HIFU: Ready for Prime Time?

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Director North Florida Research Institute
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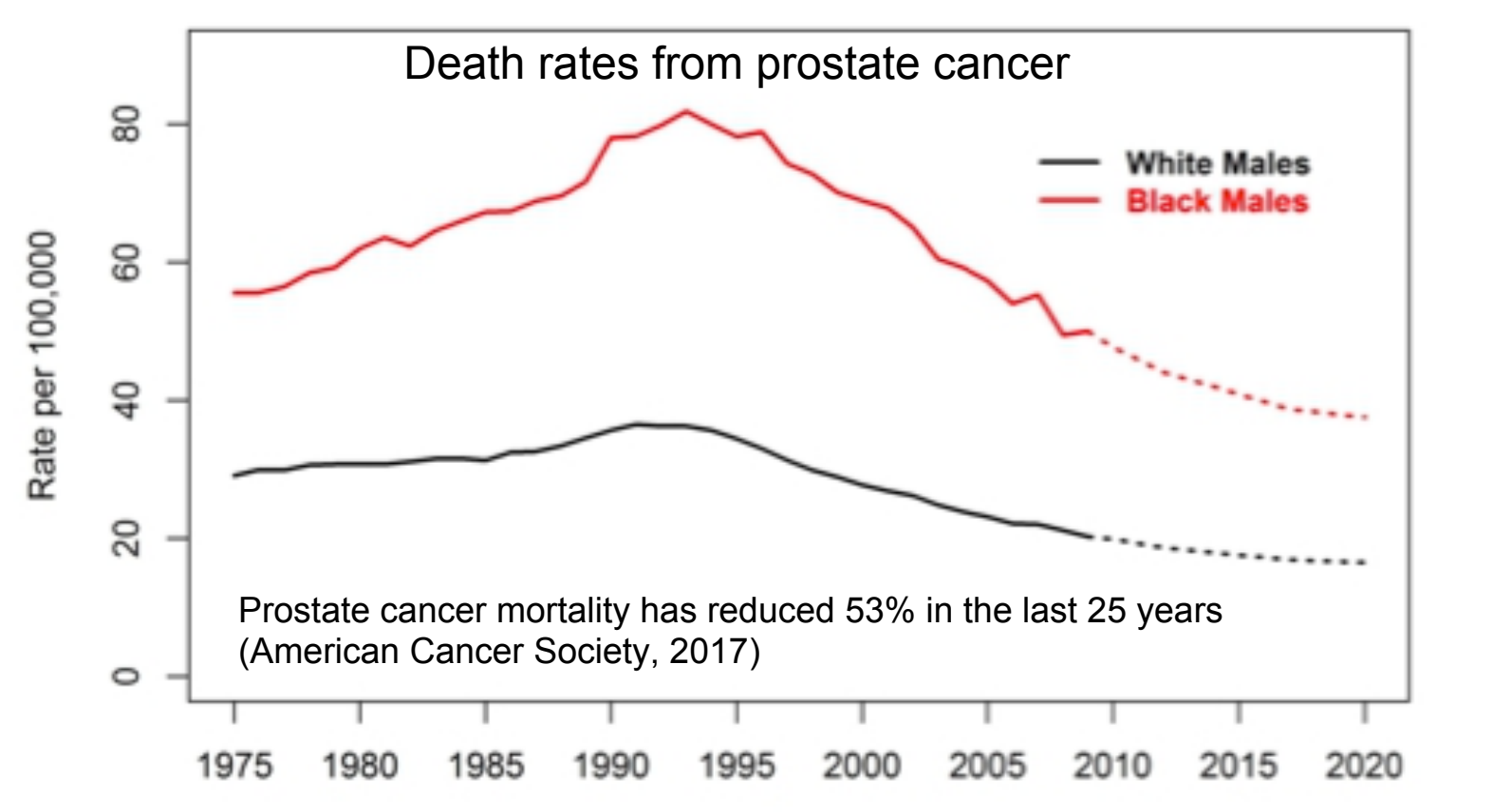
Paradigm Shifts in Prostate Cancer

- Paradigm shifts are profound changes that occur once in several decades in management of disease.
- “Revolution” in scientific thinking
- PSA revolutionized prostate cancer diagnosis and treatment in the late 80s and 90s
- 100s of papers published for and against PSA
- However, PSA took hold & clinicians enthusiastically embraced it
- Along with PSA, several other developments occurred
- There was an increase in diagnosis of prostate cancer and we changed the way we do biopsies

- PSA landmark discovery of 20th Century - American Association of Cancer Research
- Revolutionized diagnosis of prostate cancer and has shifted stage at diagnosis from T2, T3 to T1c
- Prior to PSA 5 year survival (66%)
- Currently 5 year survival (99.9%)

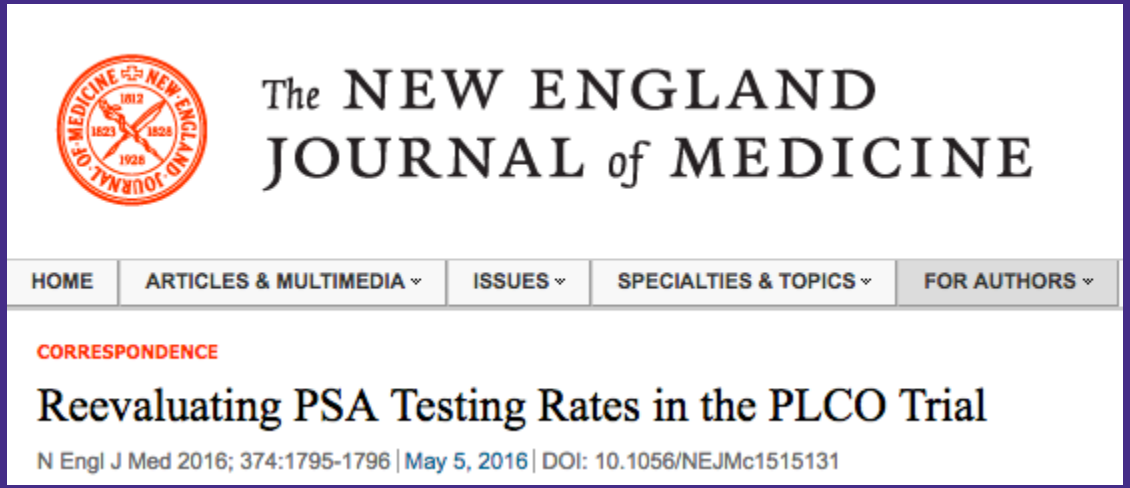
Epidemiologic Data- PSA Reduces Death Rate



The PSA Controversy-Randomized Trials

- Widespread use of PSA is driven by assumption that PSA screening reduces death rates
- Best data that PSA reduces death rate is from clinical trials
- Two randomized clinical trials have been done
- The European Trial (ERSPC): PSA reduces death rate by 21% at 13 years of f/u.
- Overdiagnosis: 27 men diagnosed to prevent 1 death.
- The PLCO trial (USA): Found no evidence of improved death rate. **However, results of this trial invalidated by re**

PLCO trial - N Engl J Med 2009; 360:1310-1319, March 26, 2009
ERSPC trial - N Engl J Med 2009; 360:1320-1328, March 26, 2009. ERSPC Lancet 2014
N Engl J Med 2016; 374:1795-1796, May 5, 2016



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CORRESPONDENCE

Reevaluating PSA Testing Rates in the PLCO Trial

N Engl J Med 2016; 374:1795-1796 | May 5, 2016 | DOI: 10.1056/NEJMc1515131

JE Shoag, S Mittal, New York Presbyterian, Jim HU Weill Cornell University

- “90% of controls in the PLCO trial had at least 1 PSA test before or during the trial.”
- “Men in control group had more testing than intervention arm.”
- “The contamination in the PLCO trial makes it unreliable to determine role of PSA on prostate cancer death rate.”

HIFU SOLUTION

PSA Reduces Death Rate

As of now, there is only 1 randomized trial of screening PSA vs. no PSA - The ERSPC trial

182,388 men - 900 cancer deaths - 13 year F/U

PSA testing every 2-4 years vs. standard care no PSA

Men aged 55-69 years at start of trial

PSA screening arm shows 21% reduction in prostate cancer death at 13 years

27 men need diagnoses to prevent 1 death

With further F/U, 5 men needed to diagnose to prevent 1 death

Schröder et al. N Engl J Med 2009; 360:1320-1328, March 26, 2009
Schröder et al. Lancet Volume 384, No. 9959, p2027–2035, 6 December 2014

Paradigm Shifts in Prostate Cancer - Increasing Costs

- Last 10 years, a second set of paradigm shifts have occurred
- This has been driven by tremendous increase in prostate cancer diagnosis and side effects of treatment
- The number of men over age 65 is expected to more than double from 40 million in 2010 to 88 million in 2050
- Medicare is under seige to cut costs
- There is an increasing uproar of complaints from many quarters that prostate cancer treatment is causing significant harms with escalating costs

Surgery and Radical Radiation is Not Preferred Anymore

- The sledgehammer approach of “war on cancer” and radical prostatectomy and radiation for every diagnosed cancer is causing escalating costs and morbidity
- Short term morbidity of surgery is 20% & occasional deaths from cardiac, respiratory, DVT, blood transfusion and others
- Long term morbidity is consistently 70-80% ED and 10-17% incontinence
- Long term studies started over 10 years ago have shown that watchful waiting and active surveillance result in 95-98% survival at 10-15 years - Pivot, ProtecT trials

USPSTF and Harms of Abandoning PSA Screening

- Because of the recognition of the harms of surgery and overdiagnosis by PSA, USPSTF declared in 2012 that PSA is not recommended for routine screening in men over 50
- 2 Studies in JAMA 2016 found that since USPSTF recommendations, PSA screening has declined by 16%
- Barocas in 2015 reported **a drop of 28% in intermediate risk cancer and a drop of 23% in high risk cancer diagnosis** after USPSTF
- In June 2016, researchers at Northwestern University in Chicago found annual incidence of **metastatic incidence increased 72% in 2013 as compared to 2004**

Jemal et al. JAMA Aug 2016; Barocas et al J Urol Dec 2015
Weiner et al Prostate Cancer Prostatic Dis. 2016 Jul 19. doi: 10.1038/pcan.2016.30

How to Reduce Overdiagnosis and Overtreatment

- Smart screening techniques of PSA recommended by NCCN, ASCO, and ACS can reduce overdiagnosis
- The 4K Test- improves PSA specificity for aggressive cancer
- mp-MRI- detects aggressive cancer, reduces overdiagnosis
- Use of 4K Test and mpMRI can reduce biopsy rate by 1/3 without missing significant cancers
- HIFU Therapy- a useful compromise between AS and radical treatment- has less side effects

Another Reason For Minimally Invasive Therapy Prostate Cancer Deaths are Increasing in Older Men

- Men over 75 screened less due to wrong perception of life expectancy
- Men 75 or older form **16% of male population but 26% of prostate cancer, 48% of metastatic disease, and 53% of deaths**
- Geriatric specialists - **health status more important than age, healthy man at 75 will live 10 yrs and should be treated**
- **Older men, however, cannot have surgery. HIFU may be a better option than radiation due to less side effects**

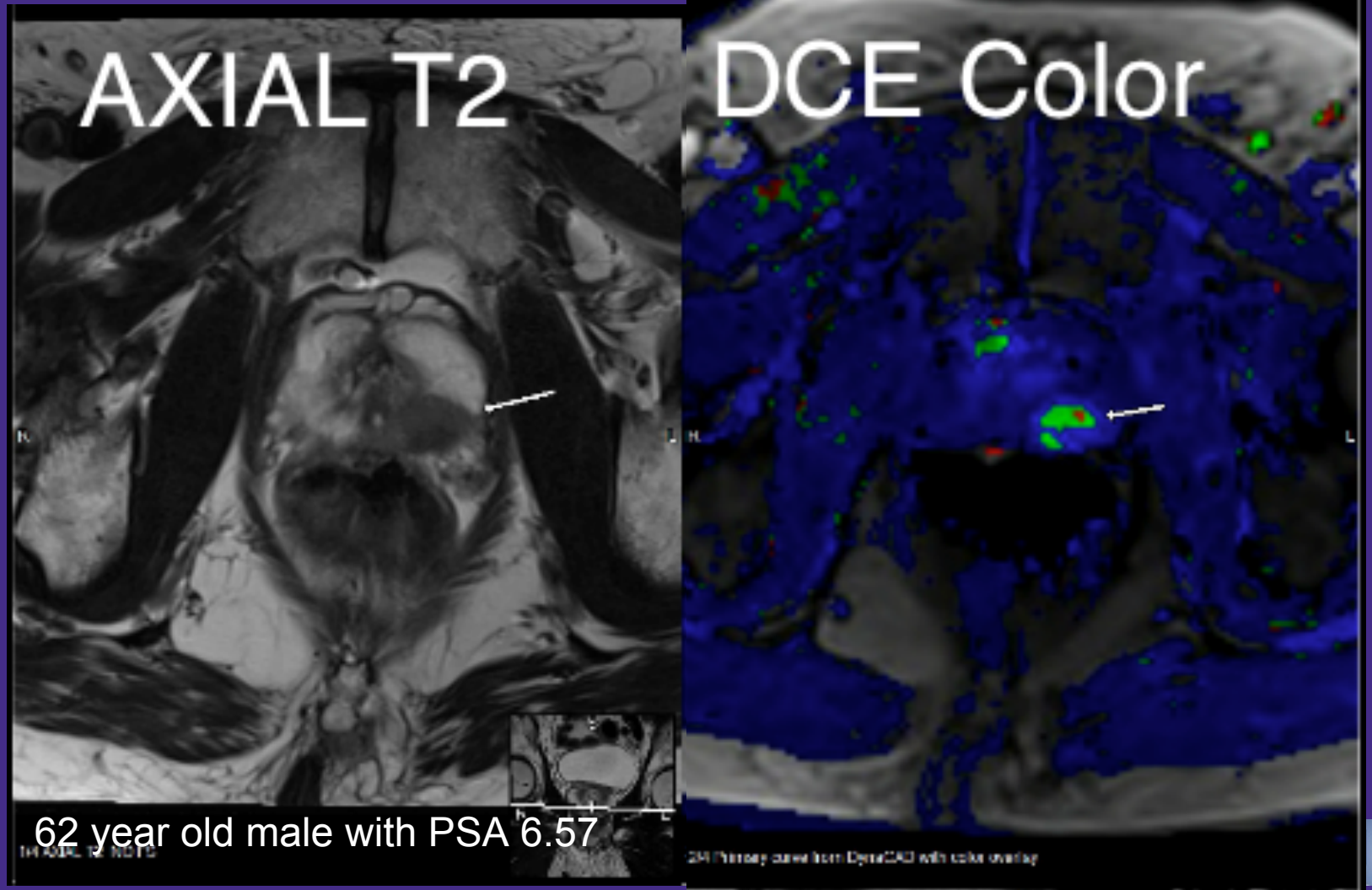
J Natl Cancer Inst Monogr. 2014 Nov;2014(49):265-74. doi: 10.1093/jncimonographs/lgu021.

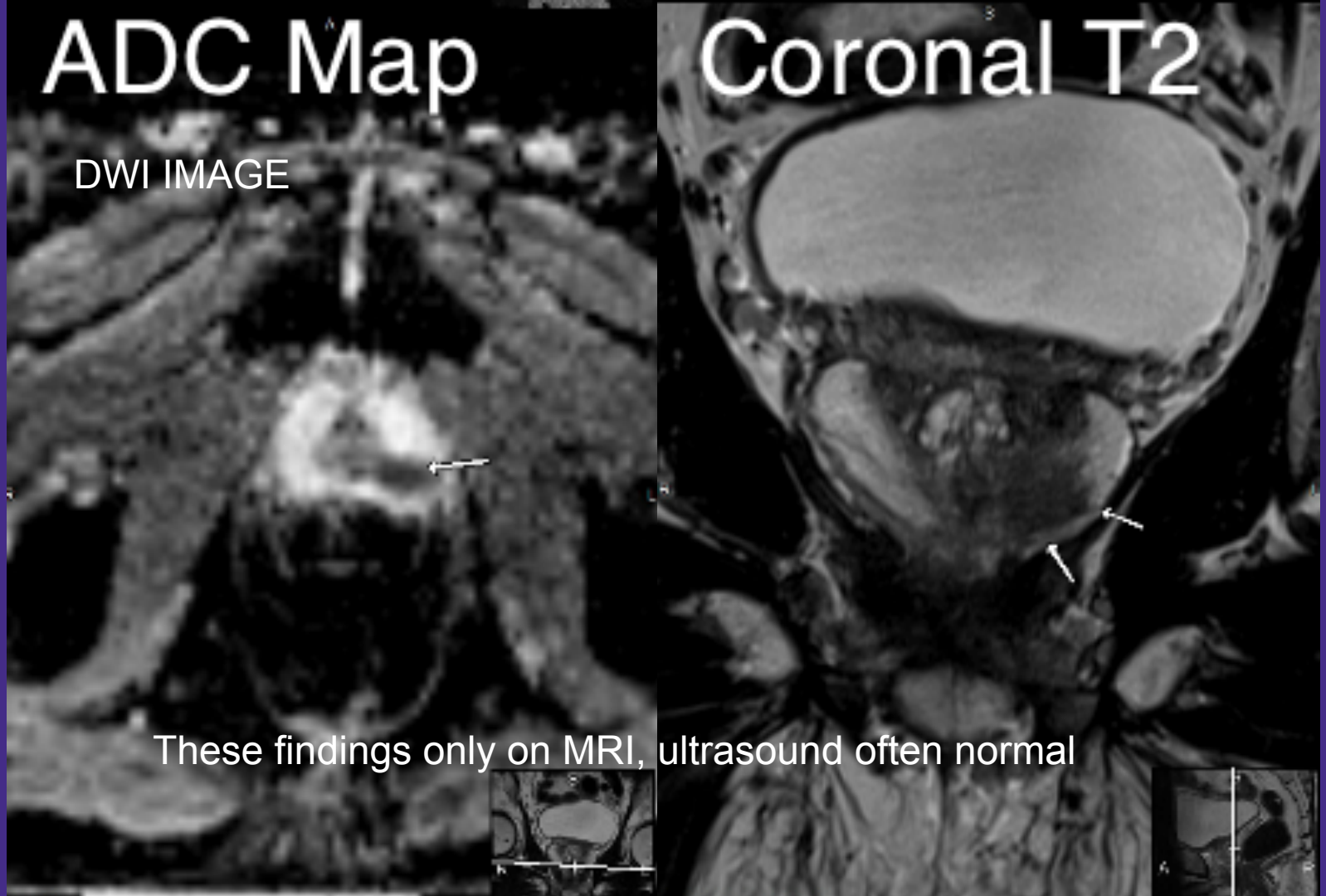
HIFU SOLUTION

Paradigm Shifts in Prostate Cancer Minimally Invasive-HIFU

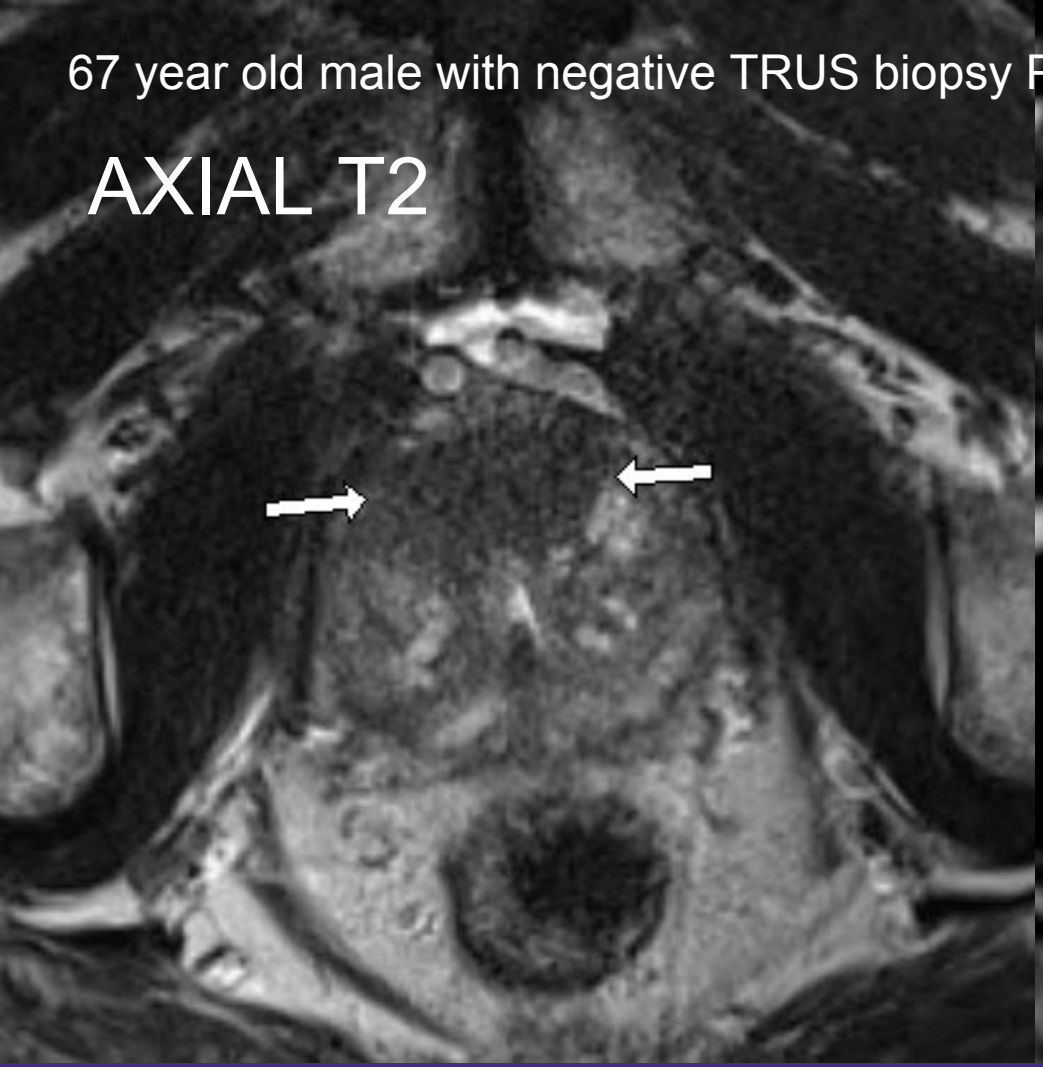
- The US FDA approval of high intensity focused ultrasound (HIFU) in October 2015 is starting to have a major impact in use of minimally invasive therapy for prostate cancer
- HIFU: the first treatment available in office with low side effects and can be used for focal Rx hemi-ablation, or whole gland treatment
- HIFU is also causing a re-assessment in other therapies such as focal cryotherapy and newer treatments such as focal radiation, IRE, and others

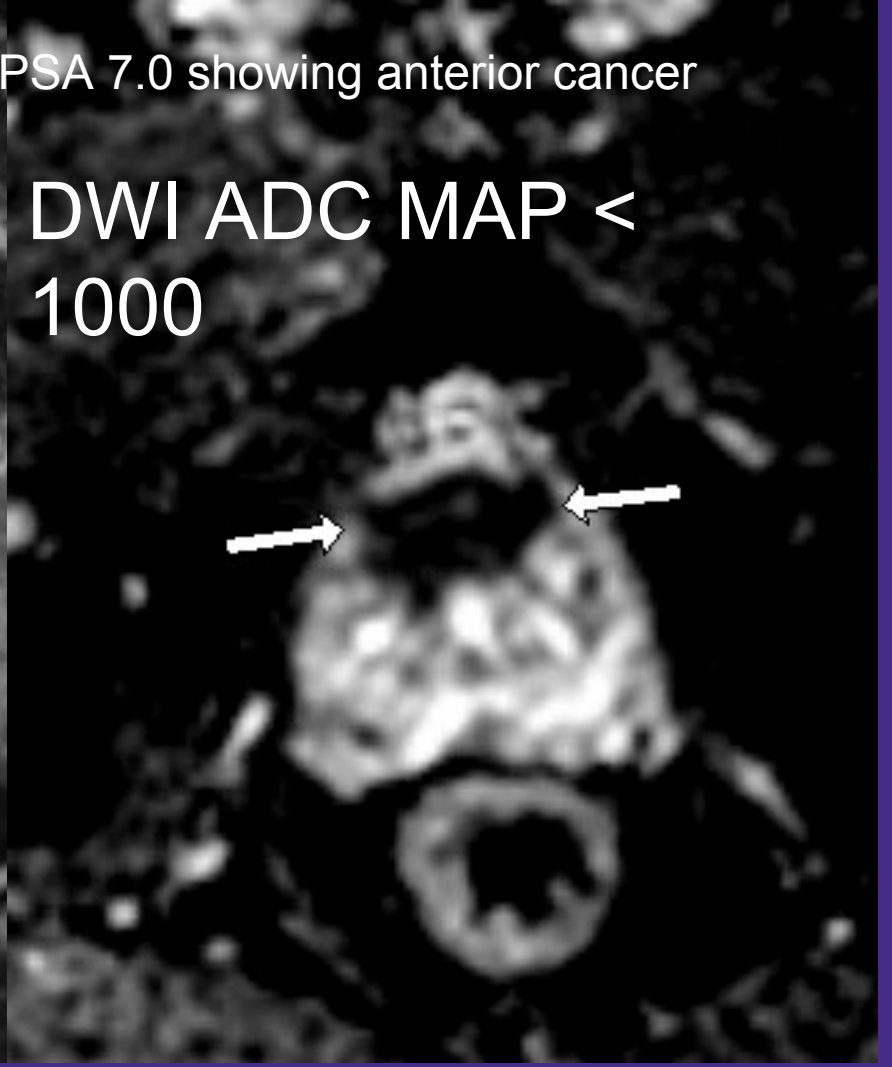
HIFU SOLUTION


AXIAL T2
DCE Color
62 year old male with PSA 6.57


ADC Map
DWI IMAGE
Coronal T2
These findings only on MRI, ultrasound often normal

67 year old male with negative TRUS biopsy PSA 7.0 showing anterior cancer

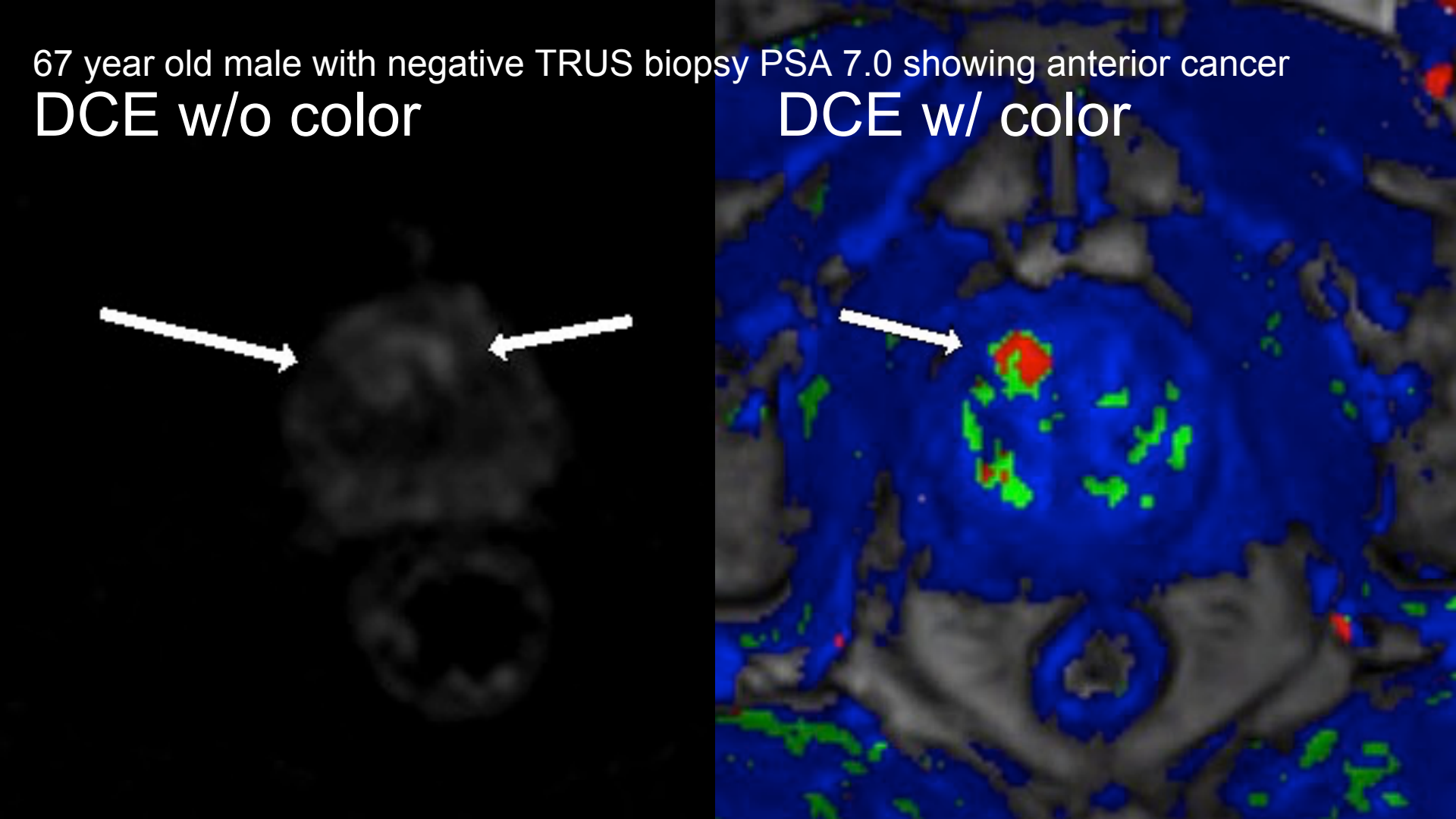




67 year old male with negative TRUS biopsy PSA 7.0 showing anterior cancer

DCE w/o color

DCE w/ color



HIFU: a technical solution to a clinical problem

- There is an unmet need for the newly diagnosed patient who, in absence of HIFU, is faced with deciding between surveillance and radical therapy
  - Whole gland HIFU is a less radical approach with similar oncologic outcomes but less morbidity
  - Hemiablation HIFU errs on the side of safety without burning any bridges for future intervention

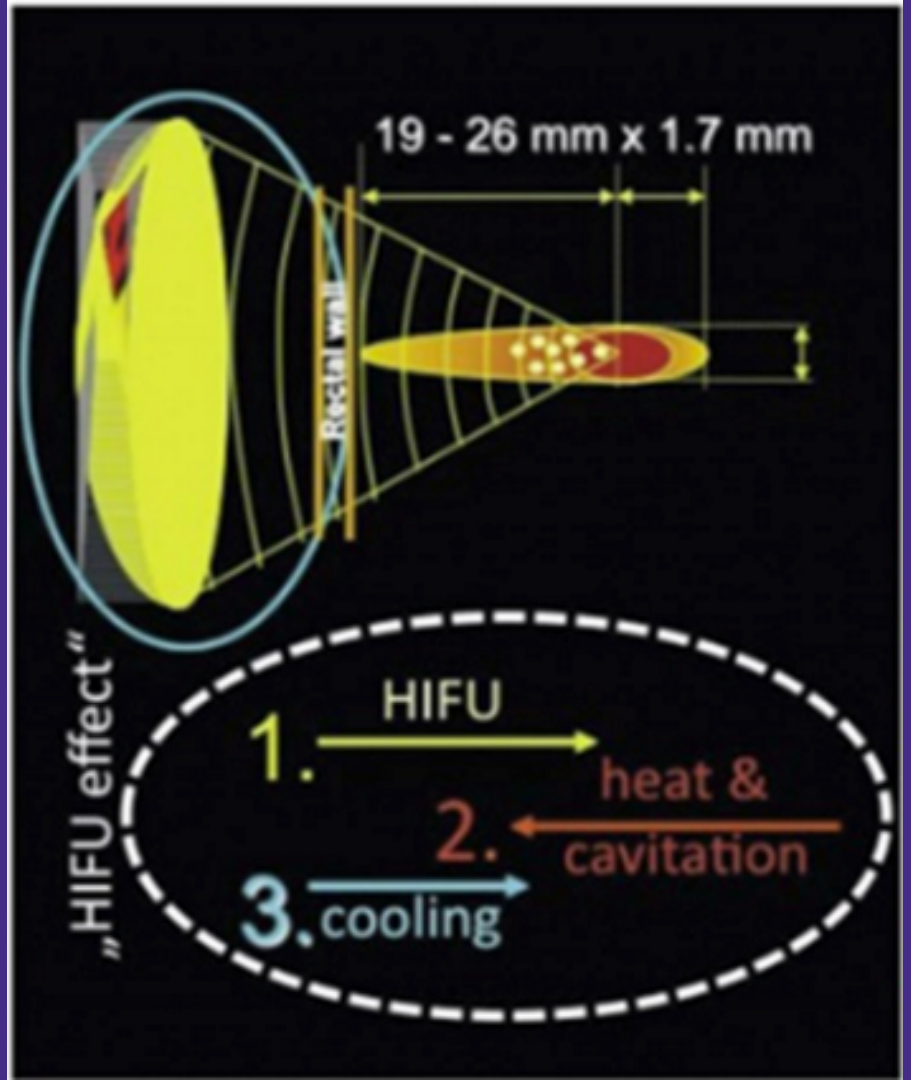
HIFU SOLUTION

Principles of HIFU - Focused High Intensity US

- As acoustic wave moves through tissue, it is absorbed and converted to heat
- With focused beams, lower temperature heat can pass through normal tissue avoiding rectal damage
- Beam is cigar shaped
- Tissue damage is a function of temperature and time of exposure
- Temperature achieved is 80-90°C
- Higher temperatures avoided to prevent boiling and microexplosions

Principles of HIFU (Cont'd)

- Ultrasound beams focused on precisely defined portion of tissue
- Robotic arm moves ultrasound beam a few mm at a time to treat a portion or entire prostate
- Anesthesia only required to prevent patient movement
- Imaging transducer will track the treatment areas as they are being treated

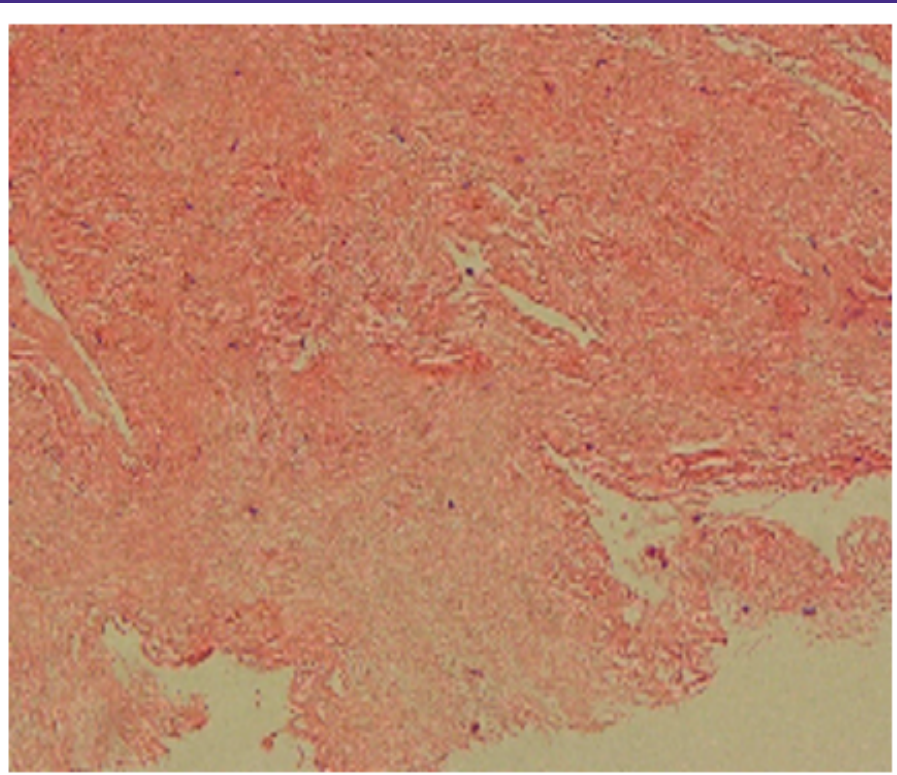


Creation of Lesion Involves Two Main Effects:

1. **Thermal effect** related to tissue temperature
2. **Cavitation effect** caused by air bubbles which absorb acoustic energy and increases tissue heating. Temperature rises to between 80-90℃

HIFU SOLUTION

HIFU Tissue Effects



Time Frame of Tissue Destruction

Immediate:

Coagulation Necrosis

After 7 Days:

Inflammatory Response

After 14 Days:

Induction of Fibrosis

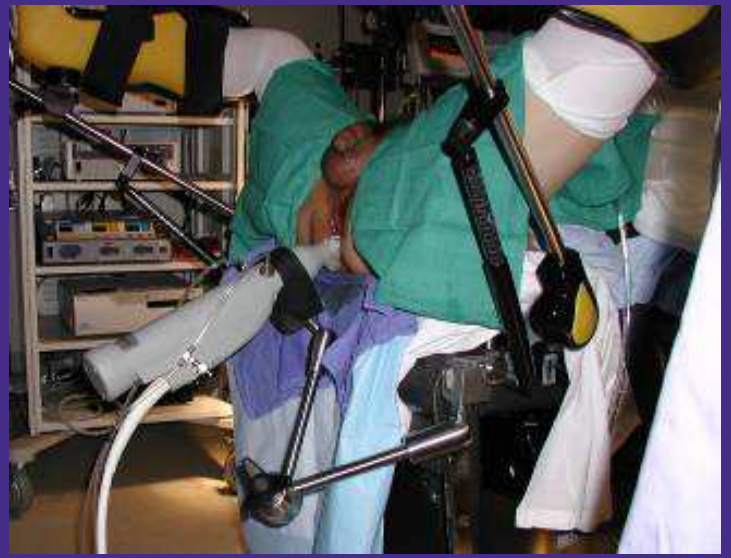
HIFU SOLUTION

HIFU Technical Considerations

Two devices FDA Approved for Ablation of Prostate Tissue October 2015

Ablatherm Robotic HIFU

Sonablate 450



FDA Clearance: HIFU Intended Use

510(k) Intended use: The Ablatherm® Integrated Imaging device is indicated for transrectal high intensity focused ultrasound (HIFU) ablation of prostate tissue.

AUANEWS February 2016 15

FDA Approves HIFU as a Prostate Ablation Tool

Jonathan P. Jarrow, MD
Silver Spring, Maryland

John H. Baxley, MS
U.S. Food and Drug Administration
Washington, DC

Two high intensity focused ultrasound (HIFU) devices were recently granted marketing authorization by the U.S. Food and Drug Administration (FDA) not as a treatment for prostate cancer, but as tools to ablate prostatic tissue. A manufacturer of a medical device must demonstrate with reasonable assurance that the device is effective and safe for its intended use in order to market it in the United States. Thereafter, the promotional activities by the manufacturer are limited to the approved indication in the labeling of that medical product.

For HIFU the manufacturers were able to provide reasonable assurance that the device could effectively ablate the targeted prostatic tissue. A good analogy is the scalpel. A scalpel is a tool to cut tissue but is not approved to treat specific diseases (eg prostate cancer or aortic aneurysm). While the studies used to establish the tool indication for the 2 marketed HIFU devices were performed in a patient population with prostate cancer, the evidence accumulated in those studies was insufficient to support a prostate cancer treatment indication.

The manufacturers of the 2 marketed devices had previously submitted applications seeking an indication for the treatment of localized prostate cancer. SonaCare Medical submitted to the FDA an interim analysis of an ongoing single arm trial of whole gland ablation using the Sonablate 450 HIFU System™ in 116 patients with recurrent prostate cancer following external beam radiation therapy. The success rate was 50% based on the preplanned analysis of effectiveness, which was the percentage of patients with a prostate specific antigen (PSA) nadir 0.5 ng/mL or less and a negative prostate biopsy 12 months after whole gland ablation. The safety profile was similar to that observed in patients treated with surgery or cryotherapy in the same post-radiation setting.

EDAP Technomed submitted to the FDA the results of a failed (due to lack of accrual) nonrandomized trial comparing whole gland ablation for patients with low risk localized prostate cancer using the Ablatherm Integrated Imaging HIFU System™ (135 patients) to cryotherapy (5 patients). The biochemical relapse-free survival using Phoenix criteria and the cumulative negative biopsy rate at 2 years were 90.5% (95% CI 85, 96) and 72%, respectively, for the HIFU arm. The safety profile of this device was comparable to that of radical prostatectomy in a previously untreated patient population.

Both applications were presented to FDA advisory panels and both panels concluded that the studies did not provide reasonable assurance that whole gland ablation with these HIFU devices resulted in long-term direct patient benefit.[1,2] Nevertheless, the short-term results using surrogate markers and safety profile were comparable to available therapies for these specific patient populations.

In this particular situation the evidence necessary to establish a tool indication for ablation of prostatic tissue is different and less burdensome than the evidence necessary to establish that these technologies offer an effective treatment for a specific disease. However, a tool indication is not granted when it would be inappropriate because it would put patients at too much risk. In the case of ablation of prostate tissue the manufacturers were able to demonstrate that the devices ablate the targeted tissue with reasonable safety. In contrast, a treatment indication that these medical devices effectively treat patients with prostate cancer requires clinical data that provide reasonable assurance of a direct clinical benefit.

A direct clinical benefit may not be difficult to achieve for a disease that has a high rate of short-term morbidity or mortality, which is not the case for prostate cancer. It takes large numbers of patients and many years of study to demonstrate a survival advantage, or even a metastasis-free survival advantage, in a population with localized prostate cancer. Unfortunately, there are no reliable surrogate markers that reasonably predict the long-term benefits of metastasis-free or overall survival of patients with localized prostate cancer. Both FDA advisory panels concluded that short-term (1 to 2 years) biochemical findings and negative prostate biopsies do not reliably predict long-term direct clinical benefit.

The short-term data on PSA, prostate volume and prostate biopsy findings could support a tool type of indication (ablation of the prostate) and the FDA approved marketing of these HIFU devices as a means to promote further evolution of the technology and foster clinical evidence generation. The manufacturers submitted new applications for which the FDA reviewed labeling of both devices states that they are "indicated for transrectal high intensity focused ultrasound (HIFU) ablation of prostatic tissue."

The FDA has the responsibility of protecting patients and ensuring that a device provides reasonable assurance of safety and efficacy for its intended use. However, it is up to physicians, patients and professional societies to determine the treatment of individual patients with prostatic disorders based on the best clinical evidence. The clinical evidence generated and submitted to the FDA does not support approval of HIFU for the specific treatment of prostate cancer.

1. July 30-31, 2014: Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee Meeting Announcement. Available at http://www.fda.gov/AdvisoryCommittees/CalendarOfMeetings/ucm404757.htm
2. October 1, 2014: Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee Meeting Announcement. Available at http://www.fda.gov/AdvisoryCommittees/CalendarOfMeetings/ucm418677.htm

"A good analogy is the scalpel. A scalpel is a tool to cut tissue but is not approved to treat specific diseases (e.g., prostate cancer or aortic aneurysm)."

Jonathan Jarrow, MD
FDA Clinical Reviewer of Ablatherm

John Baxley, MS
FDA Lead and Engineering Reviewer of Ablatherm

HIFU SOLUTION

Unique Attributes of Ablatherm HIFU

Three dimensional robotic motion

- 3 translations and 2 rotations
- Image recognition software detects rectal wall and fine tunes the probe position

Integrated ultrasound transducers avoid compromise

- 7.5 MHz imaging
- 3 MHz ablation

Patented Ablasonic™ fluid for consistent fluid transmission

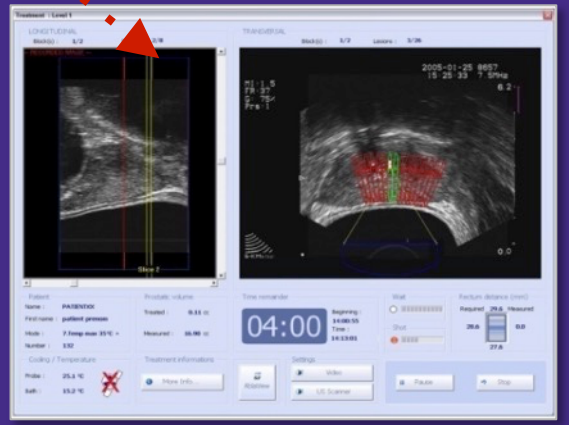
25cc/hour ablation speed

HIFU SOLUTION

Ablatherm Safety Features

Treatment module:
Patient's bed and
Technology carrier

Control module:
Treatment strategy planning
and monitoring



Endorectal applicator:
Therapy transducer (3MHz)
Imaging transducer (7.5MHz)

HIFU SOLUTION

Clinical Versatility of HIFU

Ablatherm HIFU has proven long term clinical data on more than **50,000** treatments with different approaches and patients populations:

Whole Gland Ablation

From Low Risk to locally advanced disease

Focal / Partial Ablation

For targeted disease in primary care

For targeted recurrence in salvage approach

Salvage Curative Option

From whole gland salvage to focal salvage

HIFU SOLUTION

Long-term Clinical Results - First-line Treatment

Over 85 peer-reviewed publications with Ablatherm® HIFU

Unique Safety of Ablatherm HIFU

Automatic safety features

- Rectal wall temperature monitoring
- Rectal wall detection
- Patient movement detection

	Ablatherm HIFU	Sonablate
Whole gland ablation: Incontinence (pad rate)	2.4-3.1%[1,2]	3-12%[3,4]
Post Radiation: Fistula	0.4%[5]	4-4.8%[6,7,8]

Ablatherm Robotic HIFU Equals Safety

1. Ganzer R et al BJU Int. 2013 Aug;112(3):322-9 2. Crouzet S et al Eur Urol. 2014 May;65(5):907-14 3. Uchida T et al J Urol. 2015 Jan; 193(1):103-10 4. Dickinson L et al Eur Urol 2016 epublished 5. Crouzet et al Radiother Oncol. 2012 Nov;105(2):198-202 6. Ahmed HU et al Cancer. 2012 Jun 15;118(12):3071-8 7. Uchida T et al BJU Int. 2011 Feb;107(3):378-82 8. FDA Presentation Sonacare 2014

HIFU SOLUTION

Results of Surgery for Prostate Cancer

- Radical Prostatectomy- gold standard for localized prostate cancer

		Risk Group	n	10 Year Cancer Specific Survival
Boorjian 2008 RP[1]	Mayo Clinic	Low	3283	100%
		Intermediate	2795	97%
		High	1513	95%
Stephenson 2008 RP[2]	MSK CCF U Mich	Low	5200	99%
		Intermediate	4184	96%
		High	1962	92%

- Radiotherapy is also commonly used with similar oncologic outcomes[3]

1. Boorjian et al J Urol. 2008 Apr;179(4):1354-60; 2. Stephenson et al J Clin Oncol. 2009 Sep 10;27(26):4300-5 3. Hamdy et al N Engl J Med. 2016 Oct 13;375(15):1415-1424.

Results of Whole Gland HIFU for Prostate Cancer

- HIFU efficacy similar to RRP

	Risk Group	n	10 Year Cancer Specific Survival
Ganzer (Germany)	Low	229	100%
	Moderate	211	96.22%
Thuroff (Germany)	All localized (72% mod or high)	704	99%
Crouzet (France)	Low	357	99%
	Moderate	452	98%
	High	174	92%

Ganzer R, BJU Int. 2013;112(3):322-9; Thüroff S, J Urol. 2013;190(2):702-10; Crouzet S. Eur Urol. 2014;65(5):907-14.

HIFU SOLUTION

Prostate Cancer Treatment

- 10 year Cancer Specific Survival after HIFU = RRP

	10 Year Cancer Specific Survival	
	Prostatectomy[1,2]	HIFU[3,4,5]
Low	99-100%	99-100%
Intermediate	96-97%	96-98%
High	92-95%	92%

1. Boorjian et al J Urol. 2008;179(4):1354-60; 2. Stephenson et al J Clin Oncol. 2009 10;27(26):4300-5 3. Ganzer R, BJU Int. 2013;112(3):322-9; 4. Thüroff S, J Urol. 2013;190(2):702-10; 5. Crouzet S. Eur Urol. 2014;65(5):907-14.

HIFU SOLUTION

Prostate Cancer Treatment Morbidity- ProtecT

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ORIGINAL ARTICLE

Patient-Reported Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer

Jenny L. Donovan, Ph.D., F.Med.Sci., Freddie C. Hamdy, F.R.C.S.(Urol.), F.Med.Sci., J. Athene Lane, Ph.D., Malcolm Mason, M.D., Chris Metcalfe, Ph.D., Eleanor Walsh, M.Sc., Jane M. Blazeby, Ph.D., F.R.C.S., Tim J. Peters, Ph.D., F.Med.Sci., Peter Holding, R.G.N., Susan Bonnington, R.G.N., Teresa Lennon, R.G.N., Lynne Bradshaw, R.G.N., Deborah Cooper, R.G.N., Phillipa Herbert, R.G.N., Joanne Howson, R.G.N., Amanda Jones, R.G.N., Norma Lyons, R.G.N., Elizabeth Salter, R.G.N., Pauline Thompson, R.G.N., Sarah Tidball, R.G.N., Jan Blaikie, R.G.N., Catherine Gray, R.G.N., Prasad Bollina, M.B., B.S., F.R.C.S.(Urol.), James Catto, Ph.D., F.R.C.S.(Urol.), Andrew Doble, M.S., F.R.C.S.(Urol.), Alan Doherty, F.R.C.S.(Urol.), David Gillatt, M.S., F.R.C.S.(Urol.), Roger Kockelbergh, D.M., F.R.C.S.(Urol.), Howard Kynaston, M.D., F.R.C.S.(Urol.), Alan Paul, M.D., F.R.C.S.(Urol.), Philip Powell, M.D., F.R.C.S.(Urol.), Stephen Prescott, M.D., F.R.C.S.(Urol.), Derek J. Rosario, M.D., F.R.C.S.(Urol.), Edward Rowe, M.D., F.R.C.S.(Urol.), Michael Davis, M.Sc., Emma L. Turner, Ph.D., Richard M. Martin, Ph.D., and David E. Neal, F.R.C.S., F.Med.Sci., for the ProtecT Study Group*

N Engl J Med 2016; 375:1425-1437 | October 13, 2016 | DOI: 10.1056/NEJMoa1606221

- All treatments have morbidity including surveillance

Donovan et al N Engl J Med. 2016 Oct 13;375(15):1425-1437; 2. Sponsor Executive Summary PMA P13003 (www.fda.gov)

HIFU SOLUTION

Prostate Cancer Treatment Morbidity

- All treatments have morbidity including surveillance

	Active Surveillance (ProtecT)[1]	Radiotherapy (ProtecT)[1]	Radical Prostatectomy (ProtecT)[1]
Mean age	62 years	62 years	62 years
Incontinence*	3%	4%	20%
Erectile dysfunction*	21%	66%	82%

*2 years after treatment initiation

Donovan et al N Engl J Med. 2016 Oct 13;375(15):1425-1437; 2. Sponsor Executive Summary PMA P13003 (www.fda.gov)

Comparison of HIFU Morbidity with Other Treatments

	Active Surveillance (ProtecT)[1]	Whole Gland HIFU (FDA IDE)[2]	Radiotherapy (ProtecT)[1]	RRP (ProtecT)[1]
Mean age	62 years	64 years	62 years	62 years
Incontinence*	3%	3%	4%	20%
ED*	21%	37%	66%	82%

*2 years after treatment initiation

HIFU maintains the efficacy of radical treatment with less morbidity

Donovan et al N Engl J Med. 2016 Oct 13;375(15):1425-1437; 2. Sponsor Executive Summary PMA P13003 (www.fda.gov)

HIFU SOLUTION

Further morbidity reduction with Hemiablation

Focal Ablation

Clinical Results – Partial / Focal Treatment

Institut Montsouris, Paris, European Uro
2015

- 71 pts Ablatherm Hemiablation
  Mean F/U: 21 months.
- 10 pts (14%) had postop side effects:
  - 4 UTIs & 4 urinary retentions
  - 2 retentions treated with TURP
- Mean IIEF decreased from 17.9 to 15.4
- 84% biopsy negative in treated lobe

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European Association of Urology

Platinum Priority – Prostate Cancer
Editorial by XXX on pp. xx–y of this issue

Focal High-intensity Focused Ultrasound Targeted Hemiablation for Unilateral Prostate Cancer: A Prospective Evaluation of Oncologic and Functional Outcomes

*Ernesto R. Cordeiro Feijoo, Arjun Sivaraman, Eric Barret *, Rafael Sanchez-Salas, Marc Galiano, Francois Rozet, Dominique Prapotnich, Nathalie Cathala, Annick Mombet, Xavier Cathelineau*

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Abstract

Background: In selected patients with unilateral, organ-confined prostate cancer (PCa), hemiablation of the affected lobe might be feasible to achieve acceptable cancer control with fewer complications.
Objective: To assess the oncologic and functional outcomes of focal high-intensity focused ultrasound (HIFU) hemiablation in unilateral organ-confined PCa.
Design, setting and patients: Single-center prospective evaluation of HIFU hemiablation for unilateral organ-confined PCa was performed from July 2009 through December 2013.
Intervention: Cancer localization was done with transrectal ultrasound–guided biopsy and multiparametric magnetic resonance imaging followed by HIFU hemiablation.
Outcome measurement and statistical analysis: Oncologic outcomes were analyzed with control biopsies and prostate-specific antigen (PSA) measurement. Functional outcomes were assessed with validated questionnaires for genitourinary symptoms.
Results and limitations: Of 71 HIFU hemiablation patients, 67 completed the study protocol. The mean age was 70.2 yr (standard deviation: 6.8 yr), and median PSA was 6.1 ng/ml (interquartile range [IQR]: 1.6–15.5 ng/ml). Median maximum cancer-core length was 3 mm (IQR: 2–10 mm), and total cancer length was 6.5 mm (IQR: 2–24 mm). Gleason score was 6 (3 + 3) in 58 patients (86.6%) and 7 (3 + 4) in 9 patients (13.4%). Median follow-up was 12 mo (IQR: 6–50 mo), and at 12 mo, 56 of 67 patients had a negative control biopsy in the treated lobe. At 1 mo, all patients were continent, and potency was maintained in 11 of 21 preoperatively potent patients (confidence interval, 0.18–0.69). Complications included 8% Clavien–Dindo grade 2 and 2.8% grade 3 events.
Conclusions: Focal HIFU hemiablation appears to achieve acceptable oncologic outcomes with low morbidity and minimal functional changes. Longer follow-up will establish future considerations.
Patient summary: This study showed that high-intensity focused ultrasound hemiablation in selected patients with unilateral organ-confined prostate cancer can be used for satisfactory cancer control with minimal effect on genitourinary functions.

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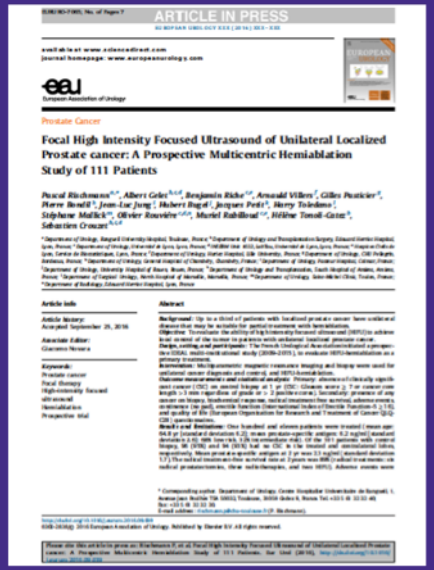
HIFU SOLUTION

Prospective Clinical Trial - Hemiablation

Focal High Intensity Focused Ultrasound of Unilateral Localized Prostate cancer: A Prospective Multicentric Hemiablation Study of 111 Patients
Rischmann et al, European Urology Eur Urol. 2017 Feb;71(2):267-27

- 111 Ablatherm pts treated at 10 centers in France
- Hemiablation with Ablatherm
- 95% no significant cancer in the treated lobe (Gleason ≥ 7 OR CCL > 3mm OR > 2 cores positive)
- Freedom from radical treatment at 2 years: 89%
- 78% preservation of erectile function at 2 years
- 3% Incontinence (pads) at 2 years



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Prostate Cancer

Focal High Intensity Focused Ultrasound of Unilateral Localized Prostate cancer: A Prospective Multicentric Hemiablation Study of 111 Patients

Morbidity Comparison: Act. Surv. vs. Hemi HIFU

	Active Surveillance (PIVOT)[1]	Active Surveillance (ProtecT)[2]	Hemi HIFU (AFU Trial)[3]
Mean age	**67 years**	**62 years**	**65 years**
De novo* Incontinence At 2 yrs	**2%** ('lots of problems' or 'large volume' or 'no control')	**3%** (pad use)	**3%** (pad use)
De novo ED* At 2 yrs	**17%** (inability to penetrate)	**21%** (sufficient for intercourse)	**22%** (maintain SHIM >16)

*proportion of population not reporting condition at baseline reporting it at follow-up

Minimal incremental morbidity with Hemiablation HIFU

[1]Wilt et al NEJM. 2012; [2]Donovan et al NEJM 2016; [3]Rischmann et al European Urology 2017

HIFU SOLUTION

Side Effects HIFU vs. Radiation & Surgery

- HEMI HIFU is essentially equivalent to Active Surveillance
- Whole gland HIFU has less side effects compared to RRP

	Act. Surv. (ProtecT)[1]	Hemi HIFU (AFU Trial)[2]	Whole Gland HIFU (FDA IDE)[2]	Radiotherapy (ProtecT)[1]	RRP (ProtecT)[1]
Mean age	62 years	65 years	64 years	62 years	62 years
Incontinence *	3%	3%	3%	4%	20%
					82%

*2 years after treatment initiation

Whole Gland HIFU maintains efficacy of radical treatment with less morbidity

Hemi HIFU: side effects = Act. Surv.; reduces need for radical treatment by 50%

HIFU SOLUTION

HIFU: a technical solution to a clinical problem

There is an unmet need for the newly diagnosed patient who, in absence of HIFU, is faced with deciding between surveillance and radical therapy

- Whole gland HIFU is a less radical approach with similar oncologic outcomes but less morbidity
- Hemiablation HIFU provides more safety without burning any bridges for future intervention

HIFU - Take Home Points

- HIFU is a non-invasive procedure that treats prostate cancer - avoids 2 most common life altering side effects seen with surgery and radiation - urinary incontinence and erectile dysfunction
- Small size & precision of HIFU beam allows dramatic decrease in side effects; no incisions needed
- Truly outpatient procedure performed in doctor's office
- Treatment takes 1.5 - 3 hours (Hemi vs. Whole Gland)
- Normal activity resumes within few days
- Minimal to no pain
- No radiation exposure
- Other treatments not contraindicated later
- Excellent results - over 10 years experience
- Approved in > 41 countries, > 50,000 patients treated

HIFU SOLUTION

Erectile dysfunction avoided by HIFU

Incontinence avoided by HIFU