Partial prostate Ablation versus Radical prosTatectomy

PART STUDY

A randomised controlled trial of *P*artial prostate *A*blation versus *R*adical pros*T*atectomy (PART)

Focal-HIFU Training Trial Specific Instruction (TSI)

Relates to OCTRU SOP:	N/A
Version Number:	1.0
Name of Author:	Steffi le Conte
Name of Reviewer:	Mr Tom Leslie, Mr Hash Ahmed
Date Finalised:	08Oct2015

PURPOSE:

This Trial Specific Instruction (TSI) describes the training involved for clinicians performing HIFU in the PART study.

INSTRUCTIONS:

Clinicians will undergo training and proctoring to ensure treatment is delivered to a standard laid down by the reference centre, UCL/UCH.

1. Urologists must read the training manual provided by the manufacturer and/or distributor of the device
2. Urologists must complete any and all compulsory online training modules provided by the manufacturer and/or distributor of the device
3. Urologists without previous HIFU experience or who have not carried out any HIFU procedures for a minimum period of one year will be required to visit a training centre (currently UCH in the UK) and observe at least 3 cases of focal HIFU (on one or two visits).
4. Urologists with previous HIFU experience who have not carried out any HIFU cases for a minimum period of one year or who are below the requisite minimum number of cases per year (currently 12) will be required to undergo proctoring.
5. Proctoring needs to be carried out at on at least the first 5 cases for those urologists who have never carried out HIFU before. This number can be less than 5 proctored cases for those urologists who have carried HIFU previously. The minimum number may be extended at the discretion of the proctor particularly if the period between proctored cases is prolonged (currently 3 months). The advice is to err on the side of caution if there is doubt and extend the proctoring period.
6. The proctored cases and the first 10 cases without proctoring should undergo case review of treatment delivery and early 1-2 week gadolinium contrast enhanced MRI centrally by an expert proctor. This review will be conducted in an iterative manner so treatments subsequent to this can also be reviewed if necessary for ongoing optimisation of treatment delivery.
7. Only approved urologists will deliver the treatment within the PART study. Each approved clinician is required to submit a case audit of the last 10 procedures to be reviewed independently. At the initiation of the trial, only one clinician per site will be proctored until competent to perform focal HIFU independently. If after this point, another clinician from a centre wishes to take part in performing focal HIFU, then this

process must be repeated after for the second urologist – training two urologists in parallel is discouraged due to dilution of cases.

8. Each urologist is currently required to perform at least 12 HIFU cases within a year to maintain independent status.
9. Any re-do focal HIFU treatments performed within the trial period should be proctored.
10. The designation of a proctor is performed by following at least one year of independent status conforming to minimum numbers and is authorized by the manufacturer/distributor on the advice of one expert proctor who will review a selection of cases from the urologist.
11. A 1-2 week mpMRI is required for the first 5 HIFU patients in sites new to performing HIFU. These scans will be centrally reviewed within the Partial Ablation Working Group.

HISTORY:

Version number Date	Significant changes from previous version
V1.0_08Oct2015	Not applicable as this is the 1st issue
	Delete or add rows as applicable.

Partial prostate Ablation versus Radical prosTatectomy

PART STUDY

A randomised controlled trial of *P*artial prostate *A*blation versus *R*adical pros*T*atectomy (PART)

Focal-HIFU Delivery
Trial Specific Instruction (TSI)

Relates to OCTRU SOP:	N/A
Version Number:	1.0
Name of Author:	Steffi le Conte
Name of Reviewer:	Mr Tom Leslie, Mr Hash Ahmed
Date Finalised:	23Jan2017

PURPOSE:

This Trial Specific Instruction (TSI) is intended as a guide for clinicians delivering HIFU in the PART study.

INSTRUCTIONS:

Signed informed consent will be taken for the focal ablation procedure using HIFU therapy. Patients will be admitted on the day of the procedure or the evening before as appropriate. A phosphate enema will be administered on the morning of surgery to ensure an empty rectum. The type of anaesthesia (regional/ general) will be discussed with the patient and depend on the anaesthetic opinion. The type of anaesthesia chosen will aim to eliminate any patient movement during HIFU treatment to avoid any adverse complications and should ideally be general anaesthetic. The patient will be placed in a relaxed lithotomy position. TED stockings and Flowtron boots will be fitted to the patient's legs for prophylaxis against any potential thrombo-embolic event. In accordance with local hospital policy sub-cutaneous heparin may be administered peri-operatively. Unless there are any contra-indications a dose of 120-160mg of intravenous Gentamicin will be given as antibiotic prophylaxis.

Catheter type should be at the discretion of the treating physician.

The HIFU probe and machine will be prepared as per the manufacturer's instructions. The probe is covered with a latex protector and primed with degassed water. The HIFU probe is then lubricated with degassed lubricant gel. About 10 to 20mls of this same gel is placed within the rectum. At this point a gentle dilatation of the anus is sometimes required. This is done using one or two digits. Once this is done the probe is introduced into the rectum as atraumatically as possible. Views of the prostate are then obtained to ensure that the images are of high quality and that the proposed therapy is technically feasible. Once satisfied, a treatment plan will be selected by the operator and the treatment commenced.

The treatment will cover the side of the gland in which the clinically significant lesion(s) have been identified by a combination of MRI and biopsy as follows:

1. Max 50-60% prostate tissue ablation
2. Tissue will be ablated in the entire lobe or quadrant affected (i.e. quadrant or hemiablation of the prostate). This will standardize treatments for the initial phase of the study when the learning curve is most pronounced. These minimum treatment zones can be extended as shown in the diagram. Treatment will reach the urethra and may cross the midline by up to 5-10 millimeters if the disease is close to the midline (minimum 5mm margin over midline) or crosses over (minimum 10mm margin over

midline) (anterior or posterior ‘dog-leg’), provided that the treatment does not cross the para-sagittal plane on that side (usually 10mm from midline.

3. At least one neurovascular bundle must be avoided by ensuring a minimum distance of ablation zone to contralateral NVB of 10mm. This would usually require preservation of the contralateral lobe but the 10mm rule ensures that in patients in whom the dog-leg is used the contralateral NVB avoids damage.
4. When cancer is seen at the extreme apical limit on mp-MRI the patient should be excluded.
5. Absence of clinically significant cancer in untreated areas (>/=3mm cancer core length and Gleason pattern >3) (the maximum number of cores with this amount of cancer core length or Gleason grade should not exceed 50% of the total biopsy volume from that corresponding side. If this number is exceeded, that lobe must be considered as equivalent to clinically significant disease).
6. One redo-HIFU to treated side is permissible, and one out-of-field focal HIFU treatment with a further redo focal therapy is permitted as per current protocols and standard practice for HIFU, if biopsies confirm cancer of a significant nature. Clinically insignificant cancer (Gleason pattern </=3 and MCCL <4mm) should be monitored post-ablation in the treated area.

There is no overall maximum gland size for patients receiving HIFU in PART. However:-

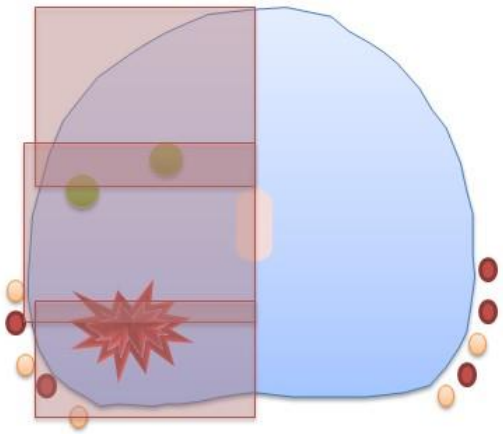
If Anterior tumour: anterior to posterior measurement on MRI must be </=3cm

If Posterior tumour: total gland volume </=60ml.

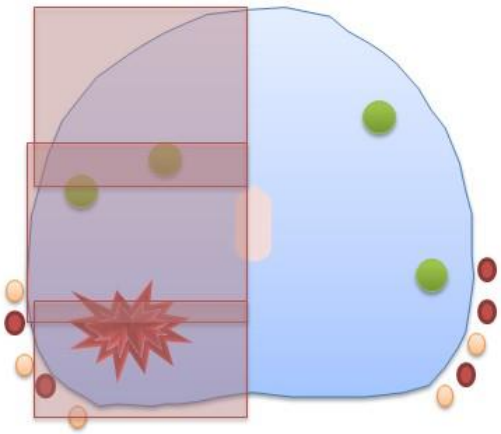
Please be aware that it is difficult to be precise as prostate compression occurs and measurements on MRI will differ from those when the HIFU probe is in situ. Both Mr Hash Ahmed and Mr Tim Dudderidge are happy to review potential PART patient scans to ensure HIFU suitability.

The following diagrams demonstrate the types of treatments that are possible within these rules – see overleaf.

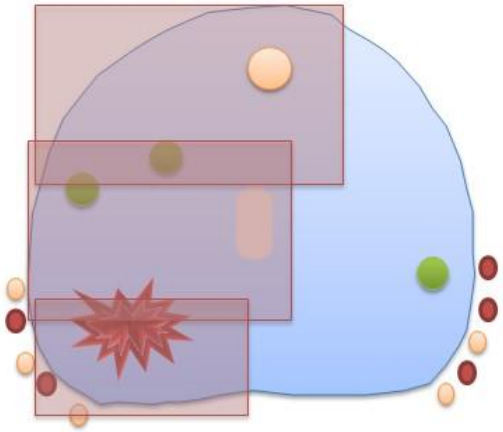
Hemiablation: Unilateral multifocal cancer



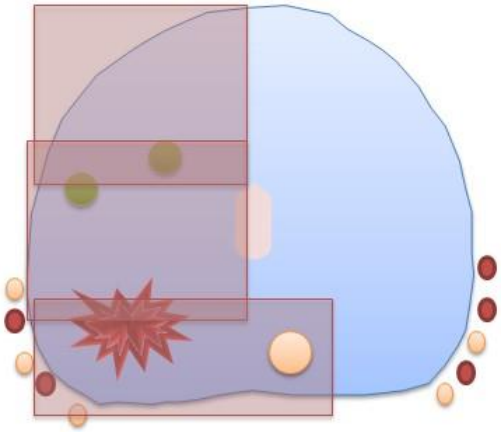
Hemiablation: Bilateral with insignificant foci on contralateral side



Hemiablation with anterior extension: Bilateral with insignificant foci on contralateral side allowed



Hemiablation: Bilateral with insignificant foci on contralateral side with insignificant foci allowed in untreated area



HISTORY:

Version number Date	Significant changes from previous version
V1.0_23Jan2017	Not applicable as this is the 1st issue