used in the included studies, which could be a major source of heterogeneity. Ictal EEG usually requires continuous EEG and video monitoring for a number of days and is a technique that directly assesses seizure onset. However, ictal EEG with surface electrodes may fail to find a seizure focus or inaccurately localise it. This is important for seizures that arise from outside the temporal lobe, particularly those arising from parts of the cerebral cortex some distance from the scalp, such as the medial frontal lobe. Ictal EEG with invasive recording (depth electrodes and/or grids) directly assesses seizure onset from cerebral grey matter, but to do so electrodes must be placed in or adjacent to the site of the seizure focus. Intracranial electrodes are placed at specific sites, the choice of site being informed by clinical characteristics and other investigation results. Despite this, electrodes may not be inserted at the site of the seizure focus, hence intra-cranial recording may also fail to locate the seizure focus. Therefore, where the results of ictal EEG and the index test disagree with respect to the site of the seizure focus, it is likely that, in some cases, the index test is correct and the ictal EEG is wrong. Similarly, it is difficult to interpret results when the ictal EEG does not locate a seizure focus but the index test does, as the accuracy of the index test cannot be verified. Different reference standards may result in greater heterogeneity between studies including patients with temporal and extra-temporal epilepsies compared with those including only patients with temporal lobe epilepsy, as outlined above.

Some studies included a combination of tests as the reference standard, which usually included ictal EEG, neuropsychological testing, Wada testing and other imaging techniques. Studies did not use the same combination of tests, which is likely to be another source of heterogeneity. One might expect a combination of tests to find a seizure focus for patients whose seizures were not localised by ictal EEG, and fewer falsely localised patients by the reference standard than for ictal EEG alone. This might improve the apparent accuracy of the index tests, although there are no clear trends from the results to support this.

Site of surgery was used as a reference standard in some studies, which has a number of limitations. First, only patients proceeding to surgery can be included, which is likely to be biased towards patients with TLE, which may be easier to localise. Second, results of the index test may have been used in making the decision to proceed with surgery. Both of these factors would tend to increase the estimated diagnostic accuracy of the index test, although no clear trends are evident from the results when studies using site of surgery as a reference standard are compared with those using other reference standards.

Despite the limitations outlined above, ictal EEG, a combination of tests and site of surgery were the best available reference standards and were considered appropriate for this review. Interictal EEG was considered inappropriate, as by definition this technique does not directly record seizure onset.

Imaging technology

Although studies have investigated the same basic technology, there are likely to be differences among studies in the exact technology used and the way it was applied. In particular, it is likely that refinements have been made in the individual technologies over time, which may improve diagnostic performance, although no trend is evident from the results when year of publication is used as a surrogate marker for change in technology to investigate heterogeneity.

For ictal SPECT, the timing of the injection of tracer relative to the time of seizure onset is likely to be extremely important, and the analyses presented here used data for patients injected immediately after seizure onset or within 30 seconds of seizure onset where possible. Studies presenting data stratified for timing of injection show improved test performance for patients with earlier injections. In studies evaluating ictal SPECT, interictal SPECT or PET, the tracer used may be another source of heterogeneity, although this was not clearly evident from our results.

Differences in MRI technologies may also be potential sources of heterogeneity. For routine MRI, there was variation in slice orientation and thickness, and also combinations of images produced including T1- and T2-weighted images, proton density and FLAIR images. MRS, MRI volumetry and T2-relaxometry were likely to be different in the way in which the technologies were applied. Although all of these factors are likely to be sources of heterogeneity, the results of this review do not allow a firm conclusion as to their impact.

One technological factor that appeared to be a source of heterogeneity was the strength of the magnet, which varied amongst included studies. Earlier studies tended to use lower field strength magnets, which ranged from 0.3 to 1.5 T. There was some suggestion from the data that the accuracy of MRI in the localisation of the seizure focus was poorer at the lower magnet strengths (≤ 1.5 T) as five of the six studies reporting <40% correctly localising scans used these lower strength magnets. This was also evident for MRS, where one study used a much more powerful magnet (4.1 T) than the other studies, which used 1.5 T magnets. This study reported a very high proportion of correctly localised scans, with only a very small proportion of incorrectly localised scans and no partially or non-localising scans. However, two routine MRI studies. one using a 0.3 T magnet, and the other a 1.5 T magnet reported a a high proportion of correctly localising scans, and a low proportion of non-localising or incorrectly localising scans. Modern scanners tend to have 1.5 T magnets and also have superior gradients, computing and more advanced software, which contribute to an increased yield. MRI is the most readily available of the technologies evaluated in this review, and the most realistic option for the NHS. However, patients must have access to good-quality, modern MRI scanners and software, with the accompanying expertise required to gather and interpret the findings.

During the evolution of the technologies investigated in this report, there have been important advances in the quality of data acquisition. This is particularly so for MRI technologies, where there have been improvements in field strengths, field gradients and software. These developments should increase the probability of these technologies finding abnormalities in keeping with an underlying seizures focus. In this report we have not been able to assess the influence of these advances upon test performance.

The interpretation of routine MRI is largely qualitative, as is SPECT and to a lesser extent PET. The interpretation of images is therefore extremely dependent on the experience of the person reporting them. Experience with these technologies has grown significantly over the past two decades. It is likely that this experience has also had an important influence on test performance. This is not a factor that we have been able to investigate in this report.

In practice, information from a wide range of sources is available to the person interpreting the results of scans, including seizure history, results of other imaging evaluations and EEG. Therefore, it is not possible for these studies to avoid both clinical review bias (the availability of different clinical information to the person interpreting the scans than would be available in practice) and test review bias (the availability of the results of the reference standard to the person interpreting the index test). Test review bias was poorly reported in the studies; however, those that did tended to report that results of the reference standard were not available to those interpreting the results of the index test. When evaluating a test it is important that results are interpreted under similar conditions to those in which the results will be interpreted in practice. This did not appear to have been the case for the majority of studies included in the review, limiting the applicability of the findings. All these variability factors (both clinical and statistical heterogeneity) precluded statistical pooling of results.

Strengths and limitations of the review

Strengths

We conducted a systematic review of the existing literature. This included detailed searches of databases, handsearching of journals, review of bibliographies and attempts to locate unpublished data. We therefore feel that it is unlikely that we have missed any important studies. Owing to the heterogeneity between studies in terms of design, neuroimaging techniques, outcome measurements, reference standards, methods of analysis and results, we decided not to conduct a meta-analysis of the results. Instead, a detailed summary and narrative synthesis of the results are presented. The quality of each included diagnostic accuracy study was assessed using QUADAS, and the quality of outcome prediction studies using the checklist for cohort studies in the CRD guidelines for undertaking systematic reviews, with the quality of

studies being taken into account in the synthesis of results. The review benefited from the multidisciplinary composition of the review team, including reviewers with experience in diagnostic accuracy studies, clinicians, economists and statisticians.

Limitations

The review was limited by the lack of available, high-quality, well-reported studies. The searches did not locate any RCTs or cohort studies comparing patient outcomes between patients who received different combinations of imaging techniques. The majority of the available studies were diagnostic accuracy studies, which were often either of poor quality or poorly reported. Study designs, population characteristics, index tests and their characteristics, outcome measurements and reference standards were variable. In many of the included studies, the spectrum of patients was different to that which would routinely be assessed in most epilepsy surgery centres. This challenges the external validity of studies, making it difficult to use results to inform practice in a routine clinical setting. Also, in the majority of studies, researchers did not set out to collect data prospectively. Instead, data were collected retrospectively or the studies did not report on whether data were collected prospectively. The retrospective analysis of imaging techniques has inherent problems, mainly because data are retrieved rather than recorded as they occur. This can lead to the introduction of selection and interpretation bias. Owing to the poor quality of the included studies, the results of the review were interpreted with caution. This review highlighted methodological inadequacies in the available research that need to be addressed in future studies.

In the studies, imaging techniques were evaluated in isolation and did not allow an assessment of the effectiveness or diagnostic accuracy of tests used in combination, and, in addition, these studies provided no data regarding the order in which tests should be carried out. These are major problems, as in current clinical practice clinicians rely upon concordance of multiple investigation results conducted in sequence when making decisions about recommending surgery. Currently, there is no general consensus of opinion as to which combination of investigations should be conducted, what order they should be conducted in, or which investigation results should carry more weight when making recommendations for surgery. It is likely that investigations are chosen and conducted on the basis of clinician preference, anecdotal evidence and resources available locally. This review does not provide data to inform either the combinations or order of tests that should be used.

One major limitation of the review is that we were unable to construct 2×2 tables from data reported in studies. The majority of the studies included in the review provided little, if any, data about the results of the investigations for patients in whom the reference standard failed to localise a seizure focus. Even when these data were available, in view of the inherent problems of the reference standards used, difficulties remained in knowing how to interpret these results. This is problematic, as for patients in whom the index test localised a seizure focus but the reference standard failed to localise a seizure focus it is unclear as to which technique was correct in these patients. In addition, it is unclear whether patients in whom both the index test and reference standard failed to identify a seizure focus really did not have a seizure focus (i.e. had a generalised onset rather than a focal onset epilepsy), or whether it was the case that none of the tests conducted managed to identify the seizure focus. This means that the data did not fit the traditional 2×2 table of test performance and hence standard measures of diagnostic performance, such as sensitivity, specificity, likelihood ratios and more clinically relevant measures such as predictive values, could not be calculated.

New advances in the structural and functional imaging of the brain are ongoing. Owing to the lack of studies, the following techniques have not been included in this review: novel MRI contrasts such as diffusion tensor imaging, magnetisation transfer ratio imaging, double inversion recovery and fast FLAIR T2 mapping. These techniques may allow the identification of brain abnormalities that may not be identified by conventional MRI. No studies investigating functional magnetic resonance imaging (fMRI) were identified. fMRI with simultaneous recording of EEG allows the identification of cerebral areas involved in the generation of interictal epileptic activity. This has opened up new possibilities for understanding the functional anatomy of normal and abnormal cerebral processes. Such new techniques may have clinical relevance when assessing patients for potential epilepsy surgery and require evaluation.

Cost-effectiveness

Owing to inadequate data we were unable to provide information on effectiveness or cost-

effectiveness. Lack of evidence on effectiveness and the absence of an agreed standard diagnostic practice in this field prevented the consideration of modelling as a way of providing the required evidence. Until those questions are resolved, assessing the cost-effectiveness analysis of neuro-imaging assessments in this field will be meaningless.

Several issues need to be addressed in order to determine which neuro-imaging techniques are cost-effective in the patient population of interest here. Although some may be addressed by conducting well-designed, controlled, prospective studies, not all the economic data required for assessing cost-effectiveness are likely to be captured in a single study. First, a clear definition needs to be identified of what the relevant options are for clinical practice. This question is complicated by the observation that diagnostic practice varies across centres in the UK and that there is no recognised standard diagnostic practice. Further, most of the available evidence from diagnostic accuracy studies relates to retrospective designs, thus raising the issue of sample selection bias. As noted before, there are key issues to be addressed around the feasibility and desirability of conducting studies that minimise bias in order to produce the evidence that is required.

Second, quality of life data associated with the negative outcomes (e.g. haemorrhage) of invasive tests (intra-cranial EEG) are needed to account properly for the trade-offs implicit in using less invasive and, possibly, less accurate imaging procedures. Ideally, those studies should use a generic instrument to derive utility scores based on the time trade-off technique such as those available for patients on continuous medical treatment.[125]

Third, there is a need for further evidence on the implications of surgical outcomes, and continuous treatment with AEDs for those not undergoing treatment, on the patient's performance of activities of daily living. One problem with existing evidence that links surgical outcomes in terms of Engel scores with productivity outcomes is that the former are sometimes expressed in relative terms (i.e. percent of seizure frequency reduction relative to baseline). A study looking at this and related outcomes for the comparators deemed to be relevant (see the section 'Future directions') would be required to inform any economic model in this field.

Future directions

The commissioning brief for this systematic review was to examine the effectiveness and cost-effectiveness of imaging techniques in the work-up for epilepsy surgery. However, existing data do not allow firm conclusions regarding effectiveness, and it was deemed unreasonable to proceed with economic modelling. It is clear that diagnostic accuracy studies of imaging techniques in the work-up for epilepsy surgery are inappropriate to answer the primary objectives of this review.

Data regarding the influence of imaging technologies upon the outcome for patients being considered for epilepsy surgery are clearly needed. The most reliable research methodology for this purpose is the RCT. RCTs could examine the influence of single tests (patients randomised to have or not have a test) or combinations of tests (patients randomised to different combinations of tests) on patient outcome. A study of a single test could evaluate the additional benefit that a particular test offers over other routinely offered tests. For example, in a study evaluating PET, all patients would receive routine tests such as MRI, EEG and Wada tests, with those in the experimental arm also receiving a PET scan. Similarly, studies could include a set of routine tests in both arms with additional combinations of tests being offered in the experimental arm. An alternative approach would be to compare different test combinations in different intervention arms. Health economic data could be collected in parallel, allowing a thorough examination of cost-effectiveness. This approach need not be restricted to examining the cost-effectiveness of individual imaging techniques and could address the whole surgical process (presurgical work-up and surgery). Advantages of an RCT include measurement of clinical and economic outcomes, no requirement for a reference standard and assessment of tests in isolation or combination. The effect of the imaging investigation on patient outcome is crucial, and cannot be adequately measured in diagnostic accuracy studies.

There would, however, be a number of significant barriers to undertaking an RCT, which require careful consideration. There will be ethical objections; for example, despite the lack of good-quality accuracy data, routine MRI is recommended for all patients with focal epilepsy, and withholding this may be deemed unethical. The same will be said for those institutions that are using technologies such as volumetric MRI,

T2-relaxometry and ictal and interictal SPECT as part of routine work-up prior to surgery. For certain tests the ethical argument against withholding them in an RCT will be persuasive, for others less so. One could also argue that it is unethical to carry out investigations for which there is insufficient evidence to inform the interpretation of results.

The feasibility of carrying out an RCT will also be questioned. Refinements in the technology over time, SPECT remaining a limited resource, the logistic problems associated with ictal SPECT, and the fact that there are still few PET scanners in the UK, may all limit the feasibility of such a study. Where resources are too scarce, an RCT might be impractical. A judgement would need to be made as to when a technology is sufficiently refined to warrant investigation in an RCT. Where resources are limited, they could be 'rationed' in the context of an RCT.

RCTs could clearly provide the evidence needed regarding the effectiveness and cost-effectiveness of imaging techniques in the work-up for epilepsy surgery. Any decision regarding the design, ethics and feasibility of RCTs of imaging tests in the work-up for epilepsy surgery would require discussion and debate among clinicians, patient groups, policy makers and health and/or research funders.

To address the question of the ability of neuroimaging techniques to predict patient outcomes following surgery, large-scale cohort studies are required. Such studies could assess the ability of imaging techniques and other factors (e.g. patient history, neurological examination and EEG) to predict which patients should undergo surgery and which will have a good outcome following surgery. A large study is ongoing in The Netherlands. The aim of this study is to quantify which combinations of the diagnostic tests provide independent prognostic information. This study has included the medical files of all patients referred to an epilepsy surgery programme over a 15-year period for evaluation for possible surgery for TLE. It will use regression analysis to investigate the predictive value of a variety of variables (such as EEG, MRI, PET, ictal SPECT, patient history and Wada test) with the consensus decision for surgery and with outcome following surgery. (Moons K, Julius Centrum voor Huisartsgeneeskunde en Patientgebonden Onderzoek, Utrecht, The Netherlands: personal communication, July 2004). In addition, Engel criteria have major limitations as an outcome measure, as they group patients into four broad categories, for which an arbitrary decision has to be made to dichotomise success and failure. It only reflects seizures outcome and does not take quality of life or surgical complications into account. There are also no clear criteria about what period of remission is required to be Engel I, whilst longitudinally, patients may move from one category to another. Regardless of this, Engel criteria are universally accepted. Change would need to be debated and decided upon by the relevant research community.

Chapter 9
Conclusions

Implications for practice

Owing to the limitations of the included studies, the results of this review do little to inform clinical practice. We are unable to provide evidence for effectiveness or cost-effectiveness of imaging techniques in the work-up for epilepsy surgery. The usefulness of diagnostic accuracy studies is limited by differences in the reference standard used, and studies are subject to both clinical and statistical heterogeneity as outlined above. Studies investigating the prognostic importance of imaging results for the outcome following epilepsy surgery suggest that abnormalities correctly identified on imaging are associated with a better clinical outcome; however, most studies did not show a significant association between a localised scan and a good outcome following surgery. Sample size may have been a factor for the lack of significant association in some studies. The MRI studies reporting a significant association between a localised scan and a good surgical outcome had two of the largest sample sizes of the MRI studies included in the review. Other studies may therefore have lacked sufficient power to detect a significant association.

Implications for research

To address the diagnostic question of whether neuroimaging techniques truly help or contribute to the decision to perform epilepsy surgery or not, a large-scale cross-sectional diagnostic study among patients who might be indicated for epilepsy surgery is needed. All patients potentially indicated for surgery should first undergo the neuroimaging tests under study (in addition to other potential diagnostic tests such as history taking, neurological examination and EEG). Subsequently for each patient, the decision 'to operate or not' should conform to the best available reference method in current practice, which is at present consensus diagnosis using an expert panel. Such a study could assess which, and to what extent, imaging techniques in combination with other diagnostics contribute to the assessment of which patients should undergo surgery.

Given the inadequacy of existing data, there is a pressing need for well-conducted and well-reported studies investigating the effectiveness and cost-effectiveness of imaging techniques in the work-up for epilepsy surgery. Studies should be reported according to the appropriate checklist (QUOROM/STARD). Diagnostic accuracy studies will not provide effectiveness or cost-effectiveness information. It is clearly important that appropriate patients are rejected from surgery, and this is an important outcome that should be measured in future studies. This outcome cannot be adequately assessed in diagnostic accuracy studies, but should be assessed in studies of effectiveness, which are sorely lacking in this field. It is important that clinicians, patient groups, policy makers and funders of healthcare and/or research meet and debate the most appropriate way to develop and implement a strategy for investigating these technologies. The following subjects require debate.

Randomised controlled trials

Debate and consensus regarding:

- The feasibility and ethical acceptability of RCTs to assess effectiveness and cost-effectiveness.
- The individual tests or combinations of tests that should be examined.
- Patient populations that should be recruited.

Evidence is also required about a test to suggest that it is worthwhile proceeding with an RCT. Diagnostic accuracy studies are one methodology that could be used to provide these data. We would need to debate the most appropriate reference standard and populations to study to obtain the appropriate information.

Prognostic studies

To address the prognostic question of whether neuroimaging techniques truly contribute to the prediction of patient outcome following epilepsy surgery, large-scale observational cohort studies of operated patients are required. Such a prognostic follow-up study could assess which and to what extent neuroimaging tests in combination with the other diagnostics are able to predict which operated patients will have favourable postoperative outcome.

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Contribution of authors

Penny Whiting (Research Fellow) was responsible for developing the review protocol, selecting and assessing studies, extracting and analysing data and writing and commenting on the final report. Rajat Gupta (Consultant Neurologist) was responsible for developing the review protocol, selecting and assessing studies, extracting and analysing data, and writing and commenting on the final report. Jane Burch (Research Fellow) was responsible for selecting and assessing studies, extracting and analysing data and writing and commenting on the final report. Ruben E Mujica Mota (Research Fellow) was responsible for the economic evaluation, including writing relevant sections of the report and commenting on the final report. Kath Wright (Information Officer) was responsible for devising and carrying out literature searches, writing literature search sections of the final report and commenting on the final report. Anthony Marson (Consultant Neurologist) was responsible for developing the review protocol, assisting with data interpretation and writing and commenting on the final report. Udo Weishmann (Consultant Neurologist) was responsible for developing the review protocol, assisting with the development of data extraction forms and data interpretation and writing and commenting on the final report. Alan Haycox (Senior Lecturer in Health Economics) was responsible for the economic evaluation, including writing relevant sections of the report and commenting on the final report. Jos Kleijnen (Director, CRD) was responsible for developing the review protocol, assisting with data interpretation and commenting on the final report. Carol Forbes (Reviews Manager) was responsible for developing the review protocol, selecting and assessing studies, extracting data and writing and commenting on the final report.

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Appendix 1

Advisory panel members

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Appendix 2

Detailed search strategies

This appendix presents the detailed searches carried out to inform the review. The following electronic databases were searched to identify papers for inclusion in the review: MEDLINE, EMBASE, Science Citation Index, Biosis Previews, Pascal, SIGLE, LILACS, NTIS, Dissertation Abstracts, Inside Conferences, NHS EED and HEED. Details of the search dates, database coverage, numbers of records retrieved and the search strategies used are given below.

MEDLINE

Via Ovid
Search date=23/6/03
Database coverage= 1966 to June Week 2 2003-06-23
Records retrieved=3550 (3279 after de-duplication)

Search strategy

1. exp Epilepsy/
2. epilep$.ti,ab.
3. 1 or 2
4. exp Magnetic Resonance Imaging/
5. exp Magnetic Resonance Spectroscopy/
6. (magnetic resonance tomograph$ or magnetic resonance scan$ or magnetic resonance imag$ or magnetic resonance spectroscop$).ti,ab.
7. (mr tomograph$ or mr scan$ or mr imag$ or mr spectroscop$).ti,ab.
8. (fmri or mri or nmr or mrs).ti,ab.
9. exp Tomography, Emission-Computed, Single-Photon/
10. (spect or single photon emission computed tomograph$).ti,ab.
11. volumetric exam$.ti,ab.
12. quantitative t2 measure$.ti,ab.
13. voxel based morphomet$.ti,ab.
14. diffusion weight$ imag$.ti,ab.
15. (diffusion weight$ imag$ or dwi).ti,ab.
16. (diffusion tensor imag$ or dti).ti,ab.
17. (fluid attentuated inversion recovery or flair).ti,ab.
18. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19. 3 and 18
20. animal.sh.
21. human.sh.
22. 20 not (20 and 21)
23. 19 not 22
24. case report.sh.
25. 23 not 24

EMBASE

Via Ovid
Search date=23/6/03
Database coverage=1980 to 2003 week 25
Records retrieved=3603 (1706 after de-duplication)

Search strategy

1. exp Epilepsy/
2. epilep$.ti,ab.
3. 1 or 2
4. exp nuclear magnetic resonance imaging/
5. exp nuclear magnetic resonance spectroscopy/
6. (magnetic resonance tomograph$ or magnetic resonance scan$ or magnetic resonance imag$ or magnetic resonance spectoscop$).ti,ab.
7. (mr tomograph$ or mr scan$ or mr imag$ or mr spectroscop$).ti,ab.
8. (fmri or mri or nmr or mrs).ti,ab.
9. exp single photon emission computer tomography/
10. spect.mp. or single photon emission computer tomograph$.ti,ab. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]
11. volumetric exam$.ti,ab.
12. quantitative t2 measure$.ti,ab.
13. voxel based morphomet$.ti,ab.
14. diffusion weight$ imag$.ti,ab.
15. (diffusion weight$ imag$ or dwi).ti,ab.
16. (fluid attentuated inversion recovery or flair).ti,ab.
17. (diffusion tensor imag$ or dti).ti,ab.
18. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19. 3 and 18
20. animal.sh.
21. human.sh.
22. 20 not (20 and 21)
23. 19 not 22
24. case report.sh.
25. 23 not 24

Science Citation Index

Via Web of Science
Search date=25/6/03
Database coverage= 1981 to present
Records retrieved=4300 (1955 after de-duplication)

Search strategy

epilep* and (magnetic resonance tomograph* or magnetic resonance scan* or magnetic resonance imag* or magnetic resonance spectroscop* or mr tomograph* or mr scan* or mr imag* or mr spectroscop* or fmri or mri or nmr or mrs or spect or single photon emission computed tomograph* or volumetric exam* or quantitative t2 measure* or voxel based morphomet* or diffusion weight* imag* or dwi or diffusion tensor imag* or dti or flair or fluid attentuated inversion recovery)

BIOSIS

via Edina
Search date=1/7/03
Database coverage=1985 to present
Records retrieved=4879 (2261 after deduplication)

Search strategy

((((((((((((((((((ts: (flair)) or (al: (fluid attentuated inversion recovery))) or (al: (dwi or diffusion tensor imag*))) or (al: (diffusion weight* imag*))) or (al: (diffusin weight* imag*))) or (al: (voxel based morphomet*))) or (al: (quantitative t2 measure*))) or (al: (volumetric exam*))) or (al: (single photon emission computed tomograph*))) or (al: (spect))) or (al: (fmri or mri or nmr or mrs))) or (al: (mr spectroscop*))) or (al: (mr imag*))) or (al: (mr scan*))) or (al: (mr tomograph*))) or (al: (magnetic resonance spectroscop*))) or (al: (magnetic resonance imag*))) or (al: (magnetic resonance scan*))) or (al: (magnetic resonance tomograph*))) and (al: (epilep*))

Pascal

Search date=21/7/03
Via Dialog
Coverage=1973 to date
Retrieved=2365(842 after deduplication)

Search strategy

s epilep?/ti,ab,de
s magnetic(w)resonance(w)tomograph?/ti,ab,de
s magnetic(w)resonance(w)scan?/ti,ab,de
s magnetic(w)resonance(w)imag?/ti,ab,de
s magnetic(w)resonance(w)spectroscop?/ti,ab,de
s mr(w)tomograph?/ti,ab,de
s mr(w)scan?/ti,ab,de
s mr(w)imag?/ti,ab,de
s mr(w)spectroscop?/ti,ab,de
s fmri or mri or nmr or mrs/ti,ab
s spect/ti,ab,de
s single(w)photon(w)emission(w)computed(w) tomograph?/ti,ab,de
s volumetric(w)exam?/ti,ab,de
s quantitative(w)t2(w)measure?/ti,ab,de
s voxel(w)based(w)morphomet?/ti,ab,de
s diffusion(w)weight?(w)imag?/ti,ab,de
s dwi/ti,ab
s diffusion(w)tensor(w)imag?/ti,ab,de
s dti/ti,ab
s fluid(w)attentuated(w)inversion(w)recovery/ ti,ab,de
s flair/ti,ab
s s2:s21
s s1 and s22
s animal/de
s human/de
s s24 not (s24 and s25)
s s23 not s26
s case(w)report/ti,de
s s27 not s28

SIGLE

Via Webspirs
Search date= 21/7/03
Date coverage=1980-2002/12
Retrieved=6

Search strategy

(epilep*) and ((flair in ti) or ((Fluid attentuated inversion recovery) in ti,ab,de) or ((mr spectroscop*)in ti,ab,de) or ((mr imag*)in ti,ab,de) or ((mr scan*)in ti,ab,de) or ((mr tomograph*)in ti,ab,de) or ((mr tomograph*)in ti,ab,de) or ((magnetic resonance spectroscop*) in ti,ab,de) or ((magnetic resonance imag*) in ti,ab,de) or ((magnetic resonance scan*) in ti,ab,de) or ((magnetic resonance tomograph*) in ti,ab,de) or (dti in ti,ab) or ((diffusion tensor imag*) in ti,ab,de) or (dwi in ti,ab) or ((diffusion weight* imag*) in ti,ab,de) or ((voxel based morphomet*) in ti,ab,de) or ((quantitative t2 measure*) in ti,ab,de) or ((volumetric exam*) in ti,ab,de) or ((single photon emission computed tomograph*) in ti,ab,de) or (spect in ti,ab,de) or ((fmri or mri or nmr or mrs) in ti,ab))

LILACS

Via:
http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&base=LILACS&lang=p

search date=21/7/03
Retrieved=176

Search strategy
epilepsy$ and (tomography$ or scan$ or imag$ or spect$ or spectropscop$ or volumetric$ or morphometric$ or flair)

NTIS

Search date=22/7/03
Via Dialog
Retrieved=9

Search strategy
s epilep?/ti,ab,de
s magnetic(w)resonance(w)tomograph?/ti,ab,de
s magnetic(w)resonance(w)scan?/ti,ab,de
s magnetic(w)resonance(w)imag?/ti,ab,de
s magnetic(w)resonance(w)spectroscop?/ti,ab,de
s mr(w)tomograph?/ti,ab,de
s mr(w)scan?/ti,ab,de
s mr(w)imag?/ti,ab,de
s mr(w)spectroscop?/ti,ab,de
s fmri or mri or nmr or mrs/ti,ab
s spect/ti,ab,de
s single(w)photon(w)emission(w)computed(w)tomograph?/ti,ab,de
s volumetric(w)exam?/ti,ab,de
s quantitative(w)t2(w)measure?/ti,ab,de
s voxel(w)based(w)morphomet?/ti,ab,de
s diffusion(w)weight?(w)imag?/ti,ab,de
s dwi/ti,ab
s diffusion(w)tensor(w)imag?/ti,ab,de
s dti/ti,ab
s fluid(w)attentuated(w)inversion(w)recovery/ti,ab,de
s flair/ti,ab
s s2:s21
s s1 and s22
s animal/de
s human/de
s s24 not (s24 and s25)
s s23 not s26
s case(w)report/ti,de
s s27 not s28

Dissertation Abstracts

Via Dialog
Search date: 22 July 2003
Retrieved: 37

Search strategy
s epilep?/ti,ab,de
s magnetic(w)resonance(w)tomograph?/ti,ab,de
s magnetic(w)resonance(w)scan?/ti,ab,de
s magnetic(w)resonance(w)imag?/ti,ab,de
s magnetic(w)resonance(w)spectroscop?/ti,ab,de
s mr(w)tomograph?/ti,ab,de
s mr(w)scan?/ti,ab,de
s mr(w)imag?/ti,ab,de
s mr(w)spectroscop?/ti,ab,de
s fmri or mri or nmr or mrs/ti,ab
s spect/ti,ab,de
s single(w)photon(w)emission(w)computed(w)tomograph?/ti,ab,de
s volumetric(w)exam?/ti,ab,de
s quantitative(w)t2(w)measure?/ti,ab,de
s voxel(w)based(w)morphomet?/ti,ab,de
s diffusion(w)weight?(w)imag?/ti,ab,de
s dwi/ti,ab
s diffusion(w)tensor(w)imag?/ti,ab,de
s dti/ti,ab
s fluid(w)attentuated(w)inversion(w)recovery/ti,ab,de
s flair/ti,ab
s s2:s21
s s1 and s22

Inside Conferences

Via Dialog
Search date: 22 July 2003
Retrieved: 209

Search strategy
s epilep?/ti,de
s ct=epilep?
s magnetic(w)resonance(w)tomograph?/ti,de
s ct=(magnetic(w)resonance(w)tomograph?)
s magnetic(w)resonance(w)scan?/ti,de
s ct=(magnetic(w)resonance(w)imag?)
s magnetic(w)resonance(w)imag?/ti,de
s ct=(magnetic(w)resonance(w)imag?)
s magnetic(w)resonance(w)spectroscop?/ti,de
s ct=(magnetic(w)resonance(w)spectroscop?)
s mr(w)tomograph?/ti,de
s ct=(mr(w)tomograph?)
s mr(w)scan?/ti,de
s ct=(mr(w)scan?)
s mr(w)imag?/ti,de
s ct=(mr(w)imag?)

s mr(w)spectroscop?/ti,de
s ct=(mr(w)spectroscop?)
s fmri or mri or nmr or mrs/ti,ab
s spect/ti,de
s ct=spect
s single(w)photon(w)emission(w)computed(w) tomograph?/ti,de
s ct=(single(w)photon(w)emission(w)computed(w) tomograph?)
s volumetric(w)exam?/ti,de
s ct=(volumetric(w)exam?)
s quantitative(w)t2(w)measure?/ti,de
s ct=(quantitative(w)t2(w)measure?)
s voxel(w)based(w)morphomet?/ti,de
s ct=(voxel(w)based(w)morphomet?)
s diffusion(w)weight?(w)imag?/ti,de
s ct=(diffusion(w)weight?(w)imag?)
s dwi/ti
s diffusion(w)tensor(w)imag?/ti,de
s ct=(diffusion(w)tensor(w)imag?)
s dti/ti
s fluid(w)attentuated(w)inversion(w)recovery/ti,de
s ct=(fluid(w)attentuated(w)inversion(w)recovery)
s flair/ti,ab
s s2:s38
s s1 and s39

NHS EED

Via CRD's B system
Search date: 24 October 2003
Results: 4 (2 after deduplication)

Search strategy

Epilepsy$
magnetic(w)resonance(w)imaging
magnetic(w)resonance(w)spectroscopy
magnetic(w)resonance
mr(w)tomograph$
mr(w)scan$
mr(w)imag$
mr(w)spectroscop$
fmri or mri or nmr or mrs
tomography(w)emission
spect
single(w)photon(w)emission(w)computed(w) tomograph$
volumetric(w)exam$
quantitative(w)t2(w)measure$
voxel(w)based(w)morphomet$
diffusion(w)weight$(w)imag$
dwi/ttl
diffusion(w)tensor(w)imag$
dti/ttl
flair
fluid(w)attentuated(w)inversion(w)recovery
s2 or s3 or s4 or s5 or s6 or s7 or s8 or s9 ot s10 or s11 or s12 or s13 or s14 or s15 or s16 or s17 or s18 or s19 or s20 or s21
s1 and s22

OHE HEED

Via CD ROM (disk coverage 1005 to October 2003)
Search date: 24 October 2003
Results: 6 (4 after deduplication)

Search strategy

epilep* AND 'magnetic resonance'
epilep* AND tomograph*
epilep* AND scan*
epilep* AND imag*
epilep* AND spectroscop*
epilep* AND fmri
epilep* AND mri
epilep* AND nmr
epilep* AND mrs
epilep* AND 'tomography emission'
epilep* AND spect
epilep* AND 'single photon'
epilep* AND 'volumetric exam*'
epilep* AND 'quantitative t2 measure*'
epilep* AND 'voxel based morphomet*'
epilep* AND 'diffusion weight*'
epilep* AND dwi
epilep* AND 'diffusion tensor'
epilep* AND dti
epilep* AND flair
epilep* AND 'fluid attentuated inversion recovery'
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21

A number of Internet-based resources [such as the GrayLit Network (http://www.osti.gov/graylit/), Economics Working Papers Archive (http://econwpa.wustl.edu/) and Current Controlled Trials (http://www.controlled-trials.com/mrct/)] were searched, but these resources did not identify any further papers. In addition, using search engines such as Google (http://www.google.com) or Copernic (http://www.copernic.com/) did not identify any further studies.

Appendix 3

Details of criteria for scoring studies

Diagnostic accuracy studies using QUADAS

1. Was the spectrum of patients representative of the patients who will receive the test in practice?

Yes Unselected prospective patients with refractory epilepsy being considered for surgery. No restrictions in terms of age or sex were applied.

No All other patient spectra including retrospectively selected patient spectra

Unclear If insufficient details were provided to make a judgement as to whether the patient spectrum would be scored as 'yes', or if it was unclear if the study was prospective or retrospective.

2. Were selection criteria clearly described?

Yes Enough details are provided of how patients were selected so that the selection process could be replicated.

No Insufficient details are presented.

Unclear Not applicable.

3. Is the reference standard likely to classify the target condition correctly?

Yes Ictal EEG or consensus decision (including site of surgery)

No All other reference standards.

Unclear If details of the reference standard are not reported.

Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?

Studies were not scored for this item as it does not apply to this topic area. Patients included in the review are already known to have epilepsy and it is very unlikely that the seizure focus will change between tests, even if there is a considerable delay between tests.

4. Did the whole sample or a random selection of the sample receive verification using a reference standard of diagnosis?

Yes If the whole sample or a random selection of the sample received a reference standard.

No If only a selected sample received the reference standard.

Unclear If it is not clear whether all the patients received the reference standard.

5. Did patients receive the same reference standard regardless of the index test result?

Yes If all patients received the same reference standard. If a combination reference standard was used with patients receiving different parts of the combination this was also considered as the 'same' reference standard.

No If some patients received a different reference standard.

Unclear If it is not clear whether all patients received the same reference standard.

6. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?

Yes If the index test and reference standard were independent.

No If the index test formed part of the reference standard.

Unclear If it is not clear if the index test and reference standard were independent.

7a. Was the execution of the index test described in sufficient detail to permit replication of the test?

Yes If sufficient details of test execution are reported so that all the required details can be completed on the data extraction forms.

No If sufficient details are not reported.

Unclear Not applicable.

7b. Was the execution of the reference standard described in sufficient detail to permit its replication?

Yes If it is clear how a decision on the seizure focus was made – it is not necessary for a study to report full details of how each of the individual tests that constitute the reference standard were conducted.

No If sufficient details are not reported.

Unclear Not applicable.

8a. Were the index test results interpreted without knowledge of the results of the reference standard?

8b. Were the reference standard results interpreted without knowledge of the results of the index test?

Yes If the index test was interpreted without knowledge of the results of the reference standard and vice versa. If one test was clearly interpreted before the results of the other test were available then this should be scored as 'yes'.

No If the person interpreting the index test was aware of the results of the reference standard or vice versa.

Unclear If no information is provided regarding whether tests were interpreted blindly.

9. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?

Yes The results of all other tests should be available to the person interpreting the results of the index test.

No If not as above.

Unclear If details on the availability of clinical data are not reported.

10. Were uninterpretable/intermediate test results reported?

Yes If details are provided on uninterpretable/intermediate test results.

No If there appear to be some uninterpretable/intermediate but the results of these are not reported.

Unclear If it is not clear whether there were any uninterpretable/intermediate test results.

11. Were withdrawals from the study explained?

Yes If all patients recruited into the study were accounted for.

No If there appear to be patients who were recruited into the study who are not accounted for.

Unclear If it is not clear whether any withdrawals occurred.

Cohort studies using checklist from CRD Report 4[20]

1. Is there sufficient description of the groups and the distribution of prognostic factors?

Yes If enough details are provided of how patients were selected so that the selection process could be replicated.

No If insufficient details are presented.

Unclear Not applicable.

Are the groups assembled at a similar point in their disease progression?

Studies included in the review were not scored on this item. Patients included in the review are already known to have epilepsy and it is very unlikely that the seizure focus will change between tests, even if there is a considerable delay between tests.

2. Was the neuroimaging test reliably evaluated?

Yes Details of test execution reported, definition of an exposed (positive) results defined, images were assessed blind to outcome following surgery.

No One or more of the above was not fulfilled.

Unclear If it was unclear whether images were assessed blind to outcome following surgery but test details and definition of a positive result were reported.

3. Were the groups comparable on all important confounding factors?

Yes A recent review found that the following items showed a significant association with outcome following epilepsy surgery: febrile seizures, mesial temporal sclerosis, tumours, EEG/MRI concordance and extent of surgical excision. Studies must therefore report on the distribution of these potential confounding factors within the groups, and groups must be comparable with respect to these factors. If any of these factors is the neuroimaging test being evaluated then this should not be included in this list.[368]

No If groups are not comparable with respect to one or more of these potential confounding factors.

Unclear If the distribution of these factors between groups is not reported.

4. Was there adequate adjustment for the effects of these confounding factors?

Yes If all the confounding factors listed above are adjusted for in the analysis.

No If one or more of these factors is not considered in the analysis.

Unclear If it is unclear whether these factors were included in the analysis.

Was a dose–response relationship between intervention and outcome demonstrated?

The neuroimaging studies would not be expected to show a dose–response and so this item was not considered relevant to these studies.

5. Was outcome assessment blind to exposure status?

Yes If outcome following surgery was assessed blinded to the results of the neuroimaging evaluations.

No If outcome assessment was not blinded.

Unclear If the authors do not report on blinding.

6. Was the follow-up long enough for the outcome to occur?

Yes If duration of follow-up following surgery was longer than 12 months in all patients.

No If duration of follow-up following surgery was <12 months.

Unclear If duration of follow-up following surgery was not reported.

7. Were study withdrawals reported?

Yes If all patients recruited into the study were accounted for.

No If there appear to be patients who were recruited into the study who are not accounted for.

Unclear If it is not clear whether any withdrawals occurred.

8. Were drop-out rates and reasons for drop-out similar across exposure groups?

Yes If drop-out rates and reasons for withdrawal were similar across exposure groups.

No If drop-out rates and reasons for withdrawal were not similar across exposure groups.

Unclear If drop-out rates and reasons for withdrawal were not reported.

Appendix 4

Details of studies excluded from the review

The reasons for exclusion from the review are highlighted in bold.

Study	Study type	Focus localisation?	At least one imaging technique and comparison technique?	No. of patients	Refractory epilepsy?	Considered for surgery?	Study design	$n \times n$ data?	Patient outcome data?
Acharya, 2000[126]	Imaging	Yes	No	≥ 20	**Not clear**	Yes		**No**	Yes
Akata, 1999[127]	Imaging	**No**							
Alving, 1999[128]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	**No**	**No**
Andersen, 1988[129]	Imaging	Yes	Yes	**<10**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Andersen, 1990[130]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Andersen, 1996[131]	Imaging	**No**							
European Federation of Neurological Societies Tasks Force, 2000[132]	**Background**								
Antar, 1991[133]	Imaging	Yes	Yes	≥ 20	**Not clear**	**Not clear**	Diagnostic accuracy	**No**	**No**
Antar, 1992[134]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Antar, 1992[135]	Imaging	**Not clear**	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Antel, 2000[136]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Asenbaum, 1999[137]	Imaging	Yes	Yes	**11–19**	**Not clear**	**Not clear**	Diagnostic accuracy	**No**	**No**
Assaf, 2001[138]	Imaging	Yes	Yes	**11–19**	Yes	Yes	**Other**	**No**	**No**
Bae, 1996[139]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Beach, 1994[140]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Not clear**	**No**	**No**
Bell, 1994[141]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	**No**	**No**
Bell, 1995[142]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Bell, 1997[143]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Berkovic, 1995[144]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Bockisch, 1990[145]	Imaging	Yes	Yes	≥ 20	**Not clear**	Yes	**Other**	**No**	**No**
Boon, 2002[146]	**Other**								
Borbely, 2001[147]	Imaging	Yes	Yes	≥ 20	**Not clear**	**Not clear**	Diagnostic accuracy	**No**	**No**
Brinkmann, 1998[148]	**Other**								
Bronen, 1996[149]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Bronen, 1996[150]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Bronen, 1997[151]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Buchpiguel, 2000[152]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Bui, 1996[153]	Imaging	Yes	Yes	≥ 20	**Not clear**	Yes	**Other**	**No**	**No**
Cascino, 1989[154]	Imaging	**No**							
Cendes, 1994[155]	Imaging	Yes	Yes	**11–19**	**Not clear**	**Not clear**	**Not clear**	**No**	**No**
Cendes, 1994[156]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	**No**
Cendes, 1997[157]	Imaging	**No**							

continued

Study	Study type	Focus localisation?	At least one imaging technique and comparison technique?	No. of patients	Refractory epilepsy?	Considered for surgery?	Study design	$n \times n$ data?	Patient outcome data?
Chan, 1996[158]	Imaging	Yes	Yes	≥ 20	**Not clear**	Yes	**Other**	**No**	**No**
Chinvarun, 1996[159]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Chung, 1998[160]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Chung, 1999[161]	Imaging	**No**							
Comair, 1994[162]	Imaging	Yes	Yes	< 10	Yes	**Not clear**	**Other**	**No**	**No**
Connelly, 1994[163]	Imaging	Yes	Yes	≥ 20	Yes	**No**	Diagnostic accuracy	Yes	
Consalvo, 2000[164]	Imaging	**No**							
Consalvo, 2001[165]	Imaging	Yes	Yes	≥ 20	**No**	**No**	Diagnostic accuracy	Yes	
Cook, 1992[167]	Imaging	Yes	**No**						
Cook, 1992[168]	Imaging	Yes	**No**				Diagnostic accuracy		
Cook, 1992[169]	Imaging	Yes	**No**				Diagnostic accuracy		
Cook, 1994[170]	**Background**								
Cook, 1996[171]	**Background**								
Crespel, 1999[172]	Imaging	Yes	**No**	≥ 20	Yes	Yes	**Other**	**No**	**No**
Cui, 2001[173]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
da Silva, 1995[174]	Imaging	**No**							
da Silva, 1997[175]	Imaging	Yes	Yes	**11–19**	Yes	Yes	**Other**	**No**	**No**
Debets, 1991[176]	**Background**								
DellaBadia, 1995[177]	Imaging	**No**							
DellaBadia, 2002[178]	Imaging	**No**							
Devaux, 2000[179]	Imaging	**No**							
Drzezga, 1998[180]	Imaging	Yes	**No**	**11–19**	**Not clear**	Yes		**No**	**No**
Duncan, 1992[181]	Imaging	**No**							
Eliashiv, 1997[182]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	**Other**	**No**	**No**
Eliashiv, 1998[183]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	**No**	**No**
Eliashiv, 1998[184]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Eliashiv, 1999[185]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Eliashiv, 2000[186]	Imaging	Yes	Yes	≥ 20	Yes	**Not clear**	Diagnostic accuracy	**No**	**No**
Eliashiv, 2002[187]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Engel, 1982[188]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Epstein, 1996[166]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Feistel, 1992[189]	Imaging	Yes	**Not clear**	< 10	Yes	Yes	**Not clear**	**No**	**No**
Fois, 1995[190]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Forster, 1998[191]	Imaging	Yes	Yes	≥ 20	**Not clear**	**Not clear**	**Other**	**No**	**No**
Frank, 2001[192]	Imaging	Yes	Yes	**< 10**	Yes	Yes	**Other**	**No**	**No**
Gallen, 1997[193]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**

continued

Study	Study type	Focus localisation?	At least one imaging technique and comparison technique?	No. of patients	Refractory epilepsy?	Considered for surgery?	Study design	$n \times n$ data?	Patient outcome data?
Garcia, 1994[194]	Imaging	**No**							
Giobbe, 1995[196]	Imaging	Yes	Yes	≥ 20	**Not clear**	**Not clear**	**Other**	**No**	**No**
Gries, 2001[197]	Imaging	Yes	Yes	≥ 20	**No**	Yes	**Other**	**No**	**No**
Guldvog, 1994[199]	Imaging	Yes	**No**	≥ 20	Yes	Yes	Cohort	No	Yes
Hajek, 1995[200]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Hammers, 1998[201]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	No	No
Hammers 2003[202]	Imaging							**No**	
Hammers 2001[203]	Imaging	Yes	**No**	≥ 20	**Not clear**	**Not clear**	Diagnostic accuracy	No	No
Hammers 2002[204]	Imaging	**No**							
Hartley, 2002[205]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	
Harvey, 1997[206]	**Background**								
He, 2001[207]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	Yes	**No**
Heinz, 1994[208]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Helveston, 1996[209]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	Yes	Yes
Ho, 1994[124]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	Yes	**No**
Hong, 2000[210]	Imaging	Yes	**No**	**11–19**	**Not clear**	**Not clear**	**Other**	**No**	**No**
Hong, 1994[211]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Hugg, 1992[212]	Imaging	Yes	**No**	**11–19**	Yes	**Not clear**	**Other**	**No**	**No**
Hugg, 1993[213]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	**No**
Jack, 1992[214]	Imaging	**No**							
Jackson, 1991[215]	Imaging	Yes	Yes	**11–19**	Yes	Yes	**Other**	**No**	**No**
Jackson, 1993[216]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	
Jackson 1993[217]	Imaging							**No**	
Jackson 1993[218]	Imaging							**No**	
Jackson 1999[219]	Imaging		**No**						
Jackson 1989[220]	Imaging							**No**	
Jackson 1992[221]	Imaging		**No**						
Jackson 1993[222]	Imaging		**No**						
Janicek, 1991[223]	Imaging	Yes	Yes	**<10**	**Not clear**	**Not clear**	Diagnostic accuracy	Yes	**No**
Jing, 2002[224]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Jutila, 1999[225]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Kalra, 2001[226]	Imaging	Yes	Yes	≥ 20	Yes	**Not clear**	**Other**	**No**	**No**
Kato, 1993[227]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	**No**	**No**
Kien, 1992[228]	Imaging	**No**							
Kikuchi, 2000[229]	Imaging	**No**							
Kim, 1999[76]	Imaging	Yes	Yes	≥ 20	**Not clear**	Yes	Diagnostic accuracy	**No**	**No**

continued

Study	Study type	Focus localisation?	At least one imaging technique and comparison technique?	No. of patients	Refractory epilepsy?	Considered for surgery?	Study design	$n \times n$ data?	Patient outcome data?
Koga, 1998[230]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Koh, 1999[231]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Konermann, 2003[232]	Imaging	Yes	**No**	**11–19**	Yes	Yes	**Other**	**No**	**No**
Koo, 1996[233]	Imaging	**No**							
Kraemer, 1995[234]	Imaging	**No**							
Krings, 1997[235]	Imaging	Yes	Yes	**<10**	**Not clear**	Yes	**Other**	**No**	**No**
Laich, 1997[236]	Imaging	**No**							
LaManna, 1989[237]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	**Other**	**No**	**No**
Lamusuo, 1996[238]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	**No**	**No**
Lamusuo, 1997[239]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	Yes	**No**
Lamusuo, 1999[240]	Imaging	Yes	Yes	**<10**	Yes	Yes	Diagnostic accuracy	Yes	Yes
Lancman, 1997[241]	Imaging	Yes	Yes	**<10**	Yes	Yes	Diagnostic accuracy	Yes	**No**
Lantz, 1992[242]	Imaging	Yes	Yes	**11–19**	Yes	Yes	**Other**	**No**	**No**
Lantz, 1994[243]	Imaging	Yes	Yes	**11–19**	Yes	Yes	**Other**	**No**	**No**
Lassen, 1989[244]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Lawson, 2000[245]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Lee, 1997[246]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Lee, 1986[247]	Imaging	**No**							
Lee, 1986[248]	**Background**								
Lee, 1988[249]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	Yes	**No**
Lee, 1992[250]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Lee, 2000[251]	Imaging	Yes	**No**	≥ 20	**Not clear**	Yes		**No**	**No**
Lemieux, 1999[252]	Imaging	Yes	**No**	**<10**	**Not clear**	**Not clear**		**No**	**No**
Leroy, 1992[253]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Lewis, 1996[254]	Imaging	Yes	Yes	**<10**	**Not clear**	**Not clear**	Diagnostic accuracy	**No**	**No**
Lukban, 1994[255]	Imaging	Yes	**Not clear**	**<10**	**Not clear**	**Not clear**	**Other**	**No**	**No**
Lynch, 1995[256]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	Yes	Yes
Mackay, 2000[18]	Imaging	**No**							
Maeda, 1992[257]	Imaging	**No**							
Magistretti, 1982[258]	Imaging	**No**							
Manno, 1994[259]	Imaging	**No**							
Markand, 1992[260]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Marks, 1992[261]	Imaging	Yes	Yes	**11–19**	**Not clear**	**No**	**Other**	**No**	**No**
Martinez, 1994[262]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Mathews, 1995[263]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Meltzer, 1996[264]	Imaging	Yes	Yes	≥ 20	Yes	**Not clear**	**Other**	**No**	**No**

continued

Study	Study type	Focus localisation?	At least one imaging technique and comparison technique?	No. of patients	Refractory epilepsy?	Considered for surgery?	Study design	$n \times n$ data?	Patient outcome data?
Meyer, 1990[265]	Imaging	Yes	Yes	**11–19**	Yes	Yes	**Other**	**No**	**No**
Meyer, 2000[266]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Mitchell, 2002[267]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Mitchell, 2002[268]	Imaging	**No**							
Miura, 1990[269]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Miura, 1992[270]	Imaging	**Not clear**	**No**	≥ 20	Yes	**Not clear**	**Other**	**No**	**No**
Morris, 2000[271]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	**No**
Moser, 2000[272]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Motamedi, 1998[195]	Imaging	Yes	Yes	**<10**	Yes	Yes	Diagnostic accuracy	Yes	Yes
Mountz, 1994[273]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	**No**
Mountz, 1997[274]	Imaging	Yes	Yes	**<10**	**Not clear**	Yes	**Other**	**No**	**No**
Mullin, 1996[275]	Imaging	Yes	Yes	**<10**	**Not clear**	Yes	**Other**	**No**	**No**
Murro, 1993[276]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	**No**	**No**
Muscas, 1990[277]	Imaging	**No**							
Muzik, 2000[278]	Imaging	**No**							
Nagata, 1994[198]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	**No**
Nagata, 1995[279]	Imaging	Yes	Yes	**<10**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Nariai, 1996[280]	Imaging	Yes	Yes	**<10**	Yes	**Not clear**	**Other**	**No**	**No**
Newton, 1994[281]	Imaging	Yes	**Not clear**	≥ 20	Yes	Yes	**Other**	**No**	**No**
Ng, 1995[282]	Imaging	Yes	**No**	**<10**	**Not clear**	Yes		**No**	**No**
Nirkko, 2001[283]	Imaging	**No**							
O'Brien, 1999[284]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Okpaku, 1999[285]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Ormson, 1986[286]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Ostertun, 1992[287]	Imaging	**No**							
O'Tuama, 1991[288]	Imaging	Yes	Yes	**<10**	Yes	**Not clear**	**Other**	**No**	**No**
O'Tuama, 1991[289]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	**No**
Packard, 1995[290]	Imaging	**No**							
Packard, 1996[291]	Imaging	Yes	Yes	**<10**	Yes	Yes	Diagnostic accuracy	Yes	**No**
Parekh, 1992[292]	Imaging	Yes	Yes	≥ 20	**Not clear**	Yes	Diagnostic accuracy	**No**	**No**
Park, 2001[293]	Imaging	**No**							
Park, 2002[294]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Pawlik, 1999[295]	Imaging	Yes	Yes	≥ 20	**Not clear**	**Not clear**	**Other**	**No**	**No**
Pozo, 1999[296]	Imaging	Yes	Yes	**11–19**	Yes	Yes	**Other**	**No**	**No**
Ramalheira, 1999[297]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Reiche, 1997[298]	Imaging	**No**							

continued

Study	Study type	Focus localisation?	At least one imaging technique and comparison technique?	No. of patients	Refractory epilepsy?	Considered for surgery?	Study design	$n \times n$ data?	Patient outcome data?
Romigi, 2001[299]	Imaging	Yes	Yes	**11–19**	**Not clear**	**Not clear**	Diagnostic accuracy	**No**	**No**
Ryvlin, 1995[300]	Imaging	Yes	Yes	≥ 20	Yes	**Not clear**	Diagnostic accuracy	**No**	**No**
Ryvlin, 1991[301]	Imaging	Yes	**No**	≥ 20	Yes	**Not clear**	**Other**	**No**	**No**
Ryvlin, 1992[302]	**Background**								
Ryvlin, 1998[303]	Imaging							**No**	
Ryvlin, 2002[304]	Imaging	**No**							
Ryvlin, 1992[305]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Sappey–Marinier, 1995[306]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Sasagawa, 2000[307]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	**No**
Savic, 1993[308]	Imaging	Yes	Yes	**<10**	Yes	Yes	Diagnostic accuracy	**No**	**No**
Schuler, 1992[309]	Imaging	Yes	Yes	≥ 20	**Not clear**	**Not clear**	Diagnostic accuracy	**No**	**No**
Seeck, 1998[310]	Imaging	Yes	Yes	**<10**	**Not clear**	**Not clear**	**Other**	**No**	**No**
Seeck, 2001[311]	**Background**								
Seo, 1996[312]	Imaging	Yes	Yes	**11–19**	**Not clear**	**Not clear**	Diagnostic accuracy	**No**	**No**
Shen, 1989[313]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Shiga, 2002[314]	Imaging	Yes	Yes	**11–19**	**Not clear**	**Not clear**	Diagnostic accuracy?	**No**	**No**
Sinha, 2003[315]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Sjoholm, 1995[316]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	**Other**	**No**	**No**
So, 2000[317]	**Background**								
Spanaki, 1998[318]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Spanaki, 1999[319]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	Yes	**No**
Spanaki, 1999[320]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Spanaki, 2001[321]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Spanaki, 1997[322]	Imaging	Yes	Yes	**<10**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Spina, 1993[323]	Imaging	Yes	Yes	≥ 20	Yes	**No**	Diagnostic accuracy	Yes	**No**
Stefan, 1987[324]	Imaging	Yes	Yes	**11–19**	**Not clear**	**Not clear**	Diagnostic accuracy	Yes	**No**
Stefan, 1994[325]	**Other**								
Sturm, 2000[326]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	**No**
Sussman, 1986[327]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	**No**	**No**
Swartz, 1992[328]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Heiss, 1995[329]	Imaging	Yes	Yes	**<10**	**Not clear**	**Not clear**	**Other**	**No**	**No**
Tallibert, 1999[330]	Imaging	Yes	**No**	≥ 20	Yes	Yes	**Other**	**No**	**No**
Tanaka, 1996[331]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	Yes
Tanaka, 1997[332]	Imaging	Yes	Yes	**<10**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Tanaka, 2000[333]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	**No**
Tecoma, 1995[334]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**

continued

Study	Study type	Focus localisation?	At least one imaging technique and comparison technique?	No. of patients	Refractory epilepsy?	Considered for surgery?	Study design	$n \times n$ data?	Patient outcome data?
Thadani, 1999[335]	Imaging	Yes	Yes	≥ 20	**Not clear**	Yes	Diagnostic accuracy	**No**	**No**
Theodore, 1986[336]	Imaging	**No**							
Thomas, 2002[337]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Thompson, 1996[338]	Imaging	Yes	Yes	**<10**	Yes	**Not clear**	**Other**	**No**	**No**
Thompson, 1997[339]	Imaging	Yes	**No**	**11–19**	Yes	**Not clear**	**Other**	**No**	**No**
Thompson, 1998[340]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	Yes	**No**
Tikofsky, 1993[341]	Imaging	**No**							
Udani, 1998[342]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Udani, 1999[343]	Imaging	Yes	Yes	≥ 20	**Not clear**	Yes	**Other**	**No**	Yes
Valenti, 2002[344]	Imaging	Yes	Yes	**<10**	Yes	Yes	Diagnostic accuracy	Yes	Yes
Valerio, 2000[345]	Imaging	**No**							
van Huffelen, 1990[346]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	**No**	**No**
van Isselt, 1990[347]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	**No**	**No**
Vera, 1997[348]	Imaging	Yes	Yes	**<10**	**Not clear**	**Not clear**	**Other**	**No**	**No**
Vera, 1998[349]	Imaging	**No**							
Verhoeff, 1992[350]	Imaging	Yes	Yes	≥ 20	**No**	**No**	**Other**	**No**	**No**
von Oertzen, 2002[351]	Imaging	Yes	Yes	≥ 20	Yes	Yes	**Other**	**No**	**No**
Warach, 1995[352]	Imaging	Yes	**Not clear**	**<10**	Yes	**Not clear**	**Other**	**No**	**No**
Wheless, 1989[353]	Imaging	**No**							
Wheless, 1991[354]	Imaging	**No**							
Wheless, 1991[355]	Imaging	**No**							
Wheless, 1991[356]	Imaging	**No**							
Wichert–Ana, 1998[357]	Imaging	Yes	Yes	**11–19**	Yes	Yes	**Other**	**No**	**No**
Wielepp, 1999[358]	Imaging	Yes	Yes	**<10**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Wissmeyer, 2001[359]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	Yes	**No**
Wissmeyer, 2001[360]	Imaging	Yes	Yes	**<10**	Yes	**Not clear**	**Other**	**No**	**No**
Wissmeyer, 2002[361]	Imaging	Yes	Yes	**11–19**	Yes	Yes	Diagnostic accuracy	**No**	**No**
Won, 1999[362]	Imaging	Yes	Yes	≥ 20	Yes	Yes	Diagnostic accuracy	**No**	**No**
Wong, 1995[363]	Imaging	Yes	**No**	≥ 20	**Not clear**	Yes	**Other**	**No**	**No**
Worrell, 2000[364]	**Other**								
Worrell, 2001[365]	**Other**								
Yeh, 1998[366]	Imaging	Yes	Yes	**11–19**	Yes	**Not clear**	Diagnostic accuracy	**No**	**No**
Ylinen, 1988[367]	Imaging	Yes	Yes	**<10**	Yes	Yes	**Other**	**No**	**No**
Yoshinaga, 1996[368]	Imaging	Yes	Yes	≥ 20	**No**	Yes	**Other**	**No**	**No**
Zubal, 1997[369]	Imaging	Yes	Yes	**11–19**	**Not clear**	Yes	Diagnostic accuracy	**No**	**No**

Appendix 5
Study details

Diagnostic accuracy studies

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Achten, 1997[29] **Study design** Prospective diagnostic cohort **Country of study** Belgium **Study objective** To compare MR spectroscopy and PET as to their effectiveness in lateralising seizure focus in patients with TLE **Aim** Lateralising **Subgroups assessed** No structural abnormality	**Population:** Children and adults **Patient spectrum:** Consecutive patients with symptoms of TLE refractory to medical treatment, with no tumours or vascular malformations, traumatic lesions or neuronal migration disease entering a presurgical evaluation programme. **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 30.2 (14–53) years **No. of patients (male):** 29 (11) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 29 **Syndrome:** Not reported	**No. of patients who underwent surgery:** 17 **Type of surgery:** **ATL:** 17 **Duration of follow-up following surgery:** 6–36 months **Outcome following surgery:** **Class I:** Engel: no further details: 11 **Class III:** 2	**Reference standard** Combination **Details:** All patients underwent clinical neurological examination and several scalp interictal and ictal EEGs; some patients also underwent video-EEG monitoring and further depth electrode EEGs **Drop-outs:** Consensus decisions not reached (n = 2); clinical/EEG presurgical evaluations non-lateralising (n = 4). Outcome data reported for 13 patients as others did not have surgery or had recent surgery	**Test 1: MRS:** Volumetric **Contrast agent:** None reported **Magnet strength:** 1.5 T **Weighting:** H MRS **Metabolites:** NAA/(Cho + Cr), 2 ppm NAA, 3 ppm Cr, 3.2 ppm Cho **What was imaged:** Mesotemporal lobes including part of hippocampus. Reference scans with the same parameters but without water suppression compensated for eddy current artefacts **Definition of a localised scan:** Areas with metabolic ratios [NAA/(Cho + Cr) below 0.70 were considered abnormal]. Asymmetry indexes (AI) were calculated. When one/both NAA/(Cho + Cr) ratios normal, AI > 0.11 considered lateralising. When ratios abnormal, AI > 0.05 considered lateralising **Test 2: MRI:** Volumetric **Magnet strength:** 1.5 T **Weighting:** T1 **Slice orientation:** Coronal **Slice thickness:** Not reported **What was imaged:** Temporal lobes and hippocampal structures **Definition of a localised scan:** Not reported **Test 3: PET:** Interictal **Tracer: FDG:** 185 MBq (5 mCi) **Camera strength:** ECAT IV scanner (n = 20) or an ECAT 951/31 scanner (n = 9) **Slice orientation:** Axial/transaxial **Slice thickness:** Not reported **Timing from injection to scan:** 30 minutes **Definition of a localised scan:** Hypometabolism

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Adams, 1992[30] **Study design** Retrospective diagnostic cohort **Country of study** Canada **Study objective** To assess the contribution of ^{99m}Tc-HmPAO SPECT to localisation of epileptiform foci **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children **Patient spectrum:** Patients with partial epilepsy **Inclusion criteria relating to outcome:** All children had to have surgery to be included **Mean age (range):** 7.5 years (4.5 months–18 years) **No. of patients (male):** 20 (7) **Duration of epilepsy:** <1–16 years **Type of epilepsy:** **Temporal:** Not reported **Mesial sclerosis:** 3 **Non-temporal:** Not reported **Other lesions:** 10 **Syndrome:** 2 with Sturge–Weber **Details:** 6 with tumours. 1 with cavernous hemangioma. 1 with porencephalic cyst and gliosis. 2 with cysts found at surgery. 4 with cortical dysplasia. 1 with Rasmussen encephalitis	**No. of patients who underwent surgery:** 20 **Type of surgery:** Not reported **Duration of follow-up following surgery:** 2–27 months **Outcome following surgery:** **Class I:** Seizure free: 8 **Class III:** >50% reduction in seizures: 6 **Class IV:** Not improved: 1	**Reference standard** Site of surgery/ pathology site **Details:** EEG using 16–21-channel recordings. Special electrodes included sphenoidal, zygomatic and supraorbital. Video-EEG telemetry used to localise ictal onset. Wada testing. ECoG performed under neuroleptic anaesthesia using a surface 4 × 4 electrode array and depth electrode. SPECT. CT and MRI (in 14 patients) also seem to have contributed	**Test 1: CT** No details reported **Test 2: SPECT: Ictal** **Tracer:** HMPAO: 15 mCi for 1.73 m^2 **Tesla/gamma camera strength:** Single-headed, rotating gamma camera. High-resolution colorimeter at 142 ± % Kev. Ramp–Hanning or Ramp–Butterworth filtering **Timing from seizure onset to injection:** <15 minutes **Slice orientation/metabolites:** Transaxial. Reconstructed sagittal and coronal **Slice thickness:** 9 mm **Timing from injection to scan:** 10–60 minutes **Definition of a localised scan:** Perfusion abnormality on two adjacent images **Drop-outs:** 16 patients did not receive ictal SPECT **Test 3: SPECT:** Interictal Details as for ictal. No details on timing from seizure to scan **Test 4: MRI** No details reported **Drop-outs:** 6 patients did not receive MRI

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Assadi, 1997[31] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To investigate the clinical application and EEG correlation of neuropsychological testing, MRI and SPECT in epilepsy focus localisation **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children **Patient spectrum:** Patients with intractable epilepsy **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 34.6 (23–68) years **No. of patients (male):** 24 (15) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 17 **Mesial sclerosis:** Not reported **Non-temporal:** 7 **Other lesions:** Not reported **Syndrome:** Not reported	**No. of patients who underwent surgery:** Not reported **Outcome following surgery:** Not reported	**Reference standard** EEG **Details:** Surface electrodes with or without sphenoidals	**Test 1: MRI** **Contrast agent:** Not reported **Tesla/gamma camera strength:** 0.5 T **Timing from seizure onset to injection/weighting:** T2, T1, proton density, FLAIR and spin-echo **Slice orientation/metabolites:** Sagittal, axial and coronal **Slice thickness:** Not reported **What was imaged:** Not reported **Definition of a localised scan:** Presence of cortical or hippocampal lesion. Uninterpretable scans were interpreted as non-localising **Test 2: SPECT**: Interictal **Tracer:** HMPAO: dose not reported **Tesla/gamma camera strength:** Not reported **Timing from seizure onset to injection:** Not reported **Slice orientation/metabolites:** Axial, coronal and sagittal **Slice thickness:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Abnormal area of decreased uptake. Uninterpretable scans were considered non-localising **Drop-outs:** 5 patients did not have SPECT scans

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Boundy, 1996[1] **Study design** Unclear: diagnostic cohort **Country of study** Australia **Study objective** To examine the relationship of IDEX binding (IDEX SPECT) to the seizure focus, interictal cerebral blood flow and MRI findings **Aim** Lateralising **Subgroups assessed** No structural abnormality	**Population:** Not reported **Patient spectrum:** Consecutive patients with intractable complex partial seizures without mass lesions on MRI **Inclusion criteria relating to outcome:** None reported **Mean age (range):** Not reported **No. of patients (male):** 23 (not clear; at least 9) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 23 **Mesial sclerosis:** 12 **Non-temporal:** Not reported **Other lesions:** Not reported **Syndrome:** Not reported	**No. of patients who underwent surgery:** 14 **Type of surgery:** **ATL:** 14 **Duration of follow-up following surgery:** >1 year **Outcome following surgery:** **Class I:** Seizure free: 9 **Class II:** >90% improvement in seizure frequency: 3	**Reference standard** Site of surgery **Details:** All patients received presurgical evaluations which included MRI, interictal EEG, ictal video-surface EEG, neuropsychological evaluations and interictal and ictal HMPAO SPECT **Drop-outs:** Outcome data not reported for 2 patients who had surgery due to <12 months follow-up	**Test 1: MRI:** Routine **Contrast agent:** None reported **Magnet strength:** 1.0 T **Weighting: T1 prepared:** rapid acquisition gradient echo sequence and T2 fast spin echo **Slice orientation:** Axial, coronal. Routine T1 and T2 axial sequences, followed by fine slices coronal to plane of temporal lobe using a T1 3D Magnetisation prepared: rapid acquisition gradient echo sequence and T2 fast spin echo. **Slice thickness:** 2–3 mm **What was imaged:** Temporal lobe **Definition of a localised scan:** Graded for hippocampal atrophy, temporal lobe atrophy and hippocampal T2 signal, making an overall assessment of normal, minor change of uncertain or definite hippocampal sclerosis **Test 2: SPECT**: Interictal **Tracer:** HMPAO: dose not reported **Gamma camera strength:** Triple-head gamma camera (TRIAD 88), ultra-high-resolution fan beam collimators **Timing from seizure onset to injection:** Not reported **Slice orientation:** Images reconstructed to produce coronal slices perpendicular to temporal lobe **Slice thickness:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Semi-automated region of interest used to calculate asymmetry index. Focal changes in perfusion noted. Images classified as normal, possible or definite temporal lobe abnormality **Test 3: SPECT**: Interictal **Tracer:** IDEX: 185 MBq (5 mCi) **Timing from seizure onset to injection:** >48 hours **Timing from injection to scan:** 6 hours later **Other details:** as for HMPAO **Definition of a localised scan:** Semi-automated region of interest used to calculate asymmetry index. Focal reductions in IDEX binding noted. Images classified as normal, possible or definite temporal lobe abnormality

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Brooks, 1990[33] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To investigate the efficacy of MR performed at a high field strength in preoperative assessment **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** Not reported **Inclusion criteria relating to outcome:** All patients underwent surgery **Mean age (range):** 26 (7–54) years **No. of patients (male):** 53 (23) **Duration of epilepsy:** 1–52 (mean 18) years **Type of epilepsy:** **Temporal:** Not reported **Mesial sclerosis:** Not reported **Non-temporal:** Not reported **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 1 with perinatal haemorrhage, 38 with mesial temporal gliosis, 4 with a history of severe head trauma, 1 of whom had evacuation of subdural haematoma at 18 months old	**No. of patients that underwent surgery:** 53 **Type of surgery:** None reported **ATL:** Not reported **AH:** Not reported **Non-TL:** Not reported **Other:** 53 **Details:** Subpial method of resection **Duration of follow-up following surgery:** 6–12 months **Outcome following surgery:** **Class I:** Seizure free: 26 **Class II:** <1–2 seizures per year: 4 **Class III:** <90% reduction in seizure frequency: 5	**Reference standard** Site of surgery **Details:** History and physical examination. Neuropsychological testing. Continuous video and EEG with scalp and sphenoidal electrodes. WADA testing. Invasive EEG for 41 patients. Invasive EEG monitoring was omitted when obvious structural lesions were seen on neuroimaging. Craniotomy in patients with seizure focus in functional area. Neuroimaging assessment	**Test 1: CT** **Contrast agent:** With and without contrast agent (agent not reported) **Magnet strength:** General Electric 9800 scanner **Slice orientation:** Transaxial non-enhanced without contrast. Section planes parallel to the long axis of the temporal lobe with contrast **Slice thickness:** 10 mm without contrast, 3 mm for temporal lobe and 10 mm for rest of brain with contrast **Definition of a localised scan:** Not reported **Drop-outs:** CT not available in 7 patients (reasons not reported) **Test 2: MRI:** Routine **Contrast agent:** Not reported **Magnet strength:** 1.5 T **Weighting:** T1, T2 **Slice orientation:** Sagittal, coronal and transaxial **Slice thickness:** T1: 3 mm with 0.6-mm interslice gap. T2: 5 mm with 2.5 mm interslice gap **What was imaged:** Not reported **Type of imaging:** ROI **Definition of a localised scan:** Not reported **Drop-outs:** Results for two patients not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Cendes, 1995[34] **Study design** Unclear: diagnostic cohort **Country of study** Canada **Study objective** To assess the usefulness of magnetic resonance spectroscopic imaging (MRSI) in the evaluation of TLE **Aim** Lateralising **Subgroups assessed** EEG focus	**Population:** Not reported **Patient spectrum:** Consecutive patients with TLE being evaluated for surgical treatment **Inclusion criteria relating to outcome:** None reported **Mean age (range):** Not reported **No. of patients (male):** 60 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 60 **Mesial sclerosis:** 0 **Non-temporal:** 0 **Other lesions:** 0 **Syndrome:** Not reported	**No. of patients who underwent surgery:** Not reported **Type of surgery:** Not reported **Duration of follow-up following surgery:** Not reported **Outcome following surgery:** Not reported	**Reference standard** EEG **Details:** Clinical-EEG lateralisation (no further details supplied)	**Test 1: Combination: MRS and MRI** MRI/MRS: 2D MRS and volumetric MRI combined **What was imaged:** Amygdala and hippocampus **Definition of a localised scan:** Values 2SD from the mean of normal controls considered abnormal for both examinations. No further details supplied **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Cendes, 1997[35] **Study design** Prospective diagnostic cohort **Country of study** Canada **Study objective** To assess the usefulness of proton MRSI and MRI in the evaluation of patients with TLE **Aim** Lateralising **Subgroups assessed** No structural abnormality	**Population:** Adults **Patient spectrum:** Consecutive patients being evaluated for medically refractory TLE **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 35 (±12.4) years **No. of patients (male):** 100 (45) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 100 **Syndrome:** Not reported	**No. of patients who underwent surgery:** 0	**Reference standard** Combination **Details:** Patient history, neurological examination, prolonged EEG using sphenoidal electrodes and ictal video-EEG. Some patients had intercranial EEG	**Test 1: MRI:** Volumetric **Magnet strength:** 1.5 T **Weighting:** 3D fast spin echo **Slice orientation:** Not reported **Slice thickness:** 1–3 mm **What was imaged:** Amygdala and hippocampal structures **Definition of a localised scan:** Asymmetry between sides (right – left)/[(right + left)/2] **Test 2: MRS** **Magnet strength:** 1.5 T **Metabolites:** NAA, Cho and Cr (NAA/Cr) **What was imaged:** Hippocampus **Definition of a localised scan:** Asymmetry of the signal intensity between the two temporal lobes (right – left)/[(right + left)/2]

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Chee, 1993[36] **Study design** Retrospective diagnostic cohort **Country of study** USA **Study objective** To determine the role of FDG PET in lateralising the epileptogenic region in patients who were diagnosed as having TLE based on clinical symptoms and EEG, and did not have a structural lesion on MRI **Aim** Lateralising **Subgroups assessed** No structural abnormality EEG focus	**Population:** Adults **Patient spectrum:** Consecutive patients with complex partial seizures diagnosed as having TLE. All patients with mass lesions on MRI were excluded. Patients with clinical seizure onsets suggestive of an extra temporal focus were excluded **Inclusion criteria relating to outcome:** Patients who underwent temporal lobectomy had at least 1 year of follow-up **Mean age (range):** 32 (18–53) years **No. of patients (male):** 40 (25) **Duration of epilepsy:** 3–36 (mean 19) years **Type of epilepsy:** **Temporal:** 40 **Mesial sclerosis:** Not reported **Syndrome:** Not reported	**No. of patients who underwent surgery:** 38 **Type of surgery:** **ATL:** 38 **AH:** 0 **Non-TL:** 0 **Other:** 0 **Details:** In those who underwent surgery, 37 had unilateral seizure origin and 1 had bilateral seizure origin **Duration of follow-up following surgery:** >1 year **Outcome following surgery:** **Class I:** Seizure free for 1 year: 28 **Class II:** <3 seizures per year: 4 **Class IV:** No improvement: 6	**Reference standard** EEG **Details:** Each patient had video-EEG, with scalp sphenoidal electrodes over 2 periods of ~5 days each. One patient was investigated using foramen ovale and epidural peg electrodes. 11 patients had orthogonally directed bitemporal flexible intracerebral-depth electrodes. Spikes were considered unilateral if ≥ 90% originated from one side. Only ictal onsets that were focal were considered in lateralising the seizure focus	**Test 1: PET** **Tracer:** FDG: 185–370 MBq **Tesla/gamma camera strength:** Posicam tomograph **Timing from seizure onset to injection:** Not reported **Slice orientation:** Images were reconstructed **Slice orientation:** Not reported **Slice thickness:** 5.1 mm **Timing from injection to scan:** 40 minutes **Definition of a localised scan:** Asymmetry in at least two contiguous slices required to be considered abnormal. Results were classified as temporal, temporal plus (extension beyond temporal lobe), bitemporal, extra-temporal or normal **Drop-outs:** None

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Chugani, 1993[38] **Study design** Unclear diagnostic cohort **Country of study** USA **Study objective** To evaluate the role of anatomical and functional neuroimaging in children undergoing surgical treatment for infantile spasms and provide follow-up data on surgical cases **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children **Patient spectrum:** Patients with infantile spasms (n = 17) or in whom spasms had evolved into refractory seizures during presurgical evaluation (n = 6) were included. Children with a remote history of infantile spasms were excluded **Inclusion criteria relating to outcome:** All children underwent cortical resection or hemispherectomy **Mean age (range):** 18.4 (5–44) months **No. of patients (male):** 23 (10) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 19 (all had additional non-temporal foci) **Non-temporal:** 23	**No. of patients who underwent surgery:** 23 **Type of surgery:** **Other:** 23 **Details:** Resections included: 10 parietal-occipitotemporal; 1 occipitotemporal; 1 frontotemporal; 1 centroparitеal; 1 parietal; 1 temporal lobectomy followed by hemispherectomy; 1 parieto-occipital; and 7 hemispherectomies **Duration of follow-up following surgery:** 28.3 (4–67) months **Outcome following surgery:** **Class I:** Seizure free (4 without medication and 10 with medication): 14 **Class II:** Continued seizures controlled with medication (1 after a period of 3 years seizure free) or 90% reduction in seizure frequency or occasional seizures: 4 **Class III:** 75% reduction: 1 **Class IV:** No improvement or >4 seizures per week: 4	**Reference standard** Surgery **Details:** Combination of EEG, MRI, CT, PET, evoked potentials, sodium thiopental activation and intraoperative ECoG **Drop-outs:** CT not performed in all patients	**Test 1: Combination MRI/CT** **Weighting:** T1, T2 No further details reported **Definition of a localised scan:** Not reported **Test 2: PET** **Tracer:** FDG (0.143 mCi/kg) **Tesla/camera strength:** NeuroECAT or CTI 831positron tomographs **Slice orientation:** Parallel to canthomeatal plane **Timing from injection to scan:** >40 minutes **Definition of a localised scan:** Not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Cross, 1996[39] **Study design** Unclear: diagnostic cohort **Country of study** UK **Study objective** To evaluate the contribution of MRS to the lateralisation and localisation of the seizure focus in children with well-characterised TLE **Aim** Lateralising **Subgroups assessed** No subgroup	**Population:** Children **Patient spectrum:** Children with TLE **Mean age (range):** 11 (5–17) years **No. of patients (male):** 20 (6) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 20 **Mesial sclerosis:** 15 with hippocampal sclerosis **Other lesions:** Not reported **Syndrome:** 9 had prolonged febrile convulsion, 6 status epilepticus, 1 simple febrile convulsion, 1 encephalitis	**No. of patients who underwent surgery:** 10 **Type of surgery:** **ATL:** 10 **Duration of follow-up following surgery:** Mean 17.5 (range 2–40) months **Outcome following surgery:** **Class I:** Seizure free: 8 **Class II:** >75% improvement: 1 **Class III:** Daily seizures: 1 **Class IV:** 0	**Reference standard** Combination **Details:** Localised on the basis of clinical history and interictal and/or ictal EEG **Drop-outs:** none reported	**Test 1: MRI:** Routine **Contrast agent:** None reported **Tesla/camera strength:** 1.5 T **Slice orientation:** Oblique, axial and coronal **Slice thickness:** 2 × 2 × 2-cm cubes **Definition of a localised scan:** Not reported **Test 2: MRS** **Tesla/camera strength:** 1.5T **Weighting:** H MRS **Metabolites:** NAA/(Cho + Cr) **Definition of a localised scan:** Values <0.72 were considered to be abnormally low (calculated from control subjects). Ratio considered lateralising if abnormally low and lower than that of contralateral side by >0.05

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Debets, 1997[40] **Study design** Unclear: diagnostic cohort **Country of study** The Netherlands **Study objective** To evaluate the contribution of FDG PET, [^{11}C]flumazenil PET and [^{123}I]iomazenil SPECT to the presurgical evaluation in patients with medically intractable complex partial seizures **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Patients with medically intractable complex partial seizures who were candidates for temporal lobe surgery based on reference testing **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 34 (13–50) years **No. of patients (male):** 23 (9) **Duration of epilepsy:** 7–45 (mean 25) years **Type of epilepsy:** **Temporal:** 23 **Mesial sclerosis:** 17 **Syndrome:** Not reported	**No. of patients who underwent surgery:** 23 **Type of surgery:** 1 patient had temporal and frontal lobe surgery. No further details supplied **Duration of follow-up following surgery:** 0.5–2.5 years (mean 1 year) **Outcome following surgery:** Engel: **Class I:** No further details: 21 **Class III:** 2 **Class IV:** 1	**Reference standard** Site of surgery **Details:** Seizure semiology from ictal recording, ictal and interictal scalp EEG, MRI. 5 patients had DEEG–EEG with intracerebral and subdural electrodes as MRI and scalp EEG were discordant. These were used to determine site of surgery. Site of surgery used as a reference standard	**Test 1: SPECT:** Interictal **Tracer:** IMZ: 4–5 mCi **Gamma camera strength:** Picker PRISM 3000 three-detector rotating gamma camera, with high-resolution fan-beam collimators. Butterworth filter **Timing from seizure onset to injection:** Not reported **Slice orientation:** Transaxial – filtered and reorientated to 'sagittal', 'oblique transaxial' and 'oblique coronal' **Slice thickness:** 7.6 mm. Spatial resolution 7.6 mm **Timing from injection to scan:** 75–80 minutes **Definition of a localised scan:** Not reported **Drop-outs:** 4 patients did not receive SPECT – reasons not reported **Test 2: PET** **Tracer:** FMZ: 20 mCi **Gamma camera strength:** 951 CTI/Siemens tomograph **Timing from seizure onset to injection:** Not reported **Slice orientation:** Transaxial **Slice thickness:** 5 mm thickness, with 3.4 mm slice separation **Timing from injection to scan:** Immediately after injection – with consecutive scans: 3 × 2, 3 × 3, 5 × 6 and 2 × 11 minutes. Scanning time 75 minutes **Definition of a localised scan:** An area of relative decrease in glucose metabolism in at least two contiguous PET slices. It is not clear if the PET scans are ictal or interictal **Test 3: PET** **Tracer:** FDG: 130 mCi **Gamma camera strength:** 951 CTI/Siemens tomograph **Timing from seizure onset to injection:** Not reported **Slice orientation:** Transaxial **Slice thickness:** 5 mm thickness, with 3.4 mm slice separation **Timing from injection to scan:** 30–60 minutes (FDG injection given on completion of C-flumazenil scan) **Definition of a localised scan:** An area of relative decrease in glucose metabolism in at least two contiguous PET slices

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Doi, 1995[41] **Study design** Unclear: diagnostic cohort **Country of study** Japan **Study objective** To investigate the ability of IMZ-SPECT to localise the seizure focus in patients with intractable localisation related epilepsy **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Adults **Patient spectrum:** Patients with intractable localisation related epilepsy being evaluated for epilepsy surgery **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 27 (20–45) years **No. of patients (male):** 25 (14) **Duration of epilepsy:** 7–13 (mean 19) years **Type of epilepsy:** **Temporal:** 14 **Mesial sclerosis:** Not reported **Non-temporal:** 9 **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 7 patients had frontal lobe epilepsy, 2 had parietal lobe epilepsy	**No. of patients who underwent surgery:** Not reported No other details given No outcome data given	**Reference standard** Combination **Details:** Clinical seizure manifestations, EEG figures and neuroimaging including MRI and regional cerebral blood flow (rCBF) SPECT	**Test 1: SPECT:** Ictal **Tracer:** rCBF with IMP 222 MBq, HMPAO and ECD. 740 MBq **Gamma camera strength:** Standard fan beam collimator for IMP, high-resolution fan beam collimator for PAO and ECD **Timing from seizure onset to injection:** Not reported **Slice orientation:** Not reported **Timing from injection to scan:** 5 minutes for PAO, 20 minutes for IMP, 30 minutes for ECD **Definition of a localised scan:** Images grouped into four groups: no abnormality (–), mild abnormality (±), definitive abnormal findings (+), definitely abnormal findings with defect or marked hyperperfusion (++) **Drop-outs:** 4 patients did not receive ictal SPECT **Test 2: SPECT:** Interictal Details as for ictal SPECT **Test 3: SPECT** **Tracer:** IMZ: 111–222 MBq **Gamma camera strength:** STECT (Headtome SET 070), Butterworth and Ramp filters used to reconstruct images, absorption correction according to Sorenson method **Timing from seizure onset to injection:** Not reported **Slice orientation:** Axial, coronal and sagittal **Slice thickness:** 4.72 mm **Timing from injection to scan:** Early scanning: 5–35 minutes **Definition of a localised scan:** As for ictal SPECT **Test 4: SPECT** Details as for IMZ SPECT **Timing from injection to scan:** Late scanning: 165–195 minutes **Test 5: MRI** **Contrast agent:** None reported **Magnet strength:** 1.5 T **Weighting:** T1 and T2 **Slice orientation:** Axial, parallel and perpendicular slices **Slice thickness:** 5 mm **What was imaged:** Not reported **Definition of a localised scan:** Not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Duncan, 1993[42] **Study design** Unclear: diagnostic cohort **Country of study** UK **Study objective** To assess the value of SPECT in localising epileptic foci in presurgical patients **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** Poorly controlled complex partial seizures, with clinical features suggesting temporal lobe involvement, who had been assessed for suitability for surgery **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 22.8 (5–36) years **No. of patients (male):** 28 (13) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 28 **Mesial sclerosis:** Not reported **Other lesions:** Not reported **Syndrome:** Not reported	**No. of patients who underwent surgery:** 23 (2 awaiting) **Type of surgery:** **ATL:** 22 **AH:** 0 **Non-TL:** 0 **Other:** 1 **Details:** 1 removal of tumour from temporal lobe, 3 rejected for surgery owing to bilateral seizure onset **Duration of follow-up following surgery:** 5–36 (median 16) months **Outcome following surgery:** **Class I:** Seizure free: 17 **Class II:** >90% improvement in seizure frequency: 5 **Class IV:** 40% reduction in seizure frequency: 1	**Reference standard** Combination **Details:** Full clinical assessment MRI, ictal and interictal EEG, neuropsychological assessment were used to localise focus and decide whether surgery was to be performed	**Test 1: SPECT:** ictal and interictal **Tracer:** HMPAO: 500 MBq **Gamma camera strength:** Strichmann 810 tomographic imager **Timing from seizure onset to injection:** After 'end of the stare' of a seizure. 8 given during seizure, 14 within 2 minutes, 5 within 15 minutes and 1 at 1.5 hours after end of seizure. Interictal: 24 patients over 24 hours from last seizure onset. 3 patients: 12–24 hours. One 2 hours since last seizure **Slice orientation:** Axial, transaxial **Slice thickness:** 12 mm **Timing from injection to scan:** Within 2 hours **Definition of a localised scan:** Uptake above or below that expected in 2 adjacent slices, limiting sensitivity to 2 cm thick. Ictal and interictal used in combination to determine localisation

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Engel, 1990[43] **Study design** Retrospective diagnostic cohort **Country of study** USA **Study objective** To compare localisation of scalp EEG, sphenoidal EEG, FDG-PET and depth electrodes in order to determine when depth electrode implantation does not provide sufficient additional information **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Patients with medically refractory partial epilepsy who underwent evaluation with depth electrodes prior to surgery **Inclusion criteria relating to outcome:** All included patients had surgery. Patients who had undergone surgical resection for lesions such as tumours or underwent surgery without depth electrodes were excluded from the study **Mean age (range):** Not reported (10–46 years) **No. of patients (male):** 153 (78) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 111 **Mesial sclerosis:** Not reported **Non-temporal:** 11 **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 4 with occipital, 7 with frontal. An additional 4 with non-localising EEG had frontal foci and resections. Focus was never identified in 31 patients	**No. of patients who underwent surgery:** 114 **Type of surgery:** **ATL:** 104 **AH:** 0 **Non-TL:** 10 **Other:** 0 **Details:** Of 109 patients with unilateral TLE, 7 did not have surgery owing to psychological problems (n = 3), discontinuance of seizures after SEEG (n = 2) or death (n = 2). Those with extra-temporal foci: 1 patient with occipital did not undergo surgery as foci not confirmed. A further 4 patients with non-localising SEEG had frontal foci and underwent frontal lobectomy No outcome data	**Reference standard** EEG **Details:** All patients underwent scalp EEG and depth electrode EEG. Site of surgery in 114	**Test 1: PET** **Tracer:** FDG: 5–10 mCi **Gamma camera strength:** 42 scans with ECAT tomograph, 90 with NeuroECAT tomograph and 15 with CTI-831 **Timing from seizure onset to injection:** Not reported **Slice thickness:** ECAT tomograph = 16 mm resolution, NeuroECAT tomograph = 8 mm resolution and CTI-831 = 5 mm resolution **Timing from injection to scan:** 40–60 minutes **Definition of a localised scan:** Localised hypointensity and discrimination of normal from abnormal variables in image intensity **Drop-outs:** Only 147 patients had PET. 2 patients were diagnosed with hemispheric hypometabolism and placed in incorrectly localised category owing to a lack of localisation

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Gilliam, 2000[44] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To determine more accurately the predictive value of presurgical MRI-identified MTS **Aim** Lateralising **Subgroups assessed** No structural abnormality EEG focus	**Population:** Children and adults **Patient spectrum:** Patients without MRI-identified foreign tissue lesions who were assessed for possible anterior temporal lobectomy **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 32 (9–54) years **No. of patients (male):** 90 (46) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 90 **Mesial sclerosis:** Not reported **Syndrome:** Not reported	**No. of patients who underwent surgery:** 77 **Type of surgery:** **ATL:** 77 **Duration of follow-up following surgery:** mean 2.3 years **Outcome following surgery:** **Class I:** Seizure free: 44 **Class III:** Continued seizures: 23	**Reference standard** Site of surgery **Details:** All patients underwent MRI, long-term video-EEG monitoring to record at least three typical seizures and neuropsychological evaluation. (At least) 13 patients had intracranial monitoring. Patients were offered an anterior temporal lobectomy if MRI, interictal EEG and ictal EEG localised abnormalities in a single anterior temporal region and neuropsychological or sodium amobarbital testing did not indicate a significant risk to memory function	**Test 1: MRI:** Routine **Contrast agent:** None reported **Magnet strength:** 1.5 T **Weighting:** T1, T2 **Slice orientation:** Axial, sagittal and coronal **Slice thickness:** 5 mm with 2.5 mm gaps for axial and sagittal slices, 3 mm with 0.5 mm gap for coronal **Type of imaging:** ROI **Definition of a localised scan:** Results were classified as either lateralised, non-lateralised or normal. If bilateral abnormal with clear asymmetry, result was classified as lateralised MTS. A lateralised scan was defined on showing asymmetry on the contralateral side **Drop-outs:** 10 patients unaccounted for

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Gram, 1988[46] **Study design** Unclear: diagnostic cohort **Country of study** Denmark **Study objective** To compare the ability of CT, MRI, a functional method and SPECT to localise epileptogenic foci demonstrated by EEG **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Patients with partial epilepsy refractive to medical treatment **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 37.3 (16–72) years **No. of patients (male):** 24 (14) **Duration of epilepsy:** 1–48 (mean 18) years **Type of epilepsy:** Not reported	**No. of patients who underwent surgery:** Not reported No outcome data	**Reference standard** EEG **Details:** Surface EEG in all patients, sphenoidal electrodes in some patients together with injection of thiopental **Drop-outs:** Not reported	**Test 1: SPECT:** Interictal **Tracer:** HMPAO: 300–500 MBq depending on height and weight **Gamma camera strength:** NOVO tomograph, 1 detector with CT picture construction **Timing from seizure onset to injection:** Not reported **Slice orientation:** Slices to the parallel to the orbital–mesial plane **Slice thickness:** Not reported **Timing from injection to scan:** Few minutes **Definition of a localised scan:** Not reported **Test 2: MRI:** Routine **Contrast agent:** Not reported **Magnet strength:** 1.5 T **Weighting:** Double spin-echo **Slice orientation:** Multiple axial and frontal scans **Slice thickness:** 5–7 mm **Definition of a localised scan:** Not reported **Test 3: CT** **Contrast agent:** With and without contrast agent (agent not reported) **Camera strength:** Siemens scanner (Somatom DRG) **Slice orientation:** Not reported **Slice thickness:** 8 mm **What was imaged:** Not reported **Definition of a localised scan:** Not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Grunwald, 1991[47] **Study design** Unclear: diagnostic cohort **Country of study** Germany **Study objective** To evaluate the predictive value of interictal SPECT using HMPAO for the outcome after temporal lobectomy in patients with complex partial seizures **Aim** Lateralising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Patients with intractable complex partial seizures who underwent a presurgical SPECT scan and a temporal lobectomy. Patients who did not reveal a clear-cut dominance for language of the left hemisphere were excluded. All patients were right-handed **Inclusion criteria relating to outcome:** Patients had to undergo surgery and be evaluated for memory performance and seizure frequency prior to and 1 year after surgery **Mean age (range):** 29 (8–48) years **No. of patients (male):** 40 (14) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 40 **Mesial sclerosis:** 18 (gliosis) **Other lesions:** 11 **Syndrome:** Not reported **Details:** 11 patients had tumours	**No. of patients who underwent surgery:** 40 **Type of surgery:** **ATL:** 40 **Details:** 21 had right temporal lobectomy and 19 had left temporal lobectomy **Duration of follow-up following surgery:** 1 year **Outcome following surgery:** **Class I:** Seizure free: 28 **Class III:** Decreased seizure frequency: 10 **Class IV:** Not seizure free: 2	**Reference standard** Combination **Details:** Interictal SPECT, neuropsychological testing and MRI/CT performed prior to surgery in all patients. Continuous video-EEG scalp monitoring and in most cases sphenoidal electrodes. In 15 cases an electrocorticogram was necessary to identify the focus	**Test 1: SPECT:** Interictal **Tracer:** HMPAO: 555 MBq (15 mCi), scaled down by body surface area for paediatric patients **Gamma camera strength:** Rotating gamma camera equipped with low-energy all-purpose parallel hole collimator **Timing from seizure onset to injection:** At least 48 hours **Slice orientation:** Reconstruction of transaxial slices was performed to give coronal and sagittal slices **Slice thickness:** 12 mm **Timing from injection to scan:** 30 minutes **Definition of a localised scan:** Evaluated visually according to clinical experience of the physicians to detect a circumscribed perfusion defect in the brain. Diagnosis established if at least four observers agreed, otherwise patient was excluded **Drop-outs:** None reported, but stated that if agreement could not be reached on interpretation of images that patients were excluded

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Hajek, 1991[49] **Study design** Unclear: diagnostic cohort **Country of study** Switzerland **Study objective** To assess the value of ^{99m}Tc-hexamethylpropylenamine oxime (HM-PAO) SPECT in the preoperative evaluation of epileptic patients with medically refractory seizures of temporal lobe origin **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Patients with medically refractory partial epilepsy with complex partial seizures, with or without secondary generalisation **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 32 (10–47) years **No. of patients (male):** 31 (15) **Duration of epilepsy:** 3–41 (mean 21) years **Type of epilepsy:** **Temporal:** 31 **Syndrome:** Not reported	**No. of patients who underwent surgery:** 31 **Type of surgery:** Not reported **Duration of follow-up following surgery:** 3–32 (mean 20) months **Outcome following surgery:** **Class I:** Seizure free: 18 **Class II:** <1–2 seizures/year: 5 **Class III:** ≥ 90% seizure reduction and marked improvement in quality of life: 4 **Class IV:** No worthwhile improvement: 4	**Reference standard** Site of surgery **Details:** Long-term radiotelemetric video split-screen EEG was performed simultaneously from scalp and bilaterally implanted foramen ovale electrodes in 29 patients. All patients underwent preoperative EEG, MRI and interictal SPECT. In two patients surgery was based on structural lesions shown by MRI with corresponding ictal scalp EEG	**Test 1: MRI:** Routine **Contrast agent:** Not reported **Magnet strength:** Not reported **Weighting:** Not reported **Slice orientation:** Not reported **Slice thickness:** Not reported **What was imaged:** Not reported **Definition of a localised scan:** Not reported – data are for lateralisation only **Test 2: SPECT:** Interictal **Tracer:** HMPAO: 600 MBq **Gamma camera strength:** Rotating scintillation camera **Timing from seizure onset to injection:** Not reported **Slice orientation:** Coronal and transversal **Slice thickness:** 1.1 cm with 1.1 cm interslice gap **Timing from injection to scan:** 10–60 minutes **Definition of a localised scan:** Presence and localisation of an abnormality were identified by visual analysis of two independent interpreters, who were blinded to EEG and clinical data

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Harvey, 1993[50] **Study design** Unclear: diagnostic cohort **Country of study** Australia **Study objective** To evaluate HMPAO SPECT in children with electroclinical features of frontal lobe epilepsy **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children **Patient spectrum:** Children with clinical seizure characteristics and EEG findings suggestive of frontal lobe epilepsy **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 10.5 (1–17) years **No. of patients (male):** 22 (8) **Duration of epilepsy:** 1–12 (mean 6) years **Type of epilepsy:** **Non-temporal:** 22 **Other lesions:** Not reported **Syndrome:** Not reported **Details:** All patients had frontal lobe epilepsy	**No. of patients who underwent surgery:** 7 **Type of surgery:** **ATL:** 0 **AH:** 0 **Non-TL:** 7 **Other:** 0 **Details:** 1 frontal corticectomy, 1 frontal biopsy insula No outcome data	**Reference standard** EEG **Details:** Video-EEG of multiple seizures using interictal and ictal scalp electrodes, 4 children had intraoperative ECoG	**Test 1: SPECT:** Interictal **Tracer:** HMPAO: 740 MBq scaled according to weight **Gamma camera strength:** Single-headed scintillation camera with cutaway head and parallel-hole, low-energy, high-resolution collimator. Images processed using Butterworth prefilter and ramp back-projection **Timing from seizure onset to injection:** At least 24 hours in 15 children, within 24 hours in 7 children **Slice orientation:** Slices reconstructed in axial, coronal and sagittal planes **Slice thickness:** 1 pixel **Timing from injection to scan:** <2 hours **Definition of a localised scan:** Images examined for asymmetric perfusion. Focal hyperperfusion and hypoperfusion were judged relative to surrounding regions. Abnormalities were classified as lobar or predominating in one of six frontal regions. Quantitative analysis was also performed

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Ho, 1995[51] **Study design** Retrospective diagnostic cohort **Country of study** Australia **Study objective** To compare ictal HMPAO SPECT and FDG PET in patients with well-lateralised TLE **Aim** Lateralising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** All patients with refractory complex partial seizures with well-lateralised TLE who underwent evaluation. Patients were excluded if localisation of the seizure focus was undetermined or extra-temporal or if functional imaging data were unavailable **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 32 (10–52) years **No. of patients (male):** 35 (20) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 35 **Mesial sclerosis:** 21 **Syndrome:** Not reported **Details:** 1 had cavernous angioma; 1 dysembryoplastic neuroepithelial tumour; 3 gangliglioma; 1 astrocytoma/hamartoma; and 1 tuber	**No. of patients who underwent surgery:** 30 **Type of surgery:** ATL: 30 **Duration of follow-up following surgery:** >1 year **Outcome following surgery:** **Class I:** Seizure free: 15 **Class II:** Nocturnal seizures only: 1	**Reference standard** Combination **Details:** Congruence of clinical seizure characteristics, ictal EEG, MRI and neuropsychological assessment. 5 patients had EEG with depth electrode	**Test 1: PET** **Tracer:** FDG: 260–370 MBq (7–10 mCi) **Gamma camera strength:** ECAT positron tomograph **Timing from seizure onset to injection:** >24 hours **Slice orientation:** After reconstruction, axial and coronal images produced **Slice thickness:** 3.375 mm **Timing from injection to scan:** 30 minutes **Definition of a localised scan:** Scans scored as TP, FP and FN by visual interpretation of two observers **Drop-outs:** None reported **Test 2: SPECT:** Ictal Tracer: HMPAO: 550–700 MBq (15–20 mCi) **Gamma camera strength:** First 28 patients, single-headed rotating gamma camera; last 7 patients, triple-headed, dedicated head scanner with low-energy, high-resolution, fan-beam collimators. Butterworth filter **Timing from seizure onset to injection:** Mean 30–129 seconds after seizure onset **Slice orientation:** Midsagittal image identified and axial slices generated. Coronal images reconstructed **Slice thickness:** 1.78 mm **Timing from injection to scan:** <2 hours **Definition of a localised scan:** Scans scored as TP, FP and FN by visual interpretation of two observers. Had to report localisation with at least 'subtle lateralisation' **Drop-outs:** Interictal scans also performed but results not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Hong, 2002[52] **Study design** Unclear: diagnostic cohort **Country of study** Korea **Study objective** To evaluate the surgical outcome and the diagnostic sensitivity of ictal scalp EEG, interictal FDG PET and ictal SPECT in non-lesional neocortical epilepsy **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Adults and children **Patient spectrum:** Consecutive patients with intractable epilepsy. All patients had surgery for neocortical epilepsy **Mean age (range):** 28 (8–44) years **No. of patients (male):** 41 (27) **Duration of epilepsy:** 14.1 years (range 3–27) years **Type of epilepsy:** **Temporal:** 11 **Non-temporal:** 30 **Details:** 7 occipital, 4 parietal, 16 frontal, 3 multifocal	**No. of patients who underwent surgery:** 41 **Type of surgery:** **ATL:** 11 **Non-TL:** 30 **Duration of follow-up following surgery:** Minimum 1 year follow-up. Mean 2.8 years **Outcome following surgery:** **Class I:** 16 **Class II:** 6 **Class III:** 11 **Class IV:** 8	**Reference standard** Surgery **Details:** Site of surgery was determined by intercranial EEG **Drop-outs:** PET was performed on 34 patients. Analysis included 28 who had a good surgical outcome (Engel I–III) Ictal SPECT was performed on 34 patients, 27 of whom had a good surgical outcome and were included in the analysis	**Test 1: PET:** Interictal **Tracer:** FDG (370 MBq) **Slice orientation:** Axial images were reconstructed and realigned in coronal and sagittal planes **Slice thickness:** 4.3 mm **Timing from injection to scan:** 60 minutes **Definition of a localised scan:** Not reported **Test 2: SPECT:** Ictal **Tracer:** HMPAO (925 MBq) **Tesla/camera strength:** Triple-headed camera with fan-beam collimator **Slice orientation:** Axial images were reconstructed to coronal and sagittal planes **Slice thickness:** 5 mm **Timing from seizure to injection:** During ictal period, no further details **Timing from injection to scan:** 1–3 hours **Definition of a localised scan:** Not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Hwang, 2001[53] **Study design** Retrospective diagnostic cohort **Country of study** Korea **Study objective** To determine the sensitivities of MRI, PET and ictal SPECT in the localisation of neocortical epileptogenic foci compared with pathological findings. **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** All patients had pathologically confirmed neocortical epilepsy **Inclusion criteria relating to outcome:** All patients underwent surgery **Mean age (range):** 28 (12–46) years **No. of patients (male):** 117 (81) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 50 **Non-temporal:** 67 **Syndrome:** 77 with neuronal migration disorder **Details:** 33 frontal, 15 occipital, 13 parietal, 2 hemispheric and 4 multifocal. 15 with tumours	**No. of patients who underwent surgery:** 117 **Type of surgery:** **ATL:** 45 (including 24 with neocortical resection) **Lesionotomy:** 10 **Other:** 86 **Details:** 60 with non-lesional neocortical resection, 24 with neocortical resection and anterior lobectomy, 2 with hemispherectomy **Duration of follow-up following surgery:** Mean 34 (range 12–67) months **Outcome following surgery:** **Class I:** Seizure free: 72 **Class II:** Rare seizures: 15 **Class III:** Worthwhile improvement (at least 75% improvement): 18 **Class IV:** No worthwhile improvement: 12	**Reference standard** Pathology at site of surgery **Details:** Site of surgery was determined by MRI and video-EEG. Invasive EEG was conducted if MRI findings were not concordant with EEG or were normal **Drop-outs:** None for MRI. Only 103 had PET scans. Only 91 had ictal SPECT scans	**Test 1: MRI:** Routine **Contrast agent:** Contrast enhancement was used in selected cases, e.g. those with tumours – no further details **Tesla/camera strength:** 1.0 or 1.5 T **Slice orientation:** Sagittal, axial and coronal **Slice thickness:** 5 mm with 1 mm interslice gap. 3 and 1.5 mm slices added in oblique plane for temporal lobe imaging **Weighting:** T1 spin-echo and T2 fast spin-echo **Definition of a localised scan:** Qualitative interpretation by experienced radiologist **Test 2: PET** **Tracer:** FDG (370 MBq) **Camera strength:** ECAT Exact; CTI siemens **Slice orientation:** Axial reconstructed to coronal and sagittal **Slice thickness:** 4.3 mm **Timing from injection to scan:** 60 minutes **Definition of a localised scan:** Area of greatest decrease of FDG uptake interpreted as the epileptogenic region on the basis of symmetry **Test 3: SPECT:** Ictal **Tracer:** HMPAO (925 MBq) **Camera strength:** Triple-headed camera with fan-beam collimator **Slice orientation:** Axial reconstructed to coronal and sagittal **Slice thickness:** 5 mm **Timing from seizure to injection:** Within 30 seconds **Timing from injection to scan:** 1–3 hours **Definition of a localised scan:** Area of hyperperfusion relative to the remaining regions considered as the epileptogenic region. When hyperperfusion was seen in multiple areas, most hyperperfused area regarded as the epileptogenic region

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Jabbari, 1991[54] **Study design** Prospective diagnostic cohort **Country of study** USA **Study objective** To study cortical localisation by EEG, CT, MRI and SPECT **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Consecutive patients with recurrent partial seizures **Inclusion criteria relating to outcome:** None reported. **Mean age (range):** 32.9 (9–72) years **No. of patients (male):** 58 (15) **Duration of epilepsy:** 1–42 (mean 12) years **Type of epilepsy:** **Temporal:** Not reported **Mesial sclerosis:** Not reported **Non-temporal:** Not reported **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 5 had low-grade astrocytomas, 3 gangliomas, 5 focal cell loss and gliosis, 2 hemangiomas, 1 focal heterotopia with gliosis	**No. of patients who underwent surgery:** 16 **Type of surgery:** **ATL:** 15 **AH:** 15 **Non-TL:** 0 **Other:** 1 **Details:** 15 patients had anterior temporal lobectomy with amygdalo-hippocampectomy, one had resection of a right posterior parietal lesion **Duration of follow-up following surgery:** 1–5 years (mean 27 months) **Outcome following surgery:** **Class I:** Seizure free: 11 **Class II:** >80% improvement in seizure frequency: 4 **Class IV:** No significant improvement: 1	**Reference standard** EEG **Details:** 3–5 days of continuous monitoring including video-telemetry and conventional EEGs. Seizures were recorded on video-EEG in 35/58 patients. Patients were offered an anterior temporal lobectomy if MRI, interictal EEG and ictal EEG localised abnormalities in a single anterior temporal region and neuropsychological or sodium amobarbital testing did not indicate a significant risk to memory function	**Test 1: SPECT:** Ictal and interictal **Tracer:** IMP: 3–5 mCi **Gamma camera strength:** General Electric 400 ACT gamma camera **Timing from seizure onset to injection:** Not reported **Slice orientation:** Transverse, transaxial, coronal and sagittal **Slice thickness:** 12 mm **Timing from injection to scan:** 10 minutes **Definition of a localised scan:** Persistent tracer uptake asymmetry of >20% was seen in two views **Drop-outs:** 1 patient was described as having a SPECT abnormality contralateral to the EEG focus, but this patient was classified as being non-localised on EEG – therefore it was unclear where to put this patient **Test 2: MRI:** Routine **Contrast agent:** Additional gadolinium enhanced scan in last 28 patients **Magnet strength:** 0.5T and 1.5T **Weighting:** T1 and T2 **Slice orientation:** axial, transverse, coronal and sagittal **Slice thickness:** 10 mm, 5 mm in 12 patients **Definition of a localised scan:** Not reported **Drop-outs:** None reported **Test 3: CT** **Contrast agent:** Diatrizoate meglumine–diatrizoate sodium: 150 ml; 9 patients received a double dose **Tesla camera strength:** 4th-generation GE scanner **Timing from injection to scan:** Scans obtained before and immediately after injection of contrast agent. The patients who received a double dose were scanned 1 hour later **Slice orientation:** Transverse and coronal sections **Slice thickness:** 10 mm **Definition of a localised scan:** Not reported **Drop-outs:** None reported **Test 4: Combination: MRI, CT and SPECT:** Details as above **Definition of a localised scan:** At least one focally abnormal neuroimaging study (CT, MRI or SPECT)

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Jack, 1990[56] **Study design** Retrospective diagnostic cohort **Country of study** USA **Study objective** To estimate the sensitivity and specificity of five different MRI-based techniques in the lateralisation of the seizure disorder in patients who underwent surgery for TLE **Aim** Lateralising **Subgroups assessed** No structural abnormality EEG focus	**Population:** Not reported **Patient spectrum:** Patients with TLE whose epilepsy origin was presumed or documented mesial sclerosis. Patients had to have adequate preoperative MRI, be right-handed, had not undergone previous cranial surgery, did not have an epileptogenic mass lesion, neuronal migration abnormality or post-traumatic lesion **Inclusion criteria relating to outcome:** Only patients who underwent surgery were included **Mean age (range):** 29.1 (not reported) years **No. of patients (male):** 41 (19) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 41 **Mesial sclerosis:** 41 **Syndrome:** Not reported	**No. of patients who underwent surgery:** 41 **Type of surgery:** **ATL:** 41 **Duration of follow-up following surgery:** 3–24 (mean 10.5) months **Outcome following surgery:** **Class I:** Seizure free: 37 **Class III:** Continued seizures but reduced postoperatively: 4	**Reference standard** Site of surgery **Details:** Preoperative seizure lateralisation based on standard clinical and video-EEG criteria. All patients underwent intraoperative electrocorticography	**Test 1: MRI** **Magnet strength:** 1.5 T **Weighting:** Not reported **Slice orientation:** Sagittal, oblique coronal, orthogonal coronal images **Slice thickness:** 5 mm with 5 mm gaps for sagittal, 4 mm without gaps for oblique coronal, 4 mm with 2 mm gap for orthogonal coronal images **What was imaged:** Medial temporal parenchyma **Definition of a localised scan:** Visual grading of unilateral signal intensity abnormalities in the medial temporal parenchyma: graded as right-side abnormality, no abnormality or left-side abnormality. **Drop-outs:** None reported **Test 2: MRI** **What was imaged:** Anterior temporal lobe (ATL) **Definition of a localised scan:** Visual grading of unilateral ATL atrophy: graded as right side, indeterminate or left side. **Other imaging details:** As Test 1 **Test 3: MRI:** Volumetric **What was imaged:** Hippocampal formation (HF) **Definition of a localised scan:** DHF (right-side minus left-side volume): Right-sided atrophy = DHF ≤ –0.2 cm^3; indeterminate = DHF –0.2 to 0.6 cm^3; left-sided atrophy = DHF ≥ 0.6 cm^3 **Other imaging details:** As Test 1 **Test 4: MRI** **What was imaged: HF** **Definition of a localised scan:** Visual grading of unilateral HF atrophy: graded as right side, indeterminate or left side **Other imaging details:** As Test 1 **Test 5: MRI:** Volumetric **What was imaged:** ATL **Definition of a localised scan:** DATL (right-side minus left-side ATL volume): right-sided atrophy = DATL ≤ –8.5 cm^3; indeterminate = DATL –8.5 to 12.7 cm^3; left-sided atrophy = DHF ≥ 12.7 cm^3 **Other imaging details:** As Test 1

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Jack, 1994[55] **Study design** Retrospective diagnostic cohort **Country of study** USA **Study objective** To compare the lateralising accuracy of interictal SPECT with MRI in non-lesional temporal lobectomy patients **Aim** Lateralising **Subgroups assessed** No structural abnormality	**Population:** Not reported **Patient spectrum:** Consecutive patients. Those who had undergone prior cranial surgery were excluded **Inclusion criteria relating to outcome:** All patients underwent surgery. Only patients with non-lesional histology were included. Patients with space-occupying lesions were excluded **Mean age (range):** 33 (not reported) years **No. of patients (male):** 53 (23) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 53	**No. of patients who underwent surgery:** 53 **Type of surgery:** **ATL:** 53 **Duration of follow-up following surgery:** 12–40 (mean 18) months **Outcome following surgery:** **Class I:** Seizure free: 37 **Class II:** Rare seizures: 6 **Class III:** Worthwhile improvement: 4 **Class IV:** No worthwhile improvement: 5 **Details:** 1 patient had significant improvement in seizures postoperatively but suffered severe postoperative memory impairment	**Reference standard** Combination **Details:** Inpatient scalp-recorded EEG, depth electrode in 4 of these, speech, language, neuropsychological and psychiatric elevation and amobarbital testing. Based predominantly on interictal and ictal electroclinical criteria. Imaging test results were known but were treated as secondary criteria	**Test 1: MRI:** Routine and volumetric **Magnet strength:** 1.5 T **Weighting:** T1 and long TR, spin-echo **Slice orientation:** Coronal **Slice thickness:** 3 or 4 mm **What was imaged:** Oblique coronal short sequence was acquired perpendicular to the long axis of the left hippocampal formation **Definition of a localised scan:** Increased hippocampal signal intensity was visually graded from images. Subjective graded for MTS was performed independently by three reviewers **Drop-outs:** Only patients in whom a satisfactory operative outcome was achieved (n = 46) were included in the analysis

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Jackson, 1990[57] **Study design** Retrospective diagnostic cohort **Country of study** Australia **Study objective** To examine the role of MRI in the preoperative evaluation of patients with intractable TLE **Aim** Lateralising **Subgroups assessed** EEG focus	**Population:** Not reported **Patient spectrum:** Consecutive patients. **Inclusion criteria relating to outcome:** None reported **Mean age (range):** Not reported (not reported) **No. of patients (male):** 81 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 27 **Hamartoma:** 5 **Oligodendroglioma:** 3 **Astrocytoma:** 3 **Ganglioglioma:** 2 **Microdysplasia:** 5 **Corpora amylacea:** 1 **Arteriovenous malformations:** 1 **Focal cortical scar:** 1 **Focal cortical infarct:** 1 **Minor pathology:** 21 (2 had dual pathology)	**No. of patients who underwent surgery:** 81 **Type of surgery:** **ATL:** 81 **Amygdalohippocampectomy:** 81 **Duration of follow-up following surgery:** Not reported **Outcome following surgery:** Not reported	**Reference standard** Site of surgery	**Test 1: MRI:** Routine **Magnet strength:** 0.3 T **Weighting:** T2. Spin-echo and inversion-recovery **Slice orientation:** Coronal, axial **Slice thickness:** 9.2 mm **What was imaged:** Hippocampus **Definition of a localised scan:** Not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Juhasz, 2003[58] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To determine the value of AMT PET compared with FDG PET in identifying the seizure focus in children without tuberous sclerosis complex with intractable neocortical epilepsy and to determine the spatial relationship between increased AMT uptake and seizure onset as defined by EEG **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children **Patient spectrum:** Children with intractable epilepsy of neocortical origin **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 6.2 (0.8–15) years **No. of patients (male):** 27 (17) **Duration of epilepsy:** Not reported **Type of epilepsy:** Not reported **Details:** 7 with dysplasia, 10 with gliosis, 1 with PMG and heterotopia, 1 with dysplasia and hamartoma and 1 with heterotopia	**No. of patients who underwent surgery:** 21 **Type of surgery:** **ATL:** 16 **Other:** 5 **Details:** 4 frontal, 5 temporal frontal, 1 frontal parietal, 1 temporal parietal frontal occipital, 4 frontal temporal parietal, 1 occipital temporal, 3 temporal parietal **Duration of follow-up following surgery:** 2–54 (mean 17) months **Outcome following surgery:** **Class I:** Seizure free: 12 **Class II:** Engel (no further details): 2 **Class III:** 4 **Details:** Outcome not reported for 3 patients	**Reference standard** Site of surgery **Details:** Ictal and interictal scalp video-EEG, 5 patients received intra-cranial EEG recording. Appears that MRI and PET data also contributed to decision on site of surgery	**Test 1: PET** **Tracer:** FDG: 0.143 mCi/kg **Gamma camera strength:** Not reported **Timing from seizure onset to injection:** 40 minutes **Slice orientation:** Axial **Slice thickness:** 3.125 mm **What was imaged:** Whole-body tomography **Definition of a localised scan:** Abnormalities identified and marked using objective method based on semi-automated software package applied to all supratentorial planes **Drop-outs:** None **Test 2: PET** **Tracer:** AMT: 0.1 mCi/kg **Gamma camera strength:** Not reported **Timing from seizure onset to injection:** 25 minutes **Slice orientation:** Not reported **Slice thickness:** 3.125 mm **What was imaged:** Whole-body tomography **Definition of a localised scan:** Regions with abnormal asymmetry of tracer were marked. Region of interest analysis was used to verify that marked AMT PET abnormalities represented increases in AMT uptake **Drop-outs:** None **Test 3: MRI:** Routine **Contrast agent:** Not reported **Magnet strength:** Not reported **Weighting:** T1, T2, FLAIR, high-resolution volumetric spoiled gradient echo **Slice orientation:** Axial and coronal **Slice thickness:** Not reported **What was imaged:** Not reported **Definition of a localised scan:** Not reported **Drop-outs:** It was unclear how best to classify two patients: MRI results correctly lateralised the focal point and identified that the cause was dysplasia but did not provide any further information on the exact location of the focal point. These patients were classified as partially localised

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Kaiboriboon, 2002[59] **Study design** Retrospective diagnostic cohort **Country of study** USA **Study objective** To prove the clinical usefulness of SISCOM and compare SICOM images derived from single- and dual-headed SPECT cameras for localisation of partial epileptic seizures **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** Consecutive patients with intractable partial epilepsy who had ictal and interictal SPECT images **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 28.2 (4–47) years **No. of patients (male):** 38 (20) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 32 (including 5 frontotemporal) **Mesial sclerosis:** Not reported **Non-temporal:** 6 **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 6 patients had frontal lobe epilepsy	**No. of patients who underwent surgery:** 21 **Type of surgery:** **ATL:** 19 **Non-TL:** 2 **Details:** Frontal surgery in 2 patients **Duration of follow-up following surgery:** 12–58 (mean 34.3) months **Outcome following surgery:** **Class I:** Seizure free: 21	**Reference standard** Site of surgery **Details:** All final surgical decision were based on EEG and MRI. Localisation was as follows: non-invasive EEG recording (n = 13); invasive video-EEG monitoring (n = 4); seizure-free outcome following surgery (n = 21) **Drop-outs:** None reported	**Test 1: SPECT:** Ictal and interictal **Tracer:** ECD: 555–1110 MBq **Gamma camera strength:** First 15 patients: Siemens Orbitor gamma camera. Last 23 patients: dual-headed gamma camera. Butterworth filter used to reconstruct images in all patients **Timing from seizure onset to injection:** At least 24 hours for interictal images, mean 38.1 (range 12–200) seconds for ictal images **Slice orientation:** First 15 patients: not reported. Last 23 patients: transaxial images. Images reconstructed I all patients, no further details **Slice thickness:** Not reported **Timing from injection to scan:** Within 2 hours **Definition of a localised scan:** Reviewers independently reviewed ictal and interictal SPECT images. Images either localised to one of 16 regions or defined as non-localising **Test 2: SISCOM:** Ictal and interictal SPECT **Tracer:** SPECT as before, no details of MRI **Definition of a localised scan:** SISCOM images were reconstructed using a Unix-based workstation with image analysis software packages. Reviewers independently reviewed SISCOM images, which were localised to one of 16 regions, or defined as non-localising

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Kaminska, 2003[60] **Study design** Retrospective diagnostic cohort **Country of study** France **Study objective** To validate the ability of ictal SPECT to localise the epileptogenic zone in children **Aim** Localising **Subgroups assessed** No subgroup EEG focus No EEG focus	**Population:** Children **Patient spectrum:** Children who received SPECT and intracranial EEG **Inclusion criteria relating to outcome:** EEG localisation or resection **Mean age (range):** 6.5 years (10 months–17 years) **No. of patients (male):** 20 (10) **Duration of epilepsy:** Age of onset 2 weeks–9 (mean 2) years **Type of epilepsy:** **Temporal:** 7 **Non-temporal:** 13 **Other lesions:** 13 **Syndrome:** Not reported **Details:** 12 had cortical dysplasia (including 4 with tuberous sclerosis), 4 dysembryoplastic neuroepithelial tumour and 2 lesions that could not be classified. 5 patients had frontal epilepsy, 1 frontal-temporal, 2 parietal, 2 occipital, 1 temporal insular and 4 tuberous sclerosis	**No. of patients who underwent surgery:** 19 **Type of surgery:** **ATL:** 7 **Non-TL:** 12 **Details:** 4 frontal, 2 parietal, 2 occipital, 1 temporal-parietal-frontal, 1 frontal temporal, 1 opperculum, 1 temporal and lingual **Duration of follow-up following surgery:** At least 1 year **Outcome following surgery:** **Class I:** Seizure free: 7 **Class II:** <2 seizures per year: 3 **Class III:** Clinically relevant improvement: 3 **Class IV:** No improvement: 6	**Reference standard** Site of surgery **Details:** 16 patients received intracranial EEG, 14 had subdural grids and depth electrodes and two only stereo EEG	**Test 1: MRI:** Routine No details given **Drop-outs:** None reported **Test 2: SISCOM:** Ictal and interictal SPECT **Tracer:** ECD: 740 MBq (20 mCi) for 1.73 m^2 **Gamma camera strength:** Double-headed rotating gamma camera equipped with ultra-high-resolution fan-beam collimators **Timing from seizure onset to injection:** Mean 18 (range 4–80) seconds **Slice orientations:** Not reported **Slice thickness:** Not reported **Timing from injection to scan:** ~1 hour **Definition of a localised scan:** Ictal and interictal SPECT images were co-registered, normalised, subtracted, smoothed and superimposed on MRI. Area of highest increased ictal perfusion **Drop-outs:** 1 patient did not receive an ictal injection. 1 patient did not undergo surgery as the epileptogenic region was multifocal

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Kang, 1997[61] **Study design** Unclear: diagnostic cohort **Country of study** Korea **Study objective** To evaluate the usefulness of ictal SPECT in patients with TLE for presurgical evaluation and also to correlate ictal SPECT patterns with the semiology of seizures **Aim** Lateralising **Subgroups assessed** No subgroup	**Population:** Not reported **Patient spectrum:** Patients with temporal lobe epilepsy with either unilateral hippocampal atrophy (18 patients), other focal temporal lesions (4 patients) and normal MRI findings (1 patient) **Inclusion criteria relating to outcome:** All patients underwent temporal lobectomy, had at least 3 months of follow-up and had good postsurgical seizure control (Engel class I) **Mean age (range):** Not reported **No. of patients (male):** 23 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 23	**No. of patients who underwent surgery:** 23 **Type of surgery:** **ATL:** 23 **Duration of follow-up following surgery:** 3–29 months **Outcome following surgery:** **Class I:** Good postsurgical seizure control: 23	**Reference standard** Site of surgery **Details:** Not clear, appears to have been site of surgery	**Test 1: SPECT:** Ictal **Tracer:** ECD: dose not reported **Gamma camera strength:** Not reported **Timing from seizure onset to injection:** 38.5 (SD = 17.3) seconds **Slice orientation:** Not reported **Slice thickness:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Presence of unilateral temporal hyperperfusion concordant with epileptic foci **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Kilpatrick, 1997[62] **Study design** Unclear: diagnostic cohort **Country of study** Australia **Study objective** To determine whether non-invasive methods are adequate for seizure focus lateralisation in TLE **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Consecutive patients with intractable partial epilepsy, experiencing at least two seizures per month **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 37 (15–58) years **No. of patients (male):** 75 (37) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 75 **Mesial sclerosis:** 34 **Syndrome:** Not reported **Details:** All temporal: 6 had dysembryoblastic neuroepithelial tumour, 4 cavernoma, 2 dysplasia, 2 ganglioglioma and 1 glioma	**No. of patients who underwent surgery:** Unclear – at least 51 **Type of surgery:** **ATL:** Unclear – at least 50 **AH:** 12 **Non-TL:** 1 **Details:** 1 patient had a frontal lobectomy. 34 with ATL who also had *en bloc* excision of neocortical structures, hippocampal formation and parahippocampal gyrus and microsurgical resection of the amygdala. Two further patients had ATL for lesions. 2 had neocorticectomy **Duration of follow-up following surgery:** 12–38 (mean 24) months **Outcome following surgery:** **Class I:** Seizure free or auras only: 39 **Class II:** >90% improvement in seizure frequency: 8 **Class III:** <90 % reduction but worthwhile improvement: 3 **Class IV:** No worthwhile improvement: 0	**Reference standard** Site of surgery **Details:** 65 patients had scalp EEG. All patients underwent video-EEG of at least three seizures and MRI. It appears SPECT and PET also contributed to the surgical decision **Drop-outs:** Only patients who had TL surgery with more than 12 months of follow-up were included ($n = 50$). Patients were excluded due to non-localised focus ($n = 7$), inoperable ($n = 3$), frontal resection ($n = 1$) or <12 months of follow-up/deferral of surgery ($n = 14$)	**Test 1: SPECT:** Ictal **Tracer:** Not reported No imaging details given **Definition of a localised scan:** Not clear – lateralisation **Test 2: SPECT:** Interictal **Tracer:** Not reported No imaging details given **Definition of a localised scan:** Localisation **Test 3: PET** **Tracer:** Not reported No imaging details given **Definition of a localised scan:** Lateralisation **Test 4: MRI:** Volumetric **Magnet strength:** 1.5 T No other imaging details given **Definition of a localised scan:** Not clear – lateralisation

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Kim, 2002[64] **Study design** Unclear: diagnostic cohort **Country of study** Korea **Study objective** To compare the sensitivity of visual and statistical parametric mapping (SPM) using FDG PET to localise epileptogenic zones in frontal lobe epilepsy **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** All participants had FLE **Inclusion criteria relating to outcome:** Good surgical outcome (Engel I or II) **Mean age (range):** 26 (12–51) years **No. of patients (male):** 29 (18) **Duration of epilepsy:** Mean 12 years **Type of epilepsy:** **Non-temporal:** 29 **Syndrome:** Not reported **Details:** 22 patients had cortical dysplasia, 1 gliosis, 1 fibrous nodule, 1 an old infarction, 1 a ganglioglioma. 1 an old contusion, 1 an astrocytoma, 1 an oligodendroglioma and 1 a cortical scar	**No. of patients who underwent surgery:** 29 **Type of surgery:** **AH:** 29 (frontal) **Details:** Radical frontal lobectomy (n = 6), standard frontal lobectomy (n = 6), partial frontal lobectomy (n = 5), lesionectomy (n = 12) **Duration of follow-up following surgery:** mean 20 months **Outcome following surgery:** **Class I:** Seizure free: 24 **Class II:** Rare seizures: 5	**Reference standard** Site of surgery **Details:** Site of surgery determined by clinical history, prolonged scalp EEG (interictal and ictal), video monitoring of seizure, MRI, FDG PET and where discrepancies arose invasive EEG	**Test 1: PET (SPM analysis)** **Tracer:** FDG: 370 MBq **Gamma camera strength:** ECAT exact scanner. 5.2 mm intrinsic strength in full width at half maximum **Slice orientation:** Transaxial, which were realigned to yield sagittal and coronal sections **Timing from injection to scan:** 30–40 minutes **Definition of a localised scan:** Normalised PET images spatially normalised into standard and non-linear transformations, smoothed by convolution with isotropic Gaussian kernel (16 mm full width at half maximum). Clusters (minimum 15 contiguous voxels) were significant. Seizure focus = the area of highest significance **Drop-outs:** Two patients showing severe hypometabolism with tissue atrophy were excluded from the SPM analysis because the spatial and count normalisations were not acceptable. Both were considered as analysis failures **Test 2: MRI** No further details reported **Drop-outs:** Unclear how to classify 1 patient with multifocal MRI scan as it was not clear whether scan identified a frontal lobe focus **Test 3: PET (visual assessment)** **Tracer:** FDG: 370 MBq **Gamma camera strength:** ECAT exact scanner. 5.2 mm intrinsic strength in full width at half maximum **Timing from seizure onset to injection:** Not reported **Slice orientation:** Transaxial, which were realigned to yield sagittal and coronal sections **Timing from injection to scan:** 30–40 minutes **Definition of a localised scan:** Cerebral cortex divided into 5 areas in each hemisphere and 2 blinded nuclear physicians assessed regional metabolism. Most hypometabolic region = seizure focus **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Kim, 1999[63] **Study design** Retrospective diagnostic cohort **Country of study** Korea **Study objective** To assess the role of each presurgical evaluation modality and to identify prognostic factors for favourable seizure outcome **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children **Patient spectrum:** Patients were included if the primary indication for surgery was relief of intractable epilepsy. This included those with brain tumours. Patients with <1 year of follow-up were excluded **Inclusion criteria relating to outcome:** Only patients who underwent surgery were included **Mean age (range):** 9.9 years (8 months–18 years) **No. of patients (male):** 38 (23) **Duration of epilepsy:** <1–17 (mean 5) years **Type of epilepsy:** **Temporal:** 25 **Mesial sclerosis:** Not reported **Non-temporal:** 13 **Other lesions:** Not reported **Syndrome:** 1 with Sturge–Weber syndrome **Details:** 7 had dysembryoplastic neuroepithelial tumour, 2 ganglioglioma, 1 oligodendroglioma, 29 cortical dysplasia, 11 with hippocampal sclerosis and 1 gliosis	**No. of patients who underwent surgery:** 38 **Type of surgery:** **ATL:** 25 **Non-TL:** 17 **Details:** 20 had temporal resection, 12 extra-temporal resection, 5 both temporal resection and extra-temporal resection and 1 callosotomy **Duration of follow-up following surgery:** 12–60 (mean 22.1) months **Outcome following surgery:** **Class I:** Seizure free: 22 **Class II:** Rare seizures: 4 **Class III:** Worthwhile improvement: 2 **Class IV:** Unchanged: 10	**Reference standard** EEG **Details:** All patients had interictal EEG and 34 had prolonged video-EEG. Localisation was based on most invasive EEG findings	**Test 1: MRI:** Routine No details reported **Definition of a localised scan:** Not reported **Test 2: PET** **Tracer:** FDG: dose not reported No further details reported **Definition of a localised scan:** Not reported **Drop-outs:** 30 patients included – no reason for drop-outs reported **Test 3: SPECT:** Interictal **Tracer:** HMPAO: dose not reported. No other details of methods for SPECT imaging reported **Definition of a localised scan:** Not reported. **Drop-outs:** 19 patients included – no reason for drop-outs reported **Test 4: SPECT:** Ictal **Tracer:** HMPAO: dose not reported No other details of methods for SPECT imaging reported **Definition of a localised scan:** Localisation **Drop-outs:** 30 patients included – no reason for drop-outs reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Knowlton, 1997[65] **Study design** Prospective diagnostic cohort **Country of study** Germany **Study objective** To compare FDG PET, hippocampal volumetry (HV), T2 relaxometry and H-MRSI in the presurgical neuroimaging lateralisation of patients with non-lesional, EEG defined unilateral TLE **Aim** Lateralising **Subgroups assessed** No structural abnormality EEG focus	**Population:** Children and adults **Patient spectrum:** Patients were excluded if epilepsy was of extra-temporal origin, had foreign tissue lesions, unclear MRSI and PET or did not undergo complete protocol for MRSI or HV. All surgical candidates were suspected to have TLE **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 38 (14–56) years **No. of patients (male):** 25 (12) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 25 **Mesial sclerosis:** 15 **Syndrome:** Not reported	**No. of patients who underwent surgery:** 24 **Type of surgery:** **ATL:** 24 **Details:** 1 patient did not undergo surgery **Duration of follow-up following surgery:** 18–31 (mean 23) months **Outcome following surgery:** Not reported	**Reference standard** EEG **Details:** All patients had scalp-sphenoidal EEG/video telemetry. 7 had subdural strip EEG and 3 had depth electrode EEG if scalp-sphenoidal EEG was non-localising	**Test 1: MRI:** Volumetric **Magnet strength:** 1.5 T **Slice thickness:** 3 mm for 3D gradient fast field echo and 6 mm for spin-echo **Slice orientation:** Sagittal (spin-echo), coronal (3D gradient fast field echo) **What was imaged:** Hippocampus **Type of imaging:** ROI **Definition of a localised scan:** Using contiguous 3-mm slices. Asymmetry index (AI) (right – left)/[(right + left)/2] × 100 (%). AI of ≥ 8%. To calculate total volume, first the slice volume was calculated by multiplying the area within the outline of the structure by the slice thickness, then these were added together **Drop-outs:** None **Test 2: MRI:** T2-relaxometry weighted **Magnet strength:** 1.5 T **Weighting:** T2 multi-spin-echo sequence **Slice thickness:** 8 mm **Slice orientation:** Coronal **What was imaged:** Hippocampus **Type of imaging:** ROI **Definition of a localised scan:** AI (right – left)/[(right + left)/2] × 100 (%). AI of ≥ 4% **Drop-outs:** 13 patients had T2 relaxometry **Test 3: MRI:** Routine **Contrast agent:** Not reported **Tesla/gamma camera strength:** 1.5 T **Weighting:** 3D SPGR, coronal T2 gradient echo and high-resolution coronal T2 fast spin-echo **Slice orientation:** Coronal. **Slice thickness:** 105 mm **Type of imaging:** ROI **Definition of a localised scan:** Volume and signal changes **Drop-outs:** None

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
				Test 4: MRS **Weighting:** H MRS **Metabolites:** NAA, Cr and ChO **Slice thickness:** Average 5 voxels (range 2–7) were selected from each hippocampus **What was imaged:** Hippocampus **Definition of a localised scan:** AI (right – left)/[(right – left)/2] × 100 (%). AI of ≥ 12% **Drop-outs:** 24 patients had HMRSI **Test 5: PET** **Tracer:** FDG: 10 mCi **Gamma camera strength:** 961 HR EXACT scanner with full width at half-maximum resolution of 3.5 mm in plane and 4.0 mm transaxially **Timing from seizure onset to injection:** Not reported **Slice orientation:** Axial, coronal and sagittal planes were reconstructed **Slice thickness:** 47 slices over a 15-cm field of view **Timing from injection to scan:** 45 minutes **Definition of a localised scan:** Evidence of relative focal hypometabolism (Hm) in 5 TL regions (pole, anterior-medial, post-medial, anterior-lateral, and post-lateral). Sum of regions was used to provide a qualitative measure of the degree of TL Hm. 3 or more regions of Hm required **Drop-outs:** 1 patient did not have PET scan

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Kuzniecky, 1993[70] **Study design** Prospective diagnostic cohort **Country of study** USA **Study objective** To evaluate the predictive value of MRI in temporal lobe epilepsy surgery **Aim** Lateralising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Patients with medically intractable complex partial seizures of temporal lobe origin referred for temporal lobectomy. Patients were excluded if they had technically inadequate MRI, previous cranial surgery, inadequate follow-up, had an anaplastic astrocytoma on pathological examination or had evidence of residual lesion postoperative MRI **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 28 (7–38) years **No. of patients (male):** 34 (14) **Duration of epilepsy:** >2 years **Type of epilepsy:** **Temporal:** 34	**No. of patients who underwent surgery:** 34 **Type of surgery:** **Details:** All patients had surgical resection according to subpial aspiration technique, including standard *en bloc* neocorticectomy **Duration of follow-up following surgery:** 12–30 (mean 22) months **Outcome following surgery:** **Class I:** Seizure free or rare seizures: 23 **Class III:** 50–80% seizure reduction: 10 **Class IV:** <50% improvement in seizures: 1	**Reference standard** Site of surgery **Details:** Interictal scalp EEG, prolonged video-EEG with sphenoidal electrodes, neuropsychological testing including amytal testing and CT. In 17 patients intracranial EEG used to confirm focus location	**Test 1: MRI** **Contrast agent:** Gadolinium enhanced in 6 patients with foreign tissue lesions **Magnet strength:** 1.5 T **Weighting:** T1 and T2 (coronal) **Slice orientation:** Axial, sagittal, coronal **Slice thickness:** 5 mm, 2.5-mm gap (axial, sagittal and coronal T2); 3 mm, 1.5-mm gap (coronal T1) **Definition of a localised scan:** Images assessed for presence of (1) anterior temporal lobe atrophy; (2) temporal horn enlargement; (3) hippocampal atrophy; (4) increased T2 weighted signal confined to hippocampus. Interpretations then grouped as normal or abnormal for each side **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Kuzniecky, 1991[67] **Study design** Retrospective diagnostic cohort **Country of study** USA **Study objective** Assess the reliability of MRI for determining lateralisation of the electrographic focus in patients with intractable TLE **Aim** Lateralising **Subgroups assessed** Structural abnormality EEG focus	**Population:** Not reported **Patient spectrum:** Patients with intractable complex partial seizures of temporal lobe origin **Inclusion criteria relating to outcome:** All patients underwent surgery; however, it is unclear as to whether this was an inclusion criterion **Mean age (range):** Not reported **No. of patients (male):** 45 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 45	**No. of patients who underwent surgery:** 45 **Type of surgery:** **ATL:** 45 **Details:** Resection included *en bloc* neocorticectomy, sparing the superior temporal gyrus and including mesial structures **Duration of follow-up following surgery:** 12–48 (mean 32) months **Outcome following surgery:** **Class I:** Seizure free: 36 **Class II:** >80% improvement in seizure frequency: 7 **Class IV:** <50% improvement in seizures: 2	**Reference standard** EEG **Details:** Prolonged 16–32-channel EEG video monitoring with scalp and sphenoidal electrodes. Focus localised by intracranial EEG ($n = 34$) and scalp sphenoidal EEG and other localising data ($n = 3$)	**Test 1: MRI:** Routine **Contrast agent:** Not reported **Magnet strength:** 0.5 or 1.5 T **Weighting:** T1 and T2 spin-echo **Slice orientation:** Transaxial, coronal and axial **Slice thickness:** Transaxial 6 mm, coronal 4 mm – all patients. Axial – not reported **Type of imaging:** ROI **Definition of a localised scan:** Reduced temporal lobe size or 50% of hippocampal (HC) volume. Temporal horn enlargement. Abnormal high signal from HC **Drop-outs:** 8 patients not included as they had evidence of structural lesions

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Kuzniecky, 1998[68] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To determine the relative utility of H MRSI and hippocampal volumetry for the lateralisation of mesial TLE in patients with intractable epilepsy **Aim** Lateralising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** Consecutive patients with intractable epilepsy and pathological confirmation of mesial temporal sclerosis. Patients were excluded if the imaging or pathological examination revealed other disease such as tumours or vascular lesions in conjunction with mesial temporal sclerosis **Inclusion criteria relating to outcome:** Only patients who underwent temporal lobectomy were included **Mean age (range):** 32 (14–47) years **No. of patients (male):** 30 (12) **Duration of epilepsy:** mean 24 years **Type of epilepsy:** **Temporal:** 30 **Mesial sclerosis:** 30	**No. of patients who underwent surgery:** 30 **Type of surgery:** **ATL:** 30 **Outcome:** not reported	**Reference standard** Site of surgery **Details:** The epileptogenic zone was identified by prolonged interictal scalp EEG, video-EEG with sphenoidal electrodes for ictal analysis and neuropsychological studies. 8 patients with divergent or bilateral abnormalities underwent intracranial EEG	**Test 1: MRS** **Magnet strength:** 4.1 T **Imaging details:** First 20 patients: single spin-echo. Last 10 patients: 2D point-resolved spectroscopy, double spin-echo **Slice orientation:** Sagittal and axial **Metabolites:** *N*-Acetylated compounds (NA) and creatine **Minimise partial volume effects:** To exclude regions from outside the head or within the ventricles, the Cr/NA ratio was set to zero in voxels where the fitted chemical shifts were >±–0.05 ppm **Definition of a localised scan:** Cr/NA > 2SDs exceeding the normal 95% CI **Drop-outs:** None **Test 2: MRI:** Volumetric **Magnet strength:** 1.5 T **Weighting:** T1 **Slice orientation:** Plane perpendicular to the long axis of the hippocampus **Slice thickness:** 1.5 mm. No inter-slice gap **What was imaged:** A volume acquisition (3D) of the entire brain **Type of imaging:** ROI **Definition of a localised scan:** Abnormal volumes were defined as being 2 SDs below the mean for the normalised data **Drop-outs:** None

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Lee, 2000[75] **Study design** Unclear: diagnostic cohort **Country of study** Korea **Study objective** To analyse the relationship between ictal EEG and ictal SPECT in presurgical evaluation **Aim** Lateralising **Subgroups assessed** No subgroup	**Population:** Adults **Patient spectrum:** Patients with unilateral medial TLE **Inclusion criteria relating to outcome:** All patients had standard anterior temporal lobectomy and had to be seizure free for at least 1 year after surgery. Patients had unilateral hippocampal sclerosis on MRI or normal brain MRI but massive and exclusive mesial temporal ictal onset confirmed by intracranial electrodes **Mean age (range):** 28.5 (not reported) years **No. of patients (male):** 68 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 68	**No. of patients who underwent surgery:** 68 **Type of surgery:** **ATL:** 68 **Duration of follow-up following surgery:** >1 (mean 2.8) years **Outcome following surgery:** **Class I:** Seizure free: 68	**Reference standard** Combination **Details:** Scalp video-EEG, interictal EEG, interictal and ictal SPECT, MRI. When results were inconclusive, additional intercranial EEG monitoring was performed	**Test 1: SPECT:** Ictal **Tracer:** HMPAO: dose not reported **Gamma camera strength:** Triple-head rotating gamma camera with high-resolution fan-beam collimator **Timing from seizure onset to injection:** Mean 29.8 seconds (SD = 14.4 seconds) **Slice orientation:** Coronal, sagittal and transaxial **Slice thickness:** Not reported **Timing from injection to scan:** Within 2 hours **Definition of a localised scan:** Lateralised – concordant hyperfusion **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Lee, 2002[73] **Study design** Prospective diagnostic cohort **Country of study** Korea **Study objective** To investigate whether repeated ictal SPECT is helpful in the localisation of epileptogenic zones and whether it can provide information confirming that the area of increased perfusion is really the epileptogenic lesion **Aim** Localising **Subgroups assessed** No structural abnormality	**Population:** Children and adults **Patient spectrum:** Patients selected from 502 with intractable epilepsy in whom presurgical localisation of epileptogenic zones was attempted with a view to possible surgical resection. 24 patients recruited from this group had ambiguous or unexpected findings on first ictal SPECT and were included in the study **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 19.2 (5–35) years **No. of patients (male):** 24 (9) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 4 **Mesial sclerosis:** Not reported **Non-temporal:** 20 **Other lesions:** 20 **Syndrome:** 1 had Sturge–Weber disease **Details:** 8 had frontal lobe epilepsy, 2 occipital lobe epilepsy, 2 parietal lobe epilepsy, 8 multifocal epilepsy, 14 focal cortical dysplasia, 2 hippocampal sclerosis, 1 oligodendroglioma and 1 old infarct	**No. of patients who underwent surgery:** 18 **Type of surgery:** **ATL:** 4 **Other:** 14 **Details:** 14 had neocortical resection **Duration of follow-up following surgery:** 20–81 months **Outcome following surgery:** Engel: **Class I:** 10 **Class III:** 6 **Class IV:** 2	**Reference standard** Combination **Details:** Scalp video-EEG, MRI, interictal EEG, FDG PET. Ictal SPECT was performed when results were inconclusive. Seizure focus was site of surgery where available, final diagnosis in other patients	**Test 1: SPECT (first and second):** Ictal **Tracer:** HMPAO: 925 MBq **Gamma camera strength:** Triple-head Prism 3000 camera with a low-energy high-resolution fan-beam collimator **Timing from seizure onset to injection:** 28 ± 21 seconds (first), 22 ± 10 seconds (second) **Slice orientation:** Transaxial – realigned to yield sagittal and coronal images **Slice thickness:** Not reported **Timing from injection to scan:** 2 hours on average **Definition of a localised scan:** Areas of hyperfusion; when these extended beyond one lobe a decision was made on whether they were lateralised. A positive result was reported when the first and second scans agreed, or one was normal and one agreed with the reference standard, or if several foci were located and the reference standard was multifocal. A negative result was when both scans were normal. A partially localising scan was when a focus was identified in one scan, with another focus incorrectly identified **Drop-outs:** 1 patient could not be classified as he/she had temporal surgery but it was not stated which side

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Lee, 2001[71] **Study design** Unclear: diagnostic cohort **Country of study** Korea **Study objective** To examine the diagnostic performance of HMPAO and ECD SPECT to localise the epileptogenic zones in mesial temporal epilepsy and neocortical epilepsy **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** No details reported **Inclusion criteria relating to outcome:** None reported **Mean age (range):** HMPAO: 23 (not reported) years; ECD: 28 (not reported) years **No. of patients (male):** HMPAO 40 (25); ECD 14 (10) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** HMPAO 17; ECD 7 **Mesial sclerosis:** Not reported **Non-temporal:** 28 **Other lesions:** HMPAO 23; ECD 7 **Syndrome:** Not reported **Details:** HMPAO 23, of whom 9 had lateral TLE, 7 frontal lobe, 4 occipital lobe and 3 parietal lobe epilepsy. ECD: 7, of whom 3 had lateral TLE, 3 frontal lobe and 1 occipital lobe epilepsy	**No. of patients who underwent surgery:** 39 **Type of surgery:** **ATL:** 20 **Other:** 19 **Details:** 19 neocortical resection. 4 with mesial TLE and 11 neocortical epilepsy patients were not operated on **Duration of follow-up following surgery:** 1.5–5 years **Outcome following surgery:** Engel: **Class I:** No further details: 30 **Class II:** 2 **Class III:** 7	**Reference standard** Combination **Details:** Scalp video-EEG, MRI, interictal EEG, PET. When results were inconclusive, additional intracranial EEG monitoring was performed **Drop-outs:** Not reported	**Test 1: SPECT:** Ictal **Tracer:** ECD: dose not reported **Gamma camera strength:** Triple-headed SPECT camera and fan-beam collimator **Timing from seizure onset to injection:** 42 ± 27 seconds **Slice orientation:** Reconstructed images were reorientated to sagittal and coronal slices. Transaxial **Slice thickness:** Not reported **Timing from injection to scan:** 1–2 hours **Definition of a localised scan:** Not reported **Test 2: SPECT:** Ictal **Tracer:** HMPAO: dose not reported **Gamma camera strength:** Triple-headed SPECT camera and fan-beam collimator **Timing from seizure onset to injection:** 52 ± 20 seconds **Slice orientation:** Reconstructed images were reorientated to sagittal and coronal slices. Transaxial **Slice thickness:** Not reported **Timing from injection to scan:** 1–2 hours **Definition of a localised scan:** Not reported **Drop-outs:** Not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Lewis, 1998[77] **Study design** Prospective diagnostic cohort **Country of study** USA **Study objective** To compare phased-array MRI and interictal cerebral perfusion SPECT in a surgical outcome analysis of partial epilepsy, using lateralisation and localisation by EEG as the indication for surgical resection **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Partial epilepsy patients who had complete data regardless of seizure type were included **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 31 (14–69) years **No. of patients (male):** 35 (18) **Duration of epilepsy:** Not reported **Type of epilepsy:** Not reported	**No. of patients who underwent surgery:** Unclear – appears to be 23 **Type of surgery:** **ATL:** 15? **AH:** Not reported **Non-TL:** 6? **Other:** 2? **Details:** 1 temporal-occipital and 1 corpus callostomy **Duration of follow-up following surgery:** 12 months–3 years **Outcome following surgery:** **Class I:** Seizure free: 10 **Class II:** >90% improvement in seizure frequency: 2 **Class III:** >75% reduction in seizures: 4 **Class IV:** <75% reduction in seizures: 4	**Reference standard** EEG **Details:** Sphenoidal/scalp interictal EEG and ictal video-EEG. The criteria for EEG localisation included ictal onsets based on examination of specific EEG patterns associated with partial seizures, and all EEG localised patients had at least three localising ictal events **Drop-outs:** Two patients were not localised on EEG and were not included in analysis	**Test 1: SPECT:** Interictal **Tracer:** HMPAO or ECD: 555–1110 MBq (15–30 mCi) **Gamma camera strength:** Gamma camera equipped with ultra-high-resolution fan-beam collimators **Timing from seizure onset to injection:** **Slice orientation:** Reformatted into sagittal, coronal and temporal lobe-axis reorientation on the transaxial plane **Slice thickness:** Reconstructed images at 2.22 mm per slice were averaged to become 6.7 mm in thickness **Timing from injection to scan:** 1 hour **Definition of a localised scan:** Focal hypoperfusion or hyperperfusion (quantitative difference in uptake relative to adjacent and contralateral homologous cortex and compared with cerebellar activity for reference as the zone with the highest uptake) **Test 2: MRI:** Routine **Contrast agent:** Not reported **Magnet strength:** 1.5 T phase-array radiofrequency coil **Weighting:** T1, T2, three-dimensional spoiled gradient-recalled **Slice orientation:** Axial, coronal **Slice thickness:** Not reported **Definition of a localised scan:** Qualitative volume loss of the hippocampal formation, increases in T2 signal within hippocampus, loss of internal hippocampal architecture. The presence of two of three findings leads to a diagnosis of mesial temporal sclerosis

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Li, 2000[78] **Study design** Unclear: diagnostic cohort **Country of study** Canada **Study objective** To assess which features of temporal lobe proton magnetic resonance spectroscopic imaging (^{1}H-MRSI) are associated with satisfactory surgical outcome in patients with intractable TLE and bilateral hippocampal atrophy **Aim** Lateralising **Subgroups assessed** EEG focus	**Population:** Adults **Patient spectrum:** Patients with electroclinical manifestations of TLE **Inclusion criteria relating to outcome:** All patients had surgical treatment for intractable TLE **Mean age (range):** 37 (16–62) years **No. of patients (male):** 21 (9) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 21 **Syndrome:** Not reported **Details:** All 21 patients had bilateral hippocampal atrophy	**No. of patients who underwent surgery:** 21 **Type of surgery:** **ATL:** 7 **Other:** Not reported **Duration of follow-up following surgery:** 12–51 months **Outcome following surgery:** **Class I:** Seizure free or <3 seizures since surgery but seizure free for ≥ 2 years: 11 **Class II:** <3 seizures per year, or >3 seizures per year after surgery but now <3/year for >2 years or nocturnal seizures only: 0 **Class III:** >90% reduction in seizure frequency: 2 **Class IV:** <90% seizure reduction: 8	**Reference standard** Site of surgery **Details:** Video-EEG, surgery. EEG was classified as unilateral when >90% of ictal EEG onsets were on one side, and bilateral when < 90% of ictal EEG seizures started from one side **Drop-outs:** None reported	**Test 1: MRI:** Routine and volumetric **Contrast agent:** None reported **Tesla:** 1.5 T **Weighting:** T1, T2. Proton density **Slice orientation:** Sagittal, coronal and axial **Slice thickness:** 1 mm **What was imaged:** Whole brain **Definition of a localised scan:** Significant lateralisation was assumed when values outside 2 SD from the normal were found. Asymmetry index (left – right)/[(left + right)/2] used for hippocampal volumes **Test 2: MRS:** Volumetric **Tesla:** 1.5 T **Imaging details:** Spin-echo. H-MRSI **Slice orientation:** Scout images in axial and sagittal, followed by a multislice transverse spin-echo MRI **Slice thickness:** Not reported **What was imaged:** The volume of interest included part of the head, body and tail of the hippocampus and portions of the grey and white matter from the mid and posterior temporal lobe **Definition of a localised scan:** Significant lateralisation was assumed when values outside 2 SD from the normal were found. Asymmetry index (left – right)/[(left + right)/2] used for hippocampal volumes. NAA/Cr ratios 2 SD below the mean were considered abnormal

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Markand, 1996[79] **Study design** Retrospective diagnostic cohort **Country of study** USA **Study objective** To compare the sensitivity of ictal ^{99m}Tc-HMPAO SPECT with interictal ^{18}F-FDG PET in the localisation of the epileptogenic focus in patients with medically intractable complex partial seizures **Aim** Lateralising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Patients with CPS with or without secondary generalised tonic clonic seizures **Inclusion criteria relating to outcome:** Patients who underwent anterior temporal lobectomy **Mean age (range):** 31 (10–55) years **No. of patients (male):** 67 (29) **Duration of epilepsy:** 1–46 (mean 21) years **Type of epilepsy:** **Temporal:** 67 **Mesial sclerosis:** Not reported	**No. of patients who underwent surgery:** 67 **Type of surgery:** **ATL:** 67 No outcome data	**Reference standard** Combination **Details:** Presurgical evaluation included clinical seminology, video-EEG, MRI, neuropsychometric tests, thiopental activation test, intracarotid sodium amytal test, interictal and ictal SPECT and interictal FDG PET 64 patients had firm localisation from surface EEG, and a further 3 from intracranial EEG	**Test 1: SPECT:** Interictal **Tracer:** HMPAO: 20–30 mCi **Gamma camera strength:** Elscint Helix dual-headed rotating gamma camera equipped with a high-resolution low-energy collimator. Butterworth filter **Timing from seizure onset to injection:** Seizure free for at least 1 day **Slice orientation:** Transaxial, sagittal and coronal **Slice thickness:** 12 mm **Timing from injection to scan:** Scan was usually completed within 1 hour of injection **Definition of a localised scan:** Not reported **Drop-outs:** 53 patients had interictal SPECT, reasons for drop-outs not reported. It was unknown if results for 9 patients were negative or partially correct **Test 2: MRI:** Routine No other details for MRI imaging given **Type of imaging:** ROI **Definition of a localised scan:** Not reported **Drop-outs:** 66 patients had MRI. 1 patient had surgery involving steel clips **Test 3: PET:** Interictal **Tracer:** FDG: 10 mCi **Gamma camera strength:** Positron two-ring tomograph **Slice orientation:** Primarily transaxial. These were then processed to acquire coronal and sagittal slices **Slice thickness:** 3.38 mm **Timing from injection to scan:** 30 minutes **Definition of a localised scan:** Not reported **Drop-outs:** 55 patients had PET, reasons for drop-outs not reported **Test 4: SPECT:** Ictal **Tracer:** HMPAO, HIPDM or ECD: 20–30 mCi **Gamma camera strength:** Elscint Helix dual-headed rotating gamma camera equipped with a high-resolution low-energy collimator. Butterworth filter **Timing from seizure onset to injection:** Not reported **Slice orientation:** Transaxial, sagittal and coronal **Slice thickness:** 12 mm **Timing from injection to scan:** Scan was usually completed within 1 hour of injection **Definition of a localised scan:** Not reported **Drop-outs:** 44 patients had ictal SPECT, reasons for drop-outs not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Markand, 1994[80] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To evaluate the usefulness of ictal and interictal SPECT to determine the epileptic focus in patients with medically intractable complex partial seizures undergoing presurgical evaluation **Aim** Lateralising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Consecutive patients with medically intractable complex partial seizures who had presurgical evaluation. Only patients who underwent anterior temporal lobectomy were included **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 31 (8–54) years **No. of patients (male):** 99 (47) **Duration of epilepsy:** 1–43 (mean 20) years **Type of epilepsy:** **Temporal:** 99 **Mesial sclerosis:** Not reported **Syndrome:** Not reported **Details:** 78 patients had gliosis, 4 low-grade glioma, 4 cavernous haemangioma, 10 heterotopia (7 of whom also had gliosis) and 3 had arachnoid cyst	**No. of patients who underwent surgery:** 99 **Type of surgery:** **ATL:** 99 **Duration of follow-up following surgery:** 6–97 (mean 37) months (outcomes only reported if follow-up >6 months) **Outcome following surgery:** **Class I:** Seizure free or auras only: 54 **Class II:** Rare seizures: 14 **Class III:** Worthwhile improvement: 12 **Class IV:** No worthwhile improvement: 10	**Reference standard** Site of surgery **Details:** Clinical semiology of seizures, EEG abnormalities, MRI, neuropsychometric testing, thiopental activation test, sodium amytal carotid test and interictal or ictal SPECT scans. In a few patients FDG-PET was also obtained. At least 3 ictal events were recorded on video-EEG in all but one patient. 13 patients did not have a focus localised by non-invasive EEG and so had intracranial electrodes used	**Test 1: SPECT:** Ictal **Tracer:** HIPDM, HMPAO or IMP: dose not reported **Gamma camera strength:** Single- or dual-headed camera. Butterworth filter with back-projection **Timing from seizure onset to injection:** HMPAO 5–7 minutes; HIPDM within 1 minute **Slice orientation:** Transaxial images obtained and data then processed to acquire coronal and sagittal slices **Slice thickness:** 12 mm **Timing from injection to scan:** Not reported **Definition of a localised scan:** Areas of regional hyperperfusion or hypoperfusion when SPECT scans visually interpreted **Drop-outs:** Scans only obtained in 82 patients **Test 2: SPECT:** Interictal **Tracer:** HIPDM, HMPAO or IMP: dose not reported **Gamma camera strength:** Single- or dual-headed camera. Butterworth filter with back-projection **Timing from seizure onset to injection:** At least 24 hours **Slice orientation:** Transaxial images obtained and data then processed to acquire coronal and sagittal slices **Slice thickness:** 12 mm **Timing from injection to scan:** Not reported **Definition of a localised scan:** Areas of regional hyperperfusion or hypoperfusion when SPECT scans visually interpreted **Drop-outs:** Scans only obtained in 94 patients

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Mastin, 1996[81] **Study design** Prospective diagnostic cohort **Country of study** USA **Study objective** To correlate prospective imaging findings in patients with intractable partial epilepsy with site of surgery and clinical outcome **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** Patients with intractable partial epilepsy who underwent interictal or postictal SPECT **Inclusion criteria relating to outcome:** Patients who eventually underwent surgical resection of non-tumoral seizure foci or resection or biopsy of a tumour **Mean age (range):** 29.8 (13–45) years **No. of patients (male):** 35 (25) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 29 **Mesial sclerosis:** Not reported **Non-temporal:** 6 **Details:** 1 with parietal venous angioma, 6 extra temporal foci, 8 arteriovenous malformation and 1 hyperfusion of the cerebellum	**No. of patients who underwent surgery:** 35 **Type of surgery:** **ATL:** Not reported **AH:** Not reported **Non-TL:** Not reported **Other:** 9 **Details:** 1 resection of ipsilateral seizure focus in patient with parietal venous angioma, 7 resections of arteriovenous malformation and 1 patient had lesion biopsy only **Duration of follow-up following surgery:** >1 year **Outcome following surgery:** **Class I:** Seizure free: 24 **Class II:** Rare seizures: 6 **Class III:** Worthwhile improvement: 4 **Class IV:** No worthwhile improvement: 0	**Reference standard** Site of surgery **Details:** Invasive EEG (n = 20), MRI (n = 8). PET(n = 25) and SPECT (ictal n = 33 and postictal n = 23)	**Test 1: SPECT:** Ictal **Tracer:** HMPAO: dose not reported **Gamma camera strength:** Triple-headed camera with 'super high-resolution' parallel-hole collimators or 'super-fine resolution' fan-beam collimators **Timing from seizure onset to injection:** Mean 8.5 (1–14) minutes **Slice orientation:** Images reconstructed by means of back-projection with a Hamming filter in the transverse, sagittal and coronal planes **Slice thickness:** 3.56 mm sections were summed to approximate 1 cm thickness **Timing from injection to scan:** Within 1 hour **Definition of a localised scan:** Asymmetric foci with perfusion increases of ≥2 colour changes (>11% asymmetry) on ≥2 contiguous images. Or asymmetric foci with perfusion increases of one colour change (1–11% asymmetry) on two or more contiguous images **Drop-outs:** 23 patients included, reasons for drop-outs not reported **Test 2: PET** **Tracer:** FDG: 185–555 MBq (5–15 mCi) **Gamma camera strength:** ECAT 951 two-ring scanner **Timing from seizure onset to injection:** Not reported **Slice orientation:** Transaxial slices were reconstructed for display in both 3.3 and 9.9 mm thick contiguous planes **Slice thickness:** Not reported **Timing from injection to scan**: 30–50 minutes **Definition of a localised scan:** Localisation **Drop-outs:** 25 patients included, reasons for drop-outs not reported **Test 3: SPECT:** Interictal **Tracer:** HMPAO: 740–1110 MBq (20–30 mCi) **Gamma camera strength:** Triple-headed camera with 'super-high resolution' parallel-hole collimators or 'super-fine resolution' fan-beam collimators **Timing from seizure onset to injection:** Not reported **Slice orientation:** Images reconstructed by means of back-projection with a Hamming filter in the transverse, sagittal and coronal planes **Slice thickness:** 3.56-mm sections were summed to approximate 1-cm thickness **Timing from injection to scan:** Within 1 hour **Definition of a localised scan:** At least two colour changes (>11% asymmetry between sides) with foci of decreased activity on ≥2 contiguous images. Or: areas with one colour change (1–11% asymmetry) and foci decrease activity in ≥2 contiguous images **Drop-outs:** 33 patients included, reasons for drop-outs not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Newton, 1994[83] **Study design** Unclear: diagnostic cohort **Country of study** Australia **Study objective** To determine the optimal time to perform SPET studies for clinical seizure lateralisation in TLE **Aim** Lateralising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** All patients being evaluated for temporal lobectomy. Consecutive patients **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 31 (12–66) years **No. of patients (male):** 73 (37) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 73 **Other lesions:** 62 **Details:** 50 with hippocampal sclerosis, 9 gangliogliomas, 1 cortical dysgenesis, 1 gliosis and 1 angioma	**No. of patients who underwent surgery:** 72 **Type of surgery:** **ATL:** 72 **Details:** One patient did not undergo surgery; the reason is not reported No outcome data	**Reference standard** Combination **Details:** Interictal SPECT, MRI, neuropsychological data. Ictal SPECT in 50 patients. Postictal SPECT in remaining 23	**Test 1: SPECT:** Postictal **Tracer:** HMPAO: dose not reported **Gamma camera strength:** Starcam 400AC gamma camera **Timing from seizure onset to injection:** 30 seconds or more after the seizure termination **Slice orientation:** Not reported **Slice thickness:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Not reported **Drop-outs:** None reported **Test 2: SPECT:** Interictal **Tracer:** HMPAO: dose not reported **Tesla/gamma camera strength:** Starcam 400AC gamma camera **Timing from seizure onset to injection:** At least 24 hours **Slice orientation:** Not reported **Slice thickness:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Lateralised **Drop-outs:** None reported **Test 3: SPECT:** Ictal **Tracer:** HMPAO: dose not reported **Gamma camera strength:** Starcam 400AC gamma camera **Timing from seizure onset to injection:** During seizure or up to 30 seconds after its electroclinical termination **Slice orientation:** Not reported **Slice thickness:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Lateralised **Drop-outs:** 52 scans were performed in 50 patients and were successful in all 50 patients. 1 scan was uninterpretable

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Newton, 1995[82] **Study design** Unclear: diagnostic cohort **Country of study** Australia **Study objective** To examine the value of SPECT in patients with refractory partial epilepsy **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** Patients investigated for refractory partial seizures **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 29 (11–60) years **No. of patients (male):** 177 (not reported) **Duration of epilepsy:** 1–49 (mean 15) years **Type of epilepsy:** **Temporal:** 126 (+9 atypical temporal) **Mesial sclerosis:** Not reported **Non-temporal:** 42 **Details:** 5 parietal, 5 frontal, 2 occipital and 30 unlocalised	**No. of patients who underwent surgery:** Not reported **Type of surgery:** Not reported No outcome data	**Reference standard** Combination **Details:** All patients underwent clinical evaluation, video-EEG, MRI and neuropsychological assessment. EEG and MRI were used to evaluate accuracy of SPECT	**Test 1: SPECT:** Interictal **Tracer:** HMPAO: 700 MBq **Gamma camera strength:** Starcam, Butterworth filter **Slice orientation:** Transaxial, reconstructed as sagittal **Slice thickness:** 3 mm **Timing from seizure onset to injection:** 24 hours **Timing from injection to scan:** Up to 2 hours **Definition of a localised scan:** Localised or not localised on the basis of finding focal hyperperfusion **Drop-outs:** Scans for 170 patients reported **Test 2: SPECT:** Postictal **Timing from seizure onset to injection:** After the 30 seconds postictal period Other imaging details as for interictal **Drop-outs:** Scans reported for 114 patients **Test 3: SPECT:** Ictal **Timing from seizure onset to injection:** TLE: within 30 seconds. Non-temporal lobe epilepsy: during seizure (no further details). Other imaging details as for interictal **Drop-outs:** Scans for 76 patients reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Ng, 1994[85] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To assess two-dimensional phase-encoded proton chemical shift imaging (MR spectroscopy) for potential clinical application in presurgical localisation of TLE **Aim** Lateralising **Subgroups assessed** No structural abnormality EEG focus	**Population:** Children and adults **Patient spectrum:** Patients with intractable epilepsy being considered for epilepsy surgery. Only patients with clinical and EEG evidence of TLE without lesions demonstrated at MRI were included **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 32 y (14–53) years **No. of patients (male):** 25 (13) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 25 **Mesial sclerosis:** Not reported	**No. of patients who underwent surgery:** Not reported **Type of surgery:** Not reported No outcome data	**Reference standard** EEG **Details:** All patients had continuous video-EEG monitoring with scalp and sphenoidal electrodes. Most patients found to have bitemporal epileptic-type abnormalities were further examined with depth electrode implantation	**Test 1: MRS:** Volumetric **Magnet strength:** 1.5 T **Weighting/imaging details:** T1 weighted images used. High spatial resolution two-dimensional phase encoded double-echo proton chemical shift imaging spectroscopy performed **Slice orientation:** sagittal, coronal and axial planes **Metabolites:** NAA, Cho **Minimising partial volume effects:** By partial volume averaging, i.e. using different voxel sizes, with smaller voxel sizes requiring a larger number of signals, averaged for adequate signal-to-noise ratio. **Definition of a localised scan:** The NAA/Cho ratio was used for threshold analysis. The threshold used was 1.13, i.e. below this regarded as being abnormal. For visual analysis, the criterion of NAA less than Cho was used to decide abnormal voxels **Drop-outs:** 4 patients only had an MRS on only one side and were therefore excluded

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
O'Brien, 2001[86] **Study design** Unclear: diagnostic cohort **Country of study** Australia **Study objective** To investigate localisation rate, accuracy and prognostic value of FDG-PET images in the presurgical evaluation of intractable partial epilepsy **Aim** Localising **Subgroups assessed** No structural abnormality	**Population:** Children and adults **Patient spectrum:** Consecutive patients. Patients referred for PET due to ambiguous localisation from other non-invasive investigations (especially MRI and ictal EEG). Guidelines were not strictly enforced and physicians could order PET if they felt it was useful **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 34 (16–63) years **No. of patients (male):** 55 (31) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 41 **Mesial sclerosis:** 2 **Non-temporal:** 14 **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 2 frontal, 4 frontalparietal, 1 temporalparietal, 1 parietal, and 6 unlocalised. 2 with focal cortical dysplasia	**No. of patients who underwent surgery:** 24 **Type of surgery:** **ATL:** 22 **Non-TL:** 2 **Details:** 9 declined surgery, 7 awaiting surgery or had <6 months follow-up, 15 not suitable surgery candidates **Duration of follow-up following surgery:** 6–42 (median 17) months **Outcome following surgery:** **Class I:** Seizure free or auras only: 19 **Class II:** >95% improvement in seizure frequency: 3 **Class III:** 80–94% reduction in seizure frequency: 1 **Class IV:** <80% reduction in seizure frequency: 1	**Reference standard** Site of surgery **Details:** Only 21 patients who underwent PET scans also underwent surgery, 20 temporal, 1 extra-temporal	**Test 1: PET** **Tracer:** FDG: 37–111 MBq (1–3 mCi) **Gamma camera strength:** PENN PET 300H tomograph scanner with sodium chloride crystals. Data were processed using a Weiner prefilter **Timing from seizure onset to injection:** Not reported **Slice orientation:** Reconstruction process created images in the transaxial, coronal sagittal and transtemporal planes **Slice thickness:** 2 mm **Timing from injection to scan:** 45–60 minutes PET was 3D whole head acquisition **Definition of a localised scan:** Single focus of decreased image intensity in ≥2 contiguous slices, in ≥2 planes. Consensus from 2 reviewers **Drop-outs:** Only results for 24 patients who underwent surgery were available

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
O'Brien, 2001[91] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To investigate the localisation rate and prognostic significance of peri-ictal SPECT in patients with medical refractory partial epilepsy associated with disorders of cortical development **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Not reported **Patient spectrum:** Consecutive patients with refractory partial epilepsy associated with disorders of cortical development **Inclusion criteria relating to outcome:** None reported **Mean age (range):** Not reported **No of patients (male):** 22 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** Not reported	**No. of patients who underwent surgery:** 17 **Type of surgery:** Not reported No outcome data	**Reference standard** EEG **Details:** Intercranial EEG	**Test 1: SISCOM** SPECT scans were co-registered with the postoperative MRI **Tracer:** Not reported **Tesla/gamma camera strength:** Not reported **Timing from seizure onset to injection:** Ictal in 18 patients and postictal in 4. No further details reported **Slice orientation:** Not reported **Slice thickness:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Not reported **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
O'Brien, 1998[88] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To determine whether SISCOM is superior to the traditional method of inspection of ictal and interictal scans, to compare seizure localisation by SISCOM with those by scalp EEG, intercranial EEG and MRI, and to assess the value of seizure localisation by SISCOM in predicting surgical outcome **Aim** Localising **Subgroups assessed** No subgroup EEG focus No EEG focus	**Population:** Children and adults **Patient spectrum:** Intractable partial epilepsy who had ictal and interictal SPECT, EEG and MRI **Inclusion criteria relating to outcome:** None reported **Mean age (range):** Median 32.5 (1.5–61) years **No. of patients (male):** 51 (26) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 12 of surgical patients **Mesial sclerosis:** Not reported **Non-temporal:** 14 of surgical patients **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 1 parietal-occipital, 8 frontal, 1 frontal-temporal, 1 frontal-parietal, 2 occipital and 1 parietal	**No. of patients who underwent surgery:** 26 **Type of surgery:** **ATL:** 12 **Non-TL:** 14 **Details:** 1 parietal-occipital, 8 frontal, 1 frontal-temporal, 1 frontal-parietal, 2 occipital, 1 parietal **Duration of follow-up following surgery:** >1 year **Outcome following surgery:** **Class I:** Seizure free or non-disabling partial seizures: 13 **Class II:** >75% improvement in seizure frequency: 7 **Class IV:** Non-favourable outcome: 6	**Reference standard** Site of surgery **Details:** All patients had video-EEG	**Test 1: MRI:** Routine/volumetric **Contrast agent:** None reported **Tesla:** 1.5 T **Weighting:** T1 **Slice orientation:** Sagittal (T1), coronal (volumetric, double spin and FLAIR) **Slice thickness:** 1.6 mm for volumetric **What was imaged:** Whole brain **Type of imaging:** ROI **Definition of a localised scan:** Not reported **Drop-outs:** 25 had not undergone surgery **Test 2: SISCOM:** Routine MRI, ictal SPECT **Tracer:** Details as for MRI and ictal SPECT **Definition of a localised scan:** Not reported **Drop-outs:** 25 had not undergone surgery **Test 3: SPECT:** Ictal and interictal **Tracer:** HMPAO 13 patients or ECD 38 patients: dose not reported **Gamma camera strength:** dual-headed gamma camera equipped with ultra-high resolution fan-beam collimator **Timing from seizure onset to injection:** Ictal: median 36 (range 6–182) seconds. Interictal: at least 24 hours **Slice orientation:** Both procedures: transaxial images were reconstructed using a Metz filter, producing transaxial, coronal, sagittal and transtemporal planes **Slice thickness:** Not reported **Timing from injection to scan:** 2–3 hours **Definition of a localised scan:** side-by-side comparison of ictal and interictal SPECT **Drop-outs:** 25 had not undergone surgery

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
O'Brien, 2000[87] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To determine whether localisation of extra-temporal epilepsy with SISCOM is predictive of outcome after resective epilepsy surgery, whether SISCOM images provide prognostically important information compared with standard tests and whether blood flow change on SISCOM images is useful in determining site and extent of excision required **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** All patients who received peri-ictal and interictal SPECT during presurgical evaluation **Inclusion criteria relating to outcome:** All patients had extra-temporal resective surgery **Mean age (range):** 25 (1.5-56) years **No. of patients (male):** 36 (23) **Duration of epilepsy:** Not reported **Type of epilepsy:** Non-temporal: 36	**No. of patients who underwent surgery:** 36 **Type of surgery:** **Other:** 36 **Details:** 19 frontal excision, 4 frontal-parietal, 4 occipital, 2 frontal-temporal, 2 parietal, 2 parieto-temporal, 2 parieto-occipital, 1 occipito-temporal. 15 had maximal frontal resection, 6 limited corticectomy, 14 lesionectomy, 1 modified hemispherectomy **Duration of follow-up following surgery:** 12–40 (median 16.5) months **Outcome following surgery:** **Class I:** Seizure free or non-disabling partial seizures: 14 **Class II:** >75% improvement in seizure frequency: 12 **Class IV:** Non-favourable outcome: 10	**Reference standard** Site of surgery **Details:** Ictal scalp EEG was localising in 22/36 patients, intercranial EEG in 18/36 patients	**Test 1: SISCOM:** Routine MRI and interictal and ictal SPECT **Tracer:** HMPAO (20 mCi) in 14 patients. ^{99m}Tc-bicisate (dose not reported) in 22 patients. None reported for MRI **Gamma camera strength:** Dual-headed gamma camera equipped with ultra-high resolution fan-beam collimators **Magnet strength:** Not reported **Weighting:** Not reported **Timing from seizure onset to injection:** Mean 43 (6–182) seconds **Slice orientation:** SPECT: transaxial images were reconstructed to create transaxial, coronal, sagittal and transtemporal planes. MRI: not reported **Slice thickness:** Not reported **Timing from injection to scan:** 2–3 hours **What was imaged:** Not reported **Type of imaging:** ROI **Definition of a localised scan:** Not reported **Drop-outs:** Not reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Oliveira, 1999[92] **Study design** Unclear: diagnostic cohort **Country of study** Brazil **Study objective** To evaluate the accuracy, feasibility and clinical value of both ictal and interictal SPECT in patients with medically refractory epilepsy **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Consecutive patients with medically refractory partial epilepsy, evaluated with a view to surgical treatment **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 25.1 (1–48) years **No. of patients (male):** 75 (38) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 48 **Mesial sclerosis:** 35 **Non-temporal:** 27 **Other lesions:** 16 **Syndrome:** Not reported **Details:** 9 had focal cortical dysplasia, 6 low-grade tumour, and 1 schizencephaly	**No. of patients who underwent surgery:** 73 **Type of surgery:** Not reported **Duration of follow-up following surgery:** 4–26 (mean 13) months **Outcome following surgery:** **Class I:** Seizure free: 47 **Class III:** Less favourable outcome (Engel classes II–IV): 16	**Reference standard** Combination **Details:** All patients had multiple prolonged video-EEG recordings with standard and sphenoidal electrodes, MRI and neurophysiological testing. Convergence of clinical, EEG, neuropsychological, structural, pathological and postsurgical follow-up data	**Test 1: SPECT:** Ictal **Tracer:** ECD: 20 mCi **Gamma camera strength:** Single-headed non-dedicated gamma camera with low-energy, high-resolution collimator. Images reconstructed with use of a Butterworth filter **Timing from seizure onset to injection:** 12–75 seconds **Slice orientation:** Reconstructed on the axial, coronal, saggital and oblique (temporal) planes **Slice thickness:** 3.99 mm **Timing from injection to scan:** 1–4 hours **Definition of a localised scan:** Presence of ictal hyperperfusion **Drop-outs:** 23 patients had ictal SPECT scans **Test 2: SPECT:** Interictal **Tracer:** ECD: 20 mCi **Timing from seizure onset to injection:** Not reported Other details as for ictal SPECT **Drop-outs:** 66 patients had interictal SPECT

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Oommen, 2004[93] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To compare the relative localising values of hypoperfusion in interictal SPECT and hyperperfusion in ictal SPECT in non-lesional patients who underwent temporal lobectomies **Aim** Lateralising **Subgroups assessed** EEG focus	**Population:** Not reported **Patient spectrum:** Patients who underwent temporal lobectomies. No further details reported **Inclusion criteria relating to outcome:** All patients had to undergo temporal lobectomies to be included **Mean age (range):** 32.1 (not reported) years **No. of patients (male):** 42 (21) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 42	**No. of patients who underwent surgery:** 42 **Type of surgery:** **ATL:** 42 No outcome data	**Reference standard** Site of surgery **Details:** Continuous video-EEG monitoring, MRI and scalp EEG. If scalp EEG was non-localising or was in conflict with MRI findings, video-EEG monitoring was repeated following implantation of subdural strip electrodes. Foci localised by reviewing edited video-EEG of at least 3 typical seizures	**Test 1: SPECT:** Interictal **Tracer:** ECD: dose not reported **Gamma camera strength:** Triple-headed scanner with high-intensity fan-beam collimator **Timing from seizure onset to injection:** At least 24 hours **Slice orientation:** Not reported **Slice thickness:** 2.89 mm/pixel **Timing from injection to scan:** Not reported **Definition of a localised scan:** Studies were reported as normal or as showing evidence of hypoperfusion or hyperperfusion **Drop-outs:** 2 patients did not have interictal scans for technical reasons **Test 2: SPECT:** Ictal **Tracer:** ECD: dose not reported **Gamma camera strength:** Triple-headed scanner with high-intensity fan-beam collimator **Timing from seizure onset to injection:** Mean 1.86 minutes **Slice orientation:** Not reported. **Slice thickness:** 2.89 mm/pixel **Timing from injection to scan:** As soon as practically feasible, usually within 3 hours **Definition of a localised scan:** Studies were reported as normal or as showing evidence of hypoperfusion or hyperperfusion **Drop-outs:** 13 patients did not have ictal scans. Reasons: patients had required seizures before next batch of isotope stocks; 2nd and 3rd seizures occurred within a 24-hour window when another injection was not permitted and patients were discharged; or seizures occurred over the weekend when scanning was not available

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Otsubo, 1995[95] **Study design** Retrospective diagnostic cohort **Country of study** Canada **Study objective** To determine whether SPECT studies improved the accuracy of locating the epileptic focus in a paediatric population **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children **Patient spectrum:** Paediatric patients with documented localisation-related epilepsy **Inclusion criteria relating to outcome:** Patients had to have undergone epilepsy surgery **Mean age (range):** 10.2 years (7 months–16 years) **No. of patients (male):** 55 (19) **Duration of epilepsy:** <1–16 (mean 5.9) years **Type of epilepsy:** **Temporal:** 33 **Mesial sclerosis:** 13 **Non-temporal:** 20 **Other lesions:** 2 **Syndrome:** 1 had West syndrome, 5 Sturge–Weber syndrome, 1 Rasmussen syndrome and 3 tuberous sclerosis **Details:** 15 had tumours and 17 migration disorders	**No. of patients who underwent surgery:** 55 **Type of surgery:** **ATL:** 30 **AH:** 13 **Non-TL:** 10 **Other:** 2 **Details:** 2 had hemidecortication, 1 infarction and 1 hemispheric Sturge–Weber syndrome. 6 had occipital lobectomy and 4 frontal lobectomy, and 13 lesionectomy (3 temporal, 5 frontal, 3 parietal and 2 occipital) No outcome data	**Reference standard** EEG **Details:** Ictal EEG abnormalities on prolonged video-EEG. Zygomatic and sphenoidal EEG was performed for patients with complex partial seizures of suspected mesial temporal origin	**Test 1: SPECT:** Interictal **Tracer:** HMPAO: 520 MBq (14 mCi). **Gamma camera strength:** Single rotating head camera with a high-resolution collimator. Filtered back-projection with a Hanning filter **Timing from seizure onset to injection:** Not reported **Slice orientation:** Transaxial slices reconstructed **Slice thickness:** 1.2 cm **Timing from injection to scan:** 20 minutes **Definition of a localised scan:** Areas of regional perfusion abnormality (hypo- and hyperperfusion). **Drop-outs:** None reported **Test 2: SPECT:** Immediate post-ictal and interictal **Timing from seizure onset to injection:** For immediate postictal SPECT within 10 minutes of seizure ending. Interictal not reported Other details as for interictal SPECT **Definition of a localised scan:** Areas of regional perfusion abnormality (hypo- and hyperperfusion) on analysis of combined immediate postictal and interictal SPECT studies **Drop-outs:** Only 17 patients had an immediate postictal SPECT and thus could have combined SPECT studies

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Park, 2001[96] **Study design** Unclear: diagnostic cohort **Country of study** Korea **Study objective** To evaluate the lateralising ability of single-voxel MRS in comparison with MR imaging and PET in patients with hippocampal sclerosis **Aim** Lateralising **Subgroups assessed** Structural abnormality (all hippocampal sclerosis)	**Population:** Children and adults **Patient spectrum:** Patients with intractable TLE whose MRI diagnosis was unilateral hippocampal sclerosis. Only patients who had MRI, MRS and PET were included **Inclusion criteria relating to outcome:** All patients had to undergo anterior temporal lobectomy and have good postsurgical outcome (Engel class I or II) **Mean age (range):** 28 (17–46) years **No. of patients (male):** 33 (21) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 33 **Mesial sclerosis:** 33 **Syndrome:** Not reported	**No. of patients who underwent surgery:** 33 **Type of surgery:** **ATL:** 33 **Duration of follow-up following surgery:** >1 year **Outcome following surgery:** **Class I:** Seizure free: **Class II:** Few seizures in a year: 33 **Class III:** >75% improvement in seizure frequency: **Class IV:** No worthwhile improvement: **Details:** All patients were Engel I and II – good surgical outcome – breakdown not reported	**Reference standard** MRI **Details:** 1.5 T. Temporal lobes and hippocampus evaluated with 2D T2-weighted fast spin-echo sequences with 3-mm thick sections and with T1-weighted 3D magentisation-prepared rapid acquisition gradient-echo sequences with 1.5-mm thick section in the oblique coronal plane perpendicular to long axis of hippocampus Diagnosis of hippocampal sclerosis: presence of unilateral atrophy and high T2 signal of the hippocampus **Drop-outs:** None reported	**Test 1: PET** **Tracer:** FDG: 370 MBq **Magnet strength:** ECAT EXACT scanner **Timing from seizure onset to injection:** Not reported **Slice orientation:** Axial and coronal, reconstructed as matrices **Slice thickness:** 2.1 × 2.1 × 3.4 mm **Timing from injection to scan:** Not reported **Definition of a localised scan:** Presence of an asymmetric decreased in FDG (asymmetry of ≥ 15%) **Test 2: MRS:** Volumetric **Tesla/gamma camera strength:** 1.5 T, single voxel proton MRS. Point-resolved spin-echo spectroscopy **Metabolites:** NAA at 2 ppm, Cr at 3 ppm and Cho at 3.2 ppm. Metabolite ratios NAA/Cho and NAA/Cr were calculated **What was imaged:** Medial temporal lobes. The ROI placement avoided potential magnetic susceptibility artefacts from skull base and sphenoidal sinus and contamination from fat in skull base **Type of imaging:** ROI **Definition of a localised scan:** Interpreted as abnormal when NAA/Cho < 0.8 or NAA/Cr <1 or both

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Rowe, 1991[100] **Study design** Unclear: diagnostic cohort **Country of study** Australia **Study objective** To determine the accuracy of seizure focus localisation with interictal SPECT by studying a large group of patients with well-defined temporal lobe seizure foci **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Not reported **Patient spectrum:** Consecutive patients with refractory complex partial seizures with well-defined temporal lobe seizure focus on EEG **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 28 (not reported) years **No. of patients (male):** 51 (Not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 51 **Mesial sclerosis:** Not reported **Syndrome:** Not reported **Details:** 4 had small tumours on MRI and 5 temporal lobe abnormalities on CT (1 tumour, 4 focal atrophy)	**No. of patients who underwent surgery:** 42 **Type of surgery:** **ATL:** 42 **Duration of follow-up following surgery:** 16–36 (mean 28) months **Outcome following surgery:** **Class I:** Seizure free: 30 **Class II:** Almost seizure free: 7 **Class IV:** No worthwhile improvement: 4 **Details:** The remaining surgical patient only had 6 months of follow-up and outcome was not reported	**Reference standard** Combination **Details:** Ictal EEG. Intracerebral electrode recordings were performed in 33/51 of patients, others had clear unilateral onset of epileptiform EEG activity on surface electrodes concordant with clinical, MRI and neuropsychological data	**Test 1: SPECT:** Interictal **Tracer:** HMPAO: 550 MBQ (15 mCi) **Gamma camera strength:** Single-headed rotating gamma camera. Butterworth filtering and change attenuation correction were performed. High-resolution collimator **Timing from seizure onset to injection:** At least 24 hours **Slice orientation:** Transaxial slices reconstructed in plane that ran from base of frontal lobe to occipital pole on a midsaggital image. Coronal slices were reconstructed perpendicular to this plane **Slice thickness:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Focal hypoperfusion used to indicate seizure focus **Drop-outs:** 6 patients had scans repeated, with the second scan used for localisation. There was difficulty in interpreting the scans for 5 patients, and these were excluded

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Rowe, 1989[97] **Study design** Unclear: diagnostic cohort **Country of study** Australia **Study objective** To evaluate localisation with interictal and postictal SPECT of cerebral perfusion in comparison with conventional ictal EEG **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Adults **Patient spectrum:** Consecutive patients referred for surgical treatment of intractable CPS **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 31 (16–64) years **No. of patients (male):** 32 (21) **Duration of epilepsy:** <1–53 (mean 19) years **Type of epilepsy:** **Temporal:** 32 **Mesial sclerosis:** 7 **Details:** 1 had oligodendroglioma, 1 glioma, 1 previous haemorrhage, 1 hamartoma, 1 mild dysplasia, and 7 with no hippocampus	**No. of patients who underwent surgery:** 27 **Type of surgery:** **ATL:** 27 **Duration of follow-up following surgery:** 12–17 months **Outcome following surgery:** **Class I:** Seizure free: 17 **Details:** 3 patients continued to experience seizures, unclear whether they are 'running down' or are surgical failures. Outcome of 7 patients not reported	**Reference standard** EEG **Details:** Consistent site of onset of ictal EEG activity from at least 3 spontaneous independent seizures. All patients had neuropsychological evaluation and continuous video-EEG monitoring. 25 had intracerebral depth electrode EEG, 4 had sphenoidal electrodes and 3 had scalp electrodes, where ictal localisation corresponded to a mass lesion on MRI **Drop-outs:** Not reported	**Test 1: SPECT:** Ictal **Tracer:** HMPAO: 550–700 MBq **Gamma camera strength:** Rotating gamma camera. Parallel hole, low-energy, high-resolution collimator **Timing from seizure onset to injection:** Initial 4 studies: >15 minutes. Remaining studies: average 5 minutes **Slice orientation:** Transverse. Midsagittal image was identified and transaxial slices were reconstructed. Coronal **Slice thickness:** Not reported **Timing from injection to scan:** Within 2 hours **Definition of a localised scan:** The cortical region showing the greatest postictal increase in perfusion relative to the interictal scan appearance was reported as the seizure focus **Test 2: SPECT:** Interictal **Tracer:** HMPAO: 550 MBq **Gamma camera strength:** Rotating gamma camera. Parallel hole, low-energy, high-resolution collimator **Timing from seizure onset to injection:** At least 24 hours **Slice orientation:** Transverse. Midsagittal image was identified and transaxial slices were reconstructed. Coronal **Slice thickness:** 3.1 mm **Timing from injection to scan:** Within 2 hours **Definition of a localised scan:** Hyperfusion visually obvious over at least three slices in comparison with opposite temporal lobe

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Runge, 1997[101] **Study design** Unclear: diagnostic cohort **Country of study** Germany **Study objective** Ictal and interictal SPECT for focus localisation **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Patients with pharmacoresistant focal epilepsy who underwent SPECT imaging **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 31 (12–45) years **No. of patients (male):** 23 (6) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 23 **Mesial sclerosis:** Not reported **Other lesions:** 17 **Details:** 5 had tumours, 8 atrophy, 1 lesion, 1 gliosis, 1 cysts and 1 defect	**No. of patients who underwent surgery:** Not reported **Type of surgery:** Not reported No outcome data	**Reference standard** EEG/ECoG **Details:** Video-EEG and ictal EEG/ECoG	**Test 1: MRI:** Routine **Contrast agent:** Not reported **Magnet strength:** 1.0 T **Weighting:** Transverse proton density, T1 and T2 weighted sequences **Slice orientation:** Coronal and transverse **Slice thickness:** Not reported **What was imaged:** Whole brain, including a special series of temporal sections **Definition of a localised scan:** Presence of morphological changes **Drop-outs:** 1 patient could not be classified as the result stated 'left/right' with no lobe stated. Reference standard stated 'left temporal' **Test 2: SPECT:** Interictal **Tracer:** ECD: 400–600 MBq **Gamma camera strength:** Single-headed camera **Timing from seizure onset to injection:** at least 24 hours **Slice orientation:** Reconstructed transaxial sections and perpendicular frontal and sagittal sections **Slice thickness:** Not reported **Timing from injection to scan:** 0.5–2 hours **Definition of a localised scan:** Comparison of perfusion patterns (hypoperfusion/hyperperfusion) were made bilaterally in 2 planes of section (transaxial and frontal). Circumscribed regional differences in perfusion of 20% interpreted as pathological **Drop-outs:** None reported **Test 3: SPECT:** Ictal **Tracer:** ECD: 300–800 MBq **Gamma camera strength:** single-headed camera **Timing from seizure onset to injection:** Mean 20 (7–30) seconds **Slice orientation:** Reconstructed transaxial sections and perpendicular frontal and sagittal sections **Slice thickness:** Not reported **Timing from injection to scan:** 2–4 hours **Definition of a localised scan:** Comparison of perfusion patterns (hypoperfusion/hyperperfusion) were made bilaterally in 2 planes of section (transaxial and frontal). Circumscribed regional differences in perfusion of 20% interpreted as pathological **Drop-outs:** No ictal recordings obtained on 2 patients

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Ryvlin, 1998[102] **Study design** Prospective diagnostic cohort **Country of study** France **Study objective** To define the specific contribution of FMZ-PET in presurgical evaluation with respect to MRI and FDG-PET **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Not reported **Patient spectrum:** Consecutive patients with refractory epilepsy **Inclusion criteria relating to outcome:** None reported **Mean age (range):** Not reported **No. of patients (male):** 100 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 52 **Frontal:** 27 **Temporal frontal:** 5 **Temporoinsulo-opercular:** 4 **Tempero-occipital:** 4 **Parietal:** 1 **Occipital:** 1 **Unknown foci:** 6	**No. of patients who underwent surgery:** 44 **Type of surgery:** Not reported No outcome data	**Reference standard** EEG (for MRI) Combination (for PET) **Details:** 40 patients had intracranial EEG. 36 patients had stereo EEG	**Test 1: MRI:** Routine **Contrast agent:** Not reported **Magnet strength:** 1.5 T **Weighting:** T1 and T2. Spin-echo **Slice orientation:** Not reported **Slice thickness:** 1 or 6 mm **Definition of a localised scan:** Asymmetry indices were calculated and compared with 20 normal people to detect unilateral hippocampal atrophy **Test 2: PET** **Tracer:** FMZ: 15 mCi **Magnet strength:** Not reported **Timing from seizure onset to injection:** Not reported **Slice orientation:** Axial and coronal, reconstructed as matrices **Slice thickness:** Not reported **Timing from injection to scan:** 20–40 minutes **Definition of a localised scan:** asymmetry indices exceeded the mean control value by ≥ 2 SDs

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Seki, 1998[103] **Study design** Unclear: diagnostic cohort **Country of study** Japan **Study objective** To compare the detection of epileptogenic areas on preoperative evaluation in patients with intractable epilepsy **Aim** Localising **Subgroups assessed** No subgroup EEG focus No EEG focus	**Population:** Adults **Patient spectrum:** Patients with intractable partial epilepsy **Inclusion criteria relating to outcome:** All patients underwent resective surgery and had a good outcome (Engel Class I or II) **Mean age (range):** 36 (17–67) years **No. of patients (male):** 33 (21) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 22 **Mesial sclerosis:** 11 **Non-temporal:** 11 **Other lesions:** 21 **Syndrome:** Not reported **Details:** 21 patients had organic lesions: 1 had encephalopathy, 1 meningioangiomatosis, 6 cavernoma, 1 dysembryoplastic neuroepithelial tumour, 3 contusion, 1 porencephalus, 2 arteriovenous malformation, 1 meningioma, 1 arachnoid cyst, 2 astrocytoma, 1 gliosis, 1 ganglioglioma	**No. of patients who underwent surgery:** 33 **Type of surgery:** Not reported **Duration of follow-up following surgery:** 12–99 (mean 43) months **Outcome following surgery:** Engel: **Class I:** No further details: 26 **Class II:** 7	**Reference standard** Site of surgery **Details:** All patients had scalp EEG, 24 had video-EEG recording >2 seizures, MRI, interictal SPECT	**Test 1: SPECT:** Interictal **Tracer:** HMPAO or ECD: 740 MBq **Gamma camera strength:** GCA-601 E and Multispect 3 (Siemens) **Timing from seizure onset to injection:** Not reported **Slice orientation:** Horizontal, coronal, sagittal **Slice thickness:** 3mm **Timing from injection to scan:** HMPAO 5 minutes; ECD 15 minutes **Definition of a localised scan:** Not reported **Drop-outs:** 7 patients did not undergo interictal SPECT **Test 2: MRI:** Volumetric and T2 weighted **Contrast agent:** Not reported **Magnet strength:** 1.5 and 1 T **Weighting:** T1 and T2, FLAIR **Slice orientation:** Horizontal, coronal, sagittal **Slice thickness:** Not reported **What was imaged:** Volumetric imaging and T2 only performed in patients with TLE **Definition of a localised scan:** Not reported **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Shen, 1990[104] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To determine if SPECT imaging would provide localising information similar to that of PET scanning **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** All patients had medically refractory and socially disabling partial seizure disorder, with IQ >70 and absence of psychosis **Inclusion criteria relating to outcome:** Patients had to have undergone temporal lobectomy **Mean age (range):** 28 (8–42) years **No. of patients (male):** 34 (18) **Duration of epilepsy:** 4–30 (mean 17) years **Type of epilepsy:** **Temporal:** 34	**No. of patients who underwent surgery:** 34 **Type of surgery:** **ATL:** 34 **Duration of follow-up following surgery:** 5–42 (mean 17) months **Outcome following surgery:** **Class I:** Seizure free: 23 **Class II:** >75% improvement in seizure frequency: 6 **Class IV:** No significant improvement: 3 **Details:** Of the 6 patients in Class II, 1 had 2 seizures in 3 months; 2 had 1 seizure in 3 months; 1 had 1 seizure/year; 1 had 2 seizures/year, and 1 had 4 nocturnal seizures in 6 months	**Reference standard** Site of surgery **Details:** Clinical semiology of seizures, focal background abnormalities on EEG, interictal epileptiform abnormalities, focal ictal EEF patterns, CT, MRI, neuropsychometric testing, thiopental activation, Wada test, interictal and ictal HIPDM SPECT. Invasive electrode monitoring was not available	**Test 1: SPECT:** Interictal **Tracer:** HIPDM: 5 mCi **Gamma camera strength:** Dual-headed camera. Butterworth filter **Timing from seizure onset to injection:** Not reported **Slice orientation:** Transaxial, sagittal, coronal and transverse **Slice thickness:** 12 mm **Timing from injection to scan:** 15–30 minutes **Definition of a localised scan:** Identification of correct temporal lobe: qualitative differences in regional cerebral perfusion **Drop-outs:** 1 patient did not receive interictal SPECT. 2 patients died (one due to malignant glioma and another to unrelated accident) and are excluded from the outcome prediction data **Test 2: SPECT:** Ictal **Tracer:** HIPDM: 5 mCi **Gamma camera strength:** Dual-headed camera. Butterworth filter **Timing from seizure onset to injection:** 1–2 minutes **Slice orientation:** Transaxial, sagittal, coronal and transverse **Slice thickness:** 12 mm **Timing from injection to scan:** 15–30 minutes **Definition of a localised scan:** Identification of correct temporal lobe: qualitative differences in regional cerebral perfusion **Drop-outs:** 4 patients did not receive ictal SPECT. 2 patients died (one due to malignant glioma and another to unrelated accident) and are excluded from the outcome prediction data

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Siegel, 2001[105] **Study design** Retrospective diagnostic cohort **Country of study** USA **Study objective** To explore the hypothesis that in patients with normal MRI, invasive monitoring can lead to localisation of the seizure-onset zone and successful surgery **Aim** Localising **Subgroups assessed** No structural abnormality	**Population:** Children and adults **Patient spectrum:** Patients who underwent intracranial EEG and had normal MRI findings **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 12.2 (0.5–40) years **No. of patients (male):** 43 (24) **Duration of epilepsy:** 2–40 (mean 19) years **Type of epilepsy:** **Temporal:** 11 **Mesial sclerosis:** Not reported **Non-temporal:** 14 **Other lesions:** 18 **Syndrome:** Not reported **Details:** 14 had frontal lobe epilepsy, 6 mesial TLE, 5 neocortical TLE, 12 multifocal origins and 6 not localised	**No. of patients who underwent surgery:** 31 **Type of surgery:** **Other:** 30 **Details:** 3 partial anterior corpus callosotomy, 26 focal cortical resections (2 of whom went on to have vagal nerve stimulators implanted), 2 others with vagal nerve stimulators implanted **Duration of follow-up following surgery:** At least 2 years **Outcome following surgery:** **Class I:** Seizure free: 15 **Class II:** Rare seizures: 5 **Class III:** III and IV combined – unable to control seizures: 4	**Reference standard** EEG **Details:** Intracranial EEG. 4 patients had two such studies	**Test 1: SISCOM:** Ictal and interictal SPECT **Tracer:** HMPAO 20 mCi or ECD 20 mCi **Gamma camera strength:** Picker Prism 3000 triple-headed camera **Timing from seizure onset to injection:** 3–48 (mean 17.6) seconds. Interictal scans performed before or after the ictal scans **Slice orientation:** Reconstructed into sagittal, coronal and axial planes **Slice thickness:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Interictal image was subtracted from ictal image and the subtracted image displayed alongside the MRI scans. An area of hyperperfusion was regarded a positive result **Drop-outs:** Ictal SPECT could not be obtained in 12 patients despite several attempts

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Sperling, 1986[106] **Study design** Prospective diagnostic cohort **Country of study** USA **Study objective** To evaluate MRI in patients in whom CT showed no focal abnormalities, and then to correlate the results with PET, EEG and findings during pathological examination **Aim** Lateralising **Subgroups assessed** No structural abnormality	**Population:** Not reported **Patient spectrum:** Consecutive patients. Prior, recent brain CT showing no focal lesions. Patients had either stereo-encephalographic telemetry evaluation with stereotactically implanted depth electrodes or resective surgery or biopsy **Inclusion criteria relating to outcome:** None reported **Mean age (range):** Not reported **No. of patients (male):** 35 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 27 **Mesial sclerosis:** 18 **Non-temporal:** 4 **Other lesions:** 4 **Syndrome:** Not reported **Details:** 4 frontal lobe, 1 heterotopia (in addition to MTS), 1 hamartoma, 2 astrocytoma and 4 with unknown seizure onset	**No. of patients who underwent surgery:** Not reported **Type of surgery:** **ATL:** 18 reported **AH:** Unclear **Non-TL:** Unclear **Other:** 1 **Details:** 1 operation for a structural lesion No outcome data	**Reference standard** Combination **Details:** CT showing no focal lesions. Either stereo-encephalographic telemetry evaluation with stereotactically implanted depth electrodes or resective surgery or biopsy. 1 patient did not have a surface EEG	**Test 1: PET** **Tracer:** FDG: dose not reported No further details reported **Drop-outs:** 2 patients with TLE, 2 with frontal lobe epilepsy and one of unknown seizure focus did not have a PET scan **Test 2: MRI:** Routine **Contrast agent:** Not reported **Tesla:** First 23 patients: 0.35 T. Last 12 patients: 0.3 T **Weighting:** T1. T2, spin-echo **Slice orientation:** Coronal in all patients. Axial in several patients **Slice thickness:** First 23 patients: 7 mm. Last 12 patients: 6 mm **What was imaged:** Not reported **Type of imaging:** ROI **Definition of a localised scan:** Not reported **Drop-outs:** 1 patient with TLE had no reference standard

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Tatlidil, 2000[107] **Study design** Retrospective diagnostic cohort **Country of study** USA **Study objective** To assess the value of same-day blood flow PET in both the identification of the language-dominant hemisphere and in the lateralisation of the epileptic focus in patients who were preoperatively evaluated for complex partial seizures **Aim** Lateralising **Subgroups assessed** No subgroup	**Population:** Adults **Patient spectrum:** The charts of patients who had temporal lobectomies were retrospectively reviewed **Inclusion criteria relating to outcome:** All patients underwent temporal lobectomies for complex partial seizures **Mean age (range):** 36 (18–58) years **No. of patients (male):** 24 (9) **Duration of epilepsy:** Mean 19 years **Type of epilepsy:** **Temporal:** 24 **Mesial sclerosis:** Not reported **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 14 had hippocampal sclerosis, 2 hippocampal gliosis, 1 hippocampal and neocortical microdysgenesis, 1 hippocampal gliosis and neocortical microdysgenesis, 1 hippocampal sclerosis and neocortical microdysgenesis, 1 hippocampal sclerosis and white matter heterotopia, 1 mesial temporal ganglioglioma and neocortical microdysgenesis and 1 hippocampal sclerosis and heterotopic neurons	**No. of patients who underwent surgery:** 24 **Type of surgery:** **ATL:** 24 **Duration of follow-up following surgery:** 4 months–3 years (mean 20 months) **Outcome following surgery:** **Class I:** Seizure free: 18 **Class II:** <3 seizures and >90% reduction in seizure frequency: 4 **Class IV:** No significant improvement: 2	**Reference standard** Site of surgery **Details:** Epileptic focus lateralisation was determined using Wada testing, EEG, MRI and PET	**Test 1: PET:** Ictal and interictal **Tracer:** [^{15}O]water: 2590 MBq (70 mCi) **Gamma camera strength:** GE scanner with transaxial field of view. A 15-slice transmission scan was performed using a ^{68}Ge/^{68}Ga source to correct for attenuation effects on raw images **Timing from seizure onset to injection:** Interictal 22, ictal 2. No further details **Slice orientation:** Transaxial **Slice thickness:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Functional asymmetry indices were used to lateralise seizure focus. Three rest scans were averaged **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Tatum, 1995[108] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To determine the sensitivity and specificity of interictal SPECT in localising an epileptogenic area by both intracranial and extra cranial recording methods **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Adults **Patient spectrum:** Patients with interictal SPECT scans were included. Patients with tumours were excluded from the analysis **Inclusion criteria relating to outcome:** None reported **Mean age (range):** Not reported (18–51 years) **No. of patients (male):** 20 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 16 **Details:** 1 had temporal-parietal and 3 were not localised	**No. of patients who underwent surgery:** 14 **Type of surgery:** **ATL:** 14 **Duration of follow-up following surgery:** 41–56 months **Outcome following surgery:** **Class I:** Seizure free: 10 **Class II:** <3 seizures/year: 2 **Class III:** >80% improved: 2 **Class IV:** 0:	**Reference standard** Combination **Details:** All patients had MRI, interictal and ictal scalp/sphenoidal EEG, neuropsychological testing, thiopental activation study and intracarotid amobarbital testing. In 11 patients, foci were not localised using non-invasive methods and intracranial monitoring was performed	**Test 1: SPECT:** Interictal **Tracer:** HMPAO: 20 mCi **Gamma camera strength:** 3700 single-headed gamma camera using a high-resolution collimator **Timing from seizure onset to injection:** At least 24 hours **Slice orientation:** Coronal, sagittal and transverse images were reconstructed **Slice thickness:** Not reported **Timing from injection to scan:** 15 minutes **Definition of a localised scan:** Hyperfusion **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Theodore, 1990[109] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To evaluate the correlation of pathology of temporal lobe foci with CT, MRI and PET. **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Adults **Patient spectrum:** Patients referred for evaluation of uncontrolled seizures. No patients had focal findings on neurological examination. Neuropsychological test results were normal or revealed only mild impairment of cognitive function in all patients **Inclusion criteria relating to outcome:** Patients had to undergo temporal lobectomies for typical CPS uncontrolled by phenytoin and carbamazepine to be included **Mean age (range):** 29 (16–39) years **No. of patients (male):** 26 (16) **Duration of epilepsy:** 5–28 (mean 20) years **Type of epilepsy:** **Temporal:** 26 **Mesial sclerosis:** 23 (gliosis) **Other lesions:** 3 **Details:** 3 had tumours: 1 oligodendroglioma, 1 mixed oligoastrocytoma and 1 ganglioglioma	**No. of patients who underwent surgery:** 26 **Type of surgery:** **ATL:** 26 **Details:** All patients underwent subpial resection technique **Duration of follow-up following surgery:** 12–55 (mean 28) months **Outcome following surgery:** **Class I:** Seizure free: 15 **Class II:** >90% improvement in seizure frequency: 7 **Class IV:** Unchanged: 4	**Reference standard** EEG **Details:** Surface ictal EEG, prolonged video-EEG telemetry with sphenoidal electrodes, selected patients had additional recordings with depth electrodes	**Test 1: PET** **Tracer:** FDG: 5 mCi **Gamma camera strength:** 4-ring, 7-slice tomograph **Timing from seizure onset to injection:** Not reported **Slice thickness:** 6 mm in plane and 11.5 mm in z-axis direction **Timing from injection to scan:** 30 minutes **Definition of a localised scan:** Asymmetry ≥ 15% in 1/3 temporal regions measured **Drop-outs:** None reported **Test 2: CT** **Contrast agent:** With and without contrast agent (agent not reported) **Magnet strength:** GE 8800 or 9800 scanner **Slice orientation:** Not reported **Slice thickness:** Not reported **Definition of a localised scan:** Not reported **Drop-outs:** None reported **Test 3: MRI:** Routine **Contrast agent:** Not reported **Magnet strength:** 0.5 T **Weighting:** T1 and T2 weighted spin-echo and inversion-recovery **Slice orientation:** Transverse and coronal scans **Slice thickness:** 10 mm **Definition of a localised scan:** Not reported **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Venz, 1994[110] **Study design** Unclear: diagnostic cohort **Country of study** Germany **Study objective** To investigate whether SPECT with [^{123}I]Iomazenil has greater sensitivity in localising the epileptic zone than [^{99m}Tc]HMPAO SPECT or MRI **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Patients with drug-resistant focal epilepsy. Only patients in whom video-EEG localised the seizure focus were included in the analysis **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 36 (8–56) years **No. of patients (male):** 33 (15) **Duration of epilepsy:** Not reported **Type of epilepsy:** Temporal: 20 (including 4 temporo-frontal and 1 temporo-parietal) **Mesial sclerosis:** 3 **Non-temporal:** 5 **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 1 central, 1 parietal-frontal, 2 right hemisphere, 1 frontal	**No. of patients who underwent surgery:** 11 **Type of surgery:** **ATL:** 9 **Non-TL:** 2 **Details:** 1 had right central seizure focus and 1 had parietal frontal seizure focus **Duration of follow-up following surgery:** 3–13 (median 8) months **Outcome following surgery:** **Details:** Authors state that 'almost all patients are seizure free'. No further details given	**Reference standard** EEG **Details:** Video-EEG, bilateral sphenoidal electrodes continuously monitored for 5–7 days. All ictal EEG changes until 20 seconds after seizure start were used for localisation. Postictal changes were also considered	**Test 1: MRI:** Routine **Contrast agent:** Gadolinium enhanced: 0.1 mmol **Magnet strength:** 1.5 T **Weighting:** T1 and T2 weighted **Slice orientation:** Reconstructed in the axial and coronal planes **Slice thickness:** Not reported **Definition of a localised scan:** Interpreted by 2 examiners blind to SPECT data. No further details given **Drop-outs:** 8 patients did not have a localised EEG and were excluded from the analysis **Test 2: SPECT** **Tracer:** Iomazenil: 111 MBq **Gamma camera strength:** Rotating single-headed gamma camera. Filtered back-projection used to reconstruct images **Timing from seizure onset to injection:** Not reported **Slice orientation:** Images reconstructed in coronal and sagittal planes **Slice thickness:** Not reported **Timing from injection to scan:** 5 and 90 minutes **Definition of a localised scan:** 2 examiners extracted results, discrepancies discussed. Visual interpretation followed by quantitative region of interest analysis **Drop-outs:** 8 patients did not have a localised EEG and were excluded from the analysis **Test 3: SPECT** **Tracer:** HMPAO: 740 MBq **Gamma camera strength:** Rotating single-headed gamma camera. Filtered back-projection used to reconstruct images **Timing from seizure onset to injection:** Not reported **Slice orientation:** Images reconstructed in coronal and sagittal planes **Slice thickness:** Not reported **Timing from injection to scan:** 10 minutes **Definition of a localised scan:** 2 examiners extracted results, discrepancies discussed. Visual interpretation followed by quantitative region of interest analysis **Drop-outs:** 8 patients did not have a localised EEG and were excluded from the analysis

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Vera, 1999[111] **Study design** Unclear: diagnostic cohort **Country of study** France **Study objective** To evaluate the usefulness of subtraction ictal SPECT co-registered to MRI for optimising the location of seizure foci in children **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children **Patient spectrum:** Children with pharmaco-resistant partial epilepsy who received ictal SPECT **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 6.6 years (3 months–18 years) **No. of patients (male):** 27 (13) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** Not reported **Syndrome:** 6 had tuberous sclerosis and 1 hemimegaloencephaly **Details:** 5 had cortical dysplasia, 2 hypothalamic haematomas, 1 hemispheric atrophy, 1 hemispheric lesion, 1 encephalitis, 1 cerebellar hamartoma and 9 were cryptogenic	**No. of patients who underwent surgery:** 12 **Type of surgery:** Not reported No outcome data	**Reference standard** Combination **Details:** Ictal video-EEG and MRI, with additional electrocorticography in 5 children	**Test 1: SISCOM:** Routine MRI and ictal and interictal SPECT **Tracer:** ECD: 740 MBq (20 mCi) for 1.73 m^2 **Tesla/gamma camera strength:** 1.5 T MRI. A double-headed DST, SMVi camera equipped with ultra-high resolution fan-beam collimators **Weighting:** T1 **Timing from seizure onset to injection:** Ictal SPECT: 5–30 (mean 15) seconds. Interictal SPECT and MRI: 48 hours later **Slice orientation:** MRI: Axial. SPECT: reconstructed to axial, sagittal and coronal **Slice thickness:** MRI: 1 mm **Timing from injection to scan:** 1 hour **Definition of a localised scan:** Ictal and interictal SPECT scans registered to MRI image and area of hyperperfusion regarded as a positive result **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Watanabe, 2002[112] **Study design** Unclear: diagnostic cohort **Country of study** Japan **Study objective** To examine the use of multi-channel NIRS during long-term video-EEG monitoring as the presurgical evaluation of patients with intractable epilepsy **Aim** Lateralising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Consecutive patients with medically intractable epilepsy **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 26 (4–46) years **No. of patients (male):** 32 (at least 10) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** Not clear, minimum 25 **Mesial sclerosis:** Not reported **Non-temporal:** Not clear, minimum 4 **Details:** 2 had frontal, 2 parietal focus and 3 not localised	**No. of patients who underwent surgery:** Not reported **Type of surgery:** Not reported No outcome data	**Reference standard** EEG **Details:** 29 cases were measured with NIRS/EEG during seizures and were further analysed. Seizure foci diagnosed by using intracranial EEG during seizures	**Test 1: NIRS** **Camera details:** Infrared light with wavelengths of 780 and 830 mm **Definition of a localised scan:** Changes in regional blood flow volume, estimated from the concentration change of oxy- and deoxyhaemoglobin during a seizure determined the seizure focus **Drop-outs:** Discrepancy between text and table make this unclear. The text states 28 patients were successfully measured with NIRS/EEG during seizures. However, results are tabulated for 29 patients. Thus from the table it appears that 3 patients did not have NIRS/EEG **Test 2: SPECT:** Ictal **Tracer:** HMPAO or ECD: dose not reported. **Gamma camera strength:** Not reported **Timing from seizure onset to injection:** Not reported **Slice orientation:** Not recorded **Slice thickness:** Not recorded **Timing from injection to scan:** Not recorded **Definition of a localised scan:** Areas of hyperperfusion **Drop-outs:** Discrepancy between text and table make this unclear. The text states 28 patients were successfully measured with NIRS/EEG during seizures. However, results are tabulated for 29 patients. Thus from the table it appears that 3 patients did not have NIRS/EEG

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Weil, 2001[113] **Study design** Retrospective diagnostic cohort **Country of study** Germany **Study objective** To investigate whether ictal SPECT distinguishes between TLE and Extra TLE and to evaluate the sensitivity of ictal SPECT in a series of patients in whom postoperative seizure control has proved that the seizure onset zone was correctly identified **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** No details **Inclusion criteria relating to outcome:** All patients had resective epilepsy surgery and excellent postoperative seizure control **Mean age (range):** 33 (11–61) years **No. of patients (male):** 30 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 21 **Non-temporal:** 9 **Syndrome:** Not reported **Details:** 1 temporo-occipital, 5 frontal, 2 parieto-occipital and 1 supplementary sensorimotor area	**No. of patients who underwent surgery:** 30 **Type of surgery:** Not reported **Duration of follow-up following surgery:** Not reported **Outcome following surgery:** **Class I:** Excellent outcome: 30	**Reference standard** Combination **Details:** EEG, MRI, FDG-PET. Patients underwent invasive EEG recordings if the results were discordant but a clear hypothesis of the seizure origin could be made	**Test 1: SPECT:** Ictal **Tracer:** ECD: 550–700 MBq **Gamma camera strength:** Triple-headed gamma camera with high-resolution parallel hole collimators **Timing from seizure onset to injection:** Not reported **Slice orientation:** Transverse **Timing from injection to scan:** 1–2 hours **Definition of a localised scan:** The ROI technique was used to estimate regional cerebral blood flow semi-quantitatively. Differences with an increase of >10% compared with the respective ROI of the opposite hemisphere were considered significant **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Weis, 1997[114] **Study design** Retrospective diagnostic cohort **Country of study** Germany **Study objective** To evaluate focus localisation by interictal and ictal SPECT **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** Patients who received ictal and interictal SPECT as part of their presurgical evaluation **Inclusion criteria relating to outcome:** All patients had undergone epilepsy surgery **Mean age (range):** 32 (14–56) years **No. of patients (male):** 87 (52) **Duration of epilepsy:** Not reported years **Type of epilepsy:** **Temporal:** 70 **Mesial sclerosis:** Not reported **Non-temporal:** 17	**No. of patients who underwent surgery:** 87 **Type of surgery:** Not reported. **Duration of follow-up following surgery:** 10–95 (mean 31) months **Outcome following surgery:** **Class I:** Seizure free: 42 **Class III:** Not seizure free: 45	**Reference standard** Site of surgery **Details:** Combined results of clinical seizure semiology, video-EEG, MRI, neuropsychological assessment and histological findings of resected brain tissue. 60 patients had intracranial EEG	**Test 1: SPECT:** Ictal **Tracer:** HMPAO (113 studies) or ECD (61 studies): 450–700 MBq **Gamma camera strength:** Dual-headed rotating scintillation camera with high-resolution collimators or single-headed gamma camera with neurofocal collimator. Butterworth filter **Timing from seizure onset to injection:** 12–150 (mean 53) seconds **Slice orientation:** Transverse slices reconstructed to create oblique slices parallel to orbito-meatal line and oblique coronal and sagittal slices **Timing from injection to scan:** 1 hour **Definition of a localised scan:** Analysed visually and using a semi-quantitative technique. Findings classified according to hypoperfusion, hyperperfusion or symmetrical brain perfusion **Drop-outs:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Wheless, 1999[115] **Study design** Prospective diagnostic cohort **Country of study** USA **Study objective** To determine the efficacy and relative contribution of several diagnostic methods in identifying the epileptogenic zone for resection **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Children and adults **Patient spectrum:** Surface EEG with at least one epileptiform discharge every 2–10 minutes, able to travel accompanied by a family member to the testing site and able to cooperate with the test requirements. These were a subset of a group of 115 patients with CPS referred to MEG studies. Patients with an incomplete battery of tests were excluded **Inclusion criteria relating to outcome:** All patients had to undergo surgery **Mean age (range):** 26.7 (7–55) years **No. of patients (male):** 58 (25) **Duration of epilepsy:** 2–43 (mean 17) years **Type of epilepsy:** Temporal: 35 **Non-temporal:** 23	**No. of patients who underwent surgery:** 58 **Type of surgery:** Not reported **Duration of follow-up following surgery:** 6–46 months **Outcome following surgery:** **Class I:** Seizure free: 37 **Class II:** Rare seizures: 5 **Class III:** >90% reduction in seizures: 9 **Class IV:** <90% reduction in seizures: 7	**Reference standard** Site of surgery **Details:** All patients underwent surface EEG, interictal and ictal continuous video-EEG and MRI. MEG studies were performed in 54 patients	**Test 1: MRI:** Routine **Contrast agent:** Not reported **Magnet strength:** 1.5 T **Weighting:** T1, T2. Many had FLAIR and 3D fast spoiled-GRASS studies **Slice orientation:** Transverse axial, sagittal and coronal **Slice thickness:** 3–5 mm **What was imaged:** Not reported **Definition of a localised scan:** Analysed visually for lesion, congenital abnormality or hippocampal sclerosis **Drop-outs:** 14 not validated

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Zhou, 1994[116] **Study design** Unclear: diagnostic cohort **Country of study** China **Study objective** To evaluate the clinical application of SPECT to the localisation of corticoepileptogenic focus of intractable epilepsy **Aim** Localising **Subgroups assessed** EEG focus	**Population:** Children and adults **Patient spectrum:** Patients who underwent surgery **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 21 (3.5–38) years **No. of patients (male):** 51 (36) **Duration of epilepsy:** >2 years **Type of epilepsy:** Not reported	**No. of patients who underwent surgery:** 51 **Type of surgery:** Surgical procedures included lesionectomy, calloectomy, anteriomedial temporal lobe resection and multiple subpial transaction No further details reported No outcome data	**Reference standard** Combination **Details:** The area of brain that was found to be abnormal preoperatively with EEG and SPECT was traced (ECoG) using subdural strip electrodes at time of surgery. Evidence of spike wave and spike-slow-wave during operation	**Test 1: SPECT** **Tracer:** ECD: 740 MBq **Gamma camera strength:** Rotatory camera. No further details reported. **Timing from seizure onset to injection:** Not reported **Slice orientation:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Region of sparse radioactivity **Dropouts:** None reported

continued

Study details	Patient spectrum	Surgery details	Reference standard	Index test
Yu, 1995[117] **Study design** Unclear: diagnostic cohort **Country of study** Taiwan **Study objective** To assess the effectiveness of delayed postictal SPECT in localisation of epileptic foci **Aim** Localising **Subgroups assessed** No subgroup	**Population:** Not reported **Patient spectrum:** None reported **Inclusion criteria relating to outcome:** Patients underwent temporal lobectomy for intractable partial seizures **Mean age (range):** Not reported **No. of patients (male):** 54 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** Temporal: 54	**No. of patients who underwent surgery:** 54 **Type of surgery: ATL:** 54 No outcome data	**Reference standard** Combination **Details:** All patients were evaluated using interictal EEG, ictal video-EEG, interictal and postictal SPECT and MR	**Test 1: SPECT:** <30 minutes postictal and interictal **Tracer:** HMPAO: dose not reported **Gamma camera strength:** Not reported **Timing from seizure onset to injection:** Ictal: within 30 minutes after seizure. Interictal: not reported **Slice orientation:** Not reported **Timing from injection to scan:** Not reported **Definition of a localised scan:** Visual assessment for regional hypoperfusion and hyperperfusion. Postictal and interictal scans were interpreted together to make the final decision on epileptic focus **Drop-outs:** 20 patients had injection <30 minutes after seizure **Test 2: SPECT:** delayed postictal (>30 minutes) and interictal **Timing from seizure onset to injection:** Over 30 minutes after seizure Other details as in Test 1. **Drop-outs:** 31 patients had injection >30 minutes after seizure **Test 3: SPECT:** immediate postictal and interictal **Timing from seizure onset to injection:** Immediately after seizure Other SPECT details as above **Drop-outs:** Only 3 patients had injection immediately after seizure

continued

Outcome prediction studies

Study details	Patient spectrum	Surgery details	Dependent variable	Variables investigated
Antel, 2002[118] **Study design** Unclear cohort **Country of study** Canada **Study objective** To develop a classifier that used MRI data to predict surgical outcome in patients with temporal lobe epilepsy	**Population:** Not clear **Patient spectrum:** Consecutive patients with pharmacological refractive suspected TLE. Patients who had extra-temporal epilepsy, space-occupying lesions or lack of peroperative volumetric MRIs or MRSI data were excluded. All patients had prolonged video-EEG to determine site of surgery **Inclusion criteria relating to outcome:** Patients who underwent surgery and had follow-up data **Mean age (range):** 35 (not reported) years **No. of patients (male):** 81 (31) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 81 **Mesial sclerosis:** Not reported **Other lesions:** Not reported	**No. of patients who underwent surgery:** 81 **Type of surgery:** **ATL:** 81 **Duration of follow-up following surgery:** Mean 38.1 (9.2–78.2) months **Outcome following surgery:** **Class I:** Seizure free: 52 **Class II:** <3 seizures/year: 1 **Class III:** >90% reduction in seizures: 12 **Class IV:** No worthwhile improvement (<90% reduction): 16	1. Seizure free 2. Worthwhile improvement (>90% reduction in seizures)	Ipsilateral, contralateral (to site of surgery) and asymmetry Z-scores for each of the following: hippocampal volume, amygdaloid volume, NAA/Cr in the midtemporal lobe and NAA Cr in the posterior temporal lobe

continued

Study details	Patient spectrum	Surgery details	Dependent variable	Variables investigated
Dupont, 2000[119] **Study design** Unclear cohort **Country of study** France **Study objective** To evaluate patients with documented medial temporal lobe epilepsy to determine if prediction of post-operative outcome is improved with the use of FDG-PET	**Population:** Not reported **Patient spectrum:** Consecutive patients with intractable MTLE who underwent PET. Patients had video-EEG, neuropsychological tests, intracarotid amobarbital test, volumetric MRI and 6 patients intracranial EEG to localising seizure focus **Inclusion criteria relating to outcome:** Patients who underwent anterior temporal lobectomies with at least 2 years of follow-up **Mean age (range):** 29 (not reported) years **No. of patients (male):** 30 (13) **Duration of epilepsy:** 30 years **Type of epilepsy:** **Temporal:** 30 **Details:** Hippocampal atrophy: 27	**No. of patients who underwent surgery:** 30 **Type of surgery:** **ATL:** 30 **Duration of follow-up following surgery:** Mean 3.5 (2.1–5.3) years **Outcome following surgery:** **A:** Completely seizure free: 14 **B:** Free of disabling seizures: 10 **C:** Rare disabling seizure or worthwhile improvement: 6	Outcome Class A compared with class C	FDG PET scans positive in the following temporal regions: 1. Temporal region: medial 2. Temporal region: pole 3. Temporal region: anterolateral 4. Temporal region: medium lateral 5. Temporal region: posterolateral

continued

Study details	Patient spectrum	Surgery details	Dependent variable	Variables investigated
O'Brien, 2000[87] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To determine where localisation of extra-temporal epilepsy with SISCOM is predictive of outcome after resective epilepsy surgery, whether SISCOM images provide prognostically important information compared with standard tests and whether blood flow change on SISCOM images is useful in determining site and extent of excision required	**Population:** Children and adults **Patient spectrum:** All patients who received peri-ictal and interictal SPECT during presurgical evaluation **Inclusion criteria relating to outcome:** Extratemporal resective surgery. All patients had at least 12 months postoperative follow-up **Mean age (range):** 25 (1.5–56) years **No. of patients (male):** 36 (23) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Non-temporal:** 36	**No. of patients who underwent surgery:** 36 **Type of surgery:** **Other:** 36 **Details:** 19 with frontal excision, 4 with frontal-parietal excision, 4 with occipital excision, 2 with frontal-temporal excision, 2 with parietal excision, 2 with parieto-temporal excision, 2 with perieto-occipital excision, 1 with occipito-temporal excision, 15 had maximal frontal resection, 6 limited corticectomy, 14 with lesionectomy, 1 had modified hemispherectomy **Duration of follow-up following surgery:** 12–40 (median 16.5) months **Outcome following surgery:** **Class I:** Seizure free or non-disabling partial seizures: 14 **Class II:** >75% improvement in seizure frequency: 12 **Class IV:** Non-favourable outcome: 10	1. Excellent outcome 2. Favourable outcome (>75% reduction in seizure frequency)	1. SISCOM (concordant vs non-concordant/non-localising) 2. Preoperative MRI (lesional vs non-lesional) 3. Ictal scalp EEG (localisation vs non-localising) And separate analysis for: 1. Extent of excision of SISCOM focus (complete excision vs non-complete or non-excision) 2. Preoperative MRI findings (focal structural lesions vs no lesion) 3. Ictal scalp EEG findings (localisation vs non-localising)

continued

Study details	Patient spectrum	Surgery details	Dependent variable	Variables investigated
O'Brien, 1998[88] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To determine whether SISCOM is superior to the traditional method of inspection of ictal and interictal scans, to compare seizure localisation by SISCOM with those by scalp EEG, intercranial EEG and MRI and to assess the value of seizure localisation by SISCOM in predicting surgical outcome	**Population:** Children and adults **Patient spectrum:** Patients with intractable partial epilepsy who had ictal and interictal SPECT, EEG and MRI **Inclusion criteria relating to outcome:** None **Mean age (range):** Median 32.5 (1.5–61) years **No. of patients (male):** 51 (26) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 12 of surgical patients **Mesial sclerosis:** Not reported **Non-temporal:** 14 of surgical patients **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 1 with parietal-occipital, 8 with frontal, 1 with frontal-temporal, 1 with frontal-parietal, 2 with occipital, 1 with parietal	**No. of patients who underwent surgery:** 26 **Type of surgery:** **ATL:** 12 **Non-TL:** 14 **Details:** 1 parietal-occipital, 8 frontal, 1 frontal-temporal, 1 frontal-parietal, 2 occipital, 1 parietal **Duration of follow-up following surgery:** >1 year **Outcome following surgery:** **Class I:** Seizure free or non-disabling partial seizures: 13 **Class II:** >75% improvement in seizure frequency: 7 **Class IV:** Non-favourable outcome: 6	1. Postoperative seizure frequency 2. Improvement in seizure frequency score (no further details)	1. SISCOM (concordant vs non-concordant or non-localising) 2. MRI (lesions vs no lesion) 3. Type of surgery (temporal vs non-temporal)

continued

Study details	Patient spectrum	Surgery details	Dependent variable	Variables investigated
O'Brien, 2001[86] **Study design** Unclear: diagnostic cohort **Country of study** Australia **Study objective** To investigate localisation rate, accuracy and prognostic value of FDG-PET images in the presurgical evaluation of intractable partial epilepsy	**Population:** Children and adults **Patient spectrum:** Consecutive patients. Patients referred for PET due to ambiguous localisation from other non-invasive investigations (especially MRI and ictal EEG). Guidelines were not strictly enforced and physicians could order PET if they felt it was useful **Inclusion criteria relating to outcome:** None reported **Mean age (range):** 34 (16–63) years **No. of patients (male):** 55 (31) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 41 **Mesial sclerosis:** 2 **Non-temporal:** 14 **Other lesions:** Not reported **Syndrome:** Not reported **Details:** 2 with frontal, 4 with frontal-parietal, 1 with temporal-parietal, 1 with parietal, and 6 unlocalised. 2 with focal cortical dysplasia	**No. of patients who underwent surgery:** 24 **Type of surgery:** **ATL:** 22 **Non-TL:** 2 **Details:** 9 declined surgery, 7 awaiting surgery or had <6 months of follow-up, 15 were not suitable surgery candidates **Duration of follow-up following surgery:** 6–42 (median 17) months **Outcome following surgery:** **Class I:** Seizure free or auras only: 19 **Class II:** >95% improvement in seizure frequency: 3 **Class III:** 80-94% reduction in seizure frequency: 1 **Class IV:** <80% reduction in seizure frequency: 1	Engel categories I–IV	1. MRI (definite focal lesions vs no focal lesion) 2. FDG-PET (localising vs non-localising)

continued

Study details	Patient spectrum	Surgery details	Dependent variable	Variables investigated
O'Brien, 2001[91] **Study design** Unclear: diagnostic cohort **Country of study** USA **Study objective** To investigate the localisation rate and prognostic significance of peri-ictal SPECT in patients with medical refractory partial epilepsy associated with disorders of cortical development	**Population:** Not reported **Patient spectrum:** Consecutive patients with refractory partial epilepsy associated with disorders of cortical development **Inclusion criteria relating to outcome:** None reported **Mean age (range):** Not reported **No. of patients (male):** 22 (not reported) **Duration of epilepsy:** Not reported **Type of epilepsy:** Not reported	**No. of patients who underwent surgery:** 17 **Type of surgery:** **ATL:** Not reported **AH:** Not reported **Non-TL:** Not reported **Other:** Not reported **Duration of follow-up following surgery:** Not reported **Outcome following surgery:** Not reported	Postoperative seizure frequency score	1. SISCOM results (no further details) 2. MRI results (no further details)

continued

Study details	Patient spectrum	Surgery details	Dependent variable	Variables investigated
Paolicchi, 2000[120] **Study design** Retrospective cohort **Country of study** USA **Study objective** To determine the correlation between pre- and perioperative variables on the outcome of children undergoing focal resections for medically intractable partial epilepsy	**Population:** Children **Patient spectrum:** Children aged <12 years with long-standing medically intractable epilepsy. Children who had incomplete follow-up or who died during the follow-up period were excluded. Resections were planned and carried out on the basis of neuroimaging and intracranially recorded electrophysiological data **Inclusion criteria relating to outcome:** All children underwent focal resection for epilepsy and had follow-up of at least 1 year **Mean age (range):** 7.7 (0.5–11.9) years **No. of patients (male):** 75 (40) **Duration of epilepsy:** Mean age at onset: 2.9 years **Type of epilepsy:** **Temporal:** 29 **Mesial sclerosis:** 6 **Non-temporal:** 37 **Other lesions:** 19 **Details:** 9 patients had both temporal and extra-temporal epilepsy Dysembryoplastic neuroepithelial tumours (n = 10), ganglioglioma (n = 3), astrocytoma (n = 3), ependymoma (n = 1), oligoglioma (n = 1), sarcoma (n = 1)	**No. of patients who underwent surgery:** 75 **Type of surgery:** **ATL:** 29 +9 **Non-TL:** 37 +9 **Details:** 9 patients had both temporal and extra-temporal resections. Temporal resections were non-standard and included the anterior neocortical and mesial limbic structures, tailored posteriorly according to EEG, lesional data and location of language cortex. Extra-temporal resection consisted of complete removal of the lesion combined with cortectomy tailored to the epileptogenic region **Duration of follow-up following surgery:** Mean 5 (range 1–10) years **Outcome following surgery:** **Class I:** Seizure free: 44 **Class II:** >90% reduction in seizures: 14 **Class III:** >50% reduction in seizures: 6 **Class IV:** Unchanged: 11	Good outcome (Engel I and II) and seizure free	1. Age at epilepsy onset 2. Duration of epilepsy before surgery 3. Presence of cognitive impairment 4. Temporal vs extra-temporal resection 5. Lesional vs non-lesional resection on MRI 6. Developmental vs acquired pathology 7. Complete vs incomplete resection

continued

Study details	Patient spectrum	Surgery details	Dependent variable	Variables investigated
Radhakrishnan, 1998[121] **Study design** Unclear: cohort **Country of study** USA **Study objective** To identify any postsurgical factors that are independently predictive of the outcome of anterior-temporal lobectomy for intractable epilepsy	**Population:** Children and adults **Patient spectrum:** Consecutive patients with medically intractable complex partial epilepsy. Seizure focus localised by clinical, neuroimaging and electrophysiological findings, depth EEG used when other tests failed to localise. ATL offered if localised to one temporal lobe **Inclusion criteria relating to outcome:** All patients underwent surgery and >2 years of postoperative follow-up. Patients with extra-temporal surgery were not included **Mean age (range):** Median 31 (7–86) years **No. of patients (male):** 175 (77) **Duration of epilepsy:** Median 19 (range <1–81) years **Type of epilepsy:** **Temporal:** 175	**No. of patients who underwent surgery:** 175 **Type of surgery:** **ATL:** 175 **Duration of follow-up following surgery:** Mean 3.6 (range 2–5.7) years **Outcome following surgery:** **Excellent:** seizure free or non-disabling seizures: 134 **Non-excellent:** 41	Excellent outcome (seizure free or non-disabling seizures)	1. Age at unprovoked seizure onset 2. Symptomatic epilepsy aetiology 3. Duration of epilepsy history 4. History of febrile seizures 5. Unilateral hippocampal formation atrophy on MRI 6. Other lesions on neuro-imaging 7. Concordant interictal epileptiform discharge (scalp EEG) 8. Age at surgery 9. Postsurgery: no epileptiform discharge on corticogram 10. Postsurgery: no epileptiform discharge at 1 week 11. Postsurgery: no epileptiform discharge at 3 months 12. Postsurgery: seizure free during 1st year 13. Postsurgery: only non-disabling seizures during 1st year 14. Postsurgery: length of follow-up

continued

Study details	Patient spectrum	Surgery details	Dependent variable	Variables investigated
Son, 1999[122] **Study design** Retrospective diagnostic cohort **Country of study** Korea **Study objective** To study the relationships between surgical outcome and localisation results of various diagnostic tests, in order to assess the predictive value of each diagnostic test	**Population:** Children and adults **Patient spectrum:** Consecutive patients with medial TLE. Patients in whom there were extra-hippocampal foci were excluded **Inclusion criteria relating to outcome:** Patients who underwent standard anterior temporal lobectomy along with amygdalohippocampectomy **Mean age (range):** 28.9 (11.51) years **No. of patients (male):** 71 (45) **Duration of epilepsy:** Not reported **Type of epilepsy:** **Temporal:** 71 **Mesial sclerosis:** 61 **Other lesions:** 10	**No. of patients who underwent surgery:** 71 **Type of surgery:** **ATL:** 71 **Duration of follow-up following surgery:** >24 months **Outcome following surgery:** **Class I:** Seizure free, auras only, or atypical general seizures with AED withdrawal: 66 **Class II:** Rare seizures: 2 **Class III:** >90% improvement in seizure frequency: 3 **Class IV:** No worthwhile improvement: 0	Engel I following surgery	1. Interictal EEG (localisation results, details unclear) 2. Video-EEG (localisation results, details unclear) 3. MRI (localisation results, details unclear) 4. PET (localisation results, details unclear) 5. Ictal SPECT (localisation results, details unclear) 6. Interictal SPECT (localisation results, details unclear) 7. Neuropsychological test (localisation results, details unclear) 8. Wada test (localisation results, details unclear)

Appendix 6
Protocol changes

We made the following changes to the methods set out in the protocol.

Inclusion criteria

We stated that studies had to report sufficient data to allow the extraction of 2 × 2 table data of test performance. Having looked more closely at the studies, it was apparent that the types of diagnostic accuracy study that were available for this topic area were not standard diagnostic accuracy studies and did not allow the extraction of 2 × 2 table data. We therefore changed the inclusion criteria to state that: "Level 3 (diagnostic accuracy) studies had to report sufficient information to extract data on the number of patients with correctly localised, not localised, partially localised and incorrectly localised scans."

We added a criterion that studies had to include at least 20 patients. For the types of study included in the review it was difficult to determine when to classify a study as a 'case series' and when to classify it as a 'diagnostic accuracy study'. We chose a cut-off point of 20 patients to make this distinction.

Data extraction

We stated that we would extract 2 × 2 table data from the studies. However, as discussed above, this type of data was not available for the included studies. Instead, we extracted the number of patients in each localisation category [see the section 'Data extraction' (p. 11) for further details].

Economic evaluations

A detailed economic evaluation was not carried out. Further details of the reasons for this are reported in the main text.

Analysis

We stated that for each test, or combination of tests, the range in sensitivity, specificity and likelihood ratios (of both positive and negative tests results) would be calculated and discussed, together with possible ranges in positive and negative predictive values which will be calculated based on a number of different estimates of disease prevalence. We also stated that diagnostic odds ratios would be calculated. We proposed to use standard methods for pooling diagnostic accuracy studies and to investigate heterogeneity. We also proposed to use regression analysis to investigate possible sources of heterogeneity.

Owing to the types of studies identified, which were not standard diagnostic accuracy studies, it was not possible to use standard methods to analyse the results from these studies. We therefore developed alternative methods, and further details of these are reported in the section 'Quality assessment' (p. 14).

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We look forward to hearing from you.

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