Health Technology Assessment 1999; Vol. 3: No. 16

Rapid review

Positron emission tomography: establishing priorities for health technology assessment

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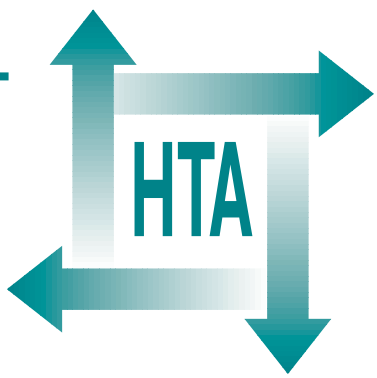
Health Technology Assessment
NHS R&D HTA Programme



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Positron emission tomography: establishing priorities for health technology assessment

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Competing interests:
none declared

Published July 1999

This report should be referenced as follows:

Robert G, Milne R. Positron emission tomography: establishing priorities for health technology assessment. *Health Technol Assess* 1999;**3**(16).

Health Technology Assessment is indexed in *Index Medicus*/MEDLINE and *Excerpta Medica*/EMBASE. Copies of the Executive Summaries are available from the NCCHTA web site (see overleaf).

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The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

This report is one of a series covering acute care, diagnostics and imaging, methodology, pharmaceuticals, population screening, and primary and community care. It was identified as a priority by the Diagnostics and Imaging Panel and funded as project number 97/03/01.

The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In particular, policy options in the area of screening will be considered by the National Screening Committee. This Committee, chaired by the Chief Medical Officer, will take into account the views expressed here, further available evidence and other relevant considerations.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The editors have tried to ensure the accuracy of this report but cannot accept responsibility for any errors or omissions. They would like to thank the referees for their constructive comments on the draft document.

ISSN 1366-5278

Published by Core Research, Alton, on behalf of the NCCHTA.
Printed on acid-free paper in the UK by The Basingstoke Press, Basingstoke.

Copies of this report can be obtained from:

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List of abbreviations

CABG	coronary artery bypass grafting
CAD	coronary artery disease
CT	computed tomography
2-D/3-D	two-/three-dimensional/dimensions
ECRI	Emergency Care Research Institute (HTA agency in the USA)
^{18}FDG	2-[^{18}F]fluoro-2-deoxy-D-glucose
HCFA	Health Care Financing Administration (USA)
HTA	health technology assessment
MIBI	technetium-99m-labelled sestamibi*
MRC	Medical Research Council (UK)
MRI	magnetic resonance imaging*
MSA	multiple system atrophy*
$^{13}NH_3$	^{13}N-ammonia
NSCLC	non-small cell lung cancer*
PD	Parkinson's disease*
PET	positron emission tomography
PTCA	percutaneous transluminal coronary angioplasty
SPECT	single photon emission computed tomography
SPN	solitary pulmonary nodule
VHA	Veterans Health Administration (USA)

* Used only in tables

Executive summary

Background

Positron emission tomography (PET) is an expensive diagnostic imaging technology. Despite the long history of PET development, the costs and effectiveness of its use in routine clinical practice remain unknown.

Against this background of uncertainty regarding the clinical role of PET, the UK Standing Group on Health Technology requested a review of its current and potential role which would enable research priorities in this area to be established.

Objectives

This 3-month project had two explicit objectives:

- to review the state of knowledge regarding the clinical applications of PET
- to determine the key health technology assessment (HTA) research questions relating to the use of PET in the UK.

Methods

A literature review to ascertain the state of knowledge regarding the clinical applications of PET and a three-round Delphi study to inform the key HTA research questions relating to the use of PET in the UK were undertaken.

The results of an earlier systematic review, published by the Veteran's Health Administration (VHA) in the USA in 1996, were used as the starting point for the literature review. The VHA review was updated and extended by means of MEDLINE and Cochrane Library database searches.

Participants in the Delphi study were selected by discussion with five individuals in the UK with an interest in, and awareness of, developments in PET. As a result of their suggestions, 43 individuals were initially invited to participate, of whom two did not feel appropriately qualified. Questionnaires were sent by facsimile to all invited participants, who were asked to return the completed forms by facsimile within a week. The content and structure of the Delphi study was informed by the results of the literature review. The responses and comments of the participants were a major source of information for this report.

Results

Clinical applications for PET have been advocated in three broad disease groups: oncology, cardiology and neuropsychiatric disorders.

There are currently four PET modalities that need to be considered when assessing its potential clinical role in the UK: full ring PET scanners operating in two or three dimensions (available at five sites); partial ring rotating PET scanners (one currently operating in the UK); coincidence imaging with modified gamma camera technology; and high-energy collimator imaging of 511 keV photons with modified gamma camera technology.

There is a paucity of available evidence relating to the cost-effectiveness of the various PET modalities in all of the clinical indications for which the technology is currently being advocated. In addition, many existing reports on the diagnostic accuracy of PET are limited because they are liable to bias and often relate only to very small patient numbers.

The results of the Delphi study indicated that the four most important research priorities for the NHS, in descending order of their importance, are:

- the relative cost-effectiveness of:
  – full ring PET
  – gamma camera PET using coincidence imaging
  – existing diagnostic strategies
  to determine staging prior to operative intervention for lung cancer
- partial ring PET compared with full ring PET in oncology
- the relative cost-effectiveness of:
  – full ring PET
  – gamma camera PET using coincidence imaging
  – existing diagnostic strategies
  to stage and monitor treatment response in breast cancer

- the relative cost-effectiveness of:
  – gamma camera PET using coincidence imaging
  – 511 keV collimated positron imaging

  for assessing myocardial viability when selecting patients for revascularisation surgery.

Vignettes describing each of the research priorities are provided in the main report.

Conclusions

The findings of this project, which was undertaken rapidly in order to inform HTA research prioritisation in the UK, provide a contemporary overview of the potential clinical role for PET in the NHS. Evidence is needed that using PET as a diagnostic technique will alter patient management. This underlies the cost-effectiveness research priorities established by this project.

Chapter 1
Background

The technology

Positron emission tomography (PET) is a method of nuclear medicine imaging that uses short-lived radiopharmaceuticals to detect and quantify the metabolic abnormalities of disease processes. Thus, whereas radiology provides data mostly on structure, nuclear medicine provides complementary information about function and metabolism.[1]

PET requires the administration of a positron-emitting radiopharmaceutical to the patient and a tomograph for imaging the patient; imaging times can vary from 30 minutes to over 1 hour.[a] The positrons travel a few millimetres in tissue before combining with negatively charged electrons and releasing two high energy (511 keV) photons, which are emitted at approximately 180 degrees to each other. The simultaneous detection of these photons by opposing detectors is then used to construct a three-dimensional (3-D) image of these events. By using the appropriate radionuclide, various aspects of tumour metabolism can be imaged.[2] For example, cancer cells have increased glucose utilisation and the radionuclide-labelled analogue of glucose, 2-[^{18}F]fluoro-2-deoxy-D-glucose (^{18}FDG), can be used to investigate tumours by exploiting the increased ^{18}FDG metabolism of malignant cells compared with non-malignant cells.

The radionuclides are produced by a cyclotron and then rapidly converted to radiopharmaceuticals using automated chemistry systems; however, an on-site cyclotron has inherent high capital and running costs.[3b] Thus, most PET imaging uses ^{18}FDG, which has a half-life of 109.8 minutes and therefore allows the operation of peripheral imaging sites at up to 2–4 hours distance in terms of travelling from the production unit. In the UK, the current supply of ^{18}FDG is limited by:

- geography (south-east England, northern Scotland)
- lack of spare capacity
- commercial supply being a secondary objective of current producers.

PET was introduced in the early 1970s after the emergence of computed tomography (CT) as a revolutionary diagnostic imaging tool. However, PET remained a research tool at academic medical centres where its development, both by the research centres and small commercial companies, continued slowly. Some of the research studies led to the recognition of the clinical applicability of PET for certain indications.

Many advances have occurred in PET technology since the initial development of the cyclotron and tomograph. Studies using PET have provided much insight into normal physiology and metabolism, and this information has been used to develop the clinical indications for PET.[4–6]

Recently, the clinical potential of PET has emerged. The major manufacturers of imaging equipment have become interested and have purchased some of the smaller companies who were developing the technology. These manufacturers have refined the technology for clinical applications and are improving PET's capabilities for research purposes. In May 1995, there were 60 PET facilities in North America, 45 in Europe, 20 in Japan and nine in other countries, including three in Australia. The International Network of Agencies for Health Technology Assessment has recently surveyed its member countries to ascertain for which indications PET is currently being reimbursed and to determine how many PET centres there are worldwide.

The Veterans Health Administration (VHA) in the USA commissioned a comprehensive systematic review of the usefulness of PET as a diagnostic test for a number of pre-defined conditions. This report was published in

[a] This has important practical implications for any comparative research between two or more PET modalities as the patient is likely to need more than one injection of a radiopharmaceutical in order for he or she to be imaged on the different modalities.

[b] Other alternatives to an on-site cyclotron exist. An ^{82}Rb generator is available for studying blood flow, particularly in cardiac studies.

October 1996[7] (see chapter 4 for the findings of this review and other contemporary reports).

In the USA in November 1997, Medicare coverage for PET imaging of lung tumours (to characterise solitary pulmonary nodules (SPN)[c] and to stage lung cancer[d]) was approved; other uses for PET were to be reviewed on a fast-track basis (within the following 18 months). This policy went into effect on 1 January 1998 and applies to lung studies obtained from full-ring PET scanners and gamma cameras modified with PET capability using coincidence imaging.[e] Although the Health Care Financing Administration (HCFA) has agreed that PET is accurate in the diagnosis of lung cancer, the effect of PET on patient care and Medicare costs is uncertain. HCFA is therefore to undertake a prospective study on the effect of PET imaging on subsequent diagnostic surgical procedures.[8] HCFA has also requested a technology assessment of PET for brain cancer and myocardial viability from the Agency for Health Care Policy and Research. A further technology assessment of PET for diagnosing and staging lung cancer, by the Emergency Care Research Institute (ECRI), was completed in mid-1998.[9] This meta-analysis concluded that the addition of PET to the diagnostic algorithm improves average life-expectancy and reduces costs, but only if the use of PET is limited to those patients with proven lung cancer and no evidence of metastasis to unresectable lymph nodes.[f] The use of PET in the diagnosis of SPN as malignant or benign decreased life-expectancy and increased costs in comparison to the reference strategy.

In the UK, the PET centre in Aberdeen began to provide clinical images in 1987, and in May 1992 the Guy's & St Thomas's PET centre in central London was established (with £4,600,000 capital funding) as a diagnostic centre utilising positron-labelled tracers; this centre currently performs more than 1000 clinical investigations per year. Mount Vernon Hospital in north-west London has also recently begun to offer a clinical PET service and is aiming to perform PET studies on 200 patients in its first year of operation.

There are currently four modalities of PET that need to be considered when assessing the potential role of the technology in the UK: full ring PET; partial ring PET; gamma camera PET (coincidence imaging); gamma camera PET (511 keV collimation). Details are presented in *Box 1*.

The two final modalities presented in *Box 1* have recently arisen because conventional gamma cameras are being adapted with thicker lead collimators or coincidence detection electronics to image the higher energy gamma rays of positron emitters.[3] All large hospitals have conventional gamma cameras but until recently it had not been possible to image positron-emitting radionuclides on such conventional scanners. Several manufacturers of gamma cameras are modifying their devices to image ^{18}FDG, thus making such imaging more available. With recent data demonstrating the potential clinical applications of ^{18}FDG, there has been a renewed interest in imaging ^{18}FDG with gamma cameras.

The first clinical investigations with gamma camera PET using coincidence imaging in the UK were undertaken in April 1997 at the Queen

[c] HCFA will pay for a PET study to characterise an SPN when the results from the CT study indicate an indeterminate or possibly malignant lesions (not > 4 cm in diameter). PET studies to screen asymptomatic patients are not covered.

[d] For cases of confirmed lung cancer, HCFA will pay for PET to stage the cancer to determine whether the patient is a candidate for surgery to remove a lesion. PET studies to monitor the disease are not covered.

[e] The electronics of gamma cameras has changed since the mid-1970s and more sophisticated computers are now available. These changes now make coincidence detection practical and most manufacturers have developed coincidence detection systems. At a meeting with HCFA in December 1997, ADAC Corporation, the largest installer of gamma cameras in the USA, presented data from an unpublished multicentre study to evaluate the effectiveness of coincidence imaging to diagnose and stage lung cancer. Data were presented for 129 patients. The trial results were consistent with preliminary results from 35 patients presented at the European Association of Nuclear Medicine Congress in August 1997. At the European meeting, researchers reported that coincidence imaging had a 96% sensitivity rate and an 80% specificity rate as confirmed by biopsy or surgery. ADAC told HCFA that these results for lung studies correlate with those obtained from full ring PET scanners. As of August 1997, there were approximately 60 camera-based PET systems installed in the USA and the number of installed systems is increasing rapidly.

[f] This analysis differed from previously published studies in that it considered all treatment costs, including non-surgical treatments and treatment of patients with recurrent cancer. It also accounted for unnecessary surgery caused by false-positive diagnosis of an SPN as malignant.

BOX 1 Modalities of PET to be considered

• Full ring PET
A full ring bismuth-germinate PET scanner operating in 2-D or 3-D is available at five sites in the UK (in London, Cambridge and Aberdeen). The capital costs associated with installation mean that each site can cost between £1 million and £4 million to establish, mainly dependent on whether a cyclotron is to be installed.

• Partial ring PET
Only one partial ring rotating PET scanner operating in 3-D* is currently operating in the UK (at the Medical Research Council (MRC) Cyclotron Unit, Hammersmith Hospital, London). Partial ring PET offers nearly the same performance of full ring PET, with capital costs of approximately £700,000. As with full ring PET, costs may be as high as £4 million if a cyclotron is also included.

• Gamma camera PET (coincidence imaging)
Coincidence imaging with modified gamma camera technology operates in 3-D and costs approximately £320,000–350,000 for camera, coincidence and attenuation, However, many imaging departments will already have a dual-headed gamma camera and will therefore only require it to be modified so that it can perform ^{18}FDG-PET; this can be achieved at a cost of only £30,000–40,000 for the coincidence software.

• Gamma camera PET (511 keV collimation)
High-energy collimator imaging of 511 keV photons with modified gamma camera technology.

** 3-D operation results in an eight-fold increase in sensitivity; this prompted the design of the partial ring scanner, in which 50% of the detectors (the major cost component) have been removed giving, for the brain, a similar performance to full ring 2-D PET.*

Elizabeth Hospital, Birmingham. In the first 10 months of operation, 44 investigations have been performed (30 in oncology and 14 in neurology). Addenbrooke's Hospital NHS Trust in Cambridge is undertaking a prospective assessment in 40–50 lung cancer and lymphoma patients of the quality of information obtained from gamma camera PET; the assessment is being funded by the Anglia and Oxford regional research and development programme. It is intended that a cost-effectiveness analysis on the basis of this work will be performed at a later date.

Imaging with modified gamma cameras is thought to be inferior to full ring PET but superior to single photon emission computed tomography (SPECT). Preliminary studies of oncology patients demonstrate that large ^{18}FDG-avid lesions can be identified (particularly in the lungs) but that small lesions (diameter < 1.5 cm) which can be detected by full-ring PET scanners, are obscured by image noise.[10] It has been suggested that several improvements in gamma camera PET need to be made prior to its routine clinical use.[11] There is some concern at the development of a sub-optimal technology and pressure for pre-mature evaluation before such systems are optimised for clinical oncology applications; this may ultimately prove to be detrimental to the clinical application of PET technology *per se*.[12] Many large imaging departments are now considering purchasing modified dual-headed gamma cameras and diffusion could be rapid; this will have a major impact on the NHS. The cameras would become widely available and would be technically simpler than PET; with further improvements in design they are likely to play a significant part in clinical nuclear medicine.[3]

Disease areas

The clinical application of PET has been advocated in three broad disease areas: oncology, cardiology and neuropsychiatric disorders.

Oncology

In the UK there are currently three PET modalities of clinical relevance for imaging cancers in oncology, principally with ^{18}FDG. These are:

(i) full ring PET scanner operating in 2-D or 3-D
(ii) partial ring rotating PET scanner operating in 3-D
(iii) coincidence imaging with modified gamma camera technology, operating in 3-D.

Each of these three modalities has a different set of performance characteristics and level of quantitative accuracy for imaging the torso where most tumours arise: full ring PET is superior in terms of performance and has been used for evaluating the role of PET in oncology principally operating in the 2-D mode.

The use of PET in oncology has increased dramatically since the development of whole body scanners and more than 70% of referrals at the majority of clinical PET centres internationally now come from oncology departments. Five years ago the only accepted application of PET was the differentiation of brain tumour recurrence from post-treatment scar and although many nuclear

medicine physicians feel there is a significant future for PET in oncology, oncologists and radiologists have expressed reservations.[13 g]

There are a number of areas in which PET potentially has a major clinical use:

- differentiating between benign and malignant tumours
- defining the extent of disease
- monitoring treatment response
- identifying recurrence
- identifying the site of primary disease.

More specifically, the applications of PET in oncology currently being undertaken or proposed are presented in *Box 2*.

BOX 2 Applications of PET in oncology

- Staging of lung cancer for surgery
- Primary staging for lymphoma
- Primary staging of sarcomas
- Primary staging of oesophageal and rectal cancer
- Distinguishing between malignant and benign pulmonary nodules
- Distinguishing between malignant and benign pancreatic masses
- Assessing doubtful bone lesions
- Determining local spread of head and neck cancer*
- Determining local extension of pelvic tumours
- Brachial plexus lesions in breast cancer
- Identifying tumour recurrence (for example, in colorectal cancer)
- Assessing response of tumours to chemotherapy and radiotherapy
- Defining residual masses following treatment (recurrence or radiation-induced necrosis, for example, in brain tumours)

** Its role is in suspected residual/recurrent disease at the primary site or in an unknown primary, for example, small nasopharyngeal cancer.*

PET imaging offers the following potential for realising cost-savings and benefits compared with existing diagnostic strategies.

a. The provision of the same diagnostic information at less cost for staging and in the assessment of relapse.
b. The provision of more accurate information to improve the staging process, in particular to decrease the number and extent of surgical procedures where it can be shown that disease is more widespread than expected. For example, Lewis and colleagues, Guy's & St Thomas's Hospitals NHS Trust, have reported on a retrospective analysis of 34 patients with 'operable' non-small cell lung cancer who underwent full ring PET after routine assessment. Management changes occurred in 14 patients (41%), including six (18%) who were changed to non-surgical therapy.[14]
c. The provision of an early prediction of disease response to chemotherapy, which will improve outcome and decrease the cost of unnecessary chemotherapy.

Cardiology

The potential applications of PET in cardiology are presented in *Box 3*.

In the first of these, PET is used to select patients with CAD who have cardiac dysfunction for revascularisation procedures by demonstrating the presence of hibernating but viable myocardium. Potential savings arise from the elimination of unnecessary angiography, angioplasty and bypass grafting in patients for whom these procedures are inappropriate.[15]

BOX 3 Applications of PET in cardiology

- Diagnosis of hibernating but viable myocardium
- Diagnosis of coronary artery disease (CAD) where other investigations are equivocal

[g] The conclusions of a SWOT analysis of the value of PET in oncology, presented by Price,[13] were as follows. **Strengths**: inherent sensitivity and specificity; potentially one of the most important tools for translation between basic biological science and patients. **Weaknesses**: difficult subject requiring a multidisciplinary approach; difficult to marry basic cancer science and therapeutic strategies with PET technology; low involvement of oncologists; do not need more diagnosis – need more effective treatment; the anatomical/functional implications of tumours are often important and so will need to be investigated further using X-ray, CT or MRI. PET is therefore an additional, not an alternative, imaging technique. **Opportunities**: clearly has a future to develop even more specific pharmacodynamic endpoints to parallel therapy assessment; PET for *in vivo* pharmacokinetic measurements has huge potential in both human tissues and tumours; PET may be one of the best methods to assess some *in vivo* gene therapy approaches to cancer. **Threats**: promises too much too soon; there are some problems in ^{18}FDG assessment of tumours.

Although the role of PET is likely to increase in oncology and neurology, there is widespread disagreement about its future in cardiology because of improvements in routine radionuclide perfusion testing and the lack of evidence that the small resolution gain with PET is of importance in assessing and managing CAD.[16] In an assessment, ECRI found that, although PET images are of higher quality (better contrast and spatial resolution) than those of SPECT, in the clinical situation, performance of PET seems to be comparable to, or only slightly better than, SPECT for detecting CAD. The American Heart Association reviewed the available data and reported that it did not find PET superior to SPECT in diagnostic accuracy.[17]

Since 1985, HCFA has financed PET studies to image perfusion of the heart. This policy restricts PET coverage to scans using the imaging agent rubidium-82, which is only used in cardiac studies. The assessment of CAD[16] and myocardial viability with PET blood flow and metabolic tracers is relatively tried and tested (including with gamma camera 511 keV collimator imaging)[18] but the use of newer radiopharmaceuticals incorporating positron-emitting radionuclides is still largely at the research stage.[3]

Neuropsychiatric disorders

Before the rapid increase in the use of PET in oncology, most clinical and research applications focused on neurological and psychiatric disease. PET can reveal lesions that are not detectable in anatomical scans, provide insight into biochemical and physiological properties (for example, metabolism, chemistry or pH) of a lesion and determine the functional integrity of the regions surrounding brain lesions.[19]

The potential clinical applications of PET in neuropsychiatric disorders include those presented in *Box 4*.

However, in order to justify the use of PET as part of routine clinical practice in these conditions, effective therapies need to be available once the neuropsychiatric disorder has been diagnosed; for many of the conditions listed in *Box 3* this is not yet the case.

BOX 4 Applications of PET in neuropsychiatric disorders

- Presurgical evaluation of epilepsy*
- Location of the optimal site of biopsy for brain tumours
- Grading primary brain tumours
- Monitoring brain tumour recurrence
- Diagnosis of dementia
- HIV (distinguishing malignancy)
- Selection of patients with stroke for appropriate interventional surgery**

** Perhaps one of most widely accepted uses of PET in neurosurgical situations is for non-invasive localisation of epileptogenic foci in patients with partial epilepsy. This application eliminates the need for many neurosurgical diagnostic EEG procedures.*

*** Baron[20] presents a personal review of the clinical applications of PET in cerebrovascular disorders, specifically: (i) assessment of the haemodynamic and metabolic effects of carotid artery disease in the perspective of surgical versus medical management; (ii) changes in brain perfusion and metabolism in acute ischaemic stroke as they relate to the issue of patient management, outcome predictability and screening in therapeutic trials; and (iii) mapping of remote metabolic effects of stroke and their clinical relevance.*

Chapter 2

Aims and objectives

In 1994 the Health Technology Assessment (HTA) programme identified *Evaluation of PET scanning* as a research priority (94/19). Subsequently, the MRC took this priority forward but no research which answered the initial HTA research priority was commissioned.

At the second meeting of the HTA Diagnostics and Imaging Panel, in the summer of 1997, the panel decided that a short (approximately 3-month) study should be commissioned urgently. This would:

(a) provide some guidance to the NHS
(b) inform a clear research agenda that could be considered by the HTA programme in 1998.

Although the intention was to pursue this by limited tender, this did not prove possible.

The Wessex Institute for Health Research and Development was then commissioned to undertake a 3-month review which ran from January to March 1998 (HTA priority 97/03).

The aim of the project was to provide information that would enable the HTA Diagnostics and Imaging Panel to agree recommendations on the most urgent research questions relating to the role of PET in the NHS. It was intended that the recommendations would be considered during the 1998 annual research prioritisation exercise.

The project had two objectives:

(i) to review the state of knowledge regarding clinical applications of PET
(ii) to determine the key HTA research questions relating to the use of PET in the UK.

Chapter 3
Methods

Review of the state of knowledge regarding PET

The methods for reviewing the state of knowledge regarding PET were as follows.

- MEDLINE and the Cochrane Library were searched for appropriate studies in order to update the VHA review, *FDG-PET as a diagnostic test for cancer and Alzheimer's disease.*[7]
- The VHA review was extended to include other indications in cardiology (myocardial perfusion, tissue viability) and neuropsychiatric disorders (dementia, stroke, epilepsy, Parkinson's disease).

Search 1

To specifically update the VHA systematic review, the Ovid MEDLINE database was searched as follows:

1 tomography, emission-computed/
2 limit 1 to year = 1996–98
3 coin lesion, pulmonary/
4 Alzheimer disease/
5 breast neoplasms/
6 lung neoplasms/
7 colorectal neoplasms/
8 head and neck neoplasms/
9 (2 & 3) or (2 & 4) or (2 & 5) or (2 & 6) or (2 & 7) or (2 & 8)

Inclusion and exclusion criteria were the same as those for the VHA review:[7]

- English language articles reporting primary data and published in a peer-reviewed journal
- studies with > 12 human subjects (not animal studies) with the disease of interest
- studies using the radiopharmaceutical ^{18}FDG.

For brief descriptions of the additional articles retrieved by Search 1, see appendix 1.

Search 2

In order to include other important indications for which PET has been proposed for routine clinical use but which were not included in the VHA review, the following search was carried out on the same database as for Search 1 with the same inclusion criteria, except that studies using all radiopharmaceuticals were included.

1 tomography, emission-computed/
2 limit 1 to year = 1996–98
3 limit 2 to (human and English language)
4 myocardium/
5 myocardial infarction/
6 dementia/
7 cerebrovascular disorders/
8 epilepsy/
9 Parkinson disease/
10 (3 & 4) or (3 & 5) or (3 & 6) or (3 & 7) or (3 & 8) or (3 & 9)

The results of Search 2 are presented in appendix 1.

Owing to the time constraints of the project, the results of applying the inclusion criteria to the results of Searches 1 and 2 are based only on analysis of the available abstracts of the full articles.

Search 3

A more general search of the MEDLINE database was also performed (1996 to January 1998), in order to provide bibliometric data on PET and to locate as many articles as possible that considered the cost-effectiveness of PET.

1 'positron emission tomography' (freetext search)
2 explode 'clinical trials'/all subheadings
3 explode 'cost-benefit-analysis'/all subheadings
4 1 and 2
5 1 and 3

In addition, through the Cochrane search described below and by contact with members of other HTA agencies, summaries of a number of reviews of PET, which are currently only available as grey literature, have been included in this review.

Search 4

Finally, the Cochrane Library (1998 #2) was searched as follows:

'positron emission tomography' or 'PET' in
– the Cochrane Database of systematic reviews

– the Database of Abstracts of Reviews of Effectiveness
– the Cochrane Controlled Trials Register
– the Cochrane Review Methodology Database.

The titles of all references retrieved from this search were scanned and details of all those that were primarily concerned with evaluating the clinical role of PET in any disease condition are presented below in the results.

Delphi study: key HTA research questions relating to the use of PET in the UK

A three-round postal Delphi study of relevant UK individuals was used to determine the key HTA research questions relating to the use of PET in the UK. The Delphi method was developed by the RAND Corporation in the 1950s and was originally used in forecasting. The aim of the RAND Corporation was to synthesise expert opinion, mainly on the emergence of new technologies. A similar method of establishing research priorities has been adopted in other areas of health care.[21–25] Participants in Delphi surveys never meet or interact directly but are sent questionnaires and asked to record their views. Often they are asked initially to suggest the factors or cues that should be considered by the group. Having contributed to drawing up the agenda, the participants are then sent a questionnaire which seeks their individual views on the items that they and their co-participants have suggested. The responses are collated by the organisers and returned to the participants in summary form, usually indicating the group judgement and the individual's initial judgement. Participants are given the opportunity to revise their judgement in the light of the group feedback. The process may be repeated a number of times before the judgements of the participants are statistically aggregated, sometimes after weighting for expertise.[21] The content and structure of our Delphi study was informed by the results of the literature review. The participants in the Delphi study, the questionnaires used, and the results generated at each stage, are presented in appendix 2.

In addition, one of the authors (GR) attended *Positron emission tomography – cost and clinical benefits*, a conference organised by the Centre for Health Planning and Management, University of Keele and North Staffordshire Hospital Trust Keele University, which was held in February 1998.[a]

[a] Relevant presentations which helped to inform the authors' thinking included: *Overview of PET and its clinical benefits*, by Dr MS O'Doherty (Guy's & St Thomas's Hospitals NHS Trust); *PET and patient management*, by Dr R Beaney (Guy's & St Thomas's Hospitals NHS Trust); *Cost–benefit modelling of PET and economic implications of PET in use*, by Dr M James and Mr K Hunt (Keele University); *Recent technological developments*, by Dr P Julyan (University Hospital Birmingham NHS Trust).

Chapter 4
Results

Review of the state of knowledge regarding PET

The results of the literature search are presented in three sections:

- update and extension of VHA systematic review
- other literature (bibliometric data, cost-effectiveness analyses and other reviews)
- conclusions (state of current knowledge and focus of future research).

Update and extension of VHA review

In the USA, the VHA commissioned an assessment of PET. They concluded that the knowledge base (up to and including September 1996[a]) supporting clinical diagnostic applications of PET has significant deficiencies and that the literature did not support widespread incorporation of PET studies into routine diagnostic strategies for the applications that the assessment addressed. Their summary findings[7] were that:

- research into clinical utility of PET in selected conditions is in its preliminary stages
- available studies have focused on the feasibility of using PET in these conditions and on defining its accuracy as a diagnostic test
- a few studies have addressed changes in treatment decisions based on PET findings.
- they were unable to locate any studies documenting changes in outcomes of care or costs of care associated with incorporating PET into diagnostic strategies.

The authors of the VHA review included a grading scheme for to assessing the methodological quality of 'diagnostic accuracy' and 'diagnostic thinking efficacy studies' (*Table 1*).

Applying these criteria to the published literature for the selected applications enabled an assessment of the quality of the studies to be made (*Table 2*).

TABLE 1 *VHA grading scheme*

Grade	Criteria
A	Studies with broad generalisability to a variety of patients and no significant flaws in research methods.
B	Studies with a narrower spectrum of generalisability, and with only a few flaws that are well-described (and impact on conclusions can be assessed).
C	Studies with several methods flaws (e.g. small sample size).
D	Studies with multiple flaws in methods (e.g. no credible reference standard for diagnosis).

TABLE 2 *Summary of VHA assessment of quality of studies*

Condition	Number	A	B	C	D
Head and neck cancer	12	–	1	1	10
Colorectal cancer	11	–	3	6	2
Breast cancer	8	–	–	4	4
Lung cancer	16	–	–	7	9
SPN	4	–	–	3	1
Alzheimer's disease*	N/A	N/A	N/A	N/A	N/A

* *All of the studies that evaluated a diagnostic test against the standard of histopathology fully met evidence-based medicine and other methodological quality criteria (i.e. received methodology grades A or B).*

The results of undertaking Search 1 in order to update this review (as specified in chapter 3) are shown in *Table 3*.

A more detailed overview of the results of the literature search is provided in appendix 1.

[a] An update (covering the period January 1997–February 1998) on some of the conditions in the original VHA review has been reported.[27]

TABLE 3 *Updated number of studies meeting VHA inclusion criteria (to April 1998)*

Condition	Number of articles identified by search	Number of articles (1996–98) meeting inclusion criteria	Updated total number of papers
Head and neck cancer	21	9	21
Colorectal cancer	17	5	16
Breast cancer	55	8	16
Lung cancer	72	14	30
SPN	4	1	5
Alzheimer's disease	69	1	9

Other literature

Bibliometric data

Figure 1 is based on the results of Search 4 and indicates how publications related to PET have increased over the period 1976–97.[b]

The Cochrane Controlled Trials Register (Search 3) had 112 references to 'PET' or 'positron emission tomography'. Of these 112 papers, only three explicitly sought to evaluate the clinical role of PET in a specific condition as opposed to using it to evaluate another specific (often pharmaceutical) intervention (none were prospective randomised controlled trials).[27–29]

Cost-effectiveness analyses

The results of papers that presented estimates of cost savings or cost–benefit ratios for PET and which were identified by Search 3 are summarised in *Table 4*.

In addition, other papers have commented broadly on the potential cost-effectiveness of PET. In one paper the role of PET compared with thallium scinitigraphy in assessing tissue viability is discussed; its authors conclude that PET is capable of assessing myocardial viability and, furthermore, may differentiate between various forms of cardiomyopathy.[30] They also conclude that more studies are needed to define

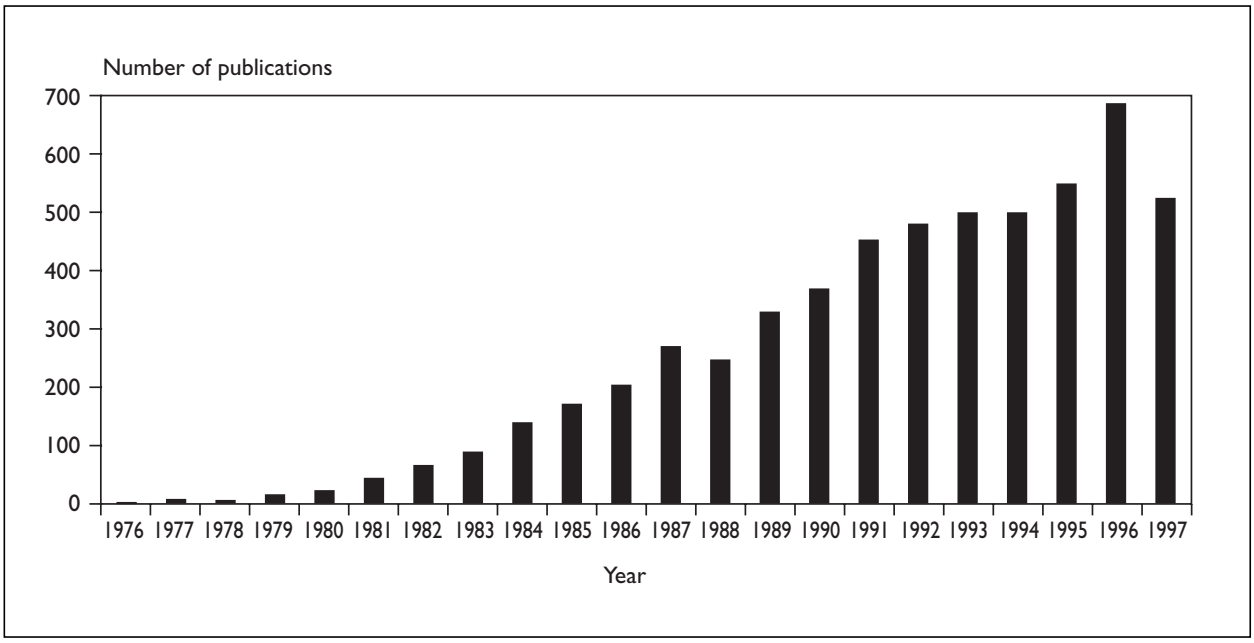

FIGURE 1 *Publication time trends for PET*

[b] At the time of the search not all 1997 publications had been indexed on MEDLINE. Thus 1996 should be taken as the last complete year for which the total numbers of publications are accurate.

TABLE 4 *Summary of studies addressing cost-effectiveness of PET*

Study, country	Design	Indications (number of patients)	Results
Madar, *et al.,* 1994 USA		Staging of non-small cell lung cancer (NSCLC) (*n* = 20).	Total cost: $25,000 for PET staging vs. $42,406 for non-PET conventional strategy.
Yao, *et al.,* 1994 USA		Staging of malignant melanoma (*n* = 59).	Cost per patient: c. $4409 for conventional imaging strategy vs. $1950 for PET strategy.
Gambhir, *et al.,* 1996 USA	Decision-tree sensitivity analysis	Staging and management of NSCLC.	CT + PET strategy showed a saving of $1154 per patient in the decision tree, without loss of life expectancy (increase of 2.96 days) compared with alternate strategy of CT alone. Effects were result of improved staging prior to surgical decision.
Valk, *et al.,* 1996 USA	Prospective evaluation; management impact assessed retrospectively	Diagnostic accuracy: staging of NSCLC (*n* = 99), detection of recurrent colorectal cancer (*n* = 57), diagnosis of metastatic melanoma (*n* = 36), staging of advanced head and neck cancer (*n* = 29). Management impact: SPN or NSCLC (*n* = 72), colorectal cancer (*n* = 68), metastatic melanoma (*n* = 45), head and neck tumours (*n* = 29).	Diagnostic accuracy: PET more accurate than anatomic imaging for determination of presence and extent of tumour and demonstration of nonresectable disease. Management impact: PET improved patient management by avoiding surgery for nonresectable tumour and for CT abnormalities that PET imaging proved to be benign. Savings from contraindicated surgical procedures exceeded costs of PET imaging by ratios of 2:1–4:1, depending on indication.
Adler, *et al.,* 1997 USA	Prospective case-series	Breast cancer (*n* = 50); ^{18}FDG PET of axilla performed before axillary lymph node dissections.	Approximately $120,000 in charges ($2300 per patient) would have been saved and 22 patients would have been spared the morbidity of axillary lymph node dissection.
Hoh, *et al.,* 1997 USA	Prospective case-series	Staging of Hogkin's disease and lymphoma (*n* = 18); whole-body PET-based staging results compared with conventional staging studies.	Accurate staging performed in 17 of 18 patients using whole-body PET-based staging algorithm compared with conventional staging algorithm in 15 of 18 patients. In five of 18 patients, whole-body PET-based staging showed additional lesions not detected by conventional staging modalities, whereas conventional staging demonstrated additional lesions in four of 18 patients not detected by whole-body PET. Total cost of conventional staging $66,292 vs. $36,250 for whole-body PET studies.
Holmberg, *et al.,* 1997 USA	Retrospective, open-label, case–control; matched patients underwent adenosine PET	CAD: 36 patients underwent dipyridoamole PET; 72 matched patients underwent adenosine PET.	Total cost of adenosine PET and dipyridamole PET was divided by their respective predictive accuracy to provide total cost adjusted for efficacy. Total cost of using dipyridamole $928 per patient, and adenosine $672 per patient. Authors suggest that adenosine may be drug of choice for pharmacological vasodilation for PET.
Mitchell, 1998 USA	Meta-analysis	Diagnosis of SPN as malignant or benign and/or staging of known primary lung cancer.	Addition of PET to diagnostic algorithm improves average life expectancy and reduces costs but only if PET limited to those patients with proven lung cancer and no evidence of metastasis to unresectable lymph nodes. Use of PET in diagnosis of an SPN as malignant or benign decreased life expectancy and increased costs compared with reference strategy. Results were subjected to thorough sensitivity analysis. Over ranges studied, changes in 14 different input variables, including all cost and prevalence variables, did not affect findings that PET is cost-effective when used to confirm that a patient's cancer is resectable, and is not cost-effective when used earlier in diagnostic algorithm.

the cost–benefit ratio of both diagnostic methods for the management of patient with CAD or cardiomyopathy. Two further papers are also reviews of the potential cost-effectiveness of PET in the treatment of ischaemic cardiomyopathy: one author suggests that a PET-driven algorithm would result in a projected cost savings for the entire patient group of cardiac transplant candidates referred to the UCLA Heart Failure Program from 1987–94 of approximately $3.9 million;[16] in the other paper several available modalities for detecting CAD are compared and the authors suggest that, while the choice of tests critically depends on patient selection, PET myocardial perfusion imaging appears to be the best non-invasive test for CAD, followed by SPECT thallium-201 and then dobutamine echocardiography.[31] In a further study to identify image parameters that would improve the specificity of PET in diagnosing chest masses and SPNs in 26 patients with benign and malignant lung lesions, the authors conclude that the recommended method could have a significant cost-effective impact on the medical/surgical management of chest masses.[32]

Reviews

The Cochrane Library (Search 4) had six entries on the database of systematic reviews and four 'other sources of information' entries relating to PET. The complete reviews were on: blood pressure and acute stroke, dietary regulation for gestational diabetes, gangliosides in acute stroke, pentoxifylline in acute stroke, prostacyclin in acute stroke, tacrine in Alzheimer's disease.

Two of the 'other sources of information' identified by the search of the Cochrane Library were reviews by HTA agencies; one by the Australian Institute of Health and Welfare (1990)[33] and one, in the USA which is reported to be 'ongoing', by the Agency for Health Care Policy and Research. The Australian review was based on a MEDLINE search and focused primarily on cardiac and neurological applications of PET. The authors concluded that a sufficient case had not yet been established for the routine use of PET as a clinical service in Australia and recommended that, if proposed PET units are introduced into Australia, they should be subject to a coordinated evaluation of costs and benefits. The American review is using the published literature from professional societies and other federal agencies, together with existing clinical trials identified on MEDLINE, to assess the safety and effectiveness of PET as a diagnostic and management tool for use in patients with coronary vascular disease, brain tumours and focal or partial epilepsy.

In a further systematic review of the cost-effectiveness of nuclear medicine (of which the authors are aware), which was conducted for the British Nuclear Medicine Society in 1994, it was concluded that further primary studies were needed.

In a technology assessment of the more than 30 uses of PET scans on non-CNS cancers, the US health insurance companies, Blue Cross and Blue Shield, reported favourably in 1997 on two uses: detection and staging of lung cancer.[c]

A Spanish review of PET diagnostic efficacy in some oncological conditions (except brain tumours) was published in October 1997.[34] The authors reported on the poor methodological quality of the analysed articles and suggested that the few number of patient cases does not allow definitive conclusions to be drawn about the relative contribution of PET in the management of cancer patients.

Conclusions

State of current knowledge

There is no good evidence in the literature to suggest how PET will affect the cost-effectiveness[d] of the diagnosis, prognosis and management of patients as the very few studies of cost-effectiveness have been largely retrospective. There has been no major prospective study of cost-effectiveness which incorporates more than a comparison of conventional compared to PET strategies. Many of the cost-effectiveness analysis studies to date have been performed by combining literature data with existing management algorithms and are, therefore, not as compelling as prospective trials.

Focus of future research

Sassi and colleagues[35] have recently reviewed the methodological challenges in the economic evaluation of diagnostic technologies, citing the capturing of the whole chain of outcomes arising from a diagnostic test as the most widely recognised problem. Fineberg[36] classified the diagnostic process into three consecutive stages (the production

[c] Cited in *J Nucl Med* 1998;**39**:25N.

[d] *Quarterly Journal of Nuclear Medicine* has an issue devoted to nuclear medicine health economics and cost-effectiveness analysis planned for publication in 1999.

of a diagnostic output, the inclusion of that output into a diagnostic strategy and choice of treatment, and the health outcome, conditional upon treatment). Kent and Larson[37] extended this to develop an evidence profile for diagnostic test assessment (*Figure 2*).

In relation to the evaluation of PET, it is clear from the published literature and from discussions with experts that although some small case-series have addressed the clinical impact of the technology (mainly in lung cancer and using full-ring PET), and a small number of studies have attempted to model the cost:benefit of PET in specific conditions, there have been no large-scale prospective studies in which the organisational impact or cost-effectiveness of PET is examined. There are numerous papers reporting on the diagnostic accuracy (sensitivity and specificity) of PET for most of the important conditions in which the technology has a potential role but this work needs to be developed to consider the utility of performing the test in routine clinical practice.

Prospective studies of cost-effectiveness are needed to assess the reproducibility of the preliminary retrospective evaluations and to determine the cost-effectiveness of PET for other indications. Two possible approaches to such studies are:

(i) prospective evaluation of management impact (which has the advantage of measuring real experience but the disadvantage of requiring large number of subjects[38])
(ii) formal decision analysis providing a synthetic means of calculating the probabilities of possible clinical outcomes and their associated desirability and cost, once the sensitivity and specificity of PET has been determined.

Delphi study: key HTA research questions relating to the use of PET in the UK

The four most important research priorities for the NHS, as informed by the Delphi study and listed in descending order of their importance, are:

(i) the relative cost-effectiveness of (a) full ring PET, (b) gamma camera PET using coincidence imaging, (c) existing diagnostic strategies to determine staging prior to operative intervention for lung cancer
(ii) partial ring PET compared with full ring PET in oncology
(iii) the relative cost-effectiveness of (a) full ring PET, (b) gamma camera PET using coincidence imaging, (c) existing diagnostic strategies to stage and monitor treatment response in breast cancer
(iv) the relative cost-effectiveness of (a) gamma camera PET using coincidence imaging, (b) 511 keV collimated positron imaging for assessing myocardial viability when selecting patients for revascularisation surgery.

Vignettes describing each of the research priorities follow below. They have been prepared in the standard format of the HTA programme. Because the Standing Group on Health Technology requires that they are available as stand-alone documents within this report, there is, of necessity, some repetition both between the vignettes and between the vignettes and other sections of this document.

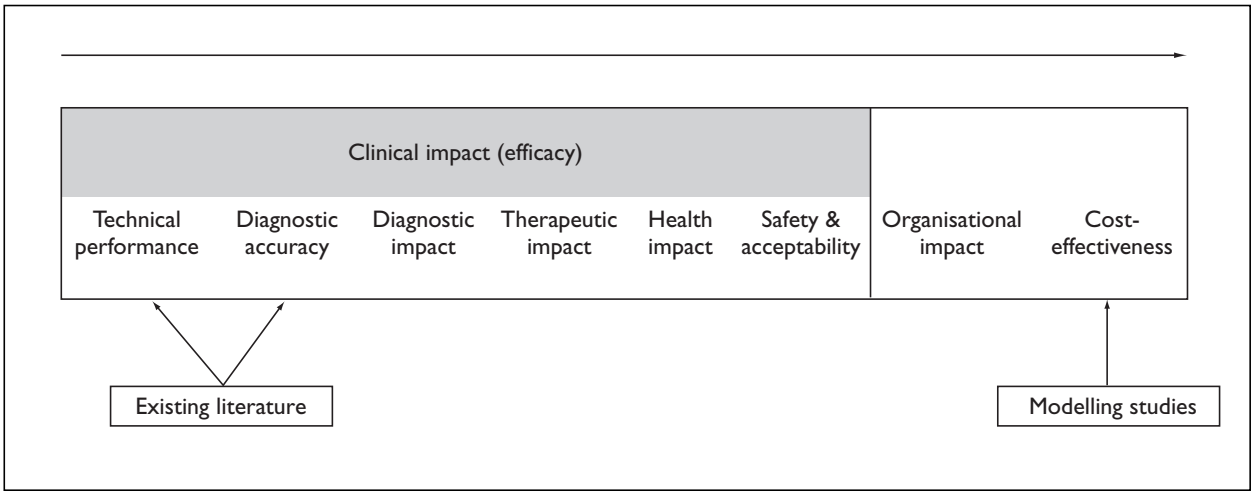

FIGURE 2 *Evidence profile for diagnostic test assessments*

The vignettes were considered by the Diagnostics and Imaging Panel of the HTA programme at its meeting in May 1998. The Panel decided that the most pressing HTA question related to the use of PET in the preoperative assessment of lung cancer. The final decision on HTA priorities is taken by the Standing Group on Health Technologies but, at its meeting in November 1998, it did not give this question a high enough priority for research commissioning to be taken forward. The question will thus be reconsidered for the HTA programme during 1999.

Vignette 1: PET in the preoperative assessment of lung cancer

Research question

To assess the relative cost-effectiveness of (a) full ring PET, (b) gamma camera PET using coincidence imaging and (c) existing diagnostic strategies (CT scanning) to determine staging prior to operative intervention for lung cancer. The focus of the research should be to determine if PET has a role in the management of lung cancer patients.

A secondary research question relates to the relative cost-effectiveness of these diagnostic modalities in the early assessment of response to chemotherapy and/or radiotherapy.

Why is research required?

It is essential to establish to what extent gamma camera PET using coincidence imaging can alter patient management in comparison to full ring PET in comparable patient groups. A study of the impact of these two modalities of PET imaging on subsequent surgical procedures in lung cancer patients will enable such a comparison to be made in one of the conditions for which routine use of PET has most frequently been advocated.

Who are the patients?

Non-small cell lung cancer patients in whom, prior to PET, an operative intervention is planned. Patients currently undergo thoraco-abdominal CT, bone scanning, bronchoscopy and respiratory function tests to exclude mediastinal or contralateral lymph node involvement or distant metastatic disease and to confirm adequate respiratory function. Despite this, 5–7% of patients have unresectable disease at surgery and 14% die within a year of 'curative' surgery.

What is the technology?

PET is a method of nuclear medicine imaging that uses short-lived radiopharmaceuticals (the commonest being ^{18}FDG) to detect and quantify the metabolic abnormalities of disease processes (e.g. tissue glucose metabolism in cancerous tumours). Recently, conventional gamma cameras have been adapted with coincidence detection electronics to image the higher-energy gamma rays of positron emitters. Conventional gamma cameras are located at all large hospitals but previously it has not been possible to image positron radionuclides on these conventional scanners. This availability is being addressed by several manufacturers of dual-headed gamma cameras who are modifying their devices to image ^{18}FDG.

Current and projected use

Many large imaging departments are now considering purchasing modified gamma cameras and diffusion could be rapid; this will have a major impact on the NHS and is the driving force behind the need for research. These cameras would be widely available and would be technically simpler than PET; with further improvements in design they are likely to play a part in clinical nuclear medicine. However, the optimisation of the image quality from gamma camera PET is still very much at an early stage. Gamma camera technology, in particular, is changing rapidly and new technology of significance is being introduced regularly.

In the UK, the Guys' and St Thomas's PET centre was established in May 1992 as a diagnostic centre utilising positron-labelled tracers, and currently performs more than 1000 clinical investigations per year using a full ring system. Mount Vernon Hospital in north-west London has also begun to offer a clinical PET service using a similar system (obtaining the ^{18}FDG from the St Thomas's cyclotron) and is aiming to perform PET studies on 200 patients in its first year of operation. The full ring systems at the two centres are slightly different and both use PET to stage lung cancer patients prior to operative intervention as well as for other indications.

Cost

Gamma camera coincidence PET costs approximately £320,000–350,000 for the camera, coincidence ability and attenuation. Many imaging departments will already have a gamma camera and will therefore only require it to be modified so that it can perform ^{18}FDG PET; this can be achieved at a cost of only £30,000–40,000 for the coincidence software, further increasing the likelihood that diffusion of this technology will be rapid. The cost of ^{18}FDG PET is in the region of £500–1000 per scan (including overheads). Costs associated with the installation and operation of a cyclotron for producing ^{18}FDG and the scanner itself mean that

each full ring PET site can cost between £1 million and £4 million to establish. By using a cyclotron at another location to supply the ^{18}FDG, the costs for the scanner alone are reduced to approximately £1,500,000.

Quantity and quality of the research so far

A systematic review by the VHA (up to and including September 1996) in the USA found 16 studies which examined the role of PET in diagnosing lung cancer; all were of a low quality, either with several flaws in their methods (e.g. small sample size) or multiple flaws in their methods (e.g. no credible reference standard for diagnosis). The HTA-funded update (97/03/01) of this review found a further 14 studies (up to and including April 1998).

In the UK, Addenbrooke's Hospital NHS Trust is undertaking a prospective assessment of the quality of information obtained from gamma camera PET in 40–50 lung cancer and lymphoma patients; this is being funded by Anglia and Oxford regional research and development programme. On the basis of this work it is intended to perform a cost-effectiveness analysis at a later date.

In the USA, ADAC Corporation, the largest installer of gamma cameras in the USA, has presented data on 129 patients (December 1997) from an unpublished multicentre study to evaluate the effectiveness of coincidence imaging to diagnose and stage lung cancer. Preliminary results from 35 patients presented at a conference in August 1997 showed that coincidence imaging had a 96% sensitivity rate and an 80% specificity rate. ADAC have said these results for lung studies correlate with those obtained from dedicated PET scanners. The ECRI technology assessment of PET for diagnosing and staging lung cancer will be completed in mid-1998. Although the HCFA has agreed that PET is accurate in the diagnosis of lung cancer, the effect of PET on patient care and Medicare costs is uncertain.

What is the potential effectiveness of the technology?

Under the best case scenario, PET may impact on the timing of existing therapies to give better local tumour control and may help patients avoid a biopsy. For example, the centre at Guy's & St Thomas's[14] has reported on a retrospective analysis of 34 patients with 'operable' non-small cell lung cancer who underwent full ring PET after routine assessment. Management changes occurred in 14 patients (41%), including 6 (18%) who were changed to non-surgical therapy.

In addition, expensive drugs are increasingly being used for chemotherapy and current practice is not to assess treatment response until after two or three cycles of treatment. Accurate and reliable assessment after one cycle using PET and other techniques, as appropriate, would be highly cost-effective. Whole body scanning with PET FDG can also improve on the detection of distant metastases, such as in brain and bone, and occasionally a synchronous or second primary malignancy.

Under the worst case scenario, PET will be a further diagnostic test which provides no additional information compared with existing strategies.

Comments

In November 1997, Medicare coverage for PET imaging of lung tumours (to characterise SPNs and to stage lung cancer) was approved. The policy went into effect on 1 January 1998 and applies to lung studies obtained from full ring PET scanners and gamma cameras modified with PET capability.

A key issue with the research design is that some patients will need to be imaged by both a full ring PET and gamma camera PET. Only one site in the UK has the facilities to do this using one radiopharmaceutical injection but the source of ^{18}FDG is not directly available. Regardless of the practical considerations relating to the supply of ^{18}FDG, issues relating to the time burden and patient acceptability would remain.

Further information supplied by:

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P Dendy, Dept of Medical Physics and Clinical Engineering, Addenbrooke's Hospital NHS Trust, Cambridge
M Maisey, Division of Radiological Sciences, Guy's & St Thomas's Hospitals NHS Trust, London

Vignette 2: Partial ring PET compared to full ring PET in oncology

Research question

To (a) provide an independent assessment of the physical performance characteristics of each system for 3-D torso imaging and quantification and (b) assess the efficacy of the technology for detection of small volume disease and quantitative measurement.

A secondary research question at this stage could be the effect of PET on management of lung cancer or the selected tumour system.

Why is research required?
There is some reduction in performance for all 3-D systems when moving from brain to body imaging. This is not reflected in standard performance measurements provided by the manufacturers of all scanners. These are made using 20 cm cylindrical objects more representative of brain imaging. The role of performance of each available technology for imaging cancer is unclear because of the lack of independent studies.

The first part of the study should be to make a physical assessment of the imaging systems with performance measurements appropriate for body imaging. In addition, the quantitative accuracy of the respective systems must be assessed. An independently funded review of the current technology would be invaluable to potential purchasers, because an evaluation of these technologies would clarify their physical and clinical performance characteristics, and assist in making an appropriate equipment selection.

Who are the patients?
Clinical studies should be targeted at one tumour system, potentially lung cancer (as this was high on the list of priorities from the Delphi study undertaken as part of this HTA-funded review). The efficacy of the technology should be assessed for detection of small volume disease, such as lymph node metastases and quantitative accuracy for monitoring alterations in tracer uptake with therapy. Stringent entry criteria should be used with appropriate comparators, biopsy and follow-up to confirm the nature of the lesions detected.

The number of patients would depend on the study design; consultation with a medical statistician at the time of commissioning the research would be required to determine the precise number of patients required for each option. The preferred option is that the same patient should be imaged on each PET imaging system within a minimal period (i.e. 1 week). The sites would need to be physically close and a second injection of the radiotracer would be necessary. The other option is to define the sensitivity and specificity of each scanner in a well-defined patient group but imaging different patient cohorts at each location. This would obviously require a larger number of patients but would facilitate assessment at locations which are geographically separated.

What is the technology?
PET is a method of nuclear medicine imaging that detects and quantifies the metabolic abnormalities of disease processes (e.g. tissue glucose metabolism in cancerous tumours). There are currently three PET modalities of clinical relevance for imaging in oncology, principally using ^{18}FDG in the UK. These are:

(i) full ring PET scanner operating in 2-D or 3-D
(ii) partial ring rotating PET scanner operating in 3-D
(iii) coincidence imaging with modified gamma camera technology operating in 3-D.

Current and projected use
There are currently approximately 11 sites worldwide, including one UK site (Department of Radiology, Hammersmith Hospital) which have a partial ring rotating PET scanner.

Dedicated PET is currently available at five locations within the UK (all in London, Cambridge or Aberdeen). In the UK, the Guy's and St Thomas's PET centre was established in May 1992 as a diagnostic centre utilising positron-labelled tracers, and it currently performs more than 1000 studies per year using a full ring system. Mount Vernon Hospital in north-west London has also begun to offer a clinical PET service using a similar system (obtaining the ^{18}FDG from the St Thomas's cyclotron) and aims to perform PET studies on 200 patients in its first year of operation. The full ring systems at the two centres are slightly different and are using PET to stage lung cancer patients prior to operative intervention as well as for other indications.

Cost
The partial ring tomograph, costing approximately £600,000–700,000 per unit, is a lower cost option than full ring PET. Costs associated with the installation and operation of a cyclotron for producing ^{18}FDG and the scanner itself mean that each full ring PET site can cost between £1 million and £4 million to establish. It is possible to obtain the ^{18}FDG from an existing cyclotron because ^{18}FDG has a half-life of 109.8 minutes, thus allowing peripheral imaging sites to operate at locations up to 2–4 hours away from the production unit. By using a cyclotron at another location the costs for the full ring system alone are reduced to approximately £1,500,000.

Quantity and quality of the research so far
Some comparison of coincidence imaging and full ring PET has been commissioned by ADAC Corporation who manufacture

coincidence imaging for gamma cameras in the USA and Germany. There are no current studies of this nature with a partial ring PET system.

The VHA in the USA commissioned an assessment of PET and concluded that the knowledge base (up to and including September 1996) supporting clinical diagnostic applications of PET has significant deficiencies and that the literature did not support widespread incorporation of PET studies into routine diagnostic strategies for the applications that the assessment addressed. Their summary findings were that:

- research into clinical utility of PET in selected conditions is in its preliminary stages
- available studies have focused on the feasibility of using PET in these conditions and on defining its accuracy as a diagnostic test
- a few studies have addressed changes in treatment decisions based on PET findings
- they were unable to locate any studies documenting changes in outcomes of care or costs of care associated with incorporating PET into diagnostic strategies.

What is the potential effectiveness of the technology?

The potential advantages of the partial ring over a full ring PET scanner is principally one of cost. There is an immediate saving using partial ring technology of approximately 50% of the capital cost of the scanner. Running costs are equivalent in terms of service contract and clinical practice. For PET to be cost-effective, the role in patient management has to be demonstrated; the question is whether the extra accuracy of full ring PET compared to partial ring PET is worth the extra cost. The requirement is for adequate sensitivity to detect small volume disease and a quantitative capability to measure alterations in radiotracer uptake for therapy response assessment.

Comments

If the study is multicentred, there must be standardisation of PET protocols. Local ethical approval and ARSAC (Administration of Radioactive Substances Advisory Committee) licences would be required.

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Vignette 3: PET to stage and monitor treatment response in breast cancer

Research question

The relative cost-effectiveness of (a) full ring PET, (b) gamma camera PET using coincidence imaging and (c) existing diagnostic strategies to stage and monitor treatment response in breast cancer.

The focus of the research should be to establish if PET has a role in the management of breast cancer patients (including the relative cost-effectiveness of this diagnostic modality in the early assessment of response to chemotherapy and/or radiotherapy).

Why is research required?

It is essential to establish to what extent gamma camera PET using coincidence imaging can alter patient management in comparison to full ring PET in comparable patient groups. A study of the impact of these two modalities of PET imaging on staging and monitoring treatment response in breast cancer patients will enable such a comparison to be made in one of the conditions for which the routine use of PET has most frequently been advocated.

Who are the patients?

Breast cancer is the most common cancer in women, accounting for 30% of all malignant neoplasms and 21% of female cancer deaths. The crude incidence rate is about 130 per 100,000 women. Few cases occur under the age of 35 years and, thereafter, incidence rates rise steeply. In an average population of 250,000 there are approximately 180 new cases of breast cancer each year. The cumulative lifetime risk of developing breast cancer is 9% (1 in 11).

^{18}FDG PET can have an important role in the assessment of patients with breasts which are difficult to evaluate by conventional means (e.g. mammographic assessment of breast lumps may be difficult in younger breasts, and even in visible lesions mammography lacks specificity).

What is the technology?

PET is a method of nuclear medicine imaging that uses short-lived radiopharmaceuticals (the commonest being ^{18}FDG) to detect and quantify the metabolic abnormalities of disease processes (e.g. tissue glucose metabolism in cancerous tumours). Recently, conventional gamma cameras have been adapted with coincidence detection electronics to image the higher-energy gamma rays of positron emitters. Conventional gamma cameras are located at all large hospitals but

previously it has not been possible to image positron radionuclides on these conventional scanners. This is being addressed by several manufacturers of dual-headed gamma cameras who are modifying their devices to image ^{18}FDG. With recent data demonstrating the clinical applications of ^{18}FDG, there has been a renewed interest in imaging ^{18}FDG with gamma cameras.

Current and projected use

Many centres are currently buying untested gamma camera systems and their use is, therefore, increasing; this is the driving force behind the need for research. However, the optimisation of the image quality from gamma camera PET is still very much at an early stage. Gamma camera technology, in particular, is changing rapidly and new technology of significance is being introduced regularly.

In the UK, the Guy's & St Thomas's PET centre was established in May 1992 as a diagnostic centre utilising positron-labelled tracers and currently performs more than 1000 studies per year using a full ring system. Mount Vernon Hospital in north-west London has also begun to offer a clinical PET service using a similar system (obtaining the ^{18}FDG from the St Thomas's cyclotron) and aims to perform PET studies on 200 patients in its first year of operating. The full ring systems at these two centres are slightly different.

Cost

Costs associated with the installation and operation of a cyclotron for producing ^{18}FDG and the scanner itself mean that each dedicated PET site can cost between £1 million and £4 million to establish. It is possible to obtain the ^{18}FDG from an existing cyclotron as ^{18}FDG has a half-life of 109.8 minutes, thus allowing peripheral imaging sites to operate up to 2–4 hours away from the production unit. By using a cyclotron at another location, the costs for the full ring system alone are reduced to approximately £1,500,000.

Gamma camera coincidence PET costs approximately £320,000–350,000 for the camera, coincidence ability and attenuation. Many imaging departments will already have a camera and will thus only require it to be modified to perform ^{18}FDG PET; this can be achieved at a cost of only £30,000–40,000 for the coincidence software, which further increases the likelihood that diffusion of this technology will be rapid. The cost of ^{18}FDG PET is in the region of £500–1000 per scan (including overheads).

Quantity and quality of the research so far

A systematic review by the VHA (up to and including September 1996) in the USA found eight studies which examined the role of PET in diagnosing breast cancer; all were of a low quality, either with several flaws in their methods (e.g. small sample size) or multiple flaws in their methods (e.g. no credible reference standard for diagnosis). The HTA-funded update (97/03/01) of this review found a further eight studies (up to and including April 1998).

The accuracy of PET is already well documented. In one study of 28 patients with 35 breast masses, full ring PET produced a sensitivity of 96% and a specificity of 100%. ^{18}FDG PET has been reported to perform well in preoperative staging of breast cancer, detecting soft tissue lesions in the contralateral breast, axillae, bone and elsewhere, with very high sensitivity, often detecting unsuspected lesions. In the post-hormone and chemotherapy evaluation of breast cancer, early reduction of ^{18}FDG uptake, compared to pre-therapy levels, is associated with a favourable response. In patients who do not respond to treatment, no significant reduction in ^{18}FDG accumulation is seen.

What is the potential effectiveness of the technology?

PET could potentially provide 'one-stop' diagnostic and staging technique, confirming the diagnosis of a primary breast cancer and staging axillary lymph nodes. This would be more cost-effective than standard imaging and axillary node surgical dissection. This technology may alter patient management although the likely magnitude of savings are hard to predict.

In addition, expensive drugs are increasingly being used for chemotherapy and current practice is not to assess treatment response until after two or three cycles of treatment. Accurate and reliable assessment after one cycle using PET and other techniques as appropriate would be highly cost-effective.

Comments

A key issue with the research design is that some patients will need to be imaged by both a full ring PET and gamma camera PET. Only one site in the UK (Addenbrooke's Hospital NHS Trust, Cambridge) has the facilities to do this using one injection but the source of ^{18}FDG (the cyclotron at the Wolfson Brain Imaging Centre, Cambridge) is not directly available. Regardless of practical considerations relating to the supply of ^{18}FDG, issues relating to the time burden and patient acceptability would remain.

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Vignette 4: PET for assessing myocardial viability when selecting patients for revascularisation surgery

Research question
What is the relative cost-effectiveness of (a) gamma camera PET using coincidence imaging and (b) 511 keV collimated positron imaging for assessing myocardial viability when selecting patients for revascularisation surgery, compared with current standard methods of assessment?

Why is research required?
Tissue revascularisation is a major operation and relatively expensive; maximum return in the form of improved patient outcome is therefore required.

A study must be made to assess the relative effectiveness of 511 keV collimated positron imaging and gamma camera coincidence imaging; high-energy collimation may be 'low tech' but if it sufficient to affect patient outcomes to the same extent as full ring or gamma camera coincidence PET then it requires further evaluation.

Who are the patients?
Those with left ventricular dysfunction who are planned to have revascularisation using either coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA). The problem to date has been in differentiating severely ischaemic but viable myocardium with wall motion abnormalities (hibernating myocardium) from infarcted, non-viable heart muscle. Using PET imaging, viable myocardium can be shown to exist in regions with severe wall motion abnormalities due to diminished perfusion, because anaerobic glycolysis is maintained. This type of assessment is particularly important for patients with low ejection fractions when mortality and morbidity are significantly higher.

There are also benefits in patients with ischaemic cardiomyoplasty who are considered for cardiac transplantation, as some may have hibernating segments suitable for revascularisation.

Large numbers of patients could be screened if PET was widely available. The total number of PTCA procedures carried out in the UK in 1996, as reported by the British Cardiovascular Intervention Society, was 20,511.

What is the technology?
PET is a method of nuclear medicine imaging that uses short-lived radiopharmaceuticals (the commonest being ^{18}FDG) to detect and quantify the metabolic abnormalities of disease processes (e.g. tissue glucose metabolism in cancerous tumours). Recently, conventional gamma cameras have been adapted with thicker lead collimators or coincidence detection electronics to image the higher-energy gamma rays of positron emitters. Conventional gamma cameras are located in all large hospitals but previously it has not been possible to image positron radionuclides on these conventional scanners. This is being addressed by several manufacturers of dual-headed gamma cameras who are modifying their devices to image ^{18}FDG. With recent data demonstrating the clinical applications of ^{18}FDG, there has been a renewed interest in imaging ^{18}FDG with gamma cameras.

Current and projected use
Many large imaging departments are now considering purchasing modified gamma cameras and diffusion could be rapid; this will have a major impact on the NHS and is the driving force behind the need for research. These cameras would be widely available and would be technically simpler than PET; with further improvements in design they are likely to play a part in clinical nuclear medicine. However, the optimisation of the image quality from gamma camera PET is still very much at an early stage. Gamma camera technology, in particular, is changing rapidly and new technology of significance is being introduced regularly.

Cost
Gamma camera coincidence PET costs approximately £320,000–350,000 for the camera, coincidence ability and attenuation. Many imaging departments will already have a camera and will thus only require it to be modified to perform ^{18}FDG PET; this can be achieved at a cost of only £30,000–40,000 for the coincidence software and further increases the likelihood that diffusion of this technology will be rapid. The cost of ^{18}FDG PET is in the region of £500–1000 per scan (including overheads).

Quantity and quality of the research so far
PET is regarded as the gold standard for non-invasive myocardial viability assessment, when measured against the true gold standard of viability,

functional recovery after revascularisation. Imaging with ^{13}N-ammonia ($^{13}NH_3$) and ^{18}FDG can accurately identify viable myocardium in patients with ischaemic disease. In one study, 93 patients were followed-up over 13 months and analysis of $^{13}NH_3$ and ^{18}FDG was found to predict patients likely to benefit from revascularisation.

What is the potential effectiveness of the technology?

Detection of hibernating myocardium using PET could better select patients for CABG or PTCA, thereby improving the likelihood of such surgery being successful. The potential impact of accurate assessment is considerable; the high costs of PET imaging may be recouped if it can accurately identify patients who will benefit from revascularisation. Additionally, the impact of the identification of significant viable myocardium, which may be undetectable by other means, in ischaemic cardiomyopathy patients who are considered for cardiac transplantation, and who may therefore benefit from revascularisation, could be large given the high management costs of these patients.

Comments

In order to obtain sufficient patient numbers a multicentre collaboration would be worthwhile.

Further information supplied by:

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Chapter 5
Discussion

This project was commissioned by the NHS Research and Development HTA programme in early 1998 and carried out in 3 months. Its aim was not to promote fundamental research affecting the future development of PET but to highlight (to a tight deadline) key HTA research questions for the 1998 prioritisation exercise in the UK. For this reason the authors consider that the report will be of interest to other HTA organisations involved in setting research priorities, as well as to those with a specific interest (research, commissioning, clinical) in PET. As outlined in chapter 1, PET technology is developing very fast and an independent HTA report on PET in one or more of the highlighted disease conditions, incorporating an economic evaluation, is considered to remain a high priority. If it is not reprioritised by the Diagnostics and Imaging Panel in 1999, the topic should be looked at again by the NHS HTA programme in 2000.

Potential neurological applications of PET have not been discussed at length in this report. In part, this is because many of the applications of PET to neurology are more research- than practice-based. Nevertheless, the authors did attempt in the Delphi survey to elicit the views of neurologists but without much success. Participants commented that "neuropsychiatric studies are still at the stage of fairly fundamental research", and that "we have not included neuropsychiatric studies on our priority list. It is our assessment that such studies will not meet our primary objective until such time as we have the necessary therapy to cure or control neuropsychiatric disease and a positive PET scan will alter patient management and patient outcome."

Given the time constraints placed upon the project, it is important to question the validity of the results with regard to both the literature review and the Delphi survey.

Literature review

The search strategy used in the literature review was, of necessity, not exhaustive, so could there be important publication bias? This is unlikely. Although time constraints meant that only the MEDLINE database and the Cochrane Library were searched, the authors sought to make the literature review as complete as possible by designing it as an update to the systematic literature review carried out by the VHA.[7] The study inclusion criteria were exactly the same as those used by the VHA. Neither the experts whose views were sought on an early draft of the report, nor the anonymous referees used by the HTA programme, have highlighted any papers that were missed which would have met the inclusion criteria.

Delphi study

It is hard to measure the validity of the Delphi technique as a means of setting research priorities. Delphi surveys unavoidably blend the subjectivity of human opinion into the more objective approach of a survey; the interests and expertise of those selected to take part in a Delphi survey crucially affect the results. In general, the contrast between the views of many of the participants (as well as some of the referees of this report) merely serves to emphasise the subjective nature of trying to establish research priorities between the different PET modalities and the numerous conditions in which the potential benefit of the technology has been suggested but not yet confirmed.

However, a shortcoming of this review is that there were not enough contributions from practising oncologists and cardiologists on the need and value of PET. Several of the Delphi participants were medically qualified but none were disease specialists. It is likely that the latter would have a different perspective on the technology than imaging specialists or physicists. Although views of oncologists (in particular) were sought as part of the survey, the authors consider that insight into the priorities of disease specialists would, with hindsight, have been useful as well. However, a much larger Delphi study would have been required in order to cover all the potential conditions in which PET might be used. Other HTA organisations which may be planning similar exercises should consider carefully the composition of the Delphi survey and whether the participation of specialists is particularly relevant to the technology under consideration.

Acknowledgements

This report was commissioned by the NHS HTA programme.

The authors would like to thank Liz Adams (Veterans Health Administration, USA), Dr Robin Dowie (Brunel University), Dr Paul Kemp (Southampton University Hospitals NHS Trust), Professor Mike Smith (University of Leeds), Dr Gillian Vivian (Plymouth Hospitals NHS Trust) and Gwyn Weatherburn (Brunel University) for their comments on an earlier draft. The authors are also grateful to all the participants in the Delphi survey (listed in appendix 2).

Particular thanks are due to Sandy Grapes for practical and secretarial support.

Our thanks are also due to the three anonymous referees for their comments on the draft report.

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Wang H, Maurea S, Mainolfi C, Fiore F, Gravina A, Panico MR, *et al.,* 1997. Tc-99m mibi scintigraphy in patients with lung cancer. Comparison with ct and fluorine-18 fdg pet imaging. *Clin Nucl Med*;**22**:243–9.

Solitary pulmonary nodules (Table 9)

Lowe VJ, Fletcher JW, Gober L, Lawson M, Kirchner P, Valk P, 1998. Prospective investigation of positron emission tomography in lung nodules. *J Clin Oncol*;**16**:1075–84.

Alzheimer's disease (Table 10)

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Parkinson's disease (Table 12)

Antonini A, Leenders KL, Vontobel P, 1997. Complementary pet studies of striatal neuronal function in the differential diagnosis between multiple system atrophy and Parkinson's disease. *Brain*;**120**:2187–95.

Ishikawa T, Dhawan V, Chaly T, 1996. Fluorodopa positron emission tomography with an inhibitor of catechol-o-methyltransferase: effect of the plasma 3-o-methyldopa fraction on data analysis. *J Cereb Blood Flow Metab*;**16**:854–63.

Otsuka M, Kuwabara Y, Ichiya Y, 1997. Differentiating between multiple system atrophy and Parkinson's disease by positron emission tomography with 18f-dopa and 18f-fdg. *Ann Nucl Med*;**11**:251–7.

Dementia (Table 13)

Hoffman JM, Hanson MW, Welsh KA, 1996. Interpretation variability of 18fdg-positron emission tomography studies in dementia. *Invest Radiol*;**31**:316–22.

Epilepsy (Table 14)

Chugani HT, da Silva E, Chugani DC, 1996. Infantile spasms: III. Prognostic implications of bitemporal hypometabolism on positron emission tomography. *Ann Neurol*;**39**:643–9.

Duncan JD, Moss SD, Bandy DJ, 1997. Use of positron emission tomography for presurgical localization of eloquent brain areas in children with seizures. *Pediatr Neurosurg*;**26**:144–56.

Ferrie CD, Marsden PK, Maisey MN, 1997. Visual and semiquantitative analysis of cortical fdg-pet scans in childhood epileptic encephalopathies. *J Nucl Med*; **38**:1891–4.

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Rintahaka PJ, Chugani HT, 1997. Clinical role of positron emission tomography in children with tuberous sclerosis complex. *J Child Neurol*;**12**:42–52.

Snead OC 3rd, Chen LS, Mitchell WG, 1996. Usefulness of [18f]fluorodeoxyglucose positron emission tomography in pediatric epilepsy surgery. *Pediat Neurol*;**2**:98–107.

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Bax JJ, Visser FC, Blanksma PK, 1996. Comparison of myocardial uptake of fluorine-18-fluorodeoxyglucose imaged with pet and spect in dyssynergic myocardium. *J Nucl Med*;**37**:1631–6.

Beanlands RS, deKemp RA, Smith S, 1997. F-18-fluorodeoxyglucose pet imaging alters clinical decision making in patients with impaired ventricular function. *Am J Cardiol*;**79**:1092–5.

Flameng WJ, Shivalkar B, Spiessens B, 1997. Pet scan predicts recovery of left ventricular function after coronary artery bypass operation. *Ann Thorac Surg*;**64**:1694–701.

Fragasso G, Chierchia SL, Rossetti E, 1997. Myocardial viability assessed with fluorodeoxyglucose and pet in patients with q wave myocardial infarction receiving thrombolysis: relationship to coronary anatomy and ventricular function. *Nucl Med Commun*;**18**:191–9.

Go RT, MacIntyre WJ, Cook SA, 1996. The incidence of scintigraphically viable and nonviable tissue by rubidium-82 and fluorine-18-fluorodeoxyglucose positron emission tomographic imaging in patients with prior infarction and left ventricular dysfunction. *J Nucl Cardiol*;**2**:96–104.

Hata T, Nohara R, Fujita M, 1996. Noninvasive assessment of myocardial viability by positron emission tomography with 11c acetate in patients with old myocardial infarction. Usefulness of low-dose dobutamine infusion. *Circulation*;**94**:1834–41.

Rubin PJ, Lee DS, Davila-Roman VG, 1996. Superiority of c-11 acetate compared with f-18 fluorodeoxyglucose in predicting myocardial functional recovery by positron emission tomography in patients with acute myocardial infarction. *Am J Cardiol*;**78**:1230–5.

Schulz G, von Dahl J, Kaiser HJ, 1996. Imaging of beta-oxidation by static pet with 14(r,s)-[18f]-fluoro-6-thiaheptadecanoic acid (ftha) in patients with advanced coronary heart disease: a comparison with 18fdg-pet and 99tcm-mibi spect. *Nucl Med Commun*;**12**:1057–64.

Stewart RE, Miller DD, Bowers TR, 1997. Pet perfusion and vasodilator function after angioplasty for acute myocardial infarction. *J Nucl Med*;**38**:770–7.

Appendix 1

Literature review

Brief descriptions of the additional articles retrieved by Search 1 which met the VHA's inclusion criteria are given in *Tables 5–10*.

The results of Search 2, which sought to extend the VHA review to cover other important indications for the period 1996–98, are presented in *Tables 11–15*.

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13 Dementia: studies meeting VHA inclusion criteria
14 Epilepsy: studies meeting VHA inclusion criteria
15 Myocardial infarction/myocardium: studies meeting VHA inclusion criteria

* Kondoh Y, Nagata K, Sasaki H, Hatazawa J. Dynamic FDG-PET study in probable Alzheimer's disease. *Ann NY Acad Sci* 1997;**826**:406–9. No abstract: unable to assess.

TABLE 5 *Head and neck cancer: additional studies meeting VHA inclusion criteria*

Role	Study	Number of cases	Authors' conclusions
Known primary site	Minn, *et al.*, 1997	37	High uptake of ^{18}FDG in untreated head and neck cancer associated with advanced disease; may portend poor survival.
Known primary site	Wong, *et al.*, 1996	30	CT/MRI, PET ^{18}FDG images provide additional clinically relevant information to that obtained from clinical evaluation or conventional CT/MRI.
Known primary site, suspected recurrent disease	Wong, *et al.*, 1997	31 (primary) 23 (recurrent)	PET ^{18}FDG more accurate than CT/MRI for identifying primary and recurrent tumours as well as metastatic lesions in neck.
Unknown primary	Braams, *et al.*, 1997	13	PET can reveal useful information that results in more appropriate treatment; it can be of value in guiding endoscopic biopsies for histological diagnosis.
Unknown primary, treatment response	Sakamoto, *et al.*, 1997	17	PET ^{18}FDG could be used to diagnose malignant tumours and evaluate treatment.
Cervical node involvement	Myers, *et al.*, 1998	14	PET showed trend in increased accuracy over CT.
Suspected recurrent disease	Anzai, *et al.*, 1996	12	PET metabolic imaging, compared with anatomical methods, has improved diagnostic accuracy for recurrent head and neck cancer.
Chemotherapy response	Lowe, *et al.*, 1997	28	PET ^{18}FDG accurate in classifying response to chemotherapy in most patients. PET ^{18}FDG may identify residual viable tumour when otherwise undetectable.
Early prediction of cancer therapy outcome	Brun, *et al.*, 1997	17	Initial low metabolic rate of glucose in primary lesions or regional metastases predicted local complete response. When high initial tumour metabolic rate of glucose found, magnitude of reduction of rate in second PET examination might be an adjunct in predicting local tumour response.

TABLE 6 *Colorectal cancer: additional studies meeting VHA inclusion criteria*

Role	Study	Number of cases	Authors' conclusions
Diagnosing primary disease	Abdel-Nabi, *et al.,* 1998	48	PET ^{18}FDG has high sensitivity and specificity for detection of colorectal carcinomas; appears to be superior to CT in staging of primary colorectal carcinoma.
Evaluation of recurrent or advanced primary	Ogunbiyi, *et al.,* 1997	58	PET ^{18}FDG more sensitive than CT in clinical assessment of patients with recurrent or metastatic cancer; provides accurate means of selecting appropriate treatment.
Evaluation of suspected or proven disease	Ruhlmann, *et al.,* 1997	59	Whole-body PET scan provides optimum conditions to locate metastatic lesions that might not be seen otherwise.
Staging recurrent disease	Delbeke, *et al.,* 1997	52	PET ^{18}FDG is most accurate non-invasive method for staging patients with recurrent metastatic colorectal carcinoma; plays an important role in management decisions in this setting.
Treatment response	Findlay, 1996	20	PET used to evaluate uptake of ^{18}FDG in tumours yields data that correlate with anti-tumour effect of chemotherapy in patients with liver metastases from colorectal cancer.

TABLE 7 *Breast cancer: additional studies meeting VHA inclusion criteria*

Role	Study	Number of cases	Authors' conclusions
Detecting primary disease	Palmedo, *et al.,* 1997	20	Diagnostic accuracy of scintimammography equivalent to that of ^{18}FDG PET. For detection of *in situ* lymph node metastases of the axilla, ^{18}FDG seems to be more sensitive.
Defining primary disease	Avril, *et al.,* 1997	73	Quantification of ^{18}FDG uptake in breast tumours provided objective criteria for differentiation between benign and malignant tissue with similar diagnostic accuracy vs. visual analysis.
Detecting regional spread	Adler, *et al.,* 1997	50	PET scans of the axilla interpreted with sufficient sensitivity for PET to serve as cost-effective screening test for axillary lymph node metastases.
Staging axillary nodes	Crippa, *et al.,* 1998	68	PET showed good overall diagnostic accuracy in detection of axillary metastases (86%). False-negative PET findings can be encountered.
Staging recurrent disease	Bender, *et al.,* 1997	75	PET ^{18}FDG detected six local recurrences, eight lymph node and seven bone metastases which were not visualized by CT/MR imaging.
Staging distant metastases	Utech, *et al.,* 1996	124	PET ^{18}FDG can be of value in evaluating axillary lymph nodes for metastatic involvement prior to surgery.
Detecting residual or recurrent tumours	Inoue, *et al.,* 1996	24	PET using ^{18}FDG and L-methyl-^{11}C-methionine appear equally effective in detecting residual or recurrent malignant tumours although ^{18}FDG uptakes slightly higher. Both showed limited diagnostic sensitivity for small (< 1.5 cm) tumours.
Evaluation of preoperative chemotherapy	Bassa, *et al.,* 1996	16	PET ^{18}FDG is valuable for monitoring effects of preoperative chemotherapy in patients with locally advanced breast cancer with better sensitivity for primary tumour and better specificity for nodal metastasis in comparison with ultrasonography.

TABLE 8 *Lung cancer: additional studies meeting VHA inclusion criteria*

Role	Study	Number of cases	Authors' conclusions
Detection of primary lung cancer and mediastinal lymph node metastases	Higashi, *et al.,* 1998a,b	33	Both ^{18}FDG PET and SPECT have clinical value for non-invasive detection of primary lung cancer of 2 cm or more in diameter. ^{18}FDG PET considered method of choice for evaluation of patients with suspected primary lung cancer of less than 2 cm in diameter.
Detecting lung tumours	Wang, *et al.,* 1997	19	Similar results for ^{99m}Tc MIBI SPECT and ^{18}FDG PET in diagnostic evaluation of patients with lung tumours. However, ^{18}FDG lung tumour uptake significantly higher compared with MIBI accumulation.
Detection of metastatic mediastinal lymph nodes	Vansteenkiste, *et al.,* 1997	50	PET significantly more accurate than CT in mediastinal lymph node staging in NSCLC. Both examinations were complementary. If results can be confirmed in larger numbers of patients, PET could reduce need for invasive surgical staging.
Detection of mediastinal lymph node metastases in NSCLC	Sasaki, *et al.,* 1996	29	^{18}FDG PET suggested to be superior to X-ray CT when used for detection of mediastinal lymph node metastases in patients with NSCLC.
Staging	Bury, *et al.,* 1997	109	Visual interpretation of whole body ^{18}FDG PET images can improve diagnostic accuracy in staging of NSCLC.
Staging of NSCLC	Bury, *et al.,* 1996a	61	Whole-body ^{18}FDG PET can improve diagnostic accuracy in staging of NSCLC.
Staging mediastinum	Bury, *et al.,* 1996b	50	PET with ^{18}FDG significantly more accurate than CT in mediastinal staging of NSCLC.
Nodal staging	Steinart, *et al.,* 1997	47	PET with ^{18}FDG appears superior to CT for nodal staging of NSCLC.
Staging lymph nodes	Guhlmann, *et al.,* 1997	46	^{18}FDG PET provides new and effective method for staging thoracic lymph nodes in patients with lung cancer; is superior to CT scanning in assessment of hilar and mediastinal nodal metastases.
Differentiating benign from metastatic adrenal masses	Erasmus, *et al.,* 1997	27	PET with ^{18}FDG is accurate, non-invasive way to differentiate benign from metastatic adrenal masses in patients with bronchogenic carcinoma.
Differentiating benign from malignant lung lesions	Hubner, *et al.,* 1996	26	^{18}FDG PET image interpretation could have significant cost-effective impact on medical/surgical management of chest masses.
Treatment response	Ichiya, *et al.,* 1996	30	^{18}FDG PET plays complementary role in both predicting and assessing therapeutic response and prognosis in patients with bronchogenic carcinoma.
Detecting residual or recurrent tumours	Inoue, *et al.,* 1996	24	PET using ^{18}FDG and L-methyl-^{11}C-methionine appear equally effective in detecting residual or recurrent malignant tumours although ^{18}FDG uptakes slightly higher. Both showed limited diagnostic sensitivity for small (< 1.5 cm) tumours.
Delineate lung cancers pre-radiotherapy and distinguish residual tumour from scarring following radiotherapy	Hebert, *et al.,* 1996	20	^{18}FDG PET may be useful for delineation of lung cancer volumes that are poorly defined by chest X-ray and/or CT scan. Value of PET in differentiating tumour from fibrosis after radiotherapy for lung cancer remains to be established.

TABLE 9 *SPNs: additional studies meeting VHA inclusion criteria*

Role	Study	Number of cases	Authors' conclusions
Discriminate between benign and malignant pulmonary nodules	Lowe, *et al.,* 1998	89	^{18}FDG PET can accurately characterise indeterminate SPNs. PET imaging provides non-invasive method of evaluating indeterminate SPNs, which can reduce need for invasive tissue biopsy.

TABLE 10 *Alzheimer's disease: additional studies meeting VHA inclusion criteria*

Role	Study	Number of cases	Authors' conclusions
Prediction of cognitive decline	Jagust, *et al.,* 1996	18	Results replicate previous findings showing that functional brain imaging is predictive of rate of cognitive decline in Alzheimer's disease.

TABLE 11 *Extension of VHA review to further indications (1996–98)*

Condition	Number of articles identified by search	Number of articles (1996–98) meeting inclusion criteria
Parkinson's disease (PD)	91	3
Cerebrovascular disease	30	0
Dementia	23	4
Epilepsy	53	7
Myocardial infarction/myocardium	156	9

TABLE 12 *Parkinson's disease: studies meeting VHA inclusion criteria*

Role	Study	Number of cases	Authors' conclusions
Differential diagnosis between multiple system atrophy (MSA) and PD	Antoni, *et al.,* 1997	9 MSA 10 PD	Striatal ^{18}FDG and particularly [^{11}C] raclopride are sensitive and effective measures of striatal function and may help characterise patients with MSA. In contrast, [^{18}F] fluorodopa measurements are accurate in detecting abnormalities of nigrostriatal dopaminergic system but may not distinguish between different forms of parkinsonism.
Differential diagnosis between MSA and PD	Otsuka, *et al.,* 1997	9 MSA 15 PD	Glucose metabolism is useful for evaluating regional metabolic activity of the brain; [^{18}F] fluorodopa study seems more useful for differentiating between MSA and PD.
Assessment of nigrostriatal dopaminergic function in PD	Ishikawa, *et al.,* 1996	12	[1231] beta CIT-FP/SPECT can provide quantitative descriptors of presynaptic dopaminergic function comparable to those obtained with [^{18}F] fluordopa/PET.

TABLE 13 *Dementia: studies meeting VHA inclusion criteria*

Role	Study	Number of cases	Authors' conclusions
Clinical evaluation	Hoffman, *et al.,* 1996	96	Intra- and inter-observer agreement of visual interpretation of ^{18}FDG PET images indicates that it is acceptable as an imaging technique in clinical evaluation of dementia patients.

TABLE 14 *Epilepsy: studies meeting VHA inclusion criteria*

Role	Study	Number of cases	Authors' conclusions
Presurgical localisation of eloquent brain areas in children with seizures	Duncan, *et al.,* 1997	15	Non-invasive presurgical brain mapping has potential to reduce risk and improve neurological outcome.
Presurgical and intraoperative localisation of eloquent brain areas	Vinas, *et al.,* 1997	12	[^{15}O]-water PET can be used for preoperative non-invasive identification of functional cortex and may be useful in neuro-surgical preplanning. Intraoperative mapping still remains main means of avoiding neurological damage as it can be performed during entire surgical procedure to avoid damage to cortex, pathways, and damage secondary to ischaemia or oedema (brain retraction).
Determination of optimal method for analysing PET scans in children being considered for epilepsy surgery	Ferrie, *et al.,* 1997	32	Semiquantitative analysis gives clinically useful information additional to that obtained from visual inspection.
Localising the epileptogenic cortex in patients who are candidates for epilepsy surgery	Lamusuo, *et al.,* 1997	18	^{18}FDG PET seemed to localise epileptogenic cortex more accurately than interictal iomazenil-SPECT in patients with complicated focal epilepsy.
Clinical role in children with tuberous sclerosis complex	Rintahaka, *et al.,* 1997	23	Usefulness of glucose metabolism PET in most patients with tuberous sclerosis complex is limited. However, if EEG, CT and MRI abnormalities are unifocal or unilateral, and surgery is being contemplated, more detailed evaluation with PET may help to determine if contralateral tubers present and evaluate functional integrity of brain as a whole.
Preoperative evaluation of children	Snead, *et al.,* 1996	56	A child with intractable partial seizures cannot be excluded from surgical consideration because interictal ^{18}FDG PET is normal; nor is there sufficient correlation between interical hypometabolic area on ^{18}FDG PET and epileptogenic zone in terms of anatomical location and size to justify forgoing chronic invasive intracranial monitoring in children with intractable partial seizures being evaluated for epilepsy surgery unless there is absolute concordance between all neuroimaging, clinical and video-EEG data.
Prognostic implications of bitemporal hypometabolism on PET	Chugani, *et al.,* 1996	18	Patients with infantile spasms and bitemporal glucose hypometabolism on PET comprise a relatively homogenous group and are typically not candidates for cortical resection. Long-term outcome of such infants is particularly poor; majority are autistic.

TABLE 15 *Myocardial infarction/myocardium: studies meeting VHA inclusion criteria*

Role	Study	Number of cases	Authors' conclusions
Prediction of left ventricular function after coronary artery bypass	Flameng, *et al.,* 1997	59	At least one low flow–high metabolism region must be present for there to be a postoperative functional benefit. When low left ventricular ejection fraction is associated with such a region, early recovery is substantial.
Impact on decision making in selection of patients for revascularisation	Beanlands, *et al.,* 1997	87	In 57% of patients, PET data influenced management decisions, indicating an important effect of myocardial viability determination on difficult therapy decisions in these patients.
Assessment of myocardial viability	Fragasso, *et al.,* 1997	36	In 'chronic' myocardial infarction, residual tissue viability as assessed by ^{18}FDG uptake does not necessarily correlate with coronary recanalisation.
Assessment of reperfusion blood flow after primary angioplasty	Stewart, *et al.,* 1997	21	PET offers the potential for accurate non-invasive serial assessment of reperfusion blood flow after primary angioplasty for acute myocardial infarction.
Diagnostic value in patients with ischaemically reduced left ventricular function	Schulz, *et al.,* 1996	21	Similarity between [^{18}F]-fluoro-6-thiaheptadecanoic acid (FTHA) and MIBI uptake suggests that static PET imaging with FTHA is of limited value when distinguishing between ischaemic or hibernating myocardium and scar.
Predicting myocardial functional recovery	Rubin, *et al.,* 1996	19	In patients with recent myocardial infarction, extent of functional recovery can be predicted accurately by measurement of regional oxidative metabolism by PET with ^{11}C-acetate; these measurements are superior to those with ^{18}FDG.
Predicting functional recovery after revascularisation	Bax, *et al.,* 1996	20	Good correlation shown between detection of viability in dyssynergic myocardium with ^{18}FDG/$^{13}NH_3$ PET and ^{18}FDG/^{201}Tl SPECT.
Evaluating tissue viability in patients with prior myocardial infarction	Go, *et al.,* 1996	155	Irreversible perfusion defects were common in patients with prior myocardial infarction and distinction between viable and non-viable tissue not possible by perfusion imaging alone. Identification of hibernating myocardium possible only with additional ^{18}F-FDG imaging in about one-third of patients. Indicates significant clinical demand for ^{18}F-FDG imaging to identify patients who will benefit from revascularisation.
Predicting functional recovery after revascularisation	Hata, *et al.,* 1996	28	^{11}C-acetate PET with dobutamine infusion can predict not only reversability of dysfunctioning myocardium after coronary revascularisation but also extent of improvement of regional wall motion in patients with old Q-wave infarction.

Appendix 2

Delphi survey

Aim

To determine research priorities for the use of PET in the UK.

Methods

Participants were selected by discussion with five individuals* with an interest in and awareness of developments in PET in the UK. From their suggestions, 43 individuals were initially invited to participate; however, two did not feel appropriately qualified. The methods for and the result of the selection of experts is an important element of the Delphi technique which is discussed further in a related paper.[39]

Three staged questionnaires were sent by facsimile to all invited participants, who were asked to return the completed forms by facsimile within 1-week. The questionnaires used in the three rounds of the survey are presented at the end of this appendix.

Results

After the initial letter and Round 1 questionnaire were sent to the 43 suggested participants, approximately 50% of the remaining 41 participants took part in the second the third rounds of the survey. The suggested priorities are presented in *Tables 16* (Round 1), *17* (Round 2) and *18* (Round 3).

Participants

The participants in the Delphi survey are shown in *Table 19*: the numbers after participants' names indicate in which rounds of the survey they took part.

* Professor M Maisey, Guy's & St Thomas's Hospitals NHS Trust, London; Professor M Smith, University of Leeds; Dr G Vivian, Plymouth Hospitals NHS Trust; Dr H Stockdale, Royal Liverpool University Hospitals NHS Trust; Mr S Ebdon-Jackson, Department of Health.

TABLE 16 *Delphi survey: Round 1 results*

Condition	Dedicated PET using ring system	Gamma camera PET using coincidence imaging	Positron imaging using a gamma camera	Partial ring system
Oncology				
Brain tumours	1	1		1
Breast cancer	5	4		
Colorectal cancer	3	2		
Head and neck cancer	2	4		
Lung cancer	5	4	1	
Lymphoma	3	3		
Rhabdomyosarcoma		1		
Neuropsychiatric				
Alzheimer's disease	2	1		
Other dementias	1	1		
Epilepsy	1	1		
Eating disorders		1		
PD	1			
Cardiology				
Tissue viability	2	3	3	
Myocardial perfusion			1	

TABLE 17 *Delphi survey: Round 2 results*

Rank	Disease group	PET technology	Mean score	Median score
1	All cancers	Partial ring	5.38	6
2	Lung cancer	Gamma camera	5.19	6
3	Lung cancer	Dedicated	4.87	6
4	Lymphoma	Gamma camera	4.86	5
5	Tissue viability	Gamma camera	4.85	5
6	Breast cancer	Dedicated	4.81	6
7	Breast cancer	Gamma camera	4.69	5.5
8	Head and neck cancer	Gamma camera	4.47	5
9	Head and neck cancer	Dedicated	4.39	5.5
10	Lymphoma	Dedicated	4.38	6
11	Tissue viability	Dedicated	4.25	5
12	Colorectal cancer	Dedicated	4.19	5
13	Epilepsy	Gamma camera	4.08	4.5
14	Myocardial perfusion	Positron imaging	4.00	5
15	Alzheimer's disease	Dedicated	4.00	5
16	PD	Dedicated	3.92	3
17	Colorectal cancer	Gamma camera	3.87	4
18	Brain tumours	Gamma camera	3.67	4
19	Rhabdomyosarcoma	Gamma camera	3.50	2.5
20	Alzheimer's disease	Gamma camera	3.36	4
21	Brain tumours	Dedicated	3.36	3
22	Tissue viability	Positron imaging	3.27	4
23	Other dementias	Dedicated	3.27	3
24	Other dementias	Gamma camera	3.09	3
25	Eating disorders	Gamma camera	2.50	1.5
26	Lung cancer	Positron imaging	2.14	2

TABLE 18 *Delphi survey: Round 3 results*

Research priority	Score
Gamma PET for staging prior to operative intervention for lung cancer	30.5
Partial ring PET compared with dedicated full ring PET in oncology	30
Full ring PET for staging prior to operative intervention for lung cancer	26.5
Full ring PET for (a) staging and (b) monitoring treatment response in breast cancer	22.5
Gamma PET for assessing myocardial tissue viability when selecting patients for revascularisation surgery	20
Gamma PET for (a) staging and (b) monitoring response to chemotherapy treatment in lymphoma	17
Full ring PET for targeting treatment and monitoring response in head and neck cancer	17
Gamma PET for (a) staging and (b) monitoring treatment response in breast cancer	15.5
Full ring PET for (a) staging and (b) monitoring response to chemotherapy treatment in lymphoma	11
Gamma PET for targeting treatment and monitoring response in head and neck cancer	11

TABLE 19 *Participants in Delphi survey*

Participant (survey rounds)	Organisation	Discipline/position
I Gordon (1, 2)	Department of Radiology, Great Ormond Street Hospital for Children NHS Trust	Radiologist
M James/K Hunt (1, 2, 3)	Centre for Health Planning and Management, Keele University	Health economist
A Peters (1, 2)	Nuclear Medicine Unit, Department of Imaging, Hammersmith Hospital	Nuclear medicine
M Maisey (1, 2, 3)	Division of Radiological Sciences, Guy's & St Thomas's Hospitals NHS Trust	Radiologist
A Murray (1, 2, 3)	University of Aberdeen	Senior Lecturer in Radiology
P Jarritt (1, 2, 3)	Institute of Nuclear Medicine, University College London	Nuclear medicine
M Rosser (1, 2)	Dementia Research Group, National Hospital for Neurology and Neurosurgery	Consultant neurologist
P Maltby (1, 2, 3)	Royal Liverpool University Hospitals NHS Trust	Radiopharmacist
T Jones (1, 2, 3)	MRC Cyclotron Unit, Hammersmith Hospital	Professor of Medical Physics: Head of PET Methodology
M Stott (1)	Brent and Harrow Health Authority	Public health medicine
H Stockdale (1, 2, 3)	Department of Nuclear Medicine, Royal Liverpool University Hospitals NHS Trust	Chief Physicist in Nuclear Medicine
P Dendy (1, 2, 3)	Department of Medical Physics and Clinical Engineering, Addenbrooke's Hospital NHS Trust	Medical physics
A Dixon (1, 2, 3)	Department of Radiology, Addenbrooke's Hospital NHS Trust	Radiologist
A Timothy (1, 2, 3)	Guy's & St Thomas's Hospitals NHS Trust	Clinical oncology
J Shaw (1, 2)	Clatterbridge Centre for Oncology NHS Trust	Oncologist
P Price (1, 2, 3)	MRC Cyclotron Unit, Hammersmith Hospital	Reader in Clinical Oncology and Head of PET Oncology Group
A Heaton (1, 2)	Picker International Ltd	Industry representative
G Vivian (1, 2, 3)	Department of Nuclear Medicine, Plymouth Hospitals NHS Trust	Consultant in nuclear medicine
P Julyan/C Boivin (2, 3)	Medical Physics Services, Queen Elizabeth Hospital, Birmingham	Research physicist/ Head of nuclear medicine
P Kemp (2, 3)	Department of Nuclear Medicine, Southampton University Hospitals NHS Trust	Consultant in nuclear medicine
A Britten (2, 3)	Department of Medical Physics, St George's Hospital NHS Trust	Medical physics
P Sharpe (1, 2)	Department of Biomedical Physics and Engineering, Aberdeen Royal Hospital NHS Trust	Biomedical physics
M O'Doherty (1, 2, 3)	Department of Nuclear Medicine, Guy's & St Thomas's Hospitals NHS Trust	Radiologist

Delphi questionnaire: Round 1

Please tick one box in sections A and B, and all boxes that apply in section C.

A: What is the imaging technique to be assessed? (select one)

Dedicated PET using a ring system	☐
Gamma camera PET using coincidence imaging	☐
Positron imaging using a gamma camera	☐
Other. Please specify	☐

Comments

B: In which disease group is it most important that (A) be assessed? (select one)

Oncology: please specify		brain tumours	☐
		breast cancer	☐
		colorectal cancer	☐
		head and neck cancer	☐
		lung cancer	☐
		lymphoma	☐
		melanoma	☐
	other (state)	.....	☐
Neuropsychiatric: please specify		Alzheimer's disease	☐
		other dementias	☐
		epilepsy	☐
		Parkinson's disease	☐
		stroke	☐
	other (state)	.....	☐
Cardiology: please specify		myocardial perfusion	☐
		tissue viability	☐
	other (state)	.....	☐

Comments

C: In which of the following do you think (A) will make an impact in (B)? (tick all boxes that apply)

Improved diagnostic sensitivity	☐
Replace other diagnostic techniques	☐
Changes in existing patient management	☐
Improved patient outcome	☐
Improved cost-effectiveness	☐
Not sure	☐

Comments

Delphi questionnaire: Round 2

Importance of suggested research priority for the NHS

Please indicate on the following pages how important you feel **each** suggested research priority is for the NHS on a scale of 1–7.

Example

If you feel the role of 'dedicated PET in brain tumours' is a very high priority for the NHS to research, then mark the scale as shown below.

A: Dedicated PET (using a ring system)

1 Oncology

	low						high	don't know
	1						7	
(i) Brain tumours							x	☐

PET compared with .....

Where possible/relevant please briefly specify the diagnostic technique against which the PET technology to be researched should be compared.

For your guidance the figure in brackets after the priority indicates the number of respondents who suggested that particular priority. If there is no figure then only one respondent suggested the priority.

When completing the form you may wish to consider the criteria currently used by the Standing Group on Health Technology to establish national research priorities.

- What are the benefits from an assessment in terms of reduced uncertainty about: outcomes for patients including acceptability, quality of life and effectiveness; cost-effectiveness to the NHS and targeting of services?
- How long might it be before benefits could be realised bearing in mind: time needed to perform the assessment; and time needed to bring about a change in practice?
- Would the assessment be likely to offer value for money?
- How important is an **early** assessment with reference to: the cost of not doing the assessment now (or in the immediate future); the likely level of demand and time trend of use; and the need for the assessment to be performed 'now or never'?
- Are there any other factors relating to the technology which might have a bearing on the importance of performing the assessment, such as: policy considerations; prevalence of the disease/condition; and social-ethical considerations?

A: Dedicated PET (using a ring system)

1 Oncology

low high don't know

(i) Brain tumours
PET compared with .....

(ii) Breast cancer (5)
PET compared with .....

(iii) Colorectal cancer (3)
PET compared with .....

(iv) Head and neck cancer
PET compared with .....

(v) Lung cancer (4)
PET compared with .....

(vi) Lymphoma (2)
PET compared with .....

2 Neuropsychiatric

(i) Alzheimer's disease (2)
PET compared with .....

(ii) Other dementias
PET compared with .....

(iii) Parkinson's disease
PET compared with .....

3 Cardiology

(i) Tissue viability (2)
PET compared with .....

Comments:

B: Gamma PET (using coincidence imaging)

	low	high	don't know
1 Oncology			
(i) Brain tumours PET compared with	1	7	☐
(ii) Breast cancer (4) PET compared with	1	7	☐
(iii) Colorectal cancer (2) PET compared with	1	7	☐
(iv) Head and neck cancer (4) PET compared with	1	7	☐
(v) Lung cancer (4) PET compared with	1	7	☐
(vi) Lymphoma (3) PET compared with	1	7	☐
(vii) Other cancer – rhabdomyosarcoma PET compared with	1	7	☐
2 Neuropsychiatric			
(i) Alzheimer's disease PET compared with	1	7	☐
(ii) Other dementias PET compared with	1	7	☐
(iii) Epilepsy PET compared with	1	7	☐
(iv) Other neuropsychiatric – eating disorders PET compared with	1	7	☐
3 Cardiology			
(i) Tissue viability (3) PET compared with	1	7	☐

Comments:

C: Positron imaging using a gamma camera

		low	high	don't know
1	**Oncology**			
	(i) Lung cancer PET compared with	1 ☐☐☐☐☐☐ 7		☐
2	**Cardiology**			
	(i) Myocardial perfusion PET compared with	1 ☐☐☐☐☐☐ 7		☐
	(ii) Tissue viability (3) PET compared with	1 ☐☐☐☐☐☐ 7		☐

Comments:

D: Other

Partial ring system

		low	high	don't know
1	**Oncology**			
	All cancers	1 ☐☐☐☐☐☐ 7		☐

Comments:

Delphi questionnaire: Round 3

Please rank your top five research priorities from the list below. Please bear in mind their urgency and importance to the NHS. Give your top priority 1, your second priority 2, etc.

The mean score for each from Round 2 is shown in parentheses for your information.

	2nd round score	Rank
A Partial ring PET compared with dedicated full ring PET in oncology	(5.4)	☐
Comments:		
B Gamma camera PET for staging prior to operative intervention for lung cancer	(5.2)	☐
Comments:		
C Dedicated PET for staging prior to operative intervention for lung cancer	(4.9)	☐
Comments:		
D Gamma camera PET for (a) staging and (b) monitoring response to chemotherapy treatment in lymphoma	(4.9)	☐
Comments:		
E Gamma camera PET for assessing myocardial tissue viability when selecting patients for revascularisation surgery	(4.9)	☐
Comments:		
F Dedicated PET for (a) staging and (b) monitoring treatment response in breast cancer	(4.8)	☐
Comments:		

G Gamma camera PET for (a) staging and (b) monitoring treatment response in breast cancer (4.7) ☐

Comments:

H Gamma camera PET for targeting treatment and monitoring response in head and neck cancer (4.5) ☐

Comments:

I Dedicated PET for targeting treatment and monitoring response in head and neck cancer (4.4) ☐

Comments:

J Dedicated PET for (a) staging and (b) monitoring response to chemotherapy treatment in lymphoma (4.4) ☐

Comments:

K Dedicated PET for assessing myocardial tissue viability when selecting patients for revascularisation surgery (4.3) ☐

Comments:

Health Technology Assessment panel membership

This report was identified as a priority by the Diagnostics and Imaging Panel.

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ISSN 1366-5278