Present and Future Hyperthermia Technology Evolution

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How are we doing?

• Reviewed 29 randomized/Phase III studies
• Reviewed criteria as reported
  – Complete response rates
  – Disease Free Survival
  – Overall survival
  – Toxicity Grade III and IV
## Randomized Studies Reviewed

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% Complete Response Overall 60% with HT vs 42% per Patient (for 2500 Patients)

- 2500AVE PerPat
- 114 Cervix
- 143 Rectal
- 306 Breast
- 44 H&N
- 40 Cervix
- 40 Esophagus
- 307 Local
- 184 H&N/Pelvic
- 76 Cerivx
- 50 Cervix

HT+RT or CT
RT or CT

Making A Difference in Cancer Care
% Overall Survival 46% with HT vs 38% per Patient (for 2300 Patients)
% Disease Free Survival 46% with HT vs 37% per Patient (for 924 Patients)

- HT + RT or CT
- RT or CT

- 924 AVERAGE/Patient
- 341 Sacoma
- 341 Sarcoma
- 40-Cervix
- 65 H&N
- 190 Bladder
- 76 Cervix
% Toxicity Grade III and IV 9% with HT vs 5% per Patient (for 1484 Patients)

- 1484 AVE/Patient
- 358 Pelvic III
- 79 Brain III+IV
- 124 Sarcoma IV
- 50 Cervix III

HT + RT or CT vs RT or CT

Making A Difference in Cancer Care

Pyrexar MEDICAL
BSD-500, 915MHz, Eight Outputs 0-60 watts or single 400 watt output channel, non-metal temperature probes with No MW artifact or interference, Superficial and interstitial applications, CE Mark

ALBA 434MHz, 0-200 Watt, Single Channel, Metal Thermocouples with MW artifact and interference. Superficial and intracavity, CE Mark

Current microwave systems
Microwave Future Thoughts

• Superficial arrays for dynamic control of surface temperature distribution
• Improved water bolus interface options
• Pretreatment planning software tools
• More conformal patient interface
• Greater implementation with Brachytherapy
Greater Clinical Use of Microwave Arrays – 8 Spiral Array Being Updated
Spiral Arrays of 8, 5 and 3 Spirals For Improved Temperature Uniformity
24 Conformal Spiral Array
Deep Heating Methods

• RF Capacitive
• RF Phased Array
• HIFU
Making A Difference in Cancer Care

Oncotherm EHY-2030, 13.56MHz, Protocol 150W Max Power, Generator 600W

Thermotron-RF8 8MHz, 1500 watts, Metal thermocouples

Capacitive electrodes have remained basically the same since 1917 in tumor treatments. Similar to modern toasters evolution.

Some Capacitive Electrodes uses cooling water bolus to reduce excess fat heating with cooling depth limited to 1.5cm of fat.
RF Phased Array Methods

- Surround a body portion with an array of RF field antennas
- Use phase and power control to steering deep focal heating location
- E-field is dominantly parallel to the body to reduce fat heating and boost central focus
Sigma30 (MAPA), SigmaEye, Sigma60

BSD-2000
ALBA 4D, 70MHz, 4 Channels 500w each, Metal thermocouples

Awaiting independent clinical validation of this configuration.

Reliability and clinical utility are yet to be established.

1981 four waveguide technology has a new look.
Deep Heating Numerical Study

- COMSOL 3D Multiphysics Model
- Homogeneous phantom cylindrical and elliptical saline or muscle dielectric and 2/3rds muscle conductivity with 1cm layer of superficial fat.
Sigma 60-8 dipole array@ 100MHz using a COMSOL numerical model of a 28cm diameter phantom 74cm long & 48cm long water bolus. This study showed more selective central heating with low fat heating near the bolus outer edges. Maximum SAR is shown in the tissue center.

Axial Slice View

Coronal Slice View

100% Central SAR

50% Fat SAR
Sigma 60-8 dipole array@ **75MHz** using a COMSOL numerical model of a 28cm diameter phantom 74cm long & 48cm long water bolus. This study showed stable and uniform surface and central heating with an increase of fat heating near bolus outer edges as compared with the heating at the center.

**Axial Slice View**

**Coronal Slice View**

- **85% Central SAR**
- **100% Fat SAR**
AMC-4 Waveguide array@ **70MHz** using a COMSOL numerical model of a 28cm diameter phantom 74cm long & **40cm** long water bolus. This study showed high superficial fat SAR potential.

Axial Slice View

Coronal Slice View

- 50% Central SAR
- 100% Fat SAR
Capacitive Electrodes Have No Energy Focus
1917 Technology

100% SAR in FAT
8% SAR below FAT
1% SAR at center

SAR, Capacitive 20cm Electrode Pair @ 13.65MHz using a COMSOL numerical model of a 28cm diameter phantom 74cm long & water bolus coupling and a 1cm fat layer. Dielectrics from Gabriel for muscle and fat.
Capacitive field divergent current

- If RF currents diverge 1.7 times the electrode diameter at depth, the expanding area at depth is $(1.7)^2 = 2.9$ times larger at the phantom center, so the RF current is $1/2.9$ times less than under fat.

- $\text{SAR} = I^2R = (1/2.9)^2 R = R/8 = 1/8^{th}$ of the muscle surface.

- For heating a central tumor or for a possible non-thermal modulation effect, the RF power must reach the target with an adequate level to be effective.
RF currents from capacitive electrodes will only converge if bone, fat, and air regions divert these currents to concentrate them. The visceral fat distribution is unique to a patient and limits any consistent deep heating results from capacitive electrodes in patients with visceral fat.
There is a limited future for capacitive electrodes in deep heating

- Superficial fat layer absorption
- Field shape is divergent with lack of control
- RF current flow paths are altered by visceral fat
- Not compatible with image guided SAR steering
- Dump and pray for an RF conductive path to reach the tumor
The Future is Phased Arrays For Deep Heating
• BSD-2000 3D/MR System

1997 - Munich - Siemens 0.2T
2001 - Berlin - Siemens Symphony 1.5T
2007 - Erlangen - Siemens Symphony 1.5T
2008 - Dusseldorf - Siemens Symphony 1.5T
2009 – Duke University - GE Signa HDxt 1.5T
2011 - Tübingen - Siemens Symphony 1.5T
2014 - Rotterdam – GE 450W 1.5T
2017 – Munich – Philips Ingenia 1.5T
2017 Munich Installation

- Universal System approved for clinical use
2019 New Developments In Process

- Universal Water System Design
- Software Controls for Universal Water System
- All-In-One Computer/Desktop Console

Making A Difference in Cancer Care
New BSD-2000 MR Water System

**Major Improvements**

- Improved Air Removal and Pressure Monitoring (7)
- Leak Catch Tub and Leak Detection (8)
- On-Board 1 Ton Chilling Unit for Improved Site Flexibility (10)
- Sensor Additions allow for Software Functionality Improvements without updated Hardware:
  - Possibility for automated Fill/Drain Capability
  - Possibility for automated Bolus Air Removal
- Addition of Pedestal LED Flow Indicator
- Addition of System Control Function Buttons on Electrical Box for Quick Troubleshooting
- No Need for Deionizing Filter due to Closed System Architecture – Breathable .3µm Filter Resists Contamination (4)
- 3 Separate Water Level Sensors for Improved Communication to Operator and Smart Controls (5)
- Added Ability to Drain and Refill System from Pedestal
- Adjustable Chilled Water Source Temperature for Patient Comfort during Circulation

Making A Difference in Cancer Care
Noninvasive brain applicator Hal.o

- Operating frequency: 915 MHz
- Array: 3 rings of 24 antennas (dipole size 9×24 mm)
- Cylindrical frame: 13 cm length, 26 cm dia. (~4cm water bolus)
Steering with different number of amplifiers

<table>
<thead>
<tr>
<th># AMP (Ptissue, Pabs)</th>
<th>72 AMP (28W, 96W)</th>
<th>24 AMP (30W, 104W)</th>
<th>8 AMP (57W, 186W)</th>
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<tbody>
<tr>
<td>YZ Plane (x=0cm)</td>
<td></td>
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<tr>
<td>XZ Plane (y=3cm)</td>
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<tr>
<td>3D view with 41°C isosurface (magenta)</td>
<td>2.7×2.0×2.1 cm³</td>
<td>2.7×1.9×1.9 cm³</td>
<td>2.7×1.9×1.9 cm³</td>
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<tr>
<td>T (°C)</td>
<td>45</td>
<td>40</td>
<td>35</td>
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Target (0,3,3) cm
Sim vs Exp MR thermometry after 3min of heating target (0,0,0)

Heat focus ~25s after power off
4 × 2 × 2 cm³

Heat focus at 25s after power off
3.9×1.9×1.9 cm³
Sim vs Exp MR thermometry: Mechanical steering

Phantom shifted vertically 1.5 cm → Focus is kept at the applicator center

MR thermometry

Simulation

Δz_{focus,exp} = 1.5 cm

Δz_{focus,sim} = 1.5 cm

ΔT (°C)
Sim vs Exp MR thermometry: Electronic phase steering

\[ \Delta y(_{\text{exp}}) = 16 \text{ mm} \]

\[ \Delta y(_{\text{sim}}) = 18 \text{ mm} \]
New deep heating practices

- Non-centered patient phase steering
- Superficial heating by power control
- Future MR image guided treatment optimization.
Making A Difference in Cancer Care

Centered phantom (0,3) cm focus

Vertical phantom +2cm (0,5) cm focus
(0,5)-(0,2)=(0,3)

Vertical phantom +2cm (0,-1) cm focus
(0,-1)-(0,2)=(0,-3)

Centered phantom (0,-3) cm focus
Sigma 60 Superficial SAR Prediction at 90MHz by SigmaHyperPlan
Using RF Power On Only 1 or 2 Power Channels
Future developments need to understand frequency dependence of field interaction caused by the cell membrane.

0.1 to 100MHz RF currents flow around the cell.

High Microwave Frequency currents pass through the cell >100MHz.

Muscle Tissue Dielectric and Conductivity Due to Cell Membrane Capacitance and Water Resonance

Dielectric
Conductivity

Water Resonance

Cell wall capacitance transition region

Numerical Advanced Study

- COMSOL 3D Multiphysics Model
- Homogeneous phantom cylindrical and elliptical saline or muscle dielectric and 2/3rds muscle conductivity with 1cm layer of superficial fat.
- More than 300 solutions with different variations evaluated.
250MHz, Center focus, 24 dipoles & RF channels, PG bolus, saline phantom, **Vol. 206cc**

100MHz, Center focus, 24 dipoles & RF channels, Water bolus, saline phantom, **Vol. 1957cc**

Patent pending
250MHz, 24 dipoles & RF channels, PG bolus, saline phantom, Vol. 206cc
250MHz, **Propylene glycol** bolus 24 dipoles & channels, muscle phantom, **Vol=176cc**
175 MHz Axial View, 3D Optimization Central Focus
24 channels and dipoles, 10.6 cm dipoles,
48 cm wide bolus, 60 cm dia. water bolus.
6.9x6.9x13.4cm, Vol.= 334cc
175MHz 24 channel System
4cm Steering
Muscle Phantom, PG Bolus
175MHz 24 channel System
4cm Steering
Muscle Phantom & PG Bolus
140MHz Sigma Eye
24 dipoles & 3 rings,
Water Bolus,
2/3rd Conductivity
Muscle Phantom
13.6x12.3x20.2cm, Vol=1,769cc
250MHz Elliptical SigmaEye, Saline Phantom, Central 3D focus, PG Bolus
4.3x6.2x11.0cm, Vol.= 143cc.
# RF vs HIFU Phased Array

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<tr>
<th>Feature</th>
<th>RF Phased Array</th>
<th>HIFU Phased Array</th>
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<tbody>
<tr>
<td>Focus</td>
<td>Large</td>
<td>Small</td>
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<tr>
<td>Focal Steering</td>
<td>Simple</td>
<td>Complex</td>
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<tr>
<td>Air &amp; Bone</td>
<td>Tolerant</td>
<td>Blockage</td>
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<tr>
<td>Large Tumors</td>
<td>Suitable</td>
<td>Limited</td>
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<tr>
<td>Dose Monitoring</td>
<td>Easy</td>
<td>Difficult</td>
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<tr>
<td>SAR Pattern</td>
<td>Uniform</td>
<td>Non-Uniform</td>
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Future Clinical Applications

• Proton therapy with HT
• Renewed interest in Brachytherapy +HT
• Immune response with HT
• Brain targeted phased array treatments
• Superficial arrays for more uniform surface heating
Treatment Tools Being Planned

- Brain phased array Hal.o
- Advanced high frequency phased array
- MR guided focused thermal therapy
- Superficial arrays
- Further evolution of current systems
- Advancements in treatment planning