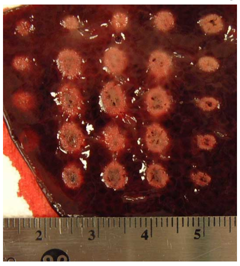
<u>BME2 – Biomedical Ultrasonics</u>

Lecture 7: Bioeffects I - Heat Deposition by Ultrasound



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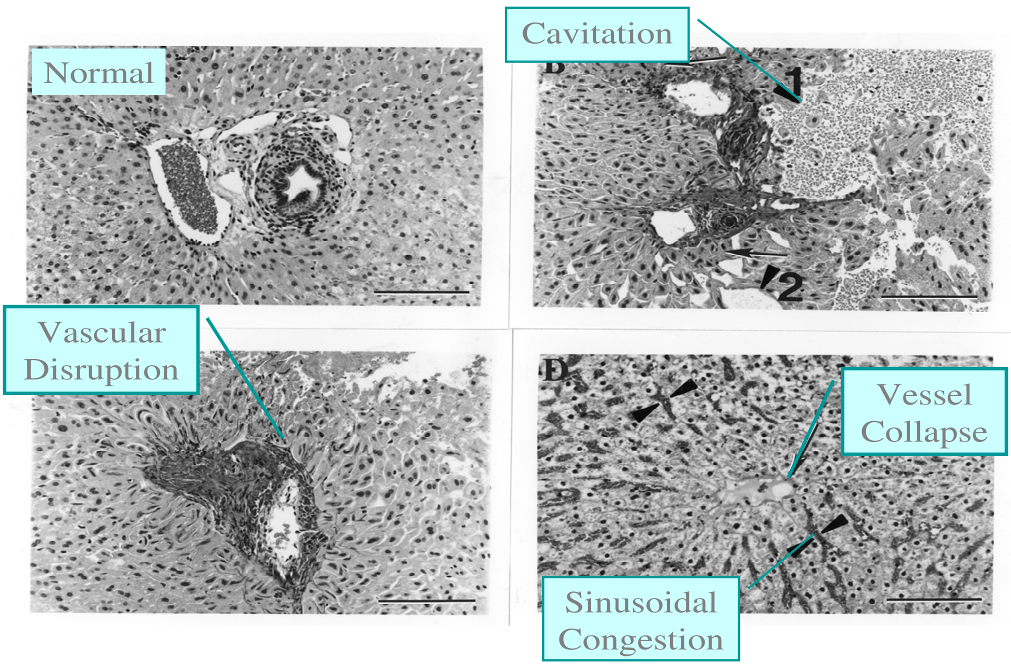
Contents

Clinical Application: *Focused Ultrasound Surgery*

- **Cancer**
  - Liver, kidney, prostate, breast, brain, skin…
- **Non Cancer**
  - Uterine fibroids, epilepsy, liver surgery, BPH, opthalmology…
- **Trauma Care**
  - Acoustic hemostasis
    - Transcutaneous
    - Intraoperative
- **Clinical Trials**
  - Columbia University
  - Univ. of Washington
  - Oxford University
  - Multiple sites in China

HAIFU 'JC-Tumor Therapy System'

Histological impact of ultrasound exposure

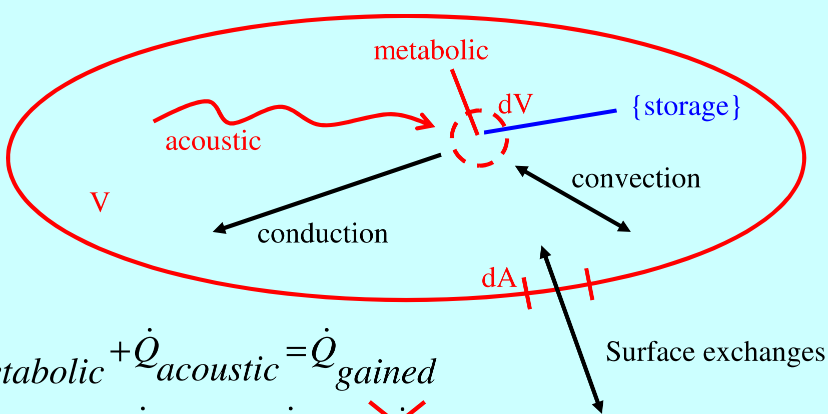


Overview of Bioheat Transfer
The Energy Balance

- Heat is continually being produced via metabolism
- Heat is continually being transferred between adjacent structures (and the environment)
- If net heat is either lost or gained, the temperature changes
- What matters???
  - Geometry & heat capacity (thermal inertia) of the organism
  - Physiological properties (blood perfusion rate, etc.)
  - Heat production from "applied energy" absorption
  - Transport effects (conductive, convective)
  - Thermoregulatory mechanisms (sweating, shivering, panting, etc.)
  - Metabolism
- The Bottom Line…

Overview of Bioheat Transfer
The Energy Balance

Energy Balance for a Control Volume V



$$\dot{Q}_{metabolic} + \dot{Q}_{acoustic} = \dot{Q}_{gained}$$

$$\dot{Q}_{gained} = \dot{Q}_{stored} + \dot{Q}_{loss} + \cancel{\dot{W}}$$

$$\dot{Q}_{loss} = \dot{Q}_{conduction} + \dot{Q}_{convection} + \cancel{\dot{Q}_{surfaces}}$$

$$\dot{Q}_{stored} = \underbrace{\left(\dot{Q}_{metabolic} + \dot{Q}_{acoustic}\right)}_{\text{energy increase}} - \underbrace{\left(\dot{Q}_{conduction} + \dot{Q}_{convection}\right)}_{\text{energy loss}}$$

Thermal Energy Production

- Heat production from metabolic processes
- Heat production from absorbed acoustic energy
- Ignore metabolic heating, the heat power gained by the control volume is:

$$\dot{Q}_{gained} = \dot{Q}_{source} = \int_V q_s(r,t)\,dV$$

- Here q_s is the power density deposited by the therapy source and r is the spatial coordinate
- The nature of q_s depends entirely on the details of how acoustic energy is converted to heat energy

Thermal Energy Storage

The Driver Behind Tissue Heating

- A net heat production leads to energy storage in the control volume
- The stored heat leads to a temperature elevation
- The rate of temperature rise is governed by the heat capacity = $\rho_t C_t$

$$\frac{\partial T(r,t)}{\partial t} = \frac{1}{\rho_t C_t} q_{stored}$$

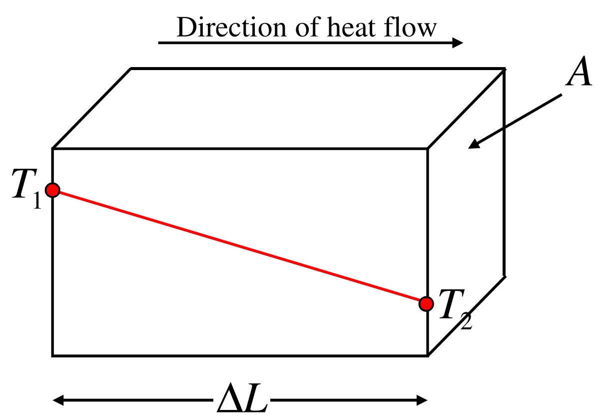
- Here q_{stored} is the power density of stored heat, ρ is the density, C is specific heat, and and subscript t refers to the tissue domain. Rearranging and integrating:

$$\dot{Q}_{stored} = \int_V \rho_t C_t \frac{\partial T(r,t)}{\partial t} dV$$

Thermal Energy Loss
1. Heat Transfer Due to Conduction

- Second Law: heat will spontaneously "flow" from a hot region to a cold, but not from cold to hot.
- Fourier Law of Heating in 1-D:

$$\frac{Q_{cond}}{\Delta t} = -KA\frac{(T_2 - T_1)}{\Delta L}$$



Thermal Energy Loss
1. Heat Transfer Due to Conduction

- The "heat flux" (f_c) is the heat energy conducted per unit area per unit time:

$$f_{cond} = \frac{Q_{cond}}{A\Delta t} = -K\frac{(T_2 - T_1)}{\Delta L} \qquad [\mathrm{W/m^2}]$$

- In the limit of infinitesimal ΔL yields the 3-D heat flux vector associated with a local temperature gradient (the Fourier Law)

$$\vec{f}_{cond} = -K_t\vec{\nabla}T \qquad [\mathrm{W/m^2}]$$

- This can be expressed in integral form by integrating the normal component of the heat flux vector over the surface of the control volume:

$$\dot{Q}_{cond} = -\int_A K_t\vec{\nabla}T(r,t)\cdot\hat{n}\,dA \qquad [\mathrm{W}]$$

Thermal Energy Loss
2. Heat Transfer Due to Convection

- Convective heat transfer is the transfer of thermal energy through a fluid due to the bulk motion of the fluid.
- Free convection: density differences between hot and cold fluid
- Forced convection: fluid motion is driven by other sources, such as blood flowing through an artery. This is the model we will consider
- The details of how heat is carried away by flow in a "pipe" are complicated. Moros *et al.** modeled this as a forced convection term applicable only in those regions of fluid flow (the "blood domain"):

$$\dot{Q}_{conv} = \int_V \rho_b C_b [\vec{u} \cdot \vec{\nabla} T(r,t)] dV \qquad \text{[W]}$$

- *b* refers to the properties of blood and $\vec{u}$ is the vector fluid flow field.

* E. G. Moros, W. L. Straube, and R. J. Myerson, "Finite difference vascular model for 3-D cancer therapy with hyperthermia," In Advances in Biological and Heat and Mass Transfer, Vol HTD-268, R. B. Roemer Ed., New York: ASME, 107- 111, 1993.

Thermal Energy Loss
2. Heat Transfer Due to Perfusion

- Representing the local contribution of blood perfusion to energy transfer is intricate… a modeling compromise is required
- Fick's Principle: The amount of "substance" taken up by a volume of tissue per unit time equals the difference in the quantities of substance in the arterial and venous flows times the blood flow rate.
- Let the "substance" be the concentration of thermal energy in the tissue and assume:
  - Blood enters the CV at the same temperature as the surrounding tissue, T_∞
  - Blood leave the CV as the local average temperature, *T*(r,t)

$$q_{perf} = w_b C_b (T - T_\infty) \qquad \text{[W/m}^3\text{]}$$

and

$$\dot{Q}_{perf} = \int_V w_b C_b [T(r,t) - T_\infty] dV \qquad \text{[W]}$$

- Here, w_b is the average blood perfusion rate.

The Bioheat Transfer Equation (BHTE)

- Recall the energy balance

$$\dot{Q}_{stored} = \dot{Q}_{acoustic} - \left(\dot{Q}_{cond} + \dot{Q}_{conv} + \dot{Q}_{perf}\right)$$

- Substitute the various source terms

$$\int_V \rho_t C_t \frac{\partial T(r,t)}{\partial t} dV = \int_V q_s(r,t) dV + \int_A K_t \vec{\nabla} T(r,t) \cdot \hat{n} dA - \int_V w_b C_b [T(r,t) - T_\infty] dV$$

$$\int_V \rho_b C_b \frac{\partial T(r,t)}{\partial t} dV = \int_V q_s(r,t) dV + \int_A K_b \vec{\nabla} T(r,t) \cdot \hat{n} dA - \int_V \rho_b C_b [\vec{u} \cdot \nabla T(r,t)] dV$$

- Apply the divergence theorem to the surface integral while noting that this energy balance applies for an arbitrary control volume and assuming the conductivity of the tissue is locally uniform …

The Bioheat Transfer Equation (BHTE)*

Tissue Domain

$$\rho_t C_t \frac{\partial T}{\partial t} = K_t \nabla^2 T - w_b C_b (T - T_\infty) + q_s$$

Blood Domain

$$\rho_b C_b \frac{\partial T}{\partial t} = K_b \nabla^2 T - \rho_b C_b (\vec{u} \cdot \nabla T) + q_s$$

Laminar Pouiseille Flow

$$\vec{u} = 2U_0 \left[1 - \left(\frac{r}{r_0}\right)^2\right]$$

* H. H. Pennes, *Journal of Applied Physiology*, 2: 93-122, 1948

The Source Term
Heat Deposition by Ultrasound Absorption

- The Westervelt equation* includes diffraction, absorption, nonlinearity and inhomogeneity

$$\left(\nabla^2 - \frac{1}{c^2}\frac{\partial^2}{\partial t^2}\right)p - \frac{1}{\rho}\nabla p\cdot\nabla\rho + \frac{\delta}{c^4}\frac{\partial^3 p}{\partial t^3} + \frac{\beta}{\rho c^4}\frac{\partial^2 p^2}{\partial t^2} = 0$$

  Where p is the propagating acoustic pressure perturbation, c is the local sound speed, ρ is the local density for the medium, δ the local acoustic diffusivity, and β is a local coefficient of nonlinearity.

- Loss mechanisms:
  - Viscous and thermal damping
  - Molecular relaxation, and others
  - Absorption coefficient is related to the acoustic diffusivity by $\alpha = \frac{\delta\omega^2}{2c^3}$

* M.F. Hamilton, and C.L. Morfey. Model equations. In: M. F. Hamilton, and D.T. lackstock,editors, *Nonlinear Acoustics*, Chapter 3, Academic Press, 1998.

The Source Term
Heat Deposition by Ultrasound Absorption

- Pierce* computes absorbed sound power density from

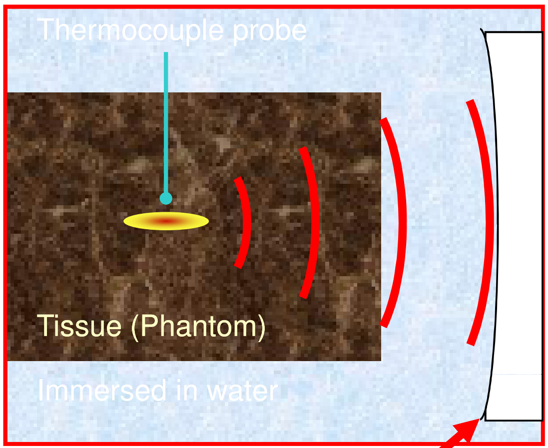
$$q_s = 2\alpha I = \frac{2\alpha}{\omega^2\rho c}\left\langle\left(\frac{\partial p}{\partial t}\right)^2\right\rangle$$

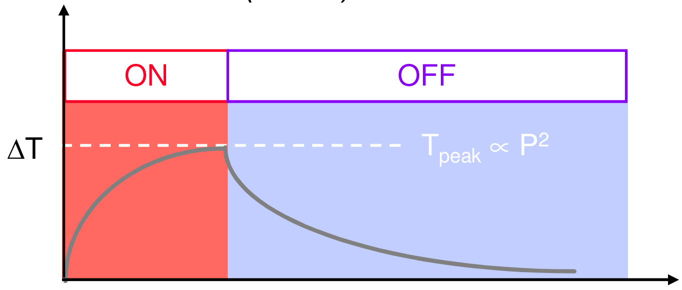
  where I is the acoustic intensity, all parameters are assumed to be functions of space and α is the attenuation coefficient.

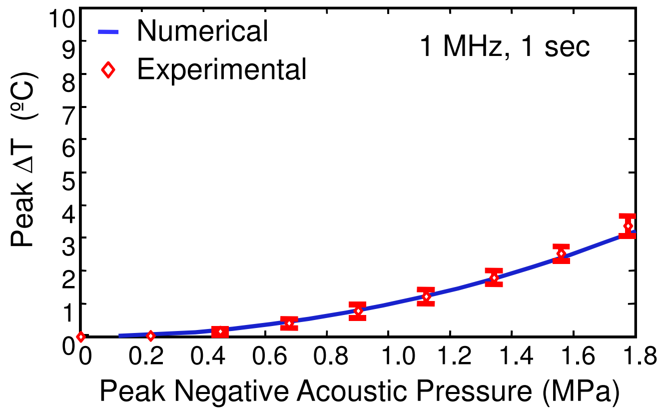
- q_s couples the pressure solution to the the bioheat equation.
- Solution is usually done numerically (FDTD, FEM, etc.)
- Issues to consider
  - The Westervelt eq. assumes a pure viscothermal medium where $\alpha \propto f^2$
  - In real tissue, $\alpha \propto f^{1.1}$
  - High amplitude beams possess nonlinearity that enhances absorption

* A. D. Pierce. *Acoustics, An introduction to its physical principles and applications*, Chap 10, McGraw-Hill Book Company, 1981.

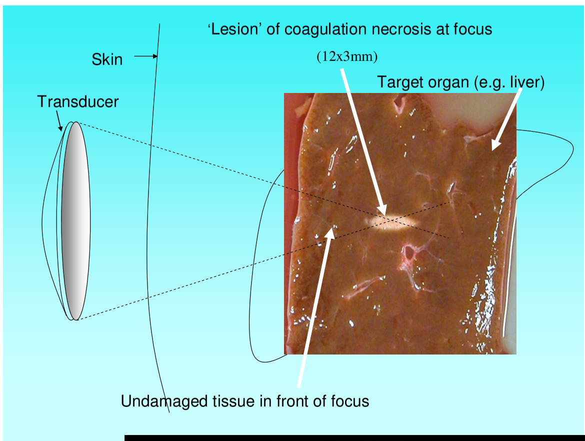
Typical Result: *Tissue Heating from High Intensity Focused Ultrasound (HIFU)*



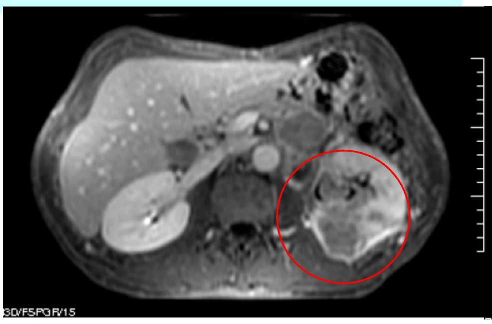




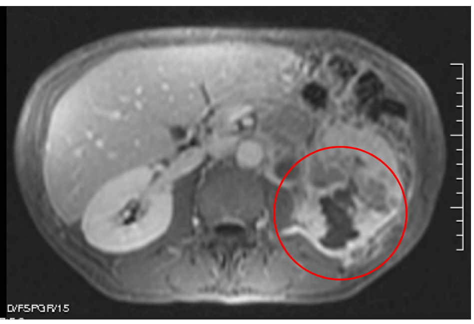
HIFU for non-invasive cancer treatment



- Aimed at creating localized cell death by thermal necrosis
- This is achieved by exceeding the threshold temperature beyond which proteins denature.

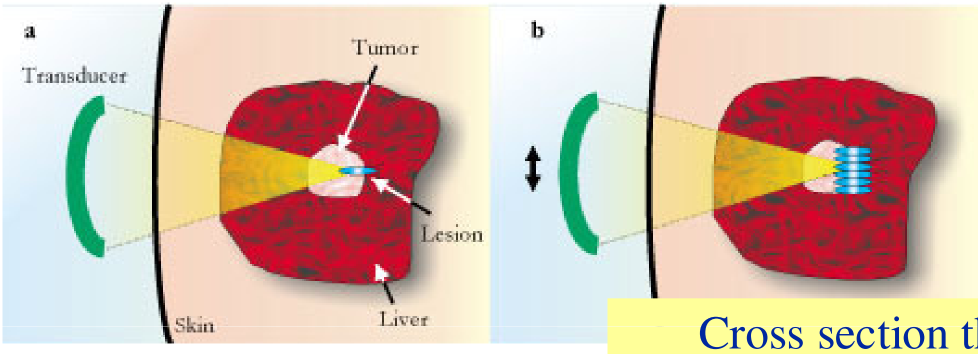


Pre-HIFU

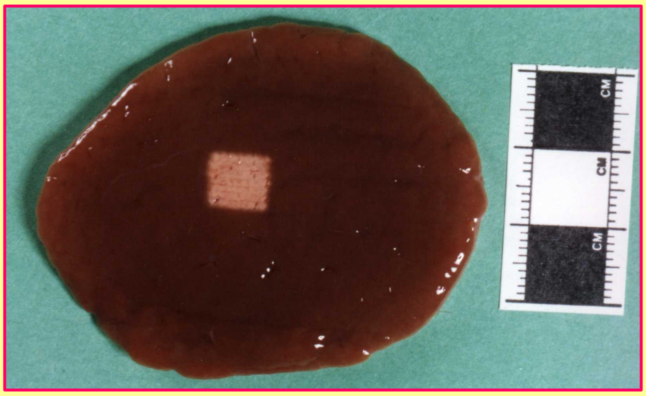


Post-HIFU

Treating a Clinically Relevant Tissue Volume



Cross section through array



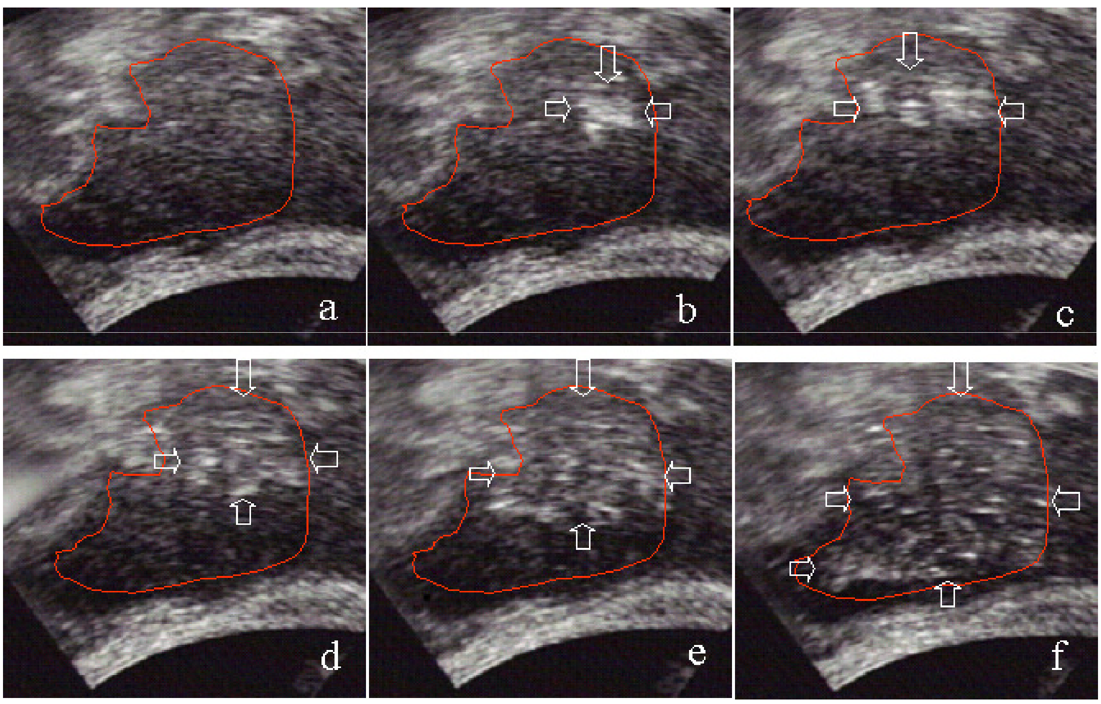
Beef Liver Exposed to HIFU

The Institute of Cancer Research

The Institute of Cancer Research

***Courtesy of Gail ter Haar, ICR, UK**

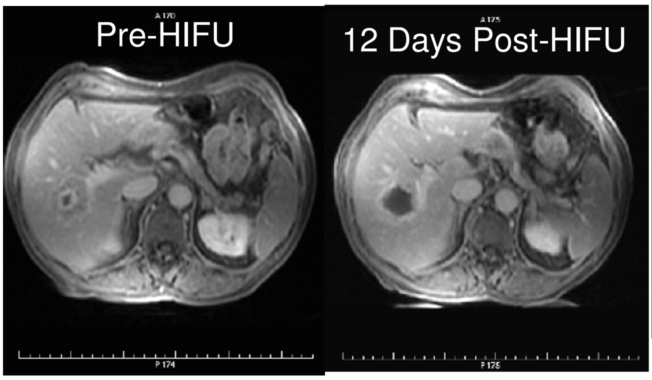
US-Monitoring of HIFU Treatment Delivery



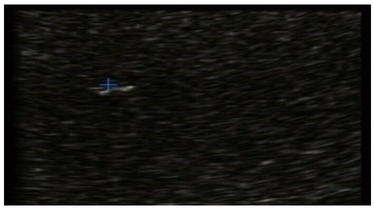
Wu F *et al*, Ann. Surg. Oncology 11: 1061-1069 (2004)

Successes and Current Limitations of HIFU Therapy

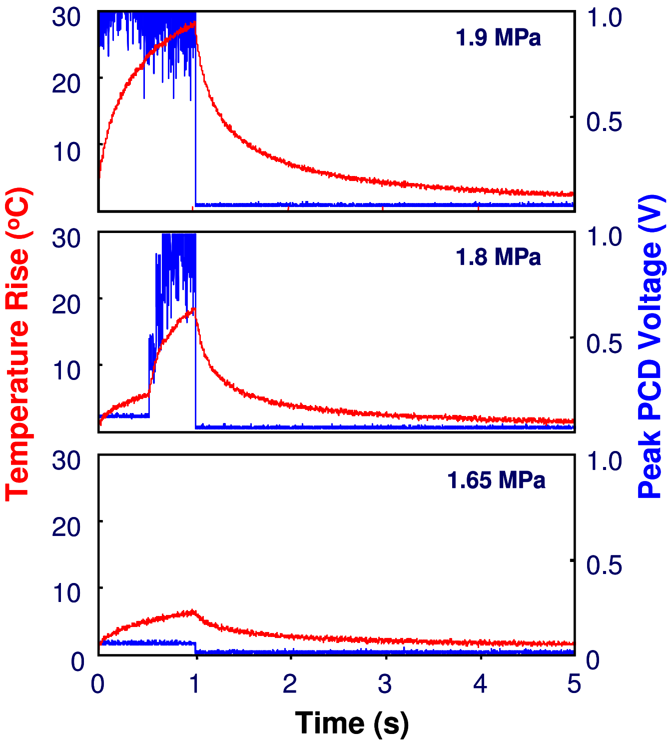
- Unique ability to create controlled heating *non-invasively* deep within the body.
- No significant side-effects, no limit to number of treatments.
- Clinical HIFU unit at the Churchill Hospital (Oxford) has treated numerous patients with solid liver and kidney tumours successfully.



- Treatment can be slow relative to invasive modalities (more than 5 hours for a 10-cm tumour)
- Treatment monitoring *during* HIFU exposure is difficult.
- Current methods of ultrasound-guided HIFU rely on appearance of bright-ups, corresponding to tissue boiling: overtreatment is likely and prefocal damage possible.



A Possible Solution: Cavitation-Enhanced Heating



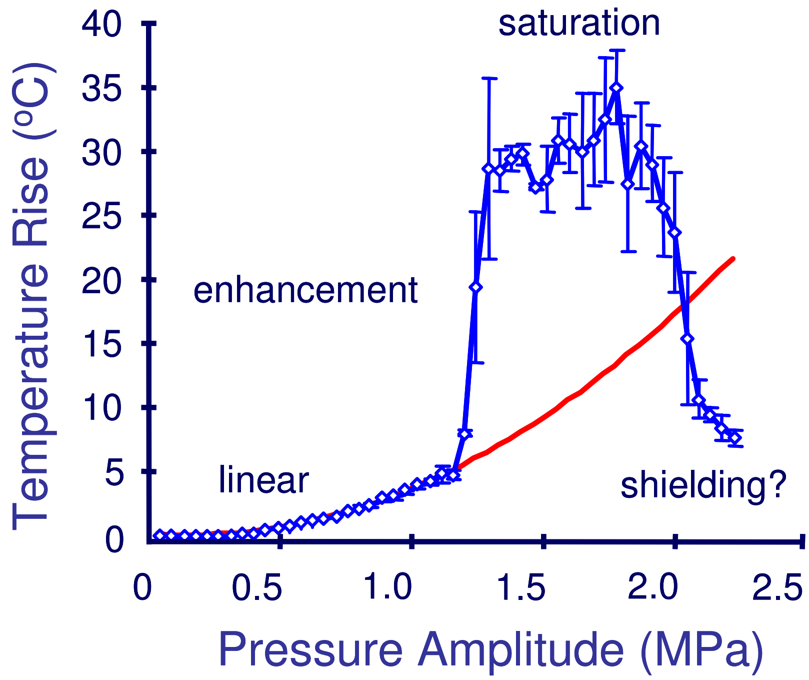
1 sec HIFU exposure
1 sec cavitation

1 sec HIFU exposure
0.5 sec cavitation

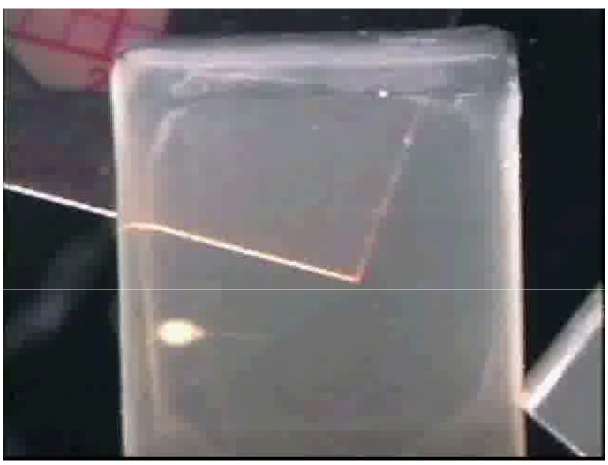
1 sec HIFU exposure
No cavitation

C-C Coussios *et al*, Int J Hyperthermia, 23(2): 105–120, 2007.
C.-C. Coussios and R.A. Roy, Annual Review of Fluid Mechanics Vol. 40:395-420 (2008).

Dependence of Temperature Rise on HIFU Pressure Amplitude below and above Cavitation Threshold

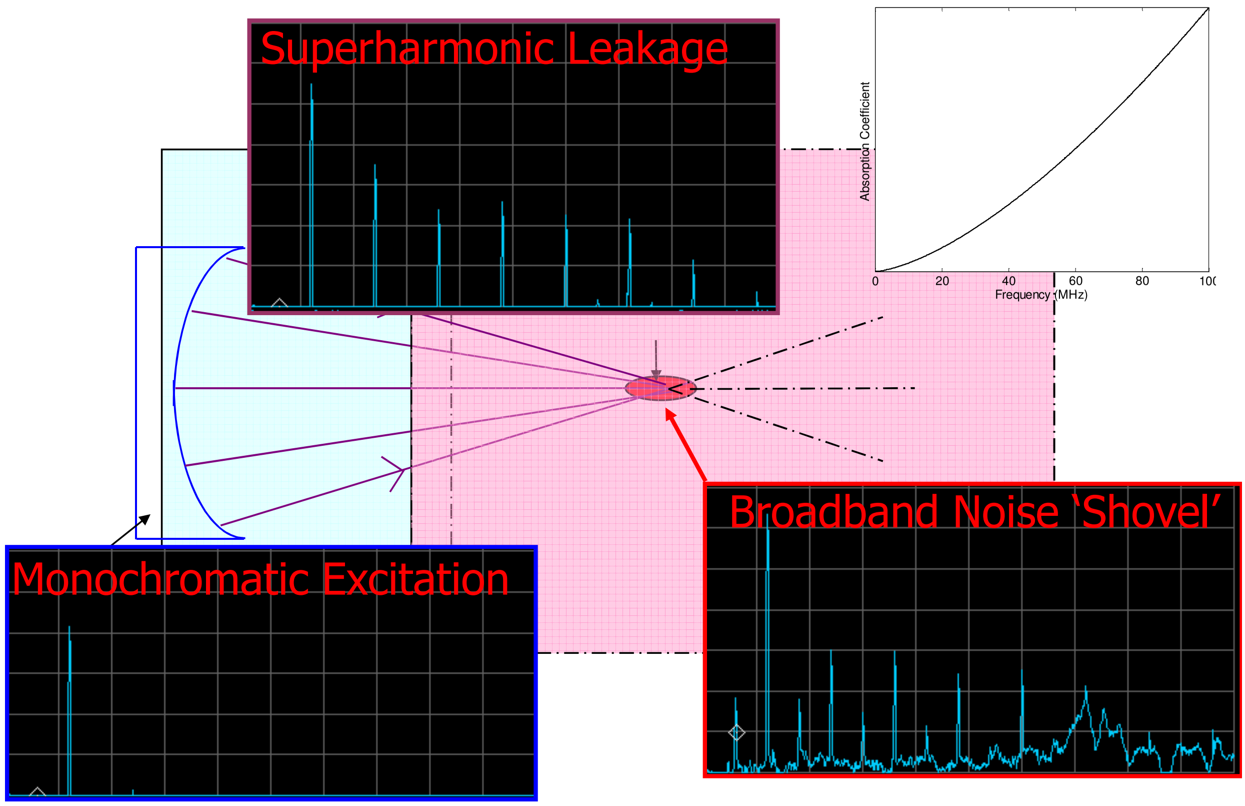


Creation of Thermal Lesion (region of T>60C)



Non-linearity *vs.* Cavitation

Enhancement Mechanism: 'The Energy Shovel'



Modelling Bubble-Enhanced Heating

$$\rho C\frac{\partial T}{\partial t} = \overbrace{K\nabla^2 T}^{\text{Conduction}} + \overbrace{q_{us} + q_{bubbles}}^{\text{SourceTerms}}$$

$$q_{bubbles} = q_{vis} + q_{rad}$$

$$q_{us} = \frac{2\alpha}{\omega^2 \rho c}\left(\frac{\partial p}{\partial t}\right)^2$$

Computed from FDTD solution to Westervelt Eq.

Related to ...
vis...
bub...
la...
hig...
Sta...
i...

$$q_{rad}(r) = 2\alpha I_{rad}(r)$$

$$q_{rad}(r) \approx \frac{\left\langle P_{rad}^2 \right\rangle_t}{\rho c}$$

$$P_{rad} \approx \frac{\rho R}{r}\left(2\dot{R}^2 + R\ddot{R}\right)e^{-\alpha(r-R)}$$

The absorption of broad-band acoustic emissions

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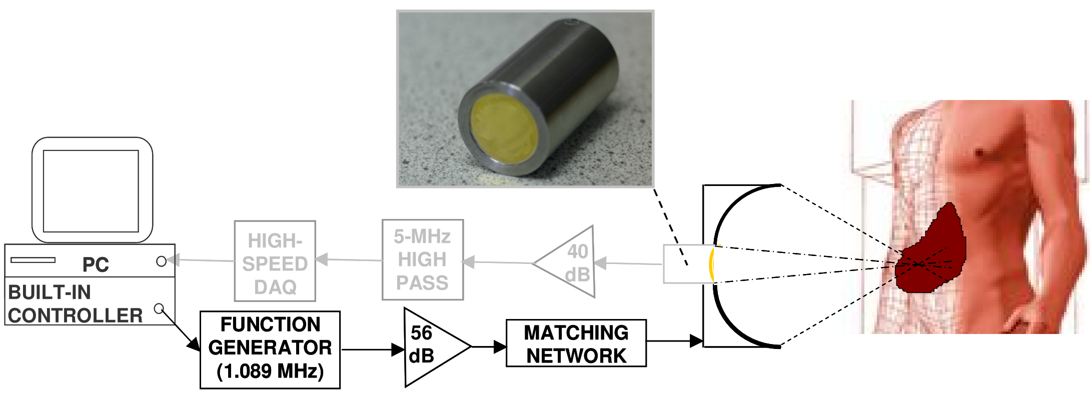
smaller bubbles
low viscosities

Inertial Cavitation is Implicated

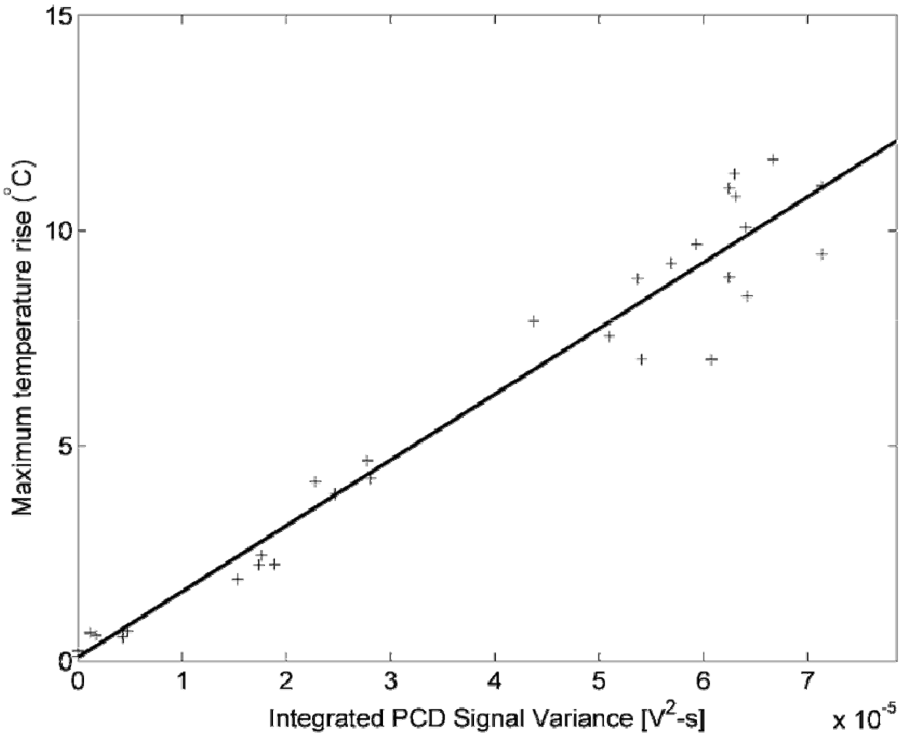
•C.-C. Coussios and R.A. Roy, Annual Review of Fluid Mechanics Vol. 40:395-420 (2008)..
•C-C Coussios *et al*, *Int J Hyperthermia*, 23(2): 105–120, 2007.

HIFU in the clinic and in the laboratory

Clinically Relevant Cavitation Detection



Non-Invasive Cavitation-Based Thermometry (in tissue phantom)



JRT Collin *et al.,* Ultrasound Med Biol., In press, 2008.

Conclusions: Cavitation-Enhanced HIFU

- Inertial cavitation locally enhances energy deposition and can result in a 600% increase in the local rate of heating
- Inertial cavitation can be detected remotely without interference from the main HIFU pulse
- Broadband noise emissions can be directly correlated to focal temperature rise *in a known, given medium.*
- Mapping cavitation activity in real time during HIFU exposure could provide a means of real-time treatment monitoring.