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)
  \( T_{90} > 40.5°C \), 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

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

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Clinical Studies - Endorectal Ultrasound Hyperthermia

- 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)

<table>
<thead>
<tr>
<th>Study</th>
<th>Tmin</th>
<th>Tave</th>
<th>Tmax</th>
<th>Tave 43°C</th>
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<tr>
<td>Fosmire 1993</td>
<td>40.4</td>
<td>43.3</td>
<td>40.1</td>
<td>42.3</td>
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<td>Hurwitz 2011</td>
<td>42.5</td>
<td>41.2</td>
<td>8.4</td>
<td>CE(M)</td>
</tr>
</tbody>
</table>

** Hurwitz, MD et al. J Cancer. 2011. 117(3)

Interstitial Ultrasound Applicators

- 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

- Peripheral Implant
- Posterior Target
- Tave >10 min.
- Tave >5 min.

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

- 30 mm x 22 mm curved transducer, 4 MHz
- ~3 x 3 x 10-12 mm^3 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

- 61 mm x 25 mm curved transducer, 3 MHz
- 45 mm focal depth
- ~1.7 x 1.7 x 18-26 mm^3 coagulation (29-36 mm^3)
- 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

*Rouviere 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

Insightec ExAblate 2100 - MRg Prostate Ablation

- 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

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

Lethal Thermal Dose Maps t<sub>43</sub>=240 min
Updated in 3D during Tx
Can modify treatment plan based on dose

Images Courtesy Dr. Christopher Cheng, MD
Singapore General Hospital

Images Courtesy of Insightec

Images Courtesy Dr. Christopher Cheng, MD

Post-Treatment T1-CE Imaging
Treatment verification
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 °C to target boundary
- Urethral cooling
- Fast and accurate ablation (+/- 3 mm)
- Pilot study for feasibility completed

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

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.

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