

Transcostal High-Intensity Focused Ultrasound : Planning Treatment Delivery for Phased Arrays

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Objective

Produce robust, integrated treatment planning software for optically registered, and ultrasonically guided and monitored, transcatheter treatment of liver tumours

... “Two years until clinical use” ... “Not yet, but it is soon” ...

Outline

1

Design of clinical set-up
how academic research questions differ from clinic engineering challenges

2

Software developments
Assumptions and numerical challenges

3

Results and lessons from recent experiments
Future and ongoing work; summary and conclusion

From bench to bedside

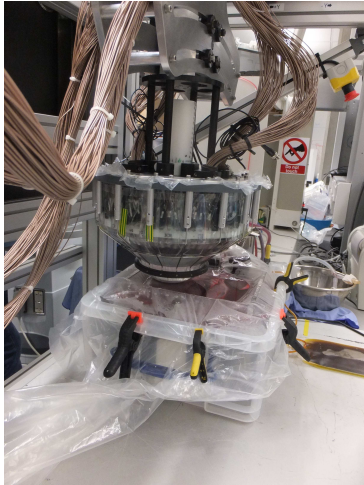
For clinical, and regulatory acceptance, as well as the successful treatment of patients, accurate and detailed treatment planning is required.

Much of the (preliminary) work is performed using small single element, spherically focused, transducers.

Although moderately computationally costly, at this scale nonlinear, multi-layered simulations can be performed, and can agree well with experimental data.

Liver Therapeutic Electronics (LTE)

If the therapy is to be used clinically, i.e. to be able to treat deep tumours, a large phased-array device is required.



Transducer Design

Phased array transducer:

- composed of 256 circular (0.575cm radius) piezo-electric elements, in a 3D printed arrangement.
- designed to operate at three frequencies: 1.1, 1.35 or 1.65MHz.
- transducer has a 19.2cm radius, with a focal depth of 19.4cm
- central aperture for monitoring and imaging
- Transducer head attached to electronically controllable gantry: providing six degrees of freedom: **location** (x, y, z) and **orientation** (α, β, γ) defined by Euler angles.

Lateral Steering Capabilities

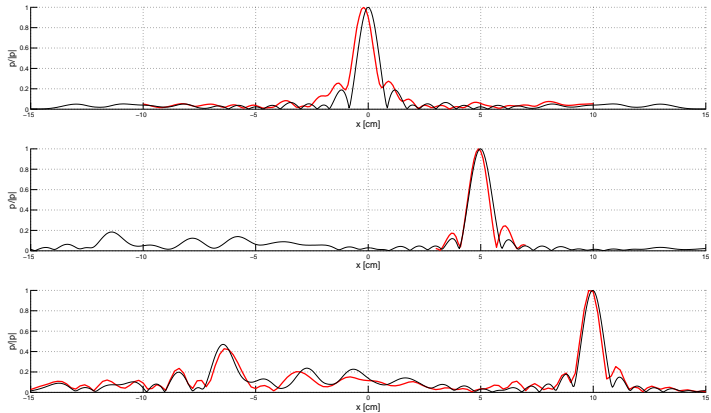


Figure: Comparison between theory, based on Rayleigh integral method, and experiment of steering predictions in a water tank at low intensities for 1.65MHz, for delay-sum focusing

Limitations of Electronic Steering

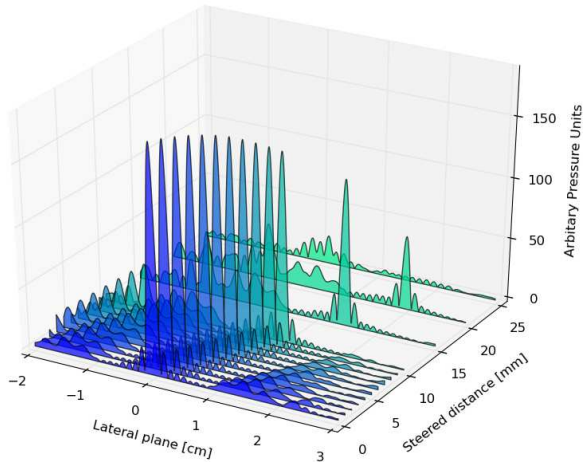


Figure: Transducer specific steering capabilities using phase-conjugation method (all 256 elements on, at 1.1MHz)

Limitations of Electronic Steering

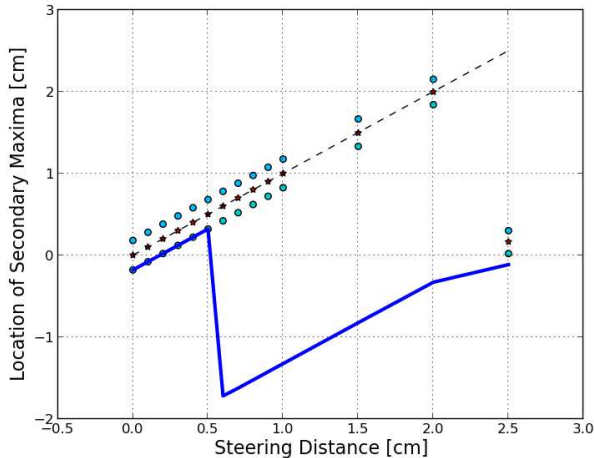


Figure: Transducer specific steering capabilities using phase-conjugation method (all 256 elements on, at 1.1MHz), showing transistion of focal peak (red), side lobes (cyan) and secondary/grating lobes (blue) due to electronic steering

Modern problems require ‘modern’ solutions

Treatment planning takes an equivalent form for both radiotherapy and ultrasound: maximize an objective functional (desired dose) given a set of constraints (side effects) for some state equation. But for HIFU

- High frequency, large propagation distances: huge spatial domain
- (Potentially) long durations: hundreds of thousands of cycles.
- Frequency dependent power-law, $\alpha = \alpha_0 |\omega|^\nu$

for example implicit, stable finite-difference time-domain codes in a clinically relevant context requires an exaflop calculations¹

$$\text{exaflop} : 10^{18} = 1,000,000,000,000,000,000$$

at each time-step, for an iterative scheme, for each subvolume — this is **extremely** computationally expensive!

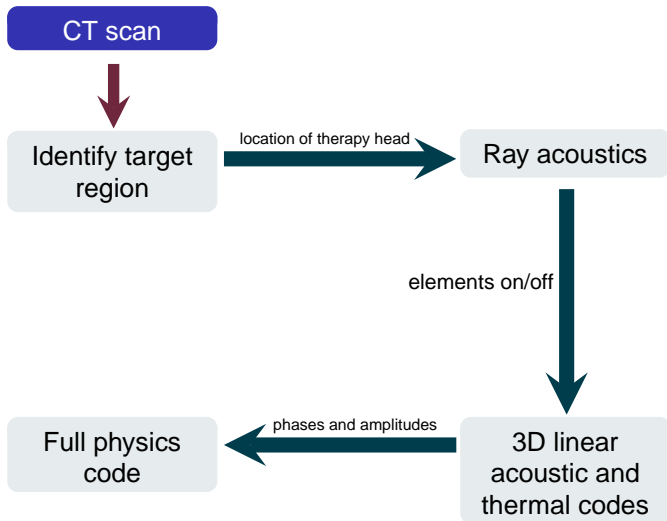
¹

Y. Jing, R. O. Cleveland, *J. Acoust. Soc. Am.* 122 (2007), pp. 1352–1364

Preclinical models have their own challenges

- **identify** possible target region suitable for given acoustic window
- **segmentation/registration** : separate mesh generation for subroutines for (i) optimal position of transducer head and (ii) phases of elements for focusing
- **surface lesions** to identify location of intended treatment sites
- **optical registration** implies constraint on location of therapy head
- **time scale**: scan-to-treatment within a week.
- **motion management**: potential limitations from electrical response of system and limits on exposure durations

Software Framework: Modular Approach



Code Suite : Ray Acoustics

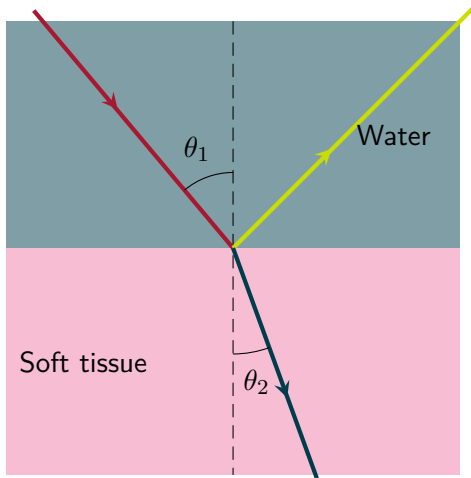
Seek to minimize a cost function which

- Maximizes total number of elements on and avoids skin burns due to reflections from ribs
- Minimizes transmission losses
- Maximizes `mean` propagation path through water
- * Avoid regions of interest such as lungs, bowels etc
- * Ensures phased array is visible to optical tracking system

Written in `fortran` and `python`, visualization using `mayavi` and handling imaging data from `VTK`, with bindings using `f2py`, output in

- `xml` so that it can be exported to the XNAT server.
- `stl` and `vtu` for registration and tracking
- `txt` to be read into the LTE

Interface Conditions



3D Linear Acoustics: Compromises

- ⇒ We assume a continuous wave so can solve the problem in the **frequency** domain, not the time domain
- ⇒ We discard the effects of nonlinearity, assume **linear** propagation
- ⇒ We assume that homogenization can be performed so that soft tissue is **uniform**

Aside from a Rayleigh integral approach, from these assumptions, we can exploit the fact we now have a Green's function and can use **boundary element method** to compute solutions on the **surface** of the ribs, rather than with a volume. However, this is a not so straight-forward ...

Boundary Element Methods

Typically, when solving any type of differential equation, it reduces to solving a system of linear equations.

1. The operator is **non-local**, i.e. at each point you need to consider the effect of the incident wave at all other points. This results in a dense matrix, which is computationally expensive to compute and store.
2. Furthermore, as a high-frequency problem the boundary element matrix can be large, i.e. 10^6 points. Inverting this matrix is also computationally expensive.

But there are methods to try and help with these problems

Krylov Spaces & Fast Multi-pole Methods

Fast multi-pole methods can reduce the time taken to compute the dense matrix, and GMRES methods (in Fortran and the Intel MKL library) can reduce time to compute a good approximation to the inverse

from SIAM News, Volume 33, Number 4

The Best of the 20th Century: Editors Name Top 10 Algorithms

By Barry A. Cipra

Algo is the Greek word for path. Algo is Latin for to do. Neither is the root for algorithms, which stems instead from al- algebras, the name of the sixth-century Arab scholar whose book of *al-jabr wa'l muqabala* devolved into today's "high school algebra" textbooks. As I have noted, the experience of mathematical procedures for solving problems. Were he named today, he'd most likely be recognized by the advances in his eponymous approach.

Some of the most beautiful of the computer age can be highlighted in the January/February 2000 issue of *Computing in Science and Engineering*, a joint publication of the American Institute of Physics and the IEEE Computer Society. Chemists and the Institute for University of Tennessee and Oak Ridge National Laboratory and French National Center for Computer Science at the Institute for Defense Analysis put together a list they call the "Top Ten Algorithms of the Century."

We easily assemble the 10 algorithms with the greatest influence on the development and practice of science and engineering in the 20th century. Designers and builders who, as with any top-10 list, their selections—and new solutions—can be found to their knowledge. When it comes to picking the top 10, their selections—and new solutions—can be found to their knowledge. When it comes to picking the top 10, their selections—and new solutions—can be found to their knowledge.

Without further ado, here's the Top 10, in chronological order (dates and names associated with the algorithms should be read as first-order approximations. Most algorithms take shape over time, with many contributors.)

1946: John von Neumann, Stan Ullman, and Nick Metropolis, all at the Los Alamos Scientific Laboratory, took up the Monte Carlo algorithm, also known as the **Markov Chain** method. The Monte Carlo algorithm uses random numbers to approximate solutions to mathematical problems with unmanageably many degrees of freedom or to combinatorial problems of factorial size, by simulating a random process. Given the digital computer's reputation for stochastic calculations, it fitting that one of its earliest applications was the generation of random numbers.



1947: George Dantzig, at the RAND Corporation, creates the **simplex method for linear programming**. In terms of widespread application, Dantzig's algorithm is one of the most successful of all time. Linear programming dominates the world of industry, where economic survival depends on the ability to optimize resources and other constraints. (Of course, the "real" problems of industry are often more complex than the one within budgetary and other constraints.) (Of course, the "real" problems of industry are often more complex than the one within budgetary and other constraints.)

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1950: Shiro Arimura, at the National Institute of Advanced Industrial Science and Technology, creates the **fast Fourier transform**. The fast Fourier transform is a mathematical algorithm for computing the discrete Fourier transform of a function. It is a key algorithm in many fields of science and engineering, including signal processing, image processing, and data analysis.

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and others (some of the computer science) have been the most important in the history of the computer science. The fast Fourier transform is a mathematical algorithm for computing the discrete Fourier transform of a function. It is a key algorithm in many fields of science and engineering, including signal processing, image processing, and data analysis.

1959-61: J.G.F. Francis of Permut Ltd., London, finds a reliable method for computing eigenvalues, known as the **QR algorithm**. Eigenvalues are arguably the most important numbers associated with matrices—and they can be the trickiest to compute. It's relatively easy to transform a square matrix into a matrix that's "almost" upper triangular, meaning one with a single entry at or below the main diagonal. But computing them, these final eigenvalues, without succumbing to an avalanche of errors, is non-trivial. The QR algorithm is the way to do it. Based on the QR decomposition, which writes A as the product of an orthogonal matrix Q and an upper triangular matrix R , this approach iteratively changes $A = QR$ into $A = RQ$, with Q and R being the same as the product of an orthogonal matrix Q and an upper triangular matrix R . This approach iteratively changes $A = QR$ into $A = RQ$, with Q and R being the same as the product of an orthogonal matrix Q and an upper triangular matrix R .

1962: Tracy Bruce of Elliott Brothers, Ltd., London, presents **Quicksort**. Picking the three of the most important numbers associated with matrices—and they can be the trickiest to compute. It's relatively easy to transform a square matrix into a matrix that's "almost" upper triangular, meaning one with a single entry at or below the main diagonal. But computing them, these final eigenvalues, without succumbing to an avalanche of errors, is non-trivial. The QR algorithm is the way to do it. Based on the QR decomposition, which writes A as the product of an orthogonal matrix Q and an upper triangular matrix R , this approach iteratively changes $A = QR$ into $A = RQ$, with Q and R being the same as the product of an orthogonal matrix Q and an upper triangular matrix R .

1963: James C. Lagarias of the IBM T.J. Watson Research Center and John T. Foster of Princeton University and AT&T Bell Laboratories, create the **fast Fourier transform**. The fast Fourier transform is a mathematical algorithm for computing the discrete Fourier transform of a function. It is a key algorithm in many fields of science and engineering, including signal processing, image processing, and data analysis.

1977: Vladimir Prokhorov and Robert Finkel of Brigham Young University advance the **integer relation detection algorithm**. The problem is to find one given a bunch of integers, say a_1, a_2, \dots, a_n , are there integers x_1, x_2, \dots, x_n such that $a_1x_1 + a_2x_2 + \dots + a_nx_n = 0$? The algorithm is a key algorithm in many fields of science and engineering, including signal processing, image processing, and data analysis.

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What new methods and algorithms will the 21st century bring? The computer science community will be known for its ability to find the most important numbers associated with matrices—and they can be the trickiest to compute. It's relatively easy to transform a square matrix into a matrix that's "almost" upper triangular, meaning one with a single entry at or below the main diagonal. But computing them, these final eigenvalues, without succumbing to an avalanche of errors, is non-trivial. The QR algorithm is the way to do it. Based on the QR decomposition, which writes A as the product of an orthogonal matrix Q and an upper triangular matrix R , this approach iteratively changes $A = QR$ into $A = RQ$, with Q and R being the same as the product of an orthogonal matrix Q and an upper triangular matrix R .

Barry A. Cipra is a mathematician and writer based in Northfield, Minnesota.

(Worst) Case Study

- Only one potential target site, with narrow available acoustic window, depth of target approx 3cm liver, 4cm skin/fat/muscle
⇒ Treatment plan gives best guess with only 40% elements on
- In order to compensate for this, close to maximum power output necessary
- Frequency chosen based on reliability of lesioning from ex vivo experiments
- Breath-hold is not applicable for moderate exposure durations, i.e. those greater than 4 seconds, 3.4 seconds

Pre-Operative CT Scan



Figure: Fiducial markers during scanning

Position for Scan is Same as Treatment

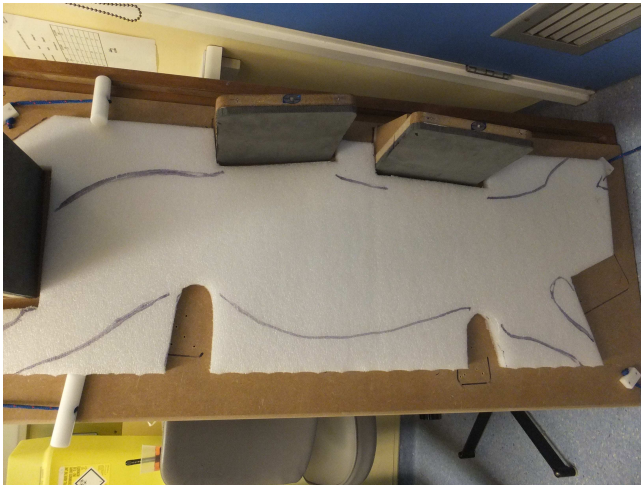


Figure: Pig bed for repositioning to ensure pig is in same location for treatment as for scanning

Segmented Surface Meshes

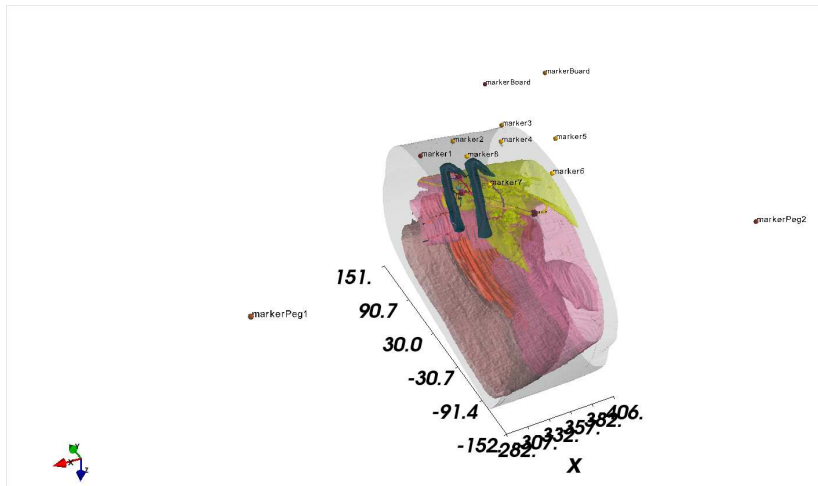


Figure: Fully segmented data set. Note location of fiducial markers also segmented.

Imaging Planes & Target Identification

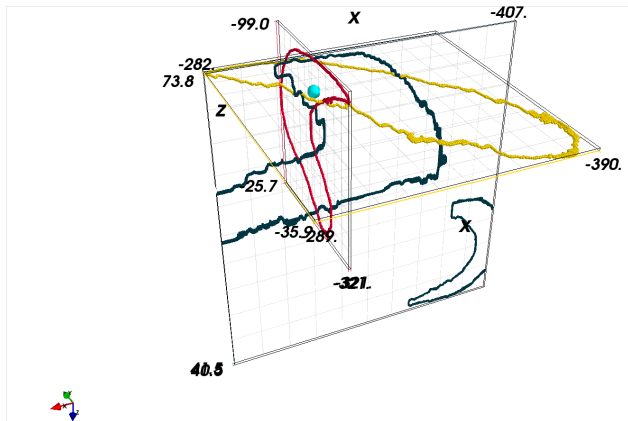


Figure: Image planes in three orthogonal planes to the optimized transducer head

Axial Imaging Plane 1

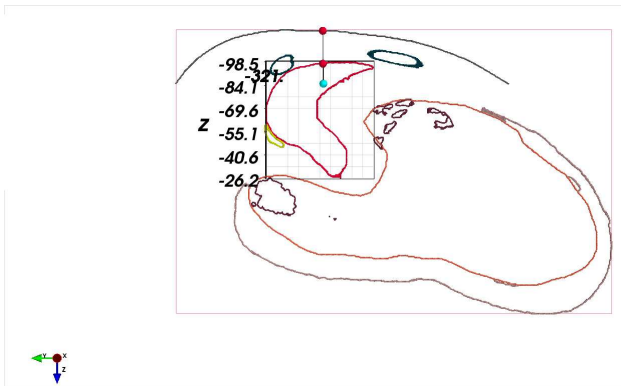


Figure: Image plane in orthogonal plane to the optimized transducer head, showing target, minimum distance to surface of liver and skin, which is same as treatment distances. This image can be registered to ultrasound image using landmark distance algorithm.

Axial Imaging Plane 2

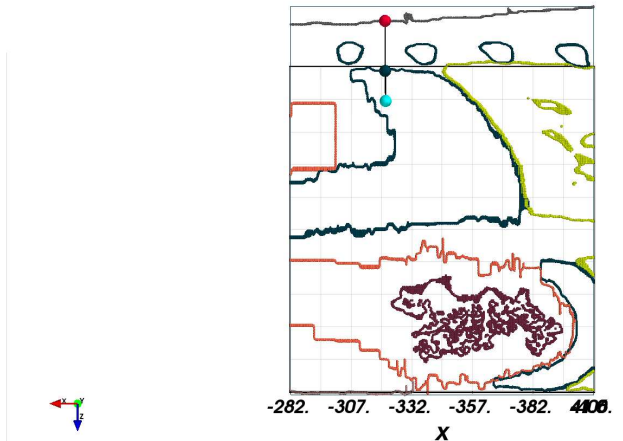


Figure: Image plane in orthogonal plane to the optimized transducer head

Lateral Imaging Plane

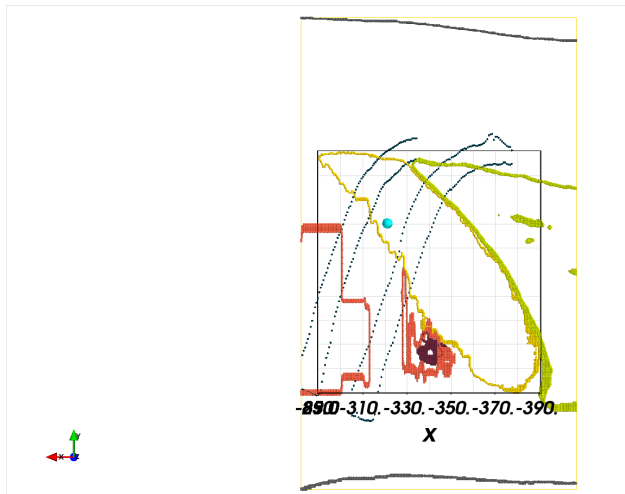


Figure: Image plane in orthogonal plane to the optimized transducer head

Direction for Electronic Steering



Figure: Rib direction characterized for use in calculation of steering direction

Visualization of Treatment Plan

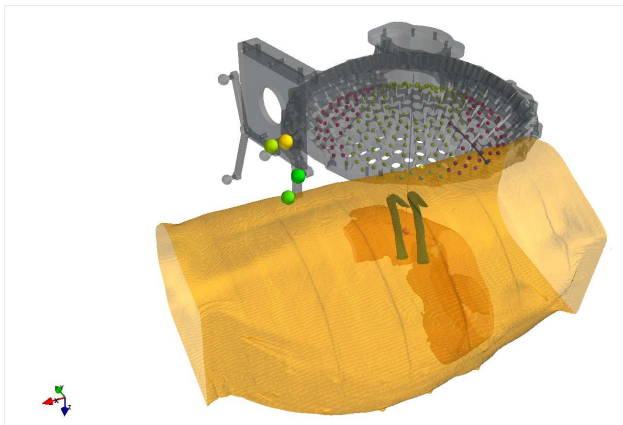


Figure: Optimal location of treatment head with respect to liver, ribs, optical trackers

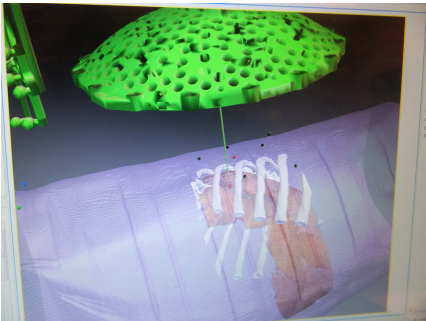


Figure: Optical registration of planned position of transducer head

Results: Skin

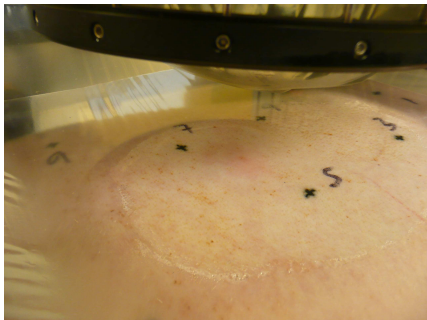


Figure: Slight marking on skin, possibly erythema or burn - samples fixed for histological studies. Note from location of mark relative to the ribs this is not due to reflections on the ribs, but perhaps due to rapid absorption of high-harmonics at skin, generated through large propagation distance through water.

Results: Lesioning in Liver

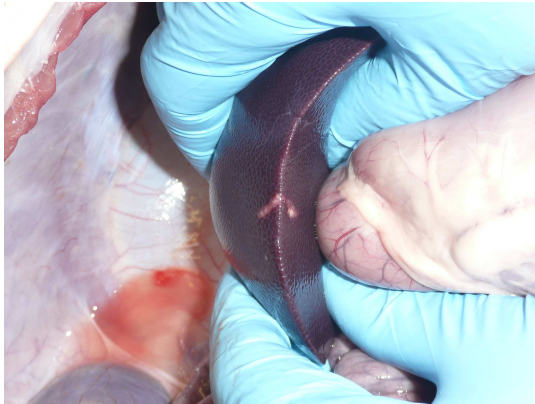


Figure: Lesioning of steered volume from edge of lobe

Conclusions

- Treatment planning for high-intensity focused ultrasound is computationally demanding, with a balance between detail in modeling and computational tractability.
 - Treatment planning must be **fully integrated** with pre-operative imaging, hardware, registration, motion management, monitoring etc.
 - Research software is bespoke, centre-dependent
 - Research models pose additional, model-dependent problems
-
- Assumptions of linearity, uniform tissue properties, continuous wave forms limit applicability.
 - Inaccuracy from solvers is often overshadowed by motion, lack of information about tissue properties etc.
 - Does every hospital need a high-performance computing facility?

Transcostal High-Intensity Focussed Ultrasound for the Treatment of Cancer

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