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°C for 30-60 min

ΔT = 4 - 8°C

Dose = Cumulative Equivalent Minutes at 43°C for the T_{90} temperature (CEM43°CT)

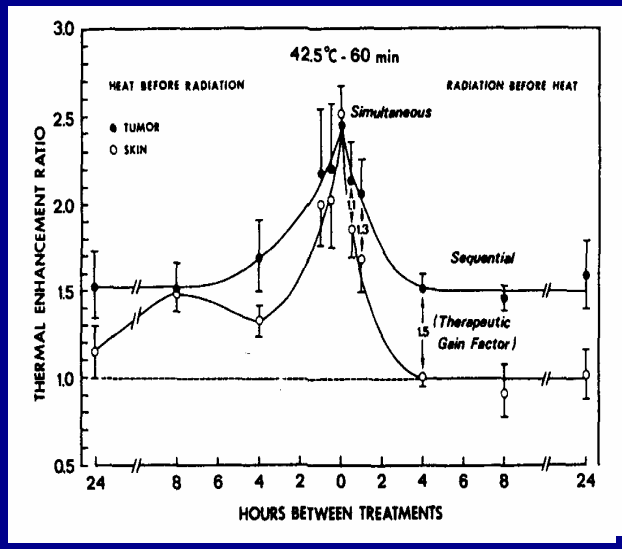
Hyperthermia Mechanisms

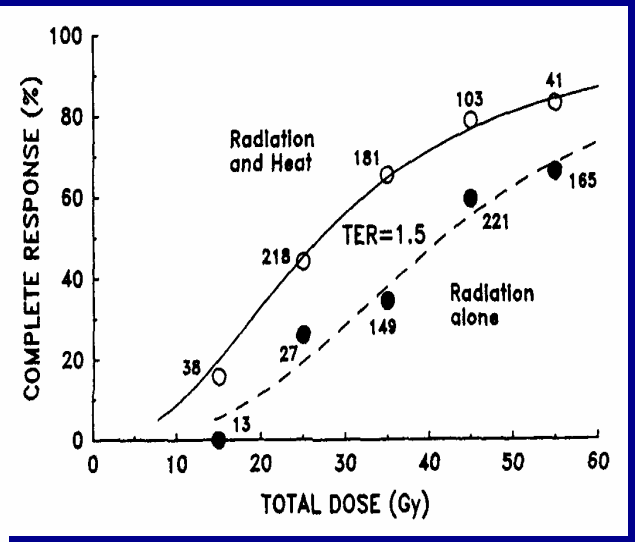
- Increases perfusion, permeability, pH, pO_2
- Increases metabolic activity, drug uptake
- Radiosensitization, Chemosensitization
- Some cell kill at higher temperatures/doses

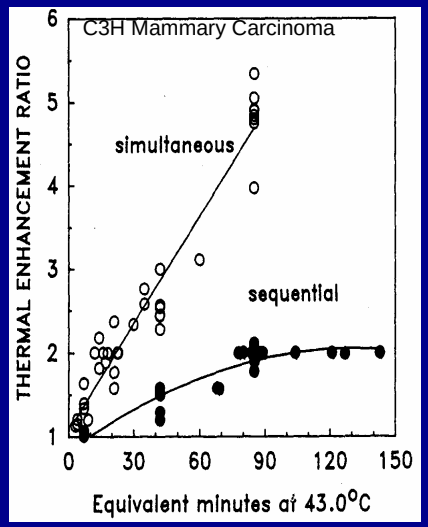
Hyperthermia Rationale

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

$$TER = \frac{RT\ dose\ without\ heat}{RT\ dose\ for\ equivalent\ effect\ with\ heat}$$



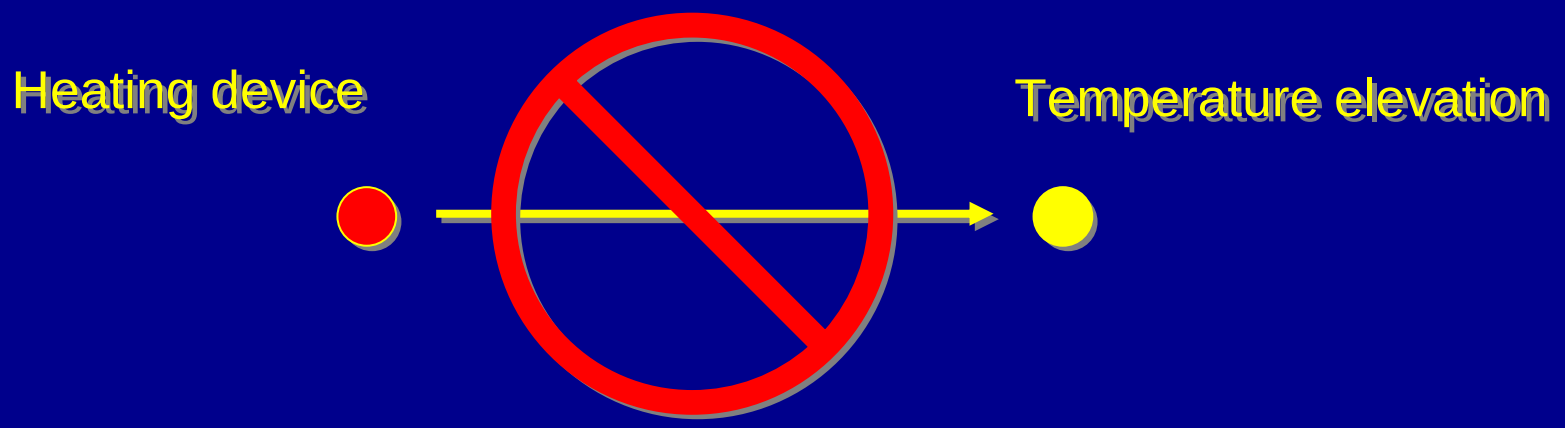




(a) (b) (c)

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 5.0 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

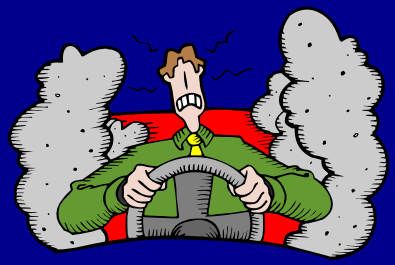
Interstitial / intracavitary

Electromagnetic
RF, MW

External

Interstitial / intracavitary

Mechanical friction
US



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°C for >10 min
ΔT = - 90°C

Mechanisms
Freeze/Thaw transition
disrupts cell membrane
Complete cellular destruction

Potential HT Techniques
Thermal Conduction

Equipment Availability
100% Commercial

Hyperthermia

T = 41-45°C for 30-60 min
ΔT = 4 - 8°C

Mechanisms
Increases perfusion, permeability, pH, pO_2
Increases metabolic activity, drug uptake
Radiosensitization, Chemosensitization
Some cell kill at higher temperatures/doses

Potential HT Techniques
External
- RF, MW, US

Interstitial - Intracavitary
- RF, MW, US
- Thermal Conduction
  - Ferroseeds, Thermorods
  - DC Resistance Wires
  - Hot Water Tubes
  - Laser/Fiberoptic Diffuser Crystals

Equipment Availability
40% Commercial
60% University - Under Development

Thermal Ablation

T > 50°C for >4-6 min
ΔT = > 13°C

Mechanisms
Protein Denaturization
Necrosis
Coagulation
Not subtle effects

Potential HT Techniques
External
- Scanned Focused US
- Large Focused US Arrays

Interstitial - Intracavitary
- RF, MW, US, Laser
- Thermal Conduction

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

25% University - Under Development

Devices and Techniques

for

Heating Tissue

Available Heating Modalities

Thermal Conduction	Equilibrium of Thermal Gradients
Electromagnetic	
Radiofrequency Current	Electron Flow between Atoms Joule Heating
Microwave Radiation	Oscillations of Polar H_2O Molecules Dielectric Heating
Laser	Absorption of Light Energy
Ultrasound	
Pressure Wave	Compression – Expansion Forces Mechanical Friction Losses

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

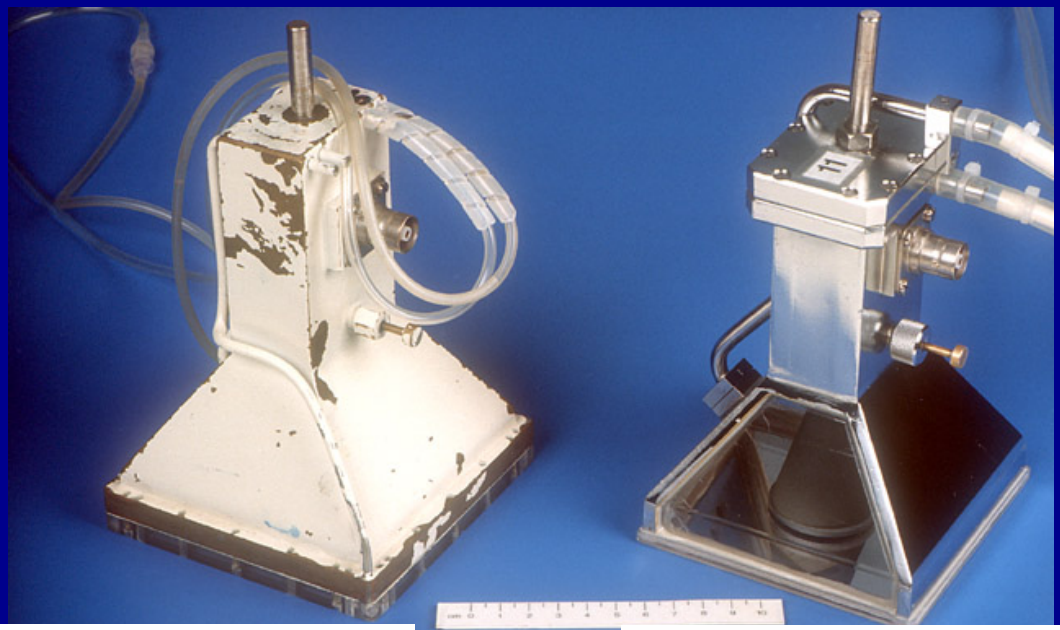
Hybrid

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

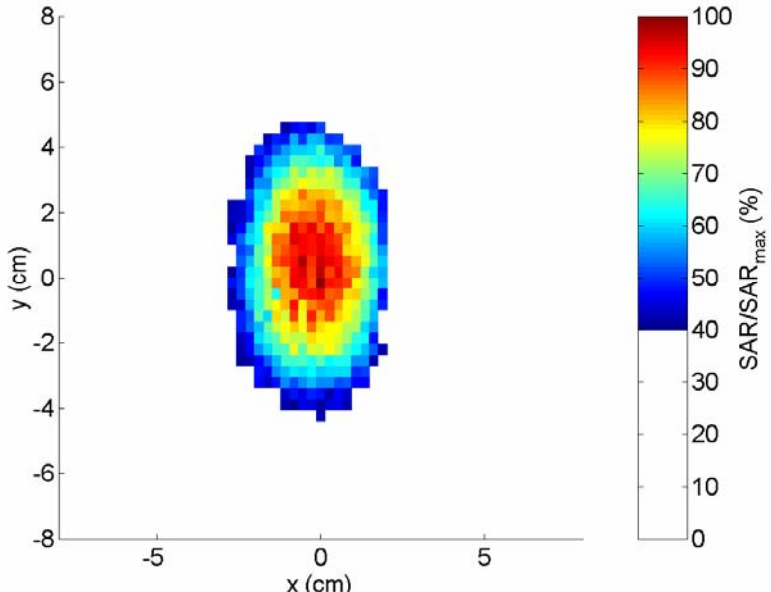
Laser

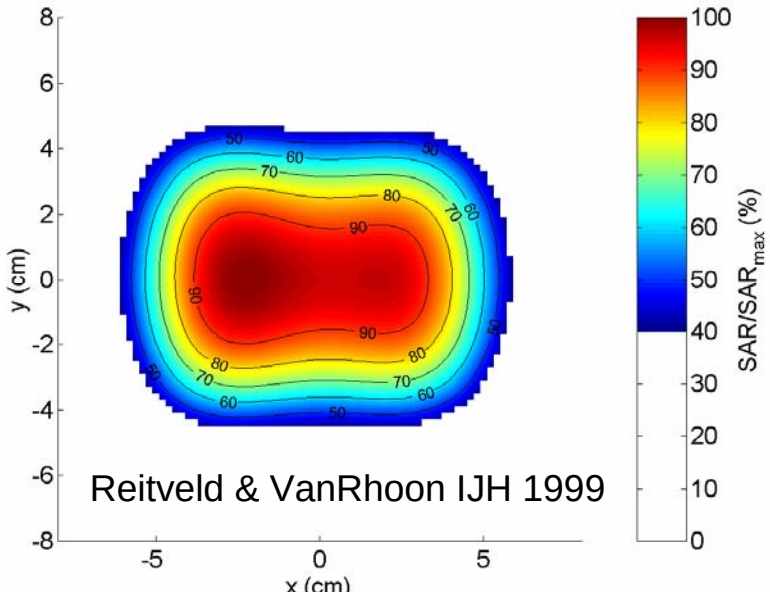
Superficial Hyperthermia
434 MHz Microwave - Deeper Penetration

Conventional 10x10 Horn Waveguide



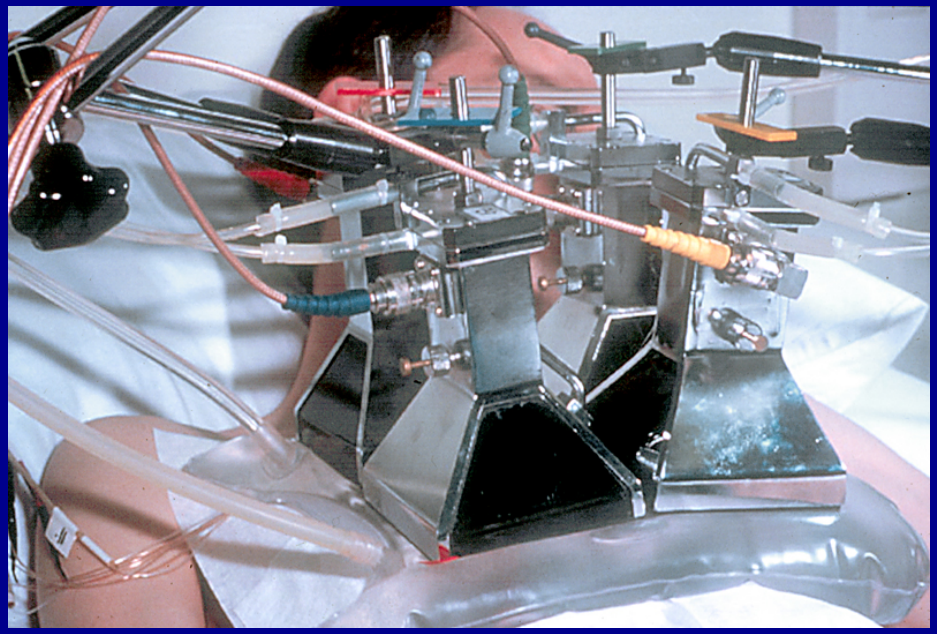
Lucite Cone Waveguide





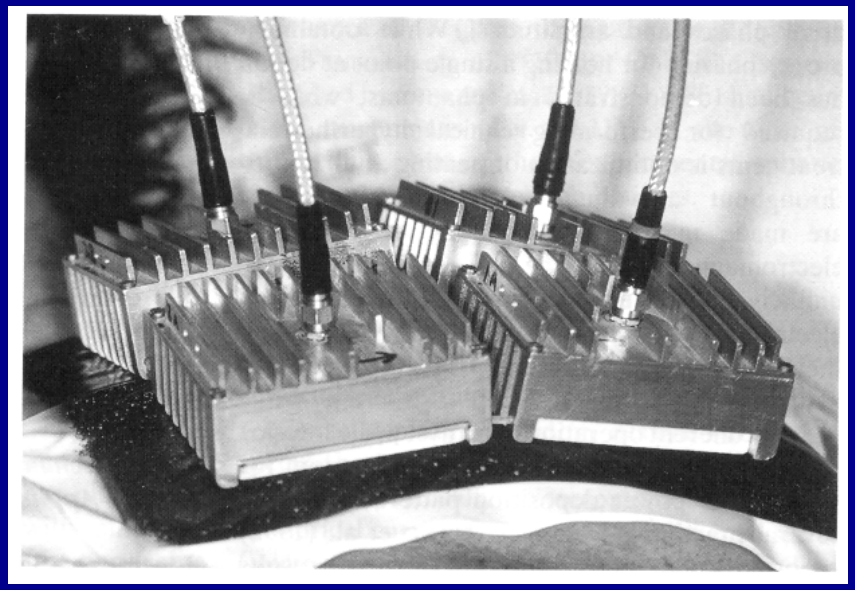
Reitveld & VanRhoon IJH 1999

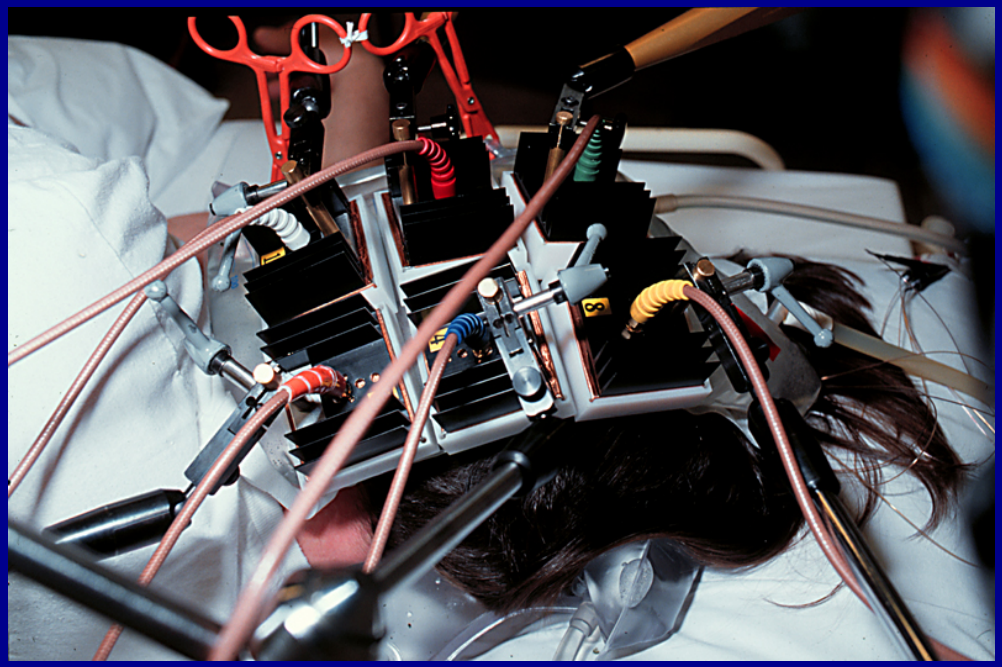
Lucite Cone Applicator

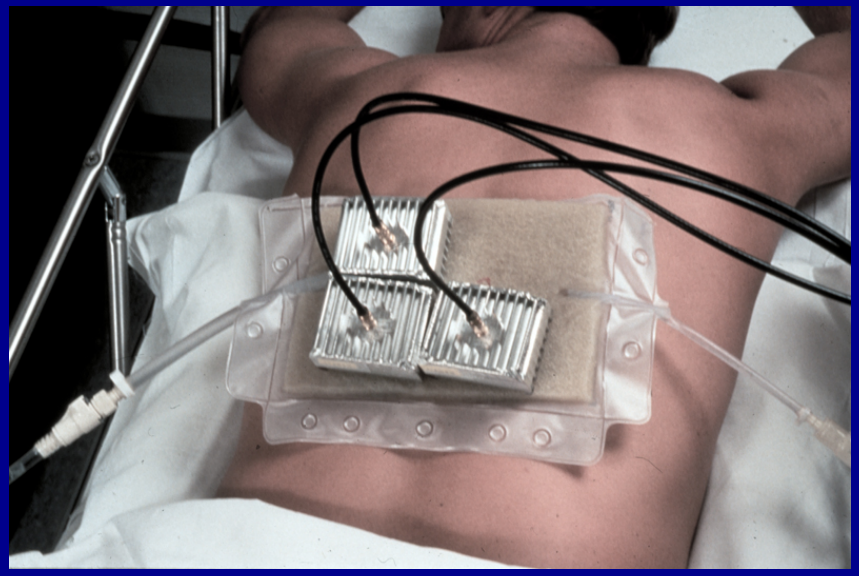


Gerard VanRhoon

Current Sheet Applicators (CSA)





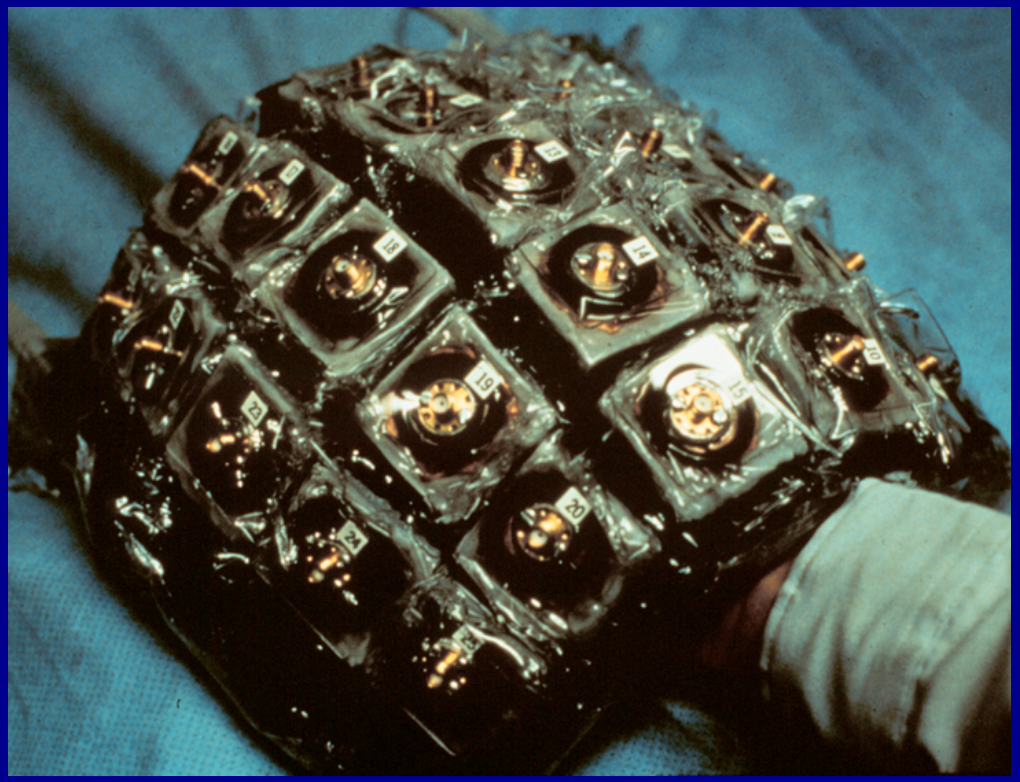


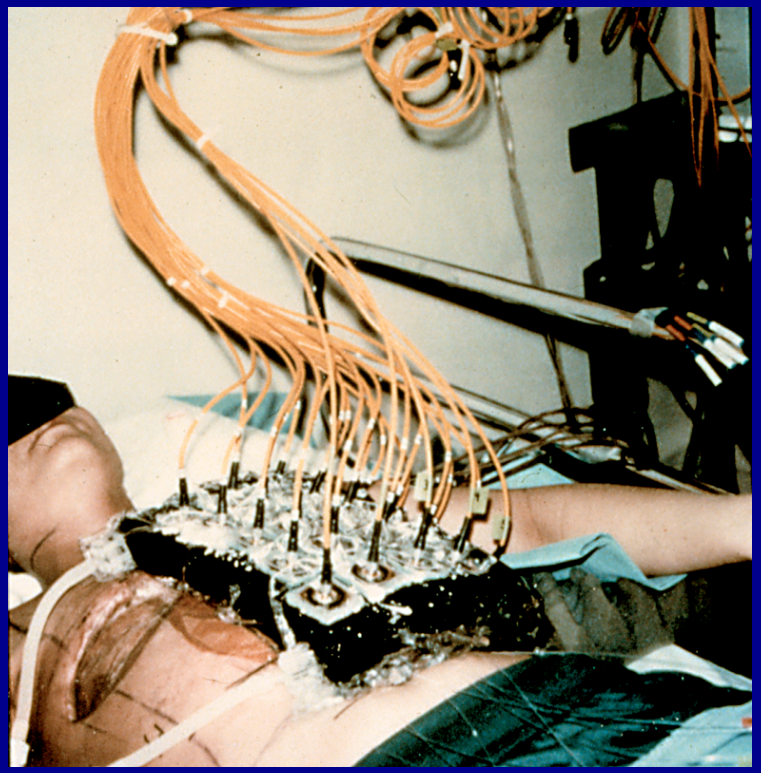
Multiple Frequencies - 915, 433
Phased Array - Deeper Penetration

J Hand, M Gopal, T Cetas

Microstrip Applicators

Stanford Blanket





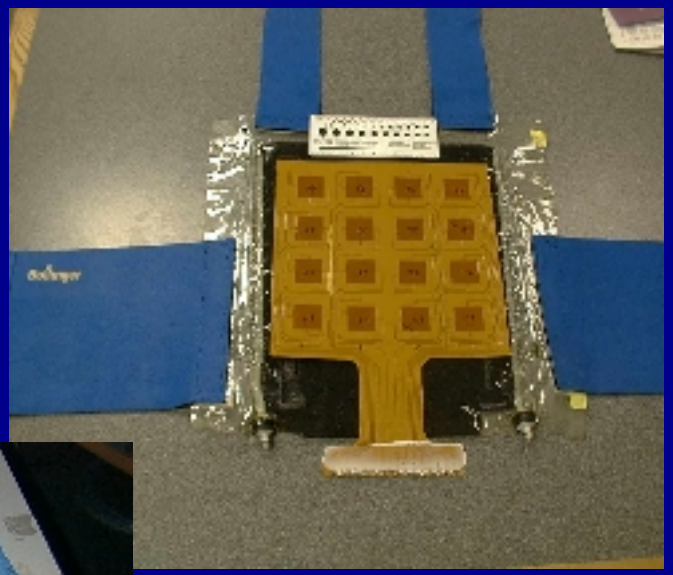
Lee, Fessenden, Kapp

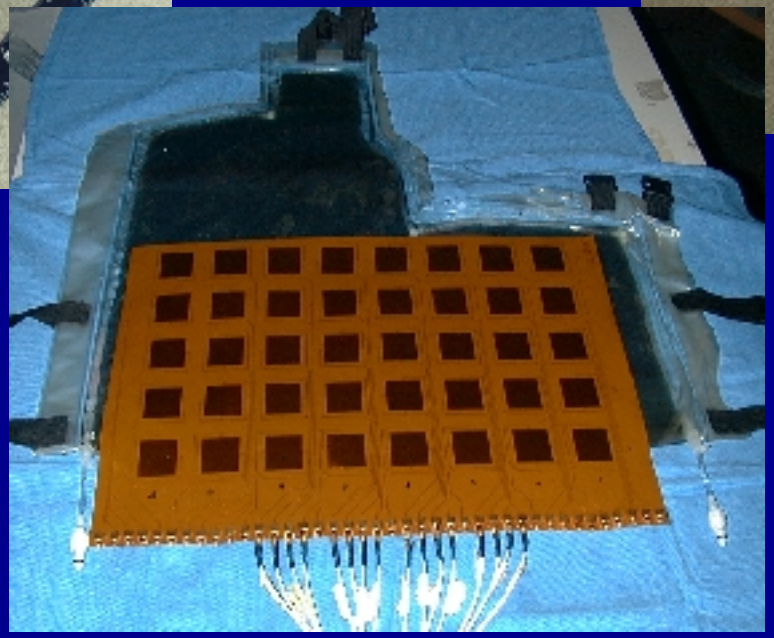
Flexible Conformal Microwave Array Applicator

6 mm Water Bolus

24 Aperture CMA

16 Aperture CMA





40 Aperture CMA

47 x 29 = 1363 cm^2

Stauffer, Rossetto, Neuman

Possible Treatment Configurations
Patient's Preference

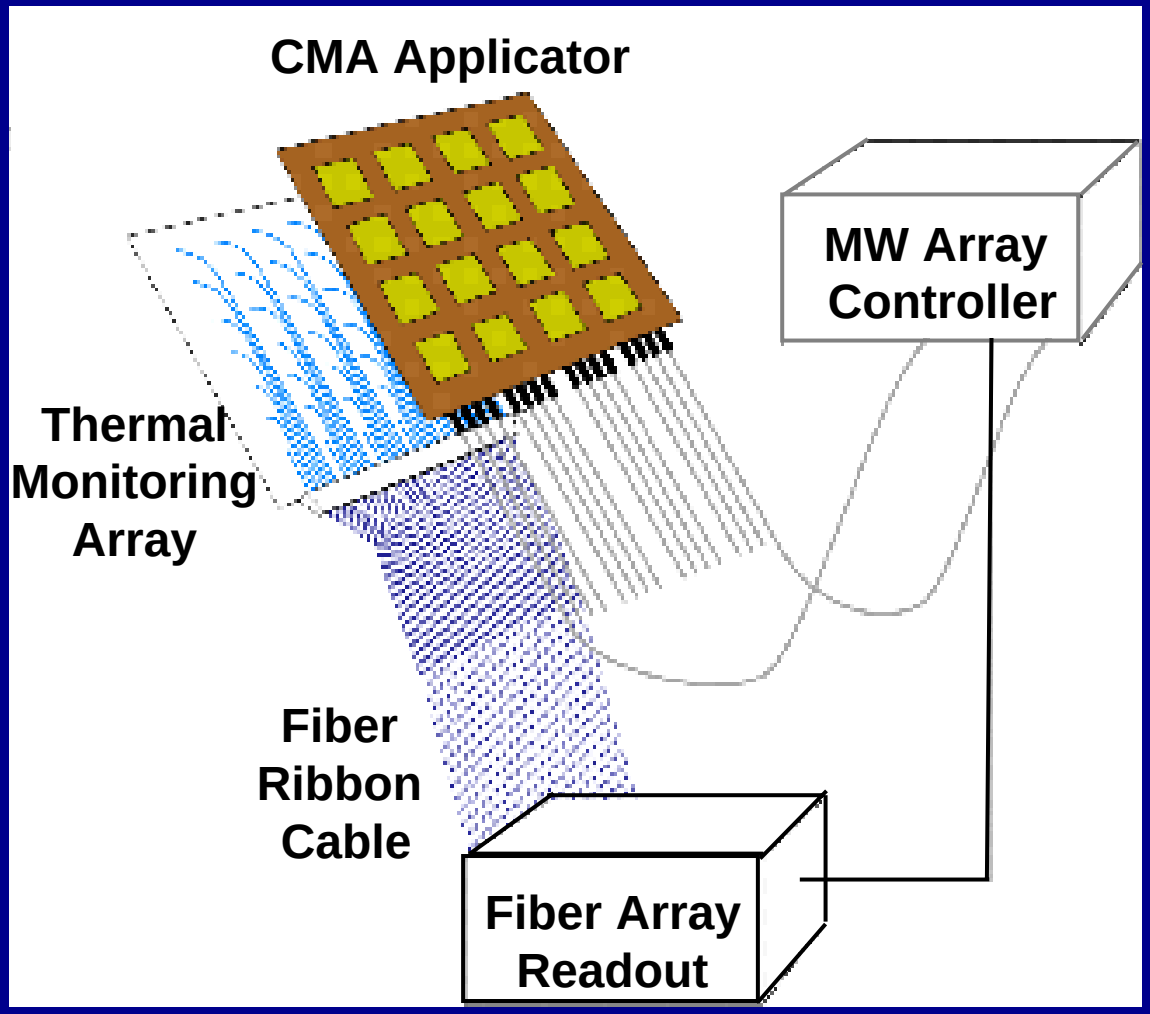
Standing - Pacing

Lying Down

Sitting

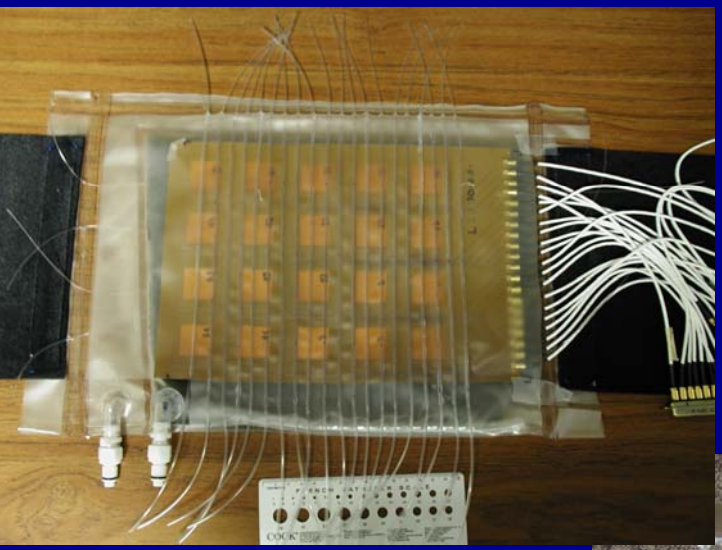
Thermometry Solutions for the Future

2D Thermal Monitoring Sheet



Ipitek Corp.

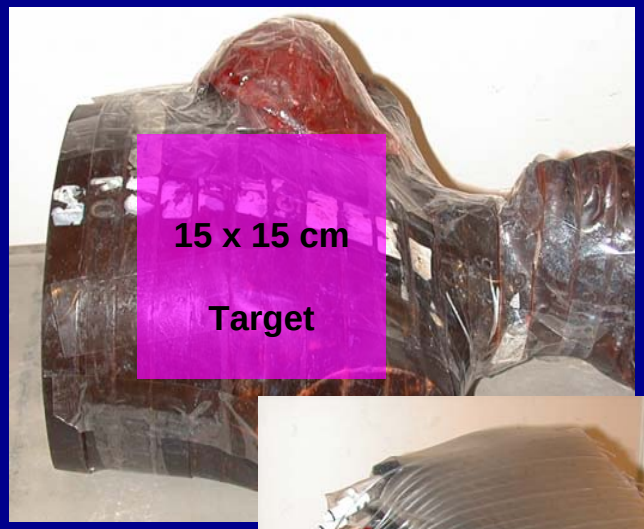
Combination Applicator
Simultaneous Heat and Brachytherapy

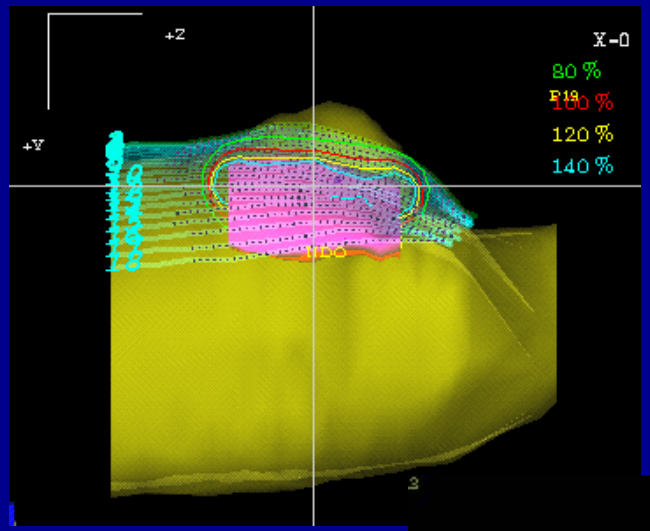


Rectangular
17 x 35 cm

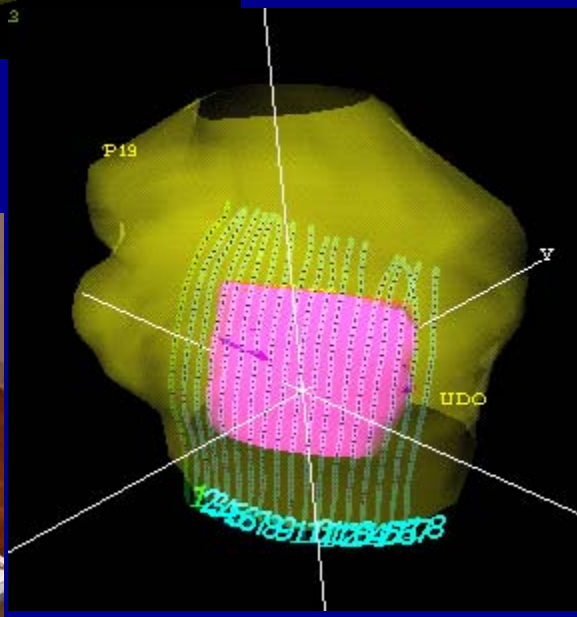
L-Shape
52 x 32 cm

Preparations for Simultaneous HT/RT Treatment Setup and Preplan



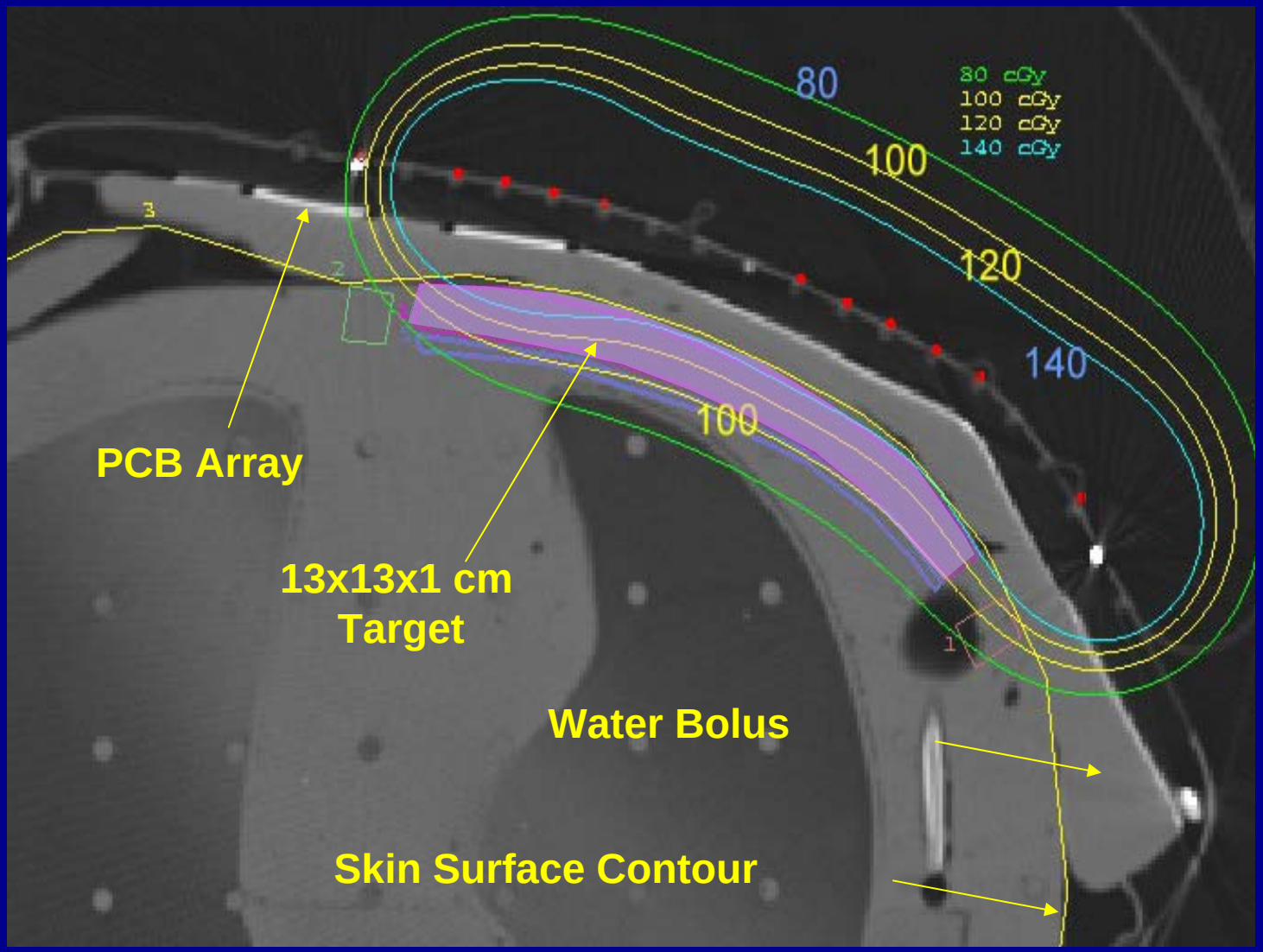


HDR



3D Conformal Dose Plan

IPSA -------> Plato



Deep Heating

Ultrasound Techniques

Piston Transducer

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

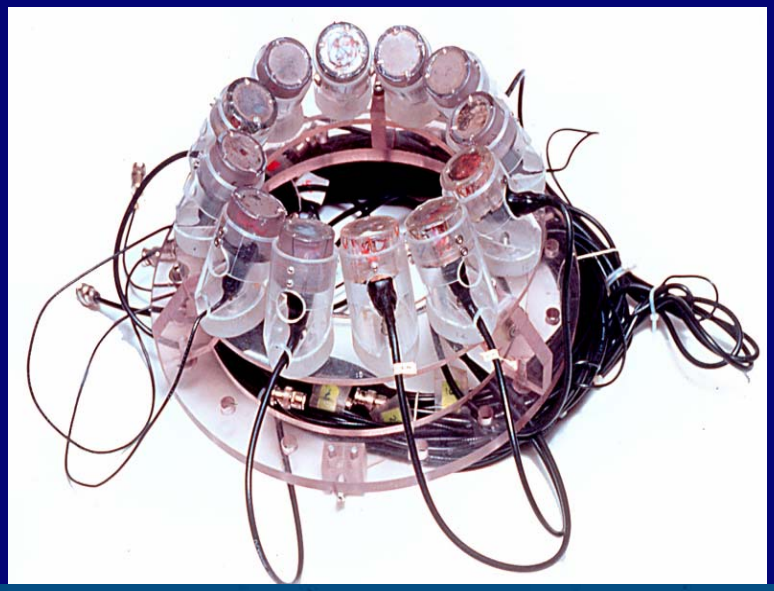
Transducer Arrays

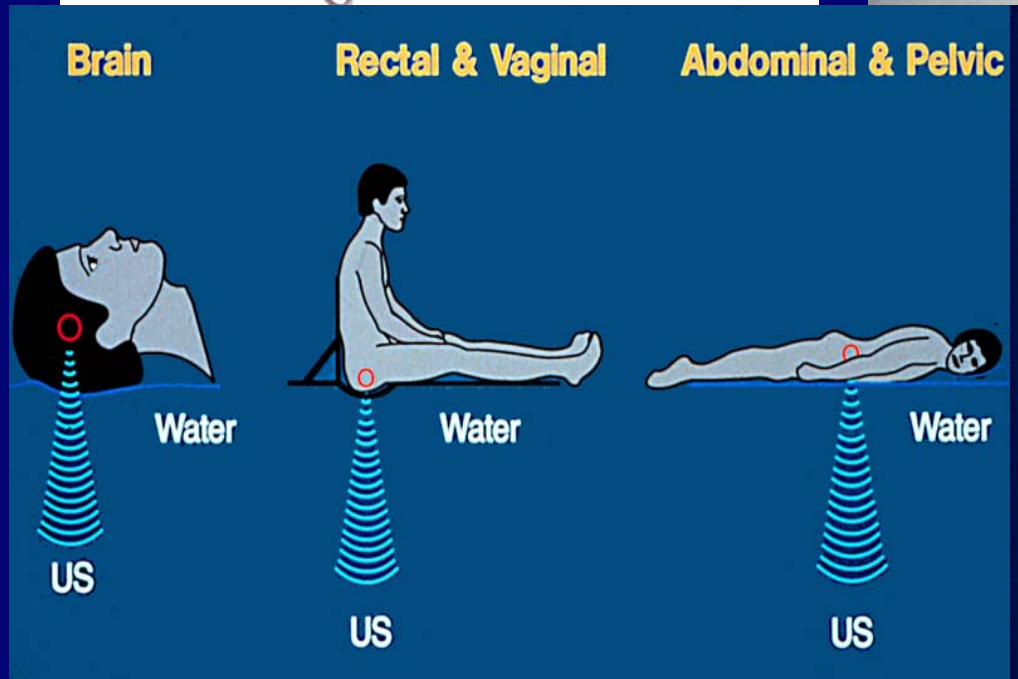
- Planar or Geometric focus
- Stationary lightly focused
- Stationary lightly focused - scanning reflector
- Mechanically or electrically scanned transducers
  - Lightly focused transducer array
  - Focused transducer array

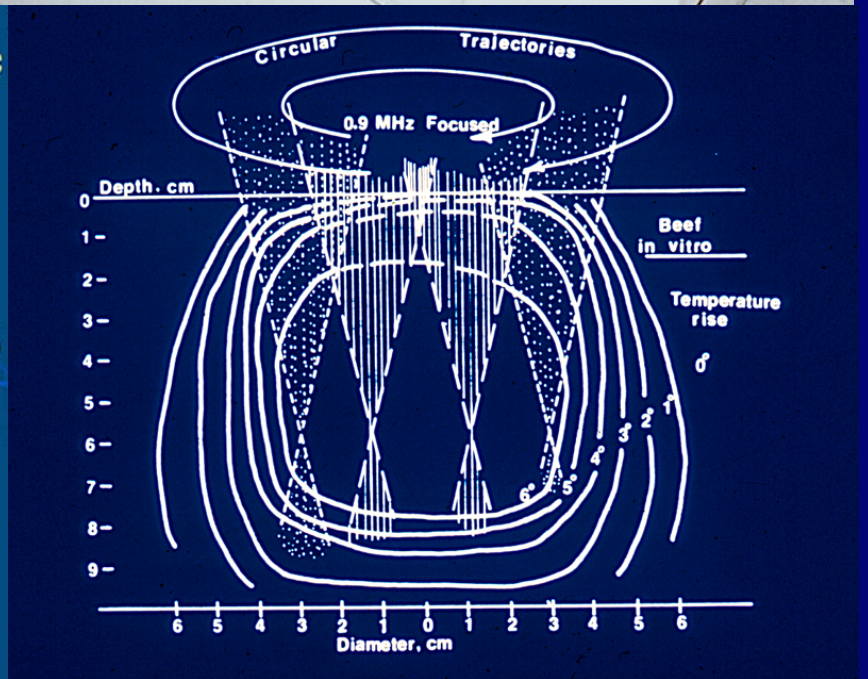
Radiofrequency Plate Electrodes

8 - 27 MHz

Scanned Focused Ultrasound

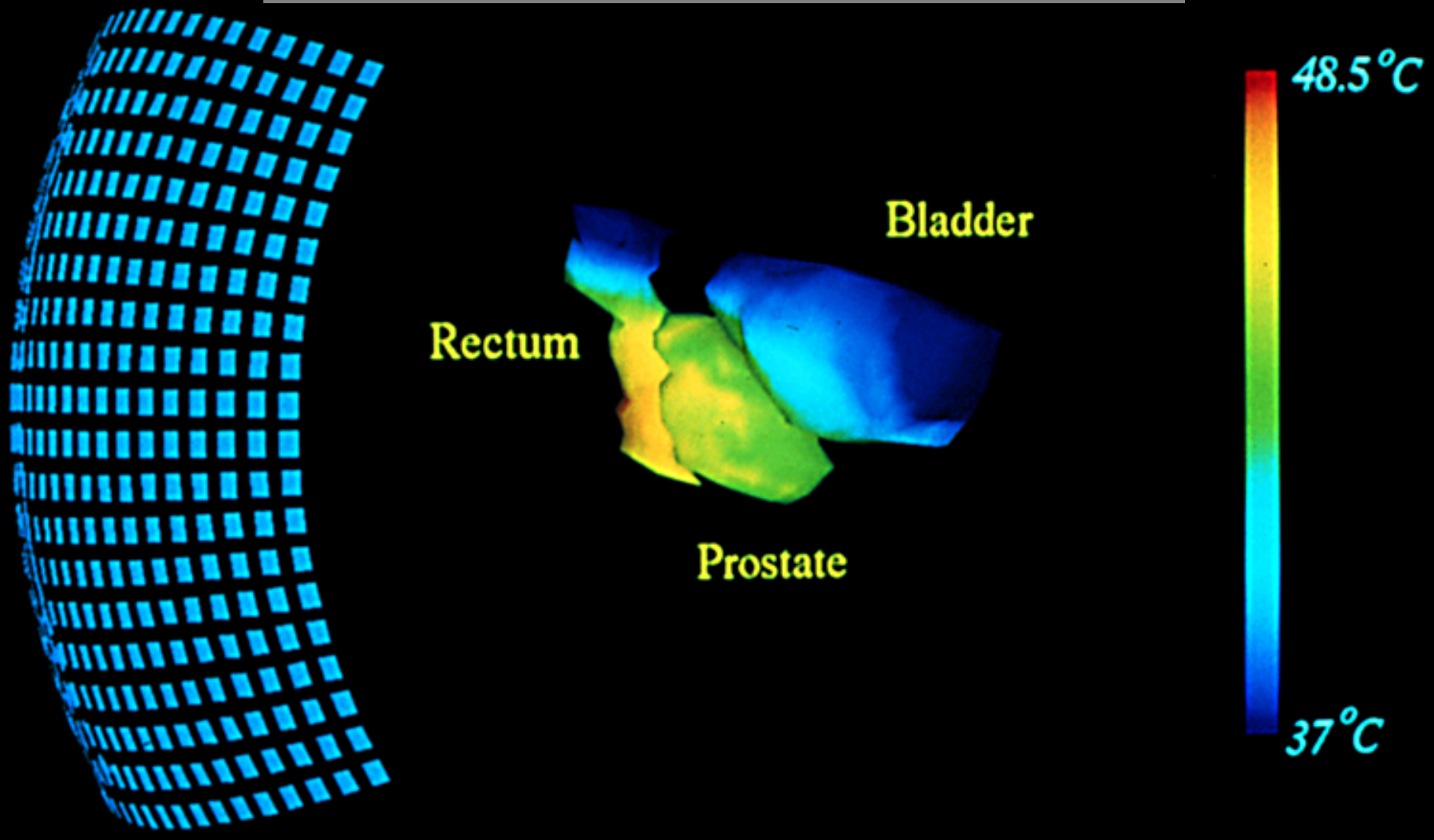




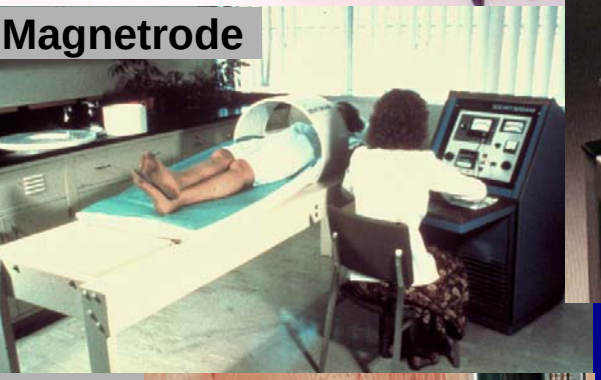


Spherical Section Array

Focused Ultrasound



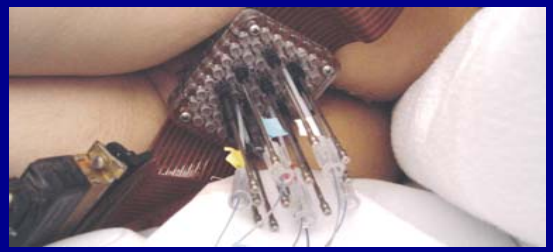
Evolving Technologies – Deep Heating



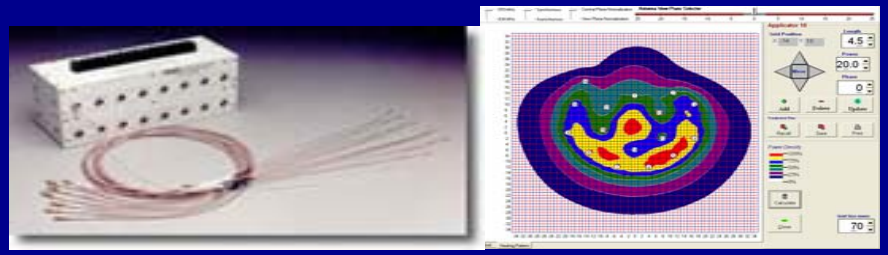
1982 1992 2002

Interstitial

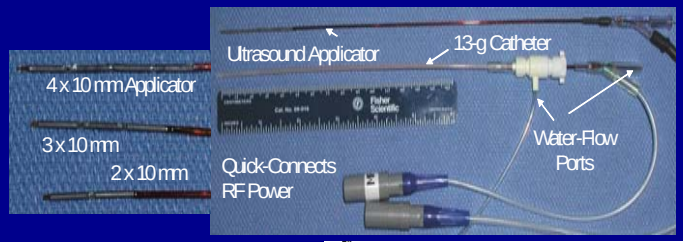
Multi-needle LCF hyperthermia system designed for hyperthermia combined with brachytherapy. (Photos courtesy of Peter Corry, William Beaumont Hospital).

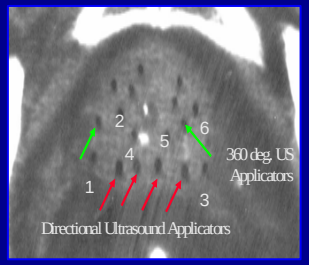


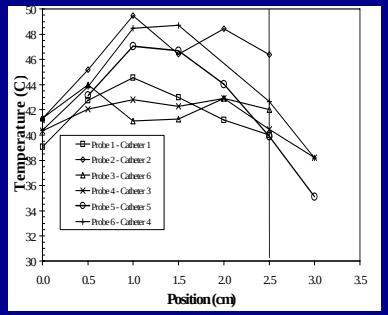
Interstitial microwave antennas suitable for hyperthermia in combination with interstitial brachytherapy (with permission from BSD Medical Corp.).



(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

Generation		
First	1980's	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)
Second	1990'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
Emerging	2000	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

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