Objectives:

1) Therapy Definitions and Goals
2) Clinical Devices for Prostate Hyperthermia
3) Clinical Devices for Prostate Ablation

Thermal Therapy for Prostate

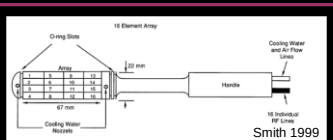
- Hyperthermia (40-43 C, 30-60 min)
  - Adjunct to radiation, chemotherapy, drug delivery
  - Increase blood flow, permeability, oxygenation
  - Radiosensitizes & directly cytotoxic (TER 1.2-1.5)
  - T_{90} >40.5 ^{o}C, thermal dose > 6-10 min @ 43 C
- Thermal Ablation (~50-90°C, > 240 EM 43°C)
  - Thermal coagulation- "Immediate" Destruction
  - Thermal necrosis & latent cell death
- Current Technology
  - Microwaves, EM, RF, Lasers, and US
  - BPH and cancer
- US has significant advantages and potential for prostate

Hyperthermia

Ablation

Endorectal Ultrasound Hyperthermia Applicator

Courtesy M. Hurwitz & K. Hynynen



Smith 1999

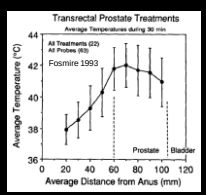
- Multi-Sectored array, 120° arc, ~6 cm length
- 1-2 MHz, ~4 cm treatment penetration
- Inflatable bolus w/temperature controlled water flow @ 37C to regulate rectal wall temp and couple US
- Sector and length control of power and heating to entire prostate

Fosmire, H., Int J Radiat Oncol Biol Phys, 1993. **26**(2); Diederich, C.J. , Medical Physics, 1990. **17**(4)
Smith, N.B., Int J Radiat Oncol Biol Phys, 1999. **43**(1) ; Hurwitz, M.D, Int J Hyperthermia, 2001. **17**(1)

Clinical Studies - Endorectal Ultrasound Hyperthermia

Thermal Dosimetry

Study	T_{MAX}	T_{MIN}	T_{AVE}	T_{90} 43°C
Fosmire 1993	43.3	40.4	42.3	—
Hurwitz 2011	42.5	40.1	41.2	8.4 (CEM)



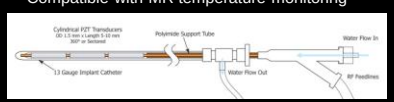
- Safe, feasible, favorable toxicity profile
- Therapeutic temperatures achieved
- Rectal temperatures to 42°C tolerated, no increased rectal toxicity**
- Disease free survival (T2a-T3a's) at 2 years-84% w/ HT + EBRT compared to 64% for RTOG92-02 (EBRT +/- androgen suppression) **
- Compatible with MR Temperature Monitoring (Silcox 2005)

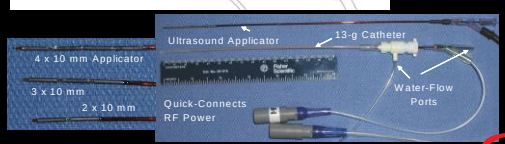
* Fosmire, H et al. Int J Radiat Oncol Biol Phys, 1993. **26**(2)
** Hurwitz, MD et al. *94-153*. Cancer, 2011. **117**(3)

Interstitial Ultrasound Applicators

Hyperthermia & Ablation

- Arrays of miniature tubular PZT radiators
- 6-10 MHz, collimated beam output
- 360° or sectored for angle control (e.g., 90°, 200°, 270°)
- Catheter-Cooled Configuration
- Compatible with MR temperature monitoring

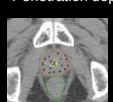




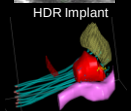
3D Control of Hyperthermia in HDR Implant

Treatment planning for two prostate target volumes w/ directional implants

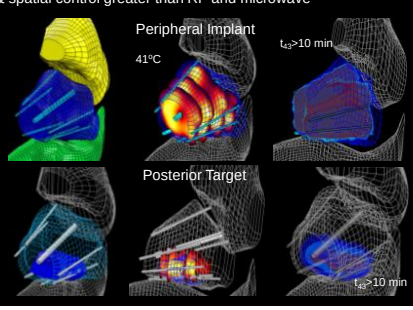
- Selection of active length, sector, and aiming
- Independent power control for conformal targeting
- Penetration depth & spatial control greater than RF and microwave



HDR Implant



Applicators
4 x 10 mm Length
180° & 270° Sectors

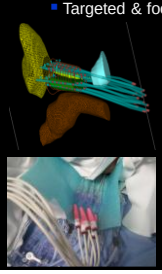


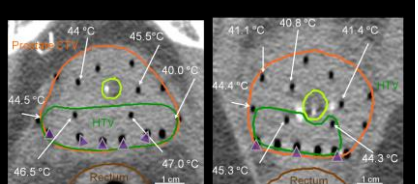
Interstitial Ultrasound & HDR Brachytherapy

Clinical Examples - Posterior Prostate

Prostate HDR+HT Implant Configuration
Locally advanced prostate cancer
60 min HT, 1 Fraction each implant, Target HTV + CTV
3x10 mm x180 deg. directional applicators, ~ 7.3 MHz

- Targeted & focal hyperthermia w/ rectal protection



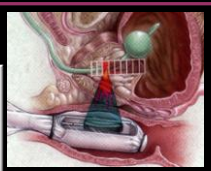


Pilot Study IDE G040168

Sonablate 500 - Transrectal HIFU for Prostate Ablation

Precise targeting with real-time ultrasound monitoring and guidance


Naren Sanghvi, Focal Surgery

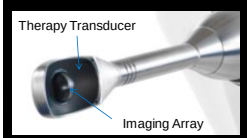


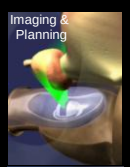

Koch et al. J Urol. 2007 Dec;178(6)

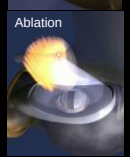
- 30 mm x 22 mm curved transducer, 4 MHz
- ~3 x 3 x 10-12 mm3 coagulation per shot
- 30-50 mm focal depth devices– selected a priori
- Split Beam- 3 & 4 cm focus; flexible targeting
- Rectal cooling & coupling
- US imaging (4 MHz) – plan and monitor
- →Anterior, middle, posterior, R/L regions

Focal Surgery, USA

Ablatherm Transrectal HIFU w/ Integrated Imaging







- 61mm x 25 mm curved transducer, 3 MHz
- 45 mm focal depth
- ~1.7 x 1.7 x 19-26 mm3 coagulation (29-36 mm3)
- Rectal cooling & coupling with T regulated flow
- Movement detection, distance detector
- Integrated US imaging (7.5 MHz) – plan and monitor
- →Apex to base in 4-6 sections
- Algorithms – primary, RT failures, HIFU retreat

EDAP TMS SA, France

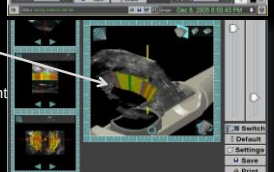
Targeting and Monitoring with Transrectal HIFU

Example of real-time ultrasound monitoring and guidance w/ Sonablate 500

NVB Detection

US Lesion Detection
And Verification –
RF/Backscatter

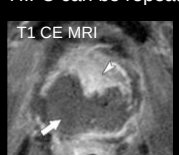
Reflectivity measurement
Quality of "Shot"



Images Courtesy Naren Sanghvi, Focal Surgery

Treatment Assessment of Transrectal HIFU

- Gadolinium-enhanced T1- MRI is gold standard
- CE-US can distinguish ablated (devascularized) and viable (enhancing) tissue after HIFU
- *30 min CE-US correlated well to 1-3 day CEUS and T1-CE MRI → practical approach
- HIFU can be repeated targeting remaining vascular areas



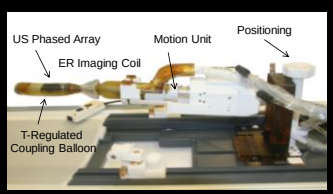
*Rouvière O, et al. Prostate cancer ablation with transrectal high-intensity focused ultrasound: assessment of tissue destruction with contrast-enhanced US, Radiology. 2011 May;259(2)

Transrectal HIFU for Prostate Cancer Therapy
Clinical Studies and Outcomes

- Two commercial systems since 90's
- Significant device improvements
- Primary Therapy (multiple studies, 3018 patients)*
  - Whole gland or hemi-ablation for focal disease
  - T1/T2 w/ curative intent
  - Overall & biochemical free survival promising
  - Complication rates acceptable (fistula <0.5%)
- Salvage Therapy (recurrence, RT failures)
  - Possibly effective treatment option for local recurrence

Crouzet et al. Int J Hyperthermia 26(8), 2010
*Warmuth et al. European Urology 58:803-815, 2010

Insightec ExAblate 2100- MRg Prostate Ablation

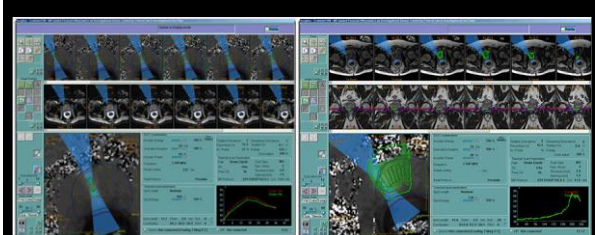



Courtesy of Insightec

- 990 element array, 2.3 MHz, 23 mm x 30 mm
- Electronic beam forming w/ mechanical
- Integrated MRI coil to improve SNR
- Rectal cooling & coupling
- Tracking coils for localization
- Adjustable focus and Macro- Sonication patterns
- MRI →accurate targeting, control, temperature & dose monitoring

MRI for treatment planning, control and monitoring

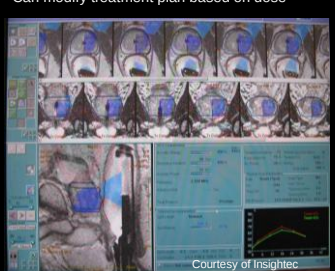
- User defined ROT, rectum, and protected tissues
- Real-time temperature monitoring and sonication control
- Cumulative thermal dose mapping (240 EM @43 C)
- Movement detection & correction



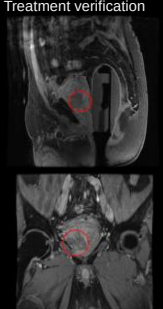
Images Courtesy Dr. Christopher Cheng, MD
Singapore General Hospital

ExAblate 2100 for Prostate Treatments
3D Thermal Dose Maps & Assessment

Lethal Thermal Dose Maps t_{43}=240 min
Updated in 3D during Tx
Can modify treatment plan based on dose


Courtesy of Insightec

Post-Treatment T1-CE Imaging
Treatment verification



Courtesy Dr. Christopher Cheng, MD

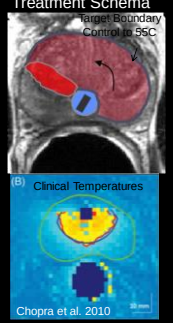
Transurethral Ablation with MR Feedback Control

Sunnybrook Health Sciences

- 3.5 mm x 20 mm planar array,8-9 MHz
- Narrow coagulation ~3mm x 5-20 mm
- Rotation under MRTI feedback control
- Coagulation extends from urethra
- 55 ºC to target boundary
- Urethral cooling
- Fast and accurate ablation (+/- 3 mm)
- Pilot study for feasibility completed

See WE-B-220-3 Chopra et al.

Treatment Schema



Chopra et al.
Int J Hyperthermia 26(8) 2010

Prostate Thermal Therapies

Summary

- Ultrasound technology provides conformal heating approaches with 3D control and image guidance
- US affords spatial and dynamic control for hyperthermia and ablation – not possible with other modalities
- US Imaging provides practical control and verification
- MR-guided systems provide accurate targeting and control
- Whole gland, unilateral or focal treatment possible
  Thermal ablation & hyperthermia
  Adjunct w/ RT or chemo, drug delivery, etc.