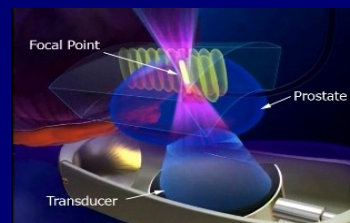


INDEX Trial



VOLUME 1, ISSUE 1

NOVEMBER 2011

SPECIAL POINTS OF INTEREST:

INDEX Trial now open for recruitment!

The aims of the INDEX trial.

Focal Therapy Outcomes so far

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INDEX Now Recruiting!

INDEX is a multi-centre prospective single arm intervention trial evaluating focal therapy for localized prostate cancer. The trial will use High Intensity Focused Ultrasound (HIFU).

INDEX aims to recruit and treat a total of 140 men with focal therapy and follow them for a period of 3 years.

The trial is currently due to run at 6 UK sites:

University College London Hospitals NHS Foundation Trust

PI: Professor Mark Emberton and Mr Hashim Uddin Ahmed

Oxford Radcliffe Hospitals

NHS Trust

PI: Mr Tom Leslie and Mr Simon Brewster

Basingstoke and North Hampshire NHS Foundation Trust, PI: Mr Richard Hindley

Imperial College Healthcare NHS Trust, PI: Mr Matthias Winkler

Royal Marsden NHS Foundation Trust, PI: Mr Chris Ogden, Dr Chris Parker and Dr Nick Van As

University Hospitals Bristol NHS Foundation Trust, PI: Mr Raj Persad

The trial opened at UCLH at the end of June 2011. To date, fourteen patients have been recruited and consented, and eight of these patients have received focal HIFU treatment.

It is expected that the other centres will be open for recruitment in the next few weeks.

The trial is sponsored by University College London. It is supported by the National Cancer Research Network. We are very grateful to US HIFU, manufacturers of the Sonablate 500 HIFU device based in USA, for a grant to support the trial.

INDEX Aims

Men who have localized prostate cancer can choose to have a number of treatments to treat the whole prostate, including radiotherapy and surgery. Active surveillance with selective delayed intervention can also be offered in many men with low-intermediate risk cancer. Those men who have treatment to the whole prostate have greater cer-

tainty that all of the cancer is treated. However, treatment to the whole prostate can affect sexual function (poor erections), urine control (urine leakage requiring pads) and can cause back passage problems (bleeding, diarrhoea or pain).

An alternative approach that is being explored within trials is to treat only the can-

cer, and not the whole prostate - so-called 'focal therapy'. There are a number of treatment modalities that can be used to treat cancer in a focal manner. The one selected for this trial is HIFU. MRI scans and template prostate mapping (TPM) biopsies will be used to localise cancer and assess success after focal therapy.



MRC

Medical
Research
CouncilPELICAN
cancer foundationProstate
ActionPROSTATE
CANCER
RESEARCH CENTRESt Peter's Trust
Kidney | Bladder | Prostate | ResearchUSHIFU
High Intensity Focused Ultrasound

What Are The Aims Of INDEX?

The aims of INDEX are several fold. They are to determine whether focal therapy using HIFU is safe, reproducible, carries fewer side-effects with less impact on quality of life and has acceptable cancer control rates in the short to medium term.

We will be treating 'clinically significant' or 'clinically important' cancers, with the option of leaving small 'clinically unimportant' cancer lesions untreated and under close surveillance. The reasons behind this strategy is that there is evidence to suggest that these clinically insignificant lesions are unlikely to cause harm to a man in his lifetime, if left untreated. The INDEX study will provide us with information on the behaviour of these untreated lesions, as they will be very closely monitored.

The **primary objectives** of the INDEX trial are:

1. To determine the proportion of men who are free from any prostate cancer in the area treated with HIFU AND are also free from any clinically significant prostate cancer in the untreated area at 36 months

after receiving focal therapy using HIFU

2. To determine the proportion of men who are free from clinically significant prostate cancer in the area treated with HIFU AND are free of clinically significant prostate cancer in the untreated area 36 months after receiving their focal therapy using HIFU.

These primary objectives will be assessed on (template) biopsies taken 36 months after HIFU treatment.

The **secondary objectives** include determining the rate of sexual, urinary and bowel problems after focal HIFU therapy. These side-effects will be assessed using validated patient questionnaires. We will also evaluate tests that could both help us to more accurately diagnose prostate cancer in the future, and tell us how successful the treatment has been. These include multi-parametric MRI and novel ultrasound imaging as well as serum and urine biomarkers, PSA tests and other biomarkers.

Focal Therapy Outcomes So Far...

There have been few prospective ethics committee approved trials worldwide that have reported outcomes after focal therapy for localized prostate cancer. A number of case series have reported encouraging outcomes using different treatment energy sources, such as cryotherapy (freezing), laser therapy, and brachytherapy (radiation). At UCLH, we have three focal HIFU trials using HIFU on the NCRN portfolio. These have treated 20 (Hemi-HIFU), 41 (Focal-HIFU) and 56 (Lesion Control HIFU) men. So far, two of these have reached completion. The first trial involved treatment of half of the prostate ('hemiblation'). The results were published in The Journal of Urology, volume 185, issue 4, in April 2011.

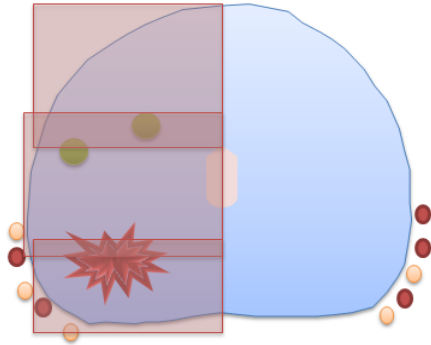
A total of 20 men underwent HIFU hemiblation. The mean age was 60.4 years with mean prostate specific antigen 7.3 ng/ml. Of the 20, 25% had low risk and 75% had intermediate risk cancer. Return of erections sufficient for penetrative sex oc-

curred in 95% of men (19 of 20). In addition, 90% of men (18 of 20) were pad-free, leak-free continent while 95% were pad-free. Mean prostate specific antigen decreased by an average of 80% to 1.5 ng/ml at 12 months. Of the men, 89% (17 of 19, 1 refused biopsy) had no histological evidence of any cancer, and no evidence of high volume or Gleason 7 or greater cancer in the treated lobe on follow-up biopsies 6 months after treatment. In addition, 89% of men achieved the trifecta status of pad-free, leak-free continence, erections sufficient for intercourse and cancer control at 12 months.

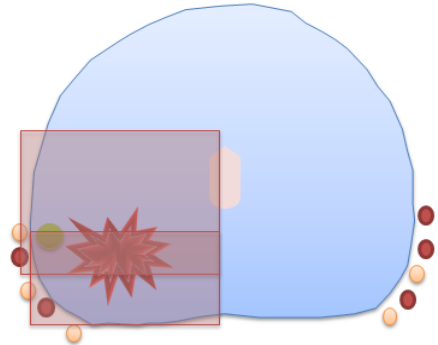
These results are encouraging. The INDEX study will now provide us with results over a longer time period in a institutional setting across a number of NHS centres. There will therefore be close monitoring and quality control of all interventions (MRI and TPM conduct and reporting and focal HIFU conduct).

Focal Therapy Rationale Diagrams

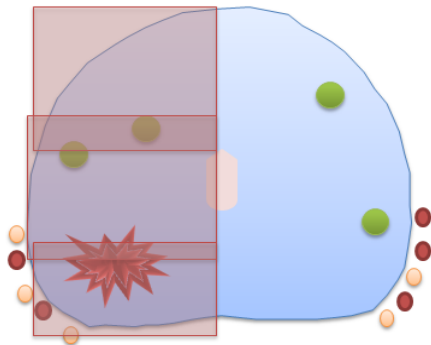
Hemiablation: Unilateral multifocal cancer



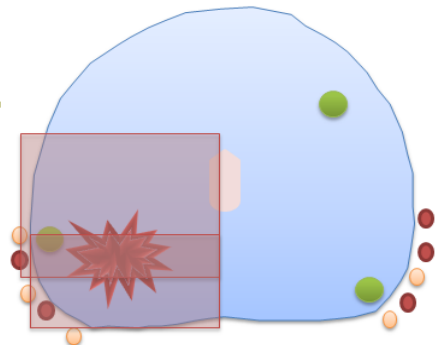
Quadrant Ablation: Unilateral/unifocal cancer



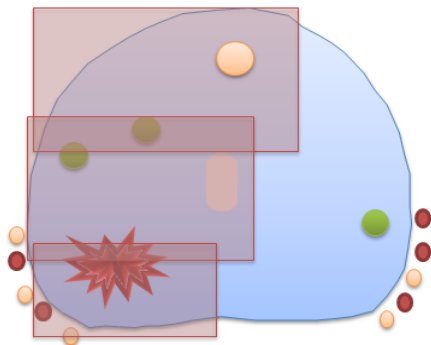
Hemiablation: Bilateral with insignificant foci on contralateral side



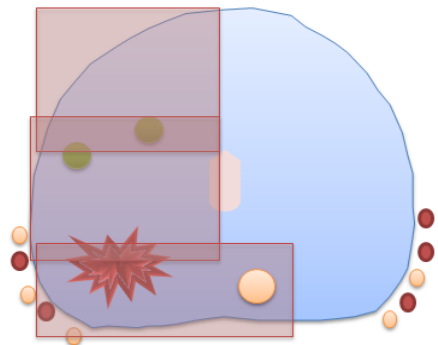
Quadrant Ablation: Unilateral/unifocal with insignificant foci in contralateral side



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



The diagrams above show the types of treatment that will be done in the INDEX trial. The type of treatment each patient will have is decided after MRI and template mapping prostate biopsies. In this study low risk cancers are considered clinically unimportant and therefore will not be treated. Medium and high risk areas will be treated.

This is what the areas mean in the diagram:

-  Low risk area of cancer (Gleason grade 3+3, 3mm or less of cancer in any one biopsy) .
-  Medium risk area of cancer (Gleason grade 3+4, 4-5mm of cancer in any one biopsy).
-  High risk area of cancer (Gleason grade 4+3, 6mm or more of cancer in any one biopsy) .

The shaded areas show the treatment areas. The white and red circles around the prostate represent the nerves and blood vessels that surround the prostate.

News and Publications

BREAKING NEWS!

Oxford and Basingstoke are both now open for recruitment!

UCLH held a successful induction day for research nurses from the centres participating in INDEX on Friday 7th October 2011. The day covered focal HIFU trials, HIFU treatment, INDEX eligibility criteria, post-operative trial flow and more. We have already held 2 successful Radiology induction days and a Pathology induction day.

Links

www.ushifu.com
www.prostate-cancer-research.org
www.prostate-cancer.org.uk
www.pelicanancer.org
www.cancerresearchuk.org
www.clinicaltrials.gov
www.prostateaction.org.uk

You can find the entry criteria for INDEX on the UKCRN (UK Clinical Research Network) database:

<http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=9945>

INDEX is also registered in the clinicaltrials.gov US NIH clinical trials registry at <http://clinicaltrials.gov/ct2/show/NCT01194648>

Publications

Ahmed HU, Pendse D, Illing R, Allen C, van der Meulen JH, Emberton M. Will focal therapy become a standard of care for men with localized prostate cancer? *Nat Clin Pract Oncol.* 2007 ;4(11):632-42.

Ahmed HU, Freeman A, Kirkham A, Sahu M, Scott R, Allen C, Van der Meulen J, Emberton M. Focal therapy for localized prostate cancer: a phase I/II trial. *J Urol.* 2011 Apr;185(4):1246-54.

Ahmed HU. The index lesion and the origin of prostate cancer. *N Engl J Med.* 2009

Contact Details

If you would like more information about the purpose of the INDEX Trial, what happens to patient's who want to take part in the trial or the conduct of the trial or would like to speak to one of the INDEX team then please contact us on the numbers below:

Professor Mark Emberton, Consultant Urological Surgeon/ INDEX Chief Investigator
 Tel: 020 3447 9194 (Secretary)

Mr Hashim Uddin Ahmed, MRC Clinician Scientist.

Email: hashim.ahmed@ucl.ac.uk

Miss Louise Dickinson, Clinical Research Fellow/ INDEX Trial Co-Ordinator

Tel: 020 3447 9194 (Via Professor Emberton's Secretary)

Email: Louise.Dickinson@uclh.nhs.uk

Helena Stone, Clinical Research Nurse/ INDEX Trial Nurse Tel: 020 3447 7364

Mobile: 07527 961138

Email: helena.stone@uclh.nhs.uk

Neil McCartan, HIFU Trials Co-Ordinator/ INDEX Trial Manager Tel: 020 3447 9404

Email: neil.mccartan@uclh.nhs.uk



INDEX

UKCRN study number is

9945 and our

Clinical Trials

Gov number

is:

NCT01194648

Men who may be suitable for INDEX are those with

localized prostate cancer

Gleason 4+3 or less

PSA \leq 15

Unilateral cancer on

TRUS biopsy

Bilateral disease on

TRUS biopsy with low

risk cancer on one

side