ICR The Institute of Cancer Research

A comparison between theory and experiment in thermal ablation of perfused livers

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Contents

Introduction

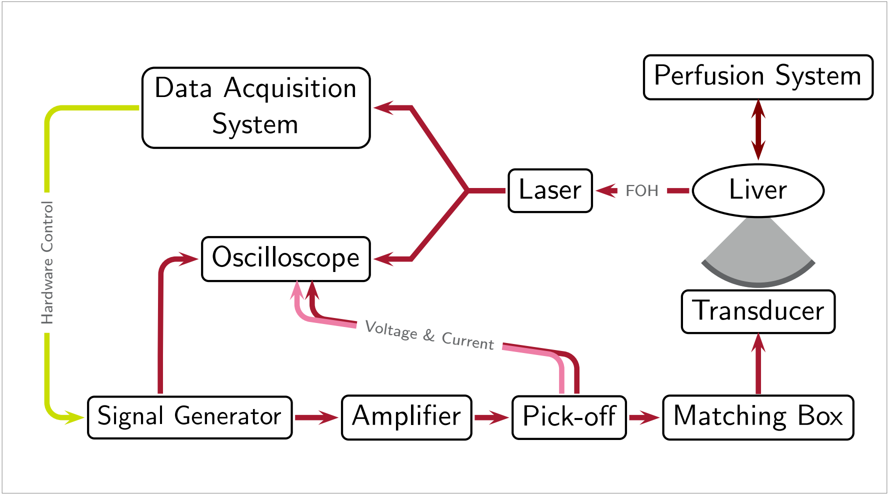
A series of experiments have been performed on perfused livers to

- Ascertain the effect of perfusion on heat deposition from high-intensity focused ultrasound for physiologically and anatomically relevant blood flow in liver.

Experiments were performed at

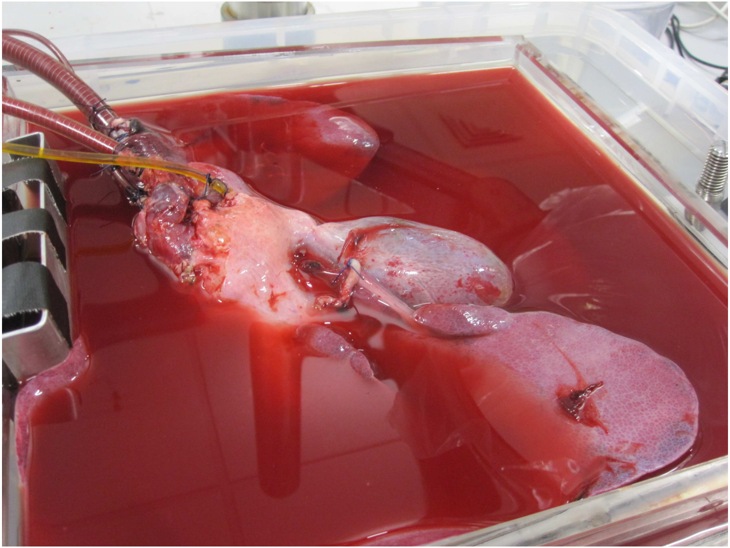
- Low intensities to enhance accuracy in monitoring, yet induce measurable temperature rises.
- Nonlinear wave propagation without shock formation.
- Both acoustic and thermal field monitored via fibre-optic hydrophone at focus of ultrasound field.
- Frequency sufficiently high to try to avoid sustained cavitation activity.

Experimental Set-up
Schematic Representation of Experimental Set-up

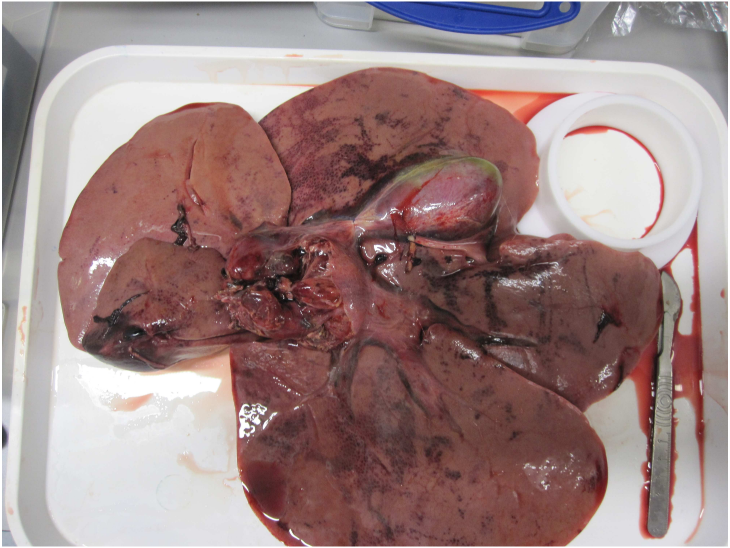


Experimental Set-up

The Liver
Before . . .



The Liver
. . . After

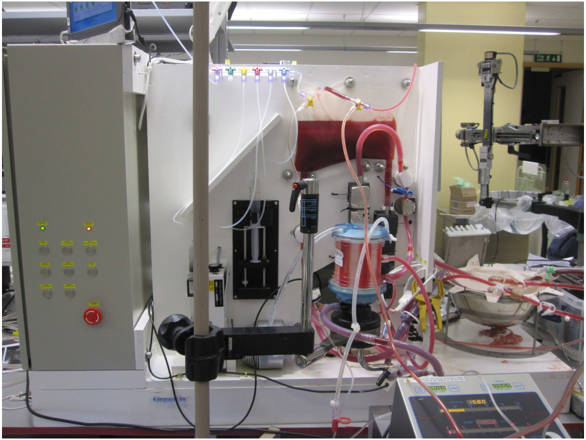


Perfusion System

The OrganOx metra controls

- blood pressures
- oxygen
- bile salts
- insulin
- nutrients
- temperature

to within physiologically relevant bounds.



Real-time diagnostic data gives information on the viability of the organ: livers may remain viable for up to 72 hours.

Computation

Water and tissue acoustic and thermal model

Khokhlov-Zabolotskaya-Kuznetsov equation

$$\frac{\partial^2 p}{\partial z \partial \tau} = \frac{c}{2}\nabla_\perp^2 p + \frac{\alpha}{2c^3}\frac{\partial^3 p}{\partial \tau^3} + \frac{\beta}{2\rho c^3}\frac{\partial^2 p^2}{\partial \tau^2}$$

$\alpha = \alpha^{\mathrm{scat}} + \alpha^{\mathrm{abs}}$ both have frequency-dependent power-laws $\alpha = \alpha_0 \left|\omega\right|^\eta$.

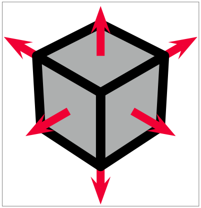
Pennes bioheat transfer equation

$$\rho C \frac{\partial T}{\partial t} = \kappa \left(\frac{1}{r}\frac{\partial T}{\partial r}\left(r \frac{\partial T}{\partial r}\right) + \frac{\partial^2 T}{\partial z^2}\right) - \omega \left(T - T_\infty\right) + q\left(r, z, t\right)$$

where $q\left(r, z, t\right) = 2 \sum_{i=1}^{N} \alpha_i^{\mathrm{abs}} \frac{p_i^2}{c\rho}$ for the N computed harmonics.

Assumptions
1. Mathematical

- Paraxial approximation in acoustic equation
- No interface conditions between liver/water
- Perfectly matched layer at acoustic boundaries
- Transducer face model via Gaussian modes[1]
- Acoustically and thermally, spatially and temporally homogeneous
- Bulk perfusion, only models the effect of perfusion on temperature, where perfusion removes thermal energy isotropically from an infinitesimal unit volume



[1] J. E. Soneson, M. R. Myers, *J. Acoust. Soc. Am.* **122** (2005) pg. 2526–2531.

Assumptions

2. Numerical

- Hybrid scheme: frequency domain for linear propagation, diffraction and attenuation, time domain for nonlinearity[1]
- Finite-difference time-domain for bioheat equation using second-order diagonal implicit Runge-Kutta scheme

1 J. E. Soneson, 8^{th} *Int. Symp. Therapeutic Ultrasound: AIP Conf. Proc.* **1113** (2009) pg. 165–169.

Simulated Acoustic Field

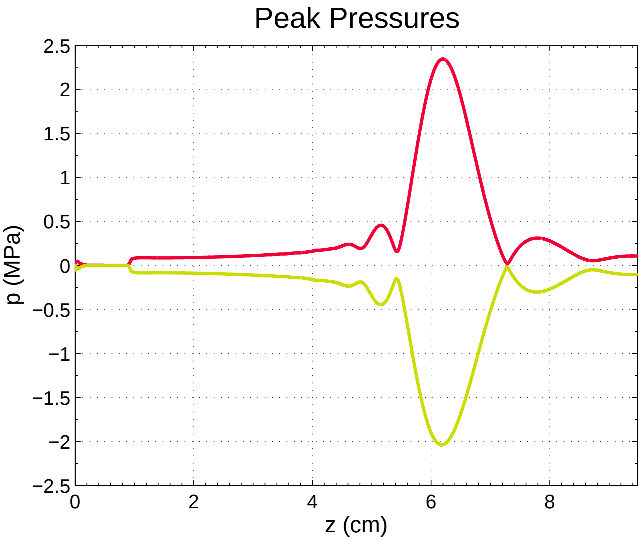
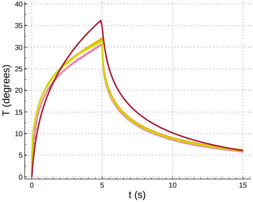
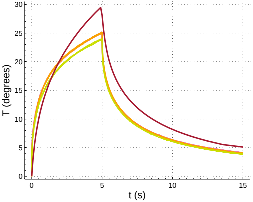


Figure: Peak pressures from a single element transducer along propagation direction

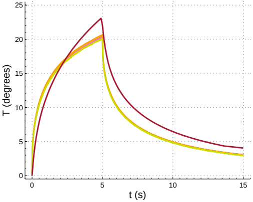
Higher or Lower?



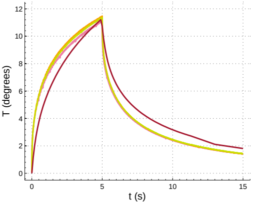
(a) setting -11dBm



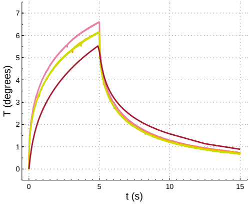
(b) setting -12dBm



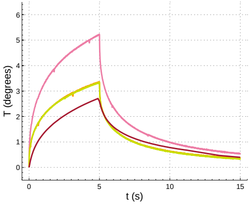
(c) setting -13dBm



(d) setting -16dBm



(e) setting -19dBm



(f) setting -22dBm

Figure: Red is simulation. At high intensities overestimates, low intensities underestimates

Variability

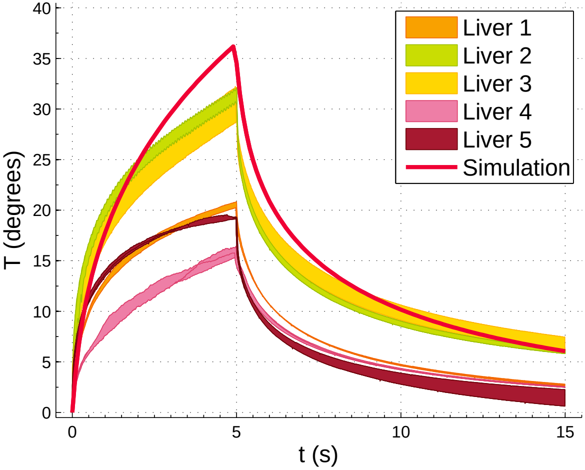


Figure: Variability in thermal profiles at the same drive levels between samples at similar depths. Note that only a limited, local knowledge of the vasculature is known.

Variability in Attenuation

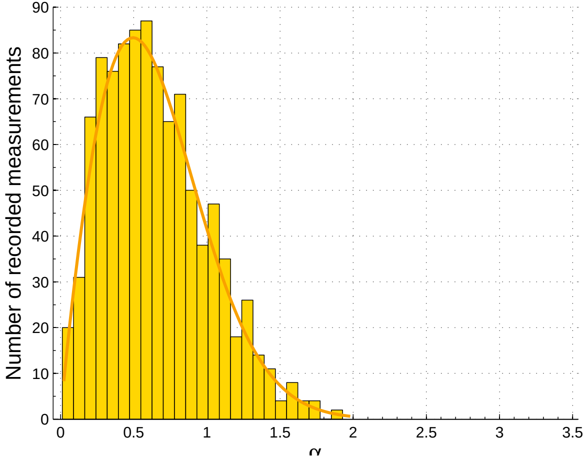


Figure: Best fit of parameters for a Weibull distribution[1] to match all experimental data at 2MHz

1 B. I. Raju, K. J. Swindells, S. Gonzalez, M. A. Srinivasan, *Ultrasound Med. Bio.* **29** (2003) pg. 825–838

Variability in Attenuation

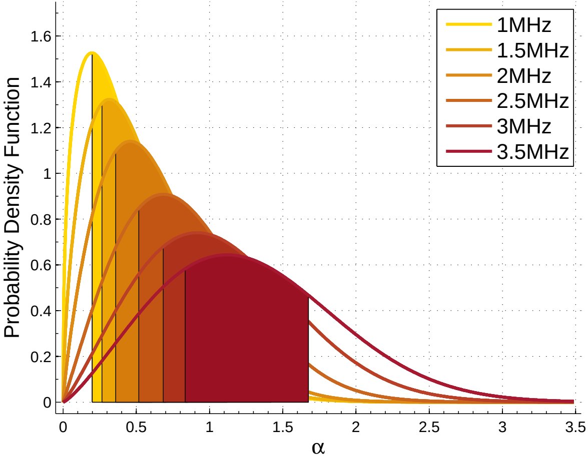


Figure: Probability density functions for Weibull distribution for range of frequencies, showing $\pm 25\%$ confidence intervals

Variability in Attenuation

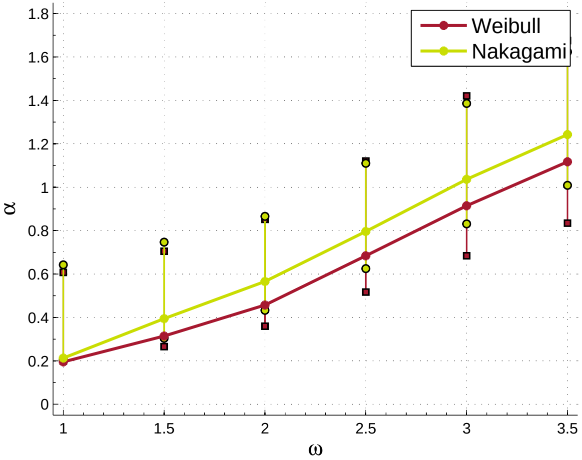


Figure: Powerlaw dependence of attenuation with frequency, with appropriate confidence intervals for Weibull and Nakagami distributions

Effects of flow

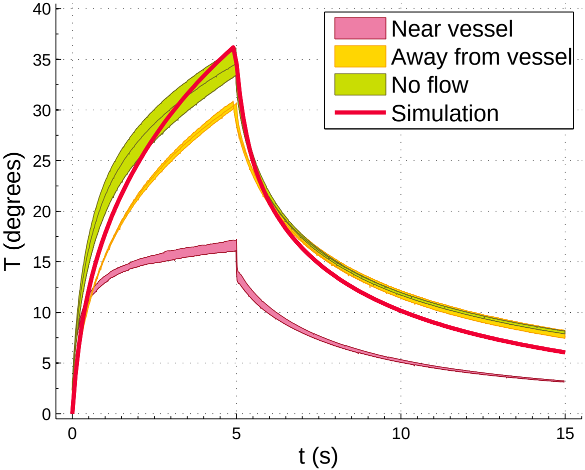


Figure: The effects of flow rates on heat desposition, in this case the vessel was a measured using Doppler imaging as being 2mm in radius and having a flow rate of 9cm/s

Cavitation

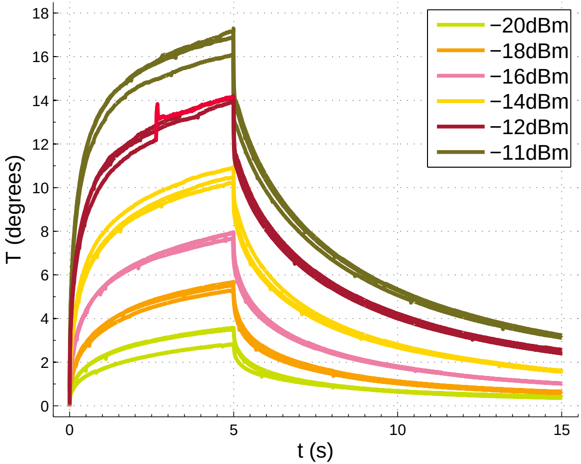


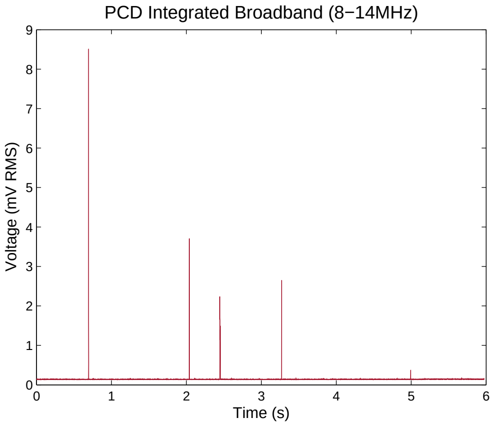
Figure: A (statistically significant) jump in the focal temperature is found for one exposure at one drive level

Cavitation

- Is this an acoustic and thermal phenomenon?
- How can it be reliably detected by both FOH and PCD?

Cavitation

A passive cavitation detect system, located within an aperture of the transducer is able to provide an overview of whether cavitation is occuring within the entire focal region.

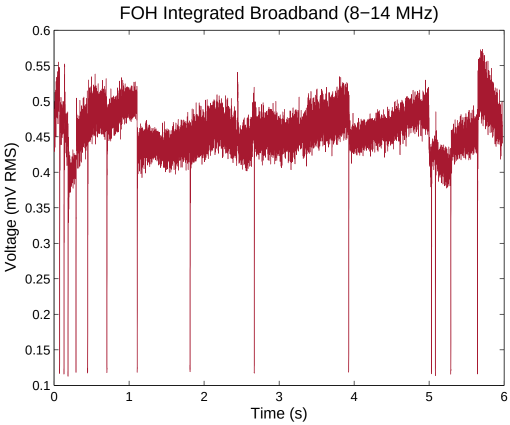


Cavitation

- The integrated broadband data suggests that the cavitation activity lasts many thousands of cycles. At the pressure amplitudes considered, it is probable that cavitation activity is from multiple events

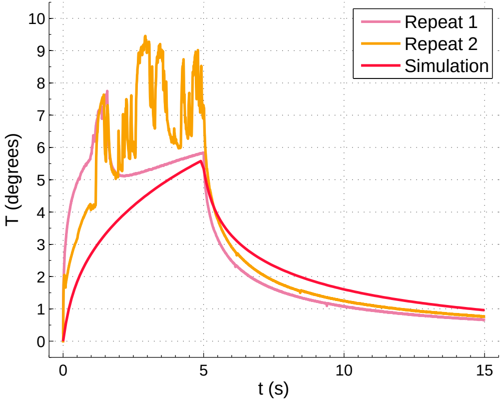
Cavitation

Acoustic data from the fibre-optic hydrophone far more localised but far less distinct



Cavitation

From the same liver at the same position, but at a greater intensity, repetitive cavitation occurs from almost the beginning of the exposure leading to enhanced heating measured at the focus



Conclusions

- Good agreement between experimental and numerical results
- Knowledge of variability between livers
- Insight into effect of large vessels and flow on necessary heating rates for ablation
- Accurate assessment of sensitivity to attenuation
- Infrequent observations of cavitation enhanced heating within the focal region.

Transcostal High-Intensity Focussed Ultrasound for the Treatment of Cancer

UCL:	Nader Saffari, Pierre Gélat, Gregory Vilensky, David Hawkes, Dean Barratt, Daniel Heanes, Lianghao Han.
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