Thermal Therapy of Cancer

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Hyperthermia

Definition
Mechanisms
Rationale: Thermal Enhancing Ratio (TER)
Dosimetry
Overview of Technology for Thermal Therapy
Clinical Applications
Hyperthermia

$T = 41-45^\circ C$ for 30-60 min

$\Delta T = 4 - 8^\circ C$

Dose = Cumulative Equivalent Minutes at $43^\circ C$
for the $T_{90}$ temperature
(CEM43°CT)
Hyperthermia Mechanisms

- Increases perfusion, permeability, pH, pO$_2$
- Increases metabolic activity, drug uptake
- Radiosensitization, Chemosensitization
- Some cell kill at higher temperatures/doses
Hyperthermia Rationale

The synergistic effect of heat and radiation is quantified by the Thermal Enhancement Ratio (TER) defined as:

\[ \text{TER} = \frac{RT \text{ dose without heat}}{RT \text{ dose for equivalent effect with heat}} \]

Fig. 2 – Rationale for combining heat and radiation for treatment of recurrent chestwall disease. Data from demonstrates: (a) increased TER for simultaneous heat and radiation in C3H mammary carcinoma, (b) clinical impact of TER=1.5 obtained from a compilation of human data in the literature, and (c) TER up to 3.0 for simultaneous heat and radiation in C3H mammary carcinoma compared to TER plateau of 2.0 for sequentially applied modalities.
Dosimetry

Body is thermally auto-regulated

Heating an organ is like bringing a heater in an air conditioned room!

Feedback Control / Power Steering
Heating Mechanisms

- Thermal conduction
- Electromagnetic (RF, MW)
- Mechanical friction (US)

Interstitial / intracavitary
External
Interstitial / intracavitary
External
Interstitial / intracavitary
Clinical Applications of Thermal Therapy

Hyperthermia (41 - 45°C or < 100 CEM)

- Cancer Therapy with Radiation or Chemotherapy
- Heat-Activated Gene Therapy, Liposome Release
- Accelerate Wound and Bone Healing
- Organ Preservation (Stimulate Heat Shock Proteins / Rewarming)
Thermal Therapy Treatment Options

**Cryotherapy**
- $T = < -50^\circ C$ for $>10$ min
- $\Delta T = -90^\circ C$

**Mechanisms**
- Freeze/Thaw transition disrupts cell membrane
- Complete cellular destruction

**Potential HT Techniques**
- Thermal Conduction

**Equipment Availability**
- 100% Commercial

**Hyperthermia**
- $T = 41-45^\circ C$ for $30-60$ min
- $\Delta T = 4-8^\circ C$

**Mechanisms**
- Increases perfusion, permeability, pH, $pO_2$
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- Some cell kill at higher temperatures/doses

**Potential HT Techniques**
- External
  - RF, MW, US
- Interstitial - Intracavitary
  - RF, MW, US
- Thermal Conduction
  - Ferro seeds, Thermorods
  - DC Resistance Wires
  - Hot Water Tubes
  - Laser/Fiberoptic Diffuser Crystals

**Equipment Availability**
- 75% Commercial
- 10% PMA
- 50% IDE Trials
- 40% Under Development
- 25% University - Under Development

**Thermal Ablation**
- $T > 50^\circ C$ for $>4-6$ min
- $\Delta T = >13^\circ C$

**Mechanisms**
- Protein Denaturization
- Necrosis
- Coagulation
- Not subtle effects

**Potential HT Techniques**
- External
  - Scanned Focused US
  - Large Focused US Arrays
- Interstitial - Intracavitary
  - RF, MW, Intracavitary
- Thermal Conduction
Devices and Techniques for Heating Tissue
## Available Heating Modalities

<table>
<thead>
<tr>
<th>Thermal Conduction</th>
<th>Equilibrium of Thermal Gradients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electromagnetic</td>
<td></td>
</tr>
<tr>
<td>Radiofrequency Current</td>
<td>Electron Flow between Atoms</td>
</tr>
<tr>
<td>Microwave Radiation</td>
<td>Oscillations of Polar H₂O Molecules</td>
</tr>
<tr>
<td>Laser</td>
<td>Dielectric Heating</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Absorption of Light Energy</td>
</tr>
<tr>
<td>Pressure Wave</td>
<td>Compression – Expansion Forces</td>
</tr>
<tr>
<td></td>
<td>Mechanical Friction Losses</td>
</tr>
</tbody>
</table>
Superficial Heating
Electromagnetic Techniques

Waveguide / Horn
- Single or multiple aperture arrays
- Phased or non-phased arrays
- Stationary or robotically scanned

Microstrip Applicators
- Single or multiple aperture
- Planar or conformal
- Spirals - Stationary or scanning
- Patches, annular slots, etc

Dipole Surface Array
- Stationary or scanning

RF Capacitive Plate

Hybrid
- Inductive loop “current sheet”
- Multimode feed “HEMA”

Laser
Superficial Hyperthermia
434 MHz Microwave - Deeper Penetration

Conventional 10x10 Horn Waveguide

Lucite Cone Waveguide

Reitveld & VanRhoon IJH 1999
Lucite Cone Applicator

Gerard VanRhoon
Current Sheet Applicators (CSA)

Multiple Frequencies - 915, 433
Phased Array - Deeper Penetration

J Hand, M Gopal, T Cetas
Microstrip Applicators

Stanford Blanket

Lee, Fessenden, Kapp
Flexible Conformal Microwave Array Applicator

6 mm Water Bolus

24 Aperture CMA

16 Aperture CMA

40 Aperture CMA
47 x 29 = 1363 cm²

Stauffer, Rossetto, Neuman
Possible Treatment Configurations
Patient’s Preference

Standing - Pacing
Lying Down
Sitting
Thermometry Solutions for the Future

2D Thermal Monitoring Sheet

CMA Applicator

MW Array Controller

Thermal Monitoring Array

Fiber Ribbon Cable

Fiber Array Readout

Ipitek Corp.
Combination Applicator
Simultaneous Heat and Brachytherapy

Rectangular
17 x 35 cm

L-Shape
52 x 32 cm
Preparations for Simultaneous HT/RT Treatment Setup and Preplan

HDR

15 x 15 cm Target
3D Conformal Dose Plan

IPSA -------> Plato

PCB Array

13x13x1 cm Target

Water Bolus

Skin Surface Contour
Deep Heating
Ultrasound Techniques

Piston Transducer
- Unfocused
- Focused - Convex shape or Focusing lens
  - Lightly - no gain
  - Tightly - high gain
- Stationary or Robotically scanned

Transducer Arrays
- Planar or Geometric focus
- Stationary lightly focused
- Stationary lightly focused - scanning reflector
- Mechanically or electrically scanned transducers
  - Lightly focused transducer array
  - Focused transducer array
Radiofrequency Plate Electrodes
8 - 27 MHz
Spherical Section Array
Focused Ultrasound
Evolving Technologies – Deep Heating

1982
1. RF-8
2. Magnetrode
3. APAS

1992
1. 4 Antenna Pairs
2. 1 Ring
3. Sigma-Eye

2002
1. 12 Ch, 24 Antennas
2. 3 Rings

Compatibility with MRI for Tx. Planning and Realtime Thermometry
Interstitial
Multi-needle LCF hyperthermia system designed for hyperthermia combined with brachytherapy. (Photos courtesy of Peter Corry, William Beaumont Hospital).

Interstitial microwave antennas suitable for hyperthermia in combination with interstitial brachytherapy (with permission from BSD Medical Corp.).

(A) Interstitial ultrasound applicators suitable for heating in combination with HDR brachytherapy; (B) CT image of a brachytherapy implant pattern in the prostate, with directional ultrasound applicators placed posterior with energy directed anterior to protect the rectum. (C) Measured temperature profiles.
### Evolutionary Trends – Heating Capabilities

<table>
<thead>
<tr>
<th>Generation</th>
<th>Description</th>
</tr>
</thead>
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| **First**  | Simple Structures (e.g. Single Waveguide, Piston)  
Centrally Peaked SAR - Power Up / Down Control  
No pre-Tx planning or real-time adjustment of SAR  
1-8 Stationary Temperature Sensors  
Small Treatment Volumes (e.g. < 3-4 cm diameter) |
| 1980's     | Planar Arrays  
2-D Treatment Planning - Lateral Adjustment of SAR  
4 - 16 Controllable Sources  
8 - 16 Temperature Sensors, Thermal Mapping  
Moderate Size Treatment Volumes |
| 1990's     | Electrically or Physically Phase Focused Arrays  
Stationary Conformal Arrays  
Site-Optimized Applicators  
Non-Invasive Temperature & Physiologic Effect Monitoring  
Patient Specific Treatment Planning - 3-D Power Steering |
| **Emerging** | |
| 2000       | |
So Why Isn’t Everyone Offering HT

(Depends on Who You Talk To)

Reimbursement rate too low                        Administrators
Space and personnel demands too high            Administrators

Can not heat all patients/sites                  Clinicians
Can not deliver precise Tdose as prescribed     Clinicians

Equipment is terrible                            Physicists
Better equipment not available commercially      Physicists

Difficult to setup and deliver in many sites    Operators
Uncomfortable for some patients                 Operators
Current Challenges - Biology

- Optimum combination of HT with RT
  - Long duration moderate vs. short duration high temp. HT
  - Pulsed vs. continuous RT with simultaneous HT

- Optimum administration of HT with CT
  - Identify best compromise of temperature/thermal dose for Vessel permeability, extravasation, cell metabolism and uptake

- Are we investigating all appropriate clinical applications
  - Can we justify treating earlier stage disease/which More aggressive combinations of HT + RT + CT