Catheter-Based Ultrasound For 3D Control of Hyperthermia & Thermal Ablation with Image Guidance

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Thermal Therapy Mediated Effects

- Non-Lethal Moderate Temperature Exposure (40-45 °C [104-113 F])
  - ↑ metabolism, inactivation of enzymes, rupture cell membranes, hyperemia, ↑ oxygenation,
  - ↑ blood vessel permeability, heat shock-stress response
  - Gene therapy, drug delivery and activation, adjunct to RT/CT
- Lethal Moderate Temperature Exposure (41-45+ °C , long duration)
  - Cellular repair mechanisms lose function or can't keep up with accumulating damage.
  - → Cell death & necrosis within 3-5 days
- Lethal High Temperature (48-50+ °C, short to long duration)
  - Cellular and tissue structural changes
  - Thermal coagulation-irreversible protein denaturation
  - Thermal necrosis & immediate cell death

Hyperthermia

Ablation

*Pearce and Thomsen 1995

Catheter-Based Ultrasound for Thermal Therapy

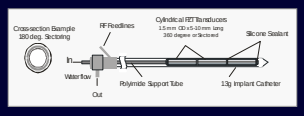
3D control of Hyperthermia & Ablation

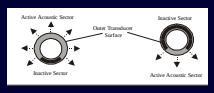
- Interstitial/Percutaneous Ultrasound Applicators
  - Arrays of Tubular Radiators
  - Prostate, Brain, GYN, Liver, Soft Tissue Sites
  - Hyperthermia and targeted ablation
- Transurethral/Intraluminal Ultrasound Applicators
  - Arrays of Tubular, Planar, & Curvilinear Radiators
  - Prostate Ablation & Intrauterine Hyperthermia
  - GI/Digestive tumors
- MR Temperature/Ablation Imaging
  - Guidance, Treatment Control, & Assessment

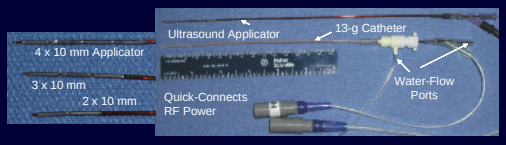
→ Extrapolate to Other Site Specific Design & Treatment

Interstitial Ultrasound Applicators

- Arrays of miniature tubular PZT radiators
- 6-10 MHz, collimated beam output
- 360° or sectored for angle control (e.g., 90°, 180°, 270°)
- Catheter-Cooled Configuration



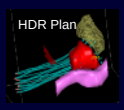




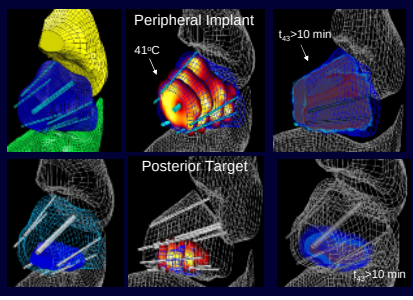
3D Control of Hyperthermia in HDR Implant

Treatment Planning for two prostate target volumes

- Selection of active length, sector, and aiming - *a priori*
- Tailor power control & conformal targeting



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

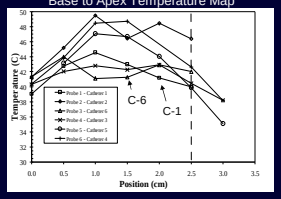


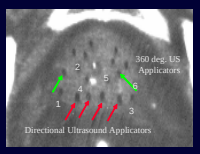
Technology Implemented for Clinical Hyperthermia

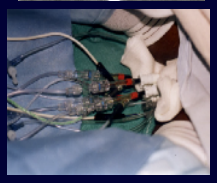
Enhanced spatial control & penetration

Prostate HDR+HT Implant Configuration
60 min HT, 1 Fraction
6-2x10 mm 13- g CC Applicators, ~ 7.3 MHz

Base to Apex Temperature Map







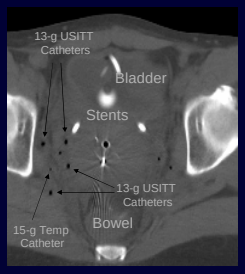
USITT - Uterine Sarcoma

HDR+HT Implant Configuration

Hyperthermia 42-45 C for 45 min, 2 Fractions
Sequential HDR Brachytherapy, 4 Fractions

Directional Applicators
- avoid bone & stent

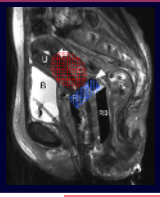
2x10 mm ~7MHz
220 and 360 deg. Applicators



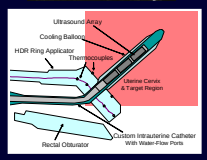
Endocavity Ultrasound Applicator

Local HT + HDR Brachytherapy for Cervical Cancer

Endocavity HDR Ring Applicator



Endocavity US HT + HDR Applicator



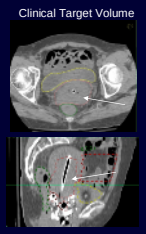
Endocavity Ultrasound Hyperthermia

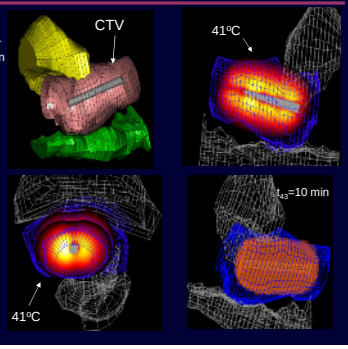
Treatment Simulation of cervix target treatment

Dual Sector Applicator

4 - 3.5 mm OD x10 mm Transducers
Dual 180°, 7 MHz, 6 mm OD Applicator
>4 cm diameter 41ºC lateral penetration
Variable length & sector control

Clinical Target Volume



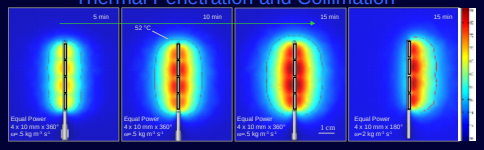


Dynamic Axial and Directional Control of Ablation

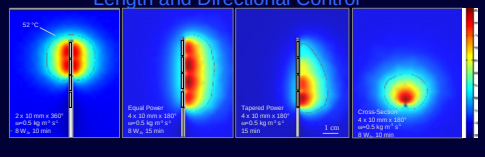
Biothermal Simulations of High-Intensity Ultrasound Devices

2.4 mm OD Interstitial Ultrasound Applicator, 4-1.5 mm OD x 10 mm, 7.5 MHz

Thermal Penetration and Collimation



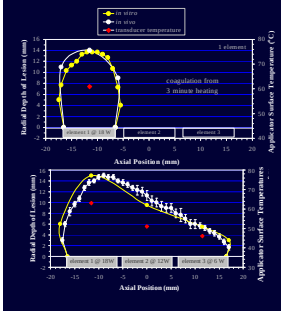
Length and Directional Control



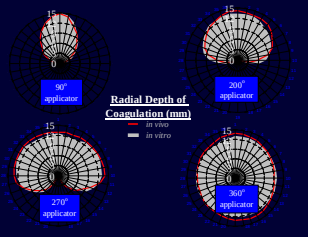
Dynamic Axial and Directional Control of Heating

Experiment – *ex vivo* and *in vivo*

Axial Control
Multiple Transducer Segments
Independent Power Control

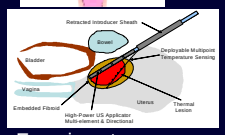


Angular Control
Sectored Tubular Radiators
Pre-Selected Directivity



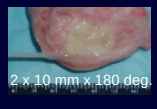
Thermal Ablation of Uterine Fibroids

Shaped Thermal Coagulation – *Ex Vivo* Specimens



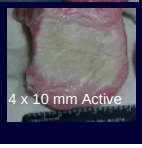
Concept

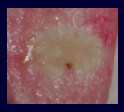
- Hysteroscopic or Laparoscopic
- Similar to RF, Laser, & Cryo
- Fast, Large Volume Ablation
- Selective Targeting, MRTI possible



Experiment

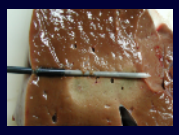
- Surgical Specimens
- 8 min Ablations
- Ex Vivo Lesions
- TTC Stained
- ~ 4 cm OD x 5 cm long





Liver Ablation
Example of Tailored Lesions Ex Vivo

3x360 ° at 13 W , 10 min
4.2 cm wide x 3.5 cm long

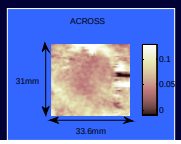


3 x 180° at 12 W, 10 min
2.0 cm radial x 3.2 cm long

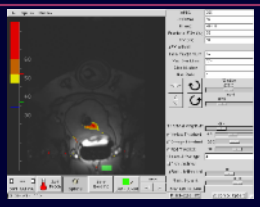
3-3 x 360° Cluster Array
7.5 cm x 4.2 cm long

→ Fast, Conformal, & Large Volume Lesions

Ultrasound Strain Imaging
Terason Imaging probe
External Compression
RF data 15fps, <1 min comp time



MRTI for Device Evaluation & Control
0.5T GE Interventional MRT, 1.5T and 3.0T GE
Applications for Prostate Ablation



MR Thermal Imaging (MRTI)

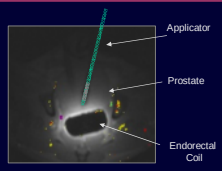
- Phase-difference mapping (PRF shift)
- SPGR (TE/TR=10-25 ms/120-190 ms,FA=60°)
- Endorectal receive coil maximizes SNR
- Resolution: 1.6 mm x 1.6 mm, 1-2 °C
- 3-5 planes simultaneously, ~10 s updates
- Integrated cooling on endorectal coil

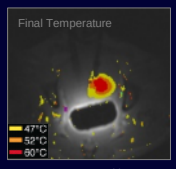
Real-Time Monitoring Software

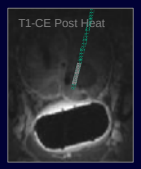
- Current Temperature
- Temperature Thresholds (52 °C)
- Thermal Dose (t_{43}>120-240 min)

Interstitial Ultrasound
Directional And Longitudinal Control of Lesion

Experimental Setup:
Applicator - 10 mm x 180 deg., 7.2 MHz
Canine Prostate – *In Vivo*
Ventral Placement, Direct Away from Urethra
Chronic Study -> Slow Controlled Heating
10-14 W Modulated for 15 min



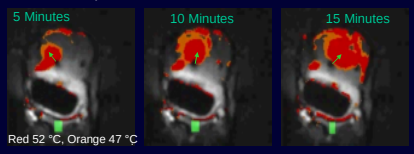




Prostate 2.9 cm Apex-Base x 3.8 Wide x 2.0 DV

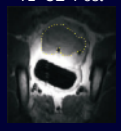
MRTI Guided USITT - *In Vivo* Prostate, 0.5 T
Dynamic Rotation of Interstitial Applicator w/MR Control

Temperature Distribution Mid-Gland



Thermal Dose

T1 -CE Post

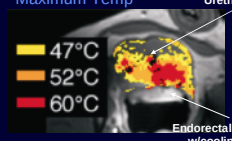


- 15–20 mm radial penetration *in vivo*
- Manual rotation/sweeping possible
- Conformal treatment

→ *Conforming Therapy to Target Boundary*

Multiple Applicator Implant
In Vivo Prostate –"Posterior" 3- 180° Applicators

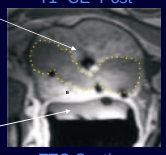
Maximum Temp



Urethral Cooling

Endorectal Coil w/cooling

T1 -CE Post



Thermal Dose

TTC Section

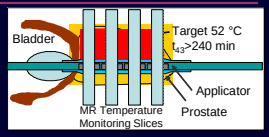
Power Applied 5-17 W, 20 min

3.8 cm AB x 4.3 cm RL x 3 cm AP

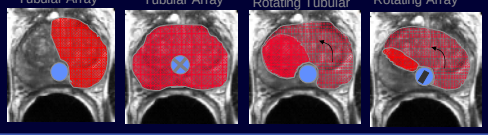
Nau et al., Medical Physics 2005

Targeted Prostate Thermal Therapy w/ MRg
Transurethral Catheter-Based Devices –BPH & Cancer

Design Schema and Strategies
- Linear Transducer Array
- Flexible Delivery Catheter
- Urethral Cooling Balloon
- Tubular, Planar, Curvilinear
- Real-time MRTI monitoring/control



Single-Sector Tubular Array | Multi-Sector Tubular Array | Single-Sector Rotating Tubular | Planar/Curvilinear Rotating Array

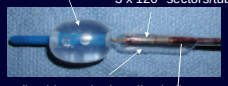


→ Develop devices and evaluate approaches for delivering conformal therapy within *in vivo* canine prostate with MR temperature monitoring.

Multi-Sectored Tubular Transurethral Applicator
Dynamic Angular & Length Control Without Movement

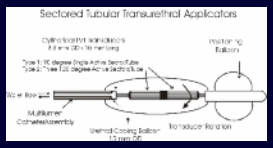
Bladder Balloon

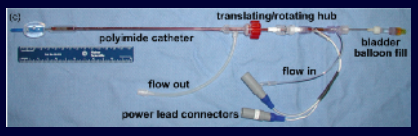
Tubular Array
3.5 mm x 6 mm PZT
3 x 120° sectors/tube



Inflatable urethral cooling balloon

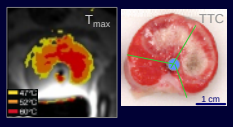
Rotation & translation of assembly for initial position



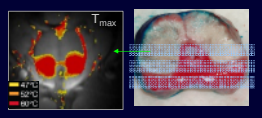


Tri-Sectored Tubular Transurethral Applicator
In Vivo Canine Prostate Evaluations (n=3) with MRTI

Case 1 – Dual-sector Control

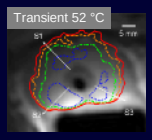


Case 2 – Translation w/ Coronal MRTI

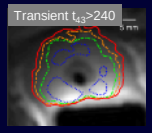


Case 3 – Tri-sector Control

Transient 52 °C



Transient t_{43}>240

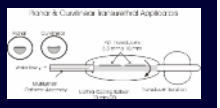


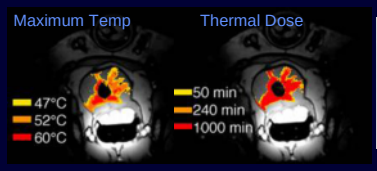
- Fast selective treatment with dynamic angular control (10-15 min)
- Practical control with MRI feedback

Kinsey et al. 2008

Curvilinear Transurethral Applicator
In Vivo Canine Prostate- Single Shots

- Lightly Focused Transducers, 6.5 MHz
- Multiple transducers (2-10mm x 3.5mm)
- 15-20 mm penetration, 1-2 minute shots
- Narrow lesions (~10-20°, 5 mm wide)
- Rotational sweeping w/ MRI compatible motor



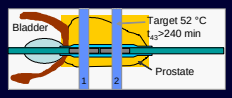


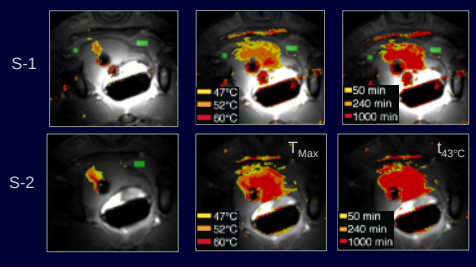
Discrete Shots

Ross, et al., Medical Physics 2005

Curvilinear Transurethral Applicator
In Vivo Canine Prostate –Conformal Targeting

- MRTI Control (Power, Position)
- ~52 °C, t_{43} > 240 min at boundary
- 6.5 MHz, 10° sequential rotation





Catheter-Based Ultrasound Thermal Therapy
Summary

- Produce 3D conformable and effective heating patterns – penetration, dynamic axial and variable angular control
- Tailor heating for sequential hyperthermia within an HDR Implant
- Transurethral and interstitial provide conformal & selective ablation
- Coupling MRTI with dynamic power control has potential for "precise" therapy targeting to prescribed boundary
- Dual mode devices – potential for delivery and guidance
- More complex but precise therapy possible
- Configurations adaptable for site and disease specific therapy

Acknowledgments

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Tony Ross
Adam Kinsey

Stanford
Kim Butts Pauly
Viola Rieke
Graham Sommer
Harchi Gil
Donna Bouley

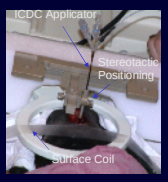
Acoustic MedSystems
E. Clif Burdette

MRTI Guided USITT

In Vivo Canine Brain Tumor

Setup:
Implanted TVT Tumor
Craniotomy/ 5 mm Burr Hole
PRF -Interleaved gradient echo EPI
(TR/TE=1000ms/40 ms,FA=60°)

ICDC Applicator:
2.2 mm OD x 10 mm, ~7.1 MHz, 360°
~4-12 W for 10 min, 20 ml/min at 22 ºC



Tumor: 1.7 cm OD