ICR The Institute of Cancer Research

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, transcostal 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

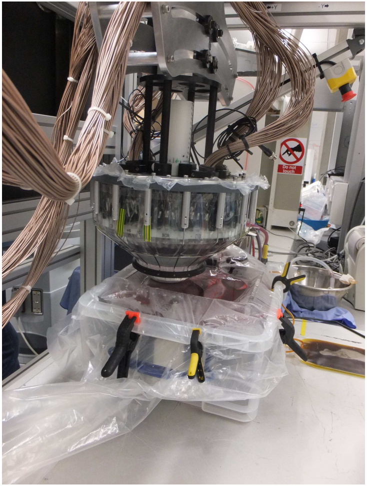
For clinical, and regulatory acceptance, as well as the successful treatment of patients, accurate and detailed treatment planning is required.

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

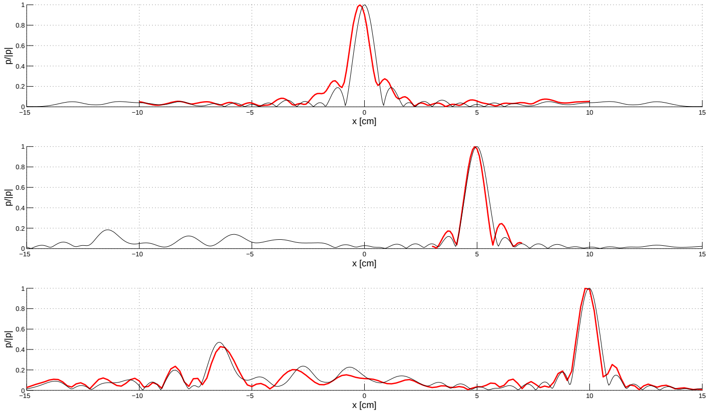


Figure: Comparison between theory, based on Rayleigh integral method, and experiment of steering predictions in a water tank at low intensities for 1.65MHz, for delay-sum focusing

Limitations of Electronic Steering

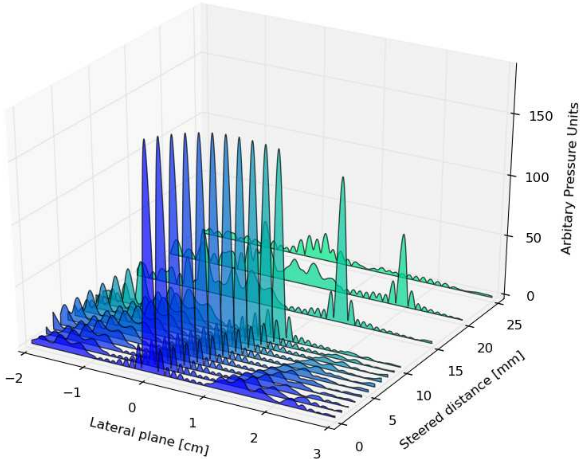


Figure: Transducer specific steering capabilities using phase-conjugation method (all 256 elements on, at 1.1MHz)

Limitations of Electronic Steering

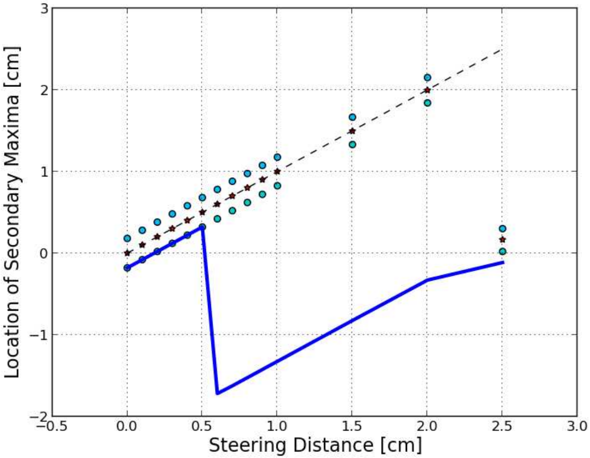


Figure: Transducer specific steering capabilities using phase-conjugation method (all 256 elements on, at 1.1MHz), showing transistion of focal peak (red), side lobes (cyan) and secondary/grating lobes (blue) due to electronic steering

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, $\alpha = \alpha_0 \left|\omega\right|^{\nu}$

for example implicit, stable finite-difference time-domain codes in a clinically relevant context requires an exaflop calculations[1]

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

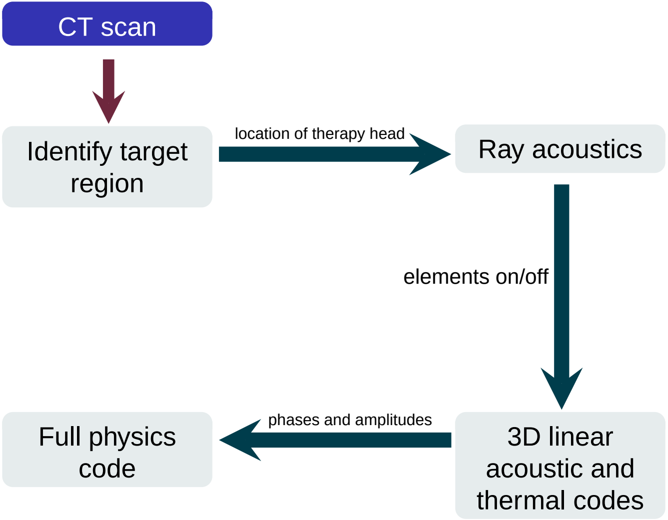
at each time-step, for an iterative scheme, for each subvolume — this is extremely computationally expensive!

[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

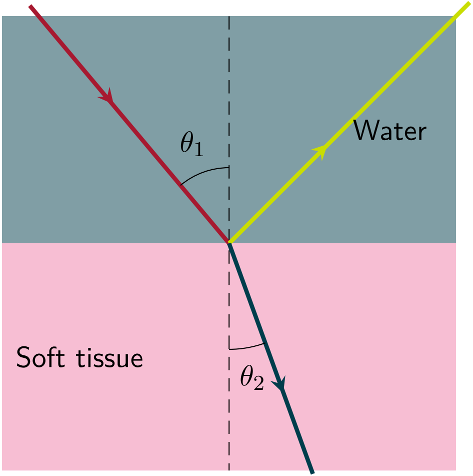
Seek to minimize a cost function which

- 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.

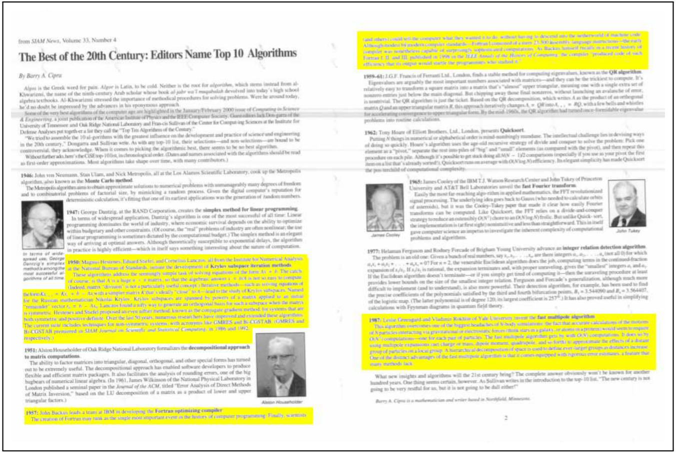
1. The operator is non-local, i.e. at each point you need to consider the effect of the incident wave at all other points. This results is a dense matrix, which is computationally expensive to compute and store.

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 Subspaces & 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

(Worst) Case Study

- Only one potential target site, with narrow available acoustic window, depth of target approx 3cm liver, 4cm skin/fat/muscle
  - $\Rightarrow$ 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

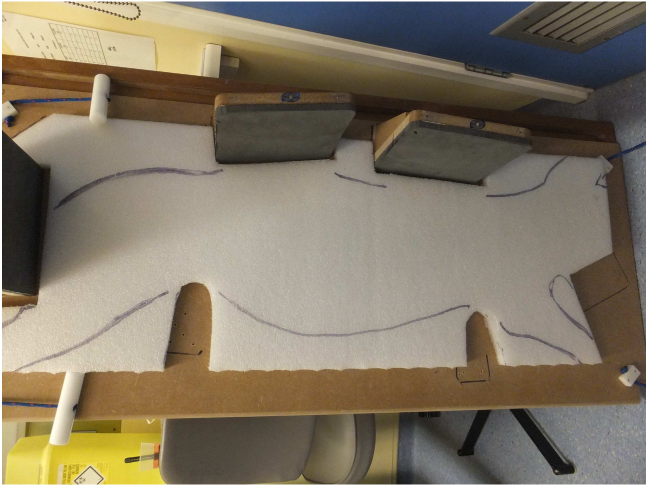


Figure: Pig bed for repositioning to ensure pig is in same location for treatment as for scanning

Segmented Surface Meshes

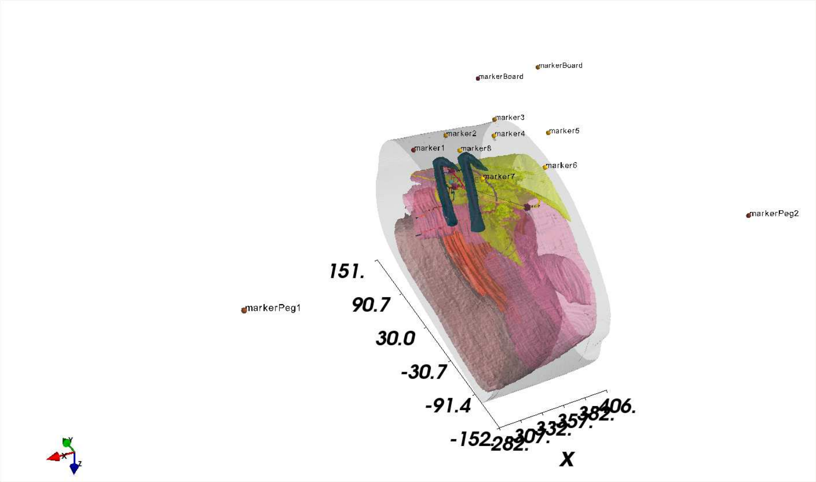


Figure: Fully segmented data set. Note location of fiducial markers also segmented.

Imaging Planes & Target Identification

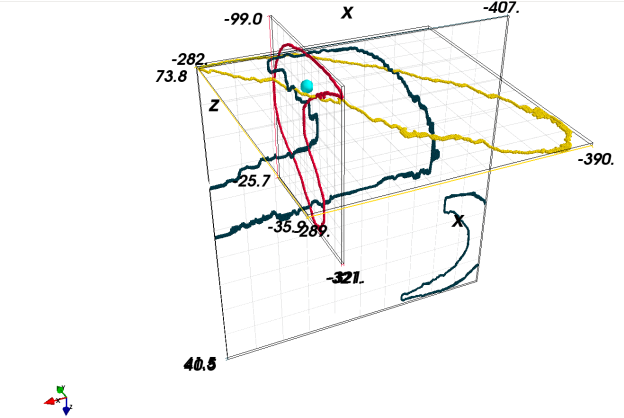


Figure: Image planes in three orthogonal planes to the optimized transducer head

Axial Imaging Plane 1

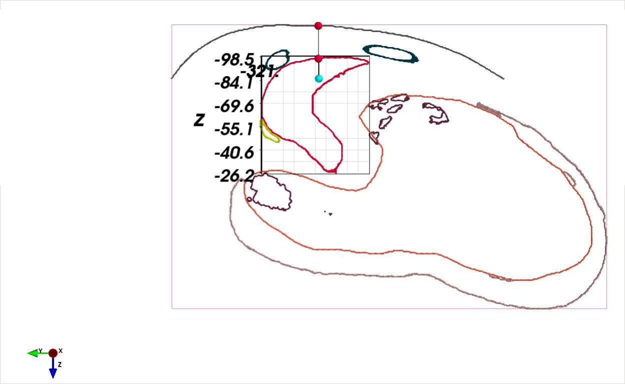


Figure: Image plane in orthogonal plane to the optimized transducer head, showing target, minimum distance to surface of liver and skin, which is same as treatment distances. This image can be registered to ultrasound image using landmark distance algorithm.

Axial Imaging Plane 2

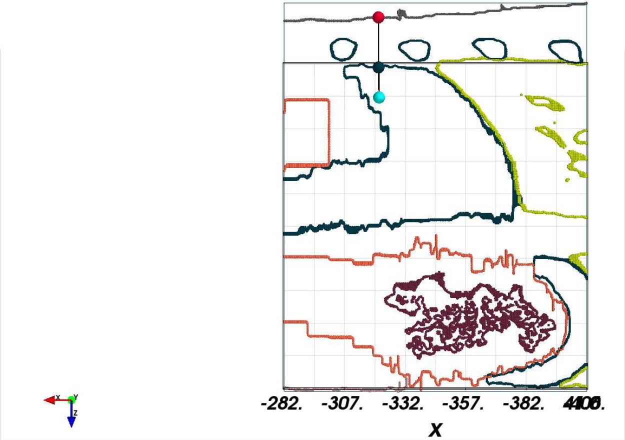


Figure: Image plane in orthogonal plane to the optimized transducer head

Lateral Imaging Plane

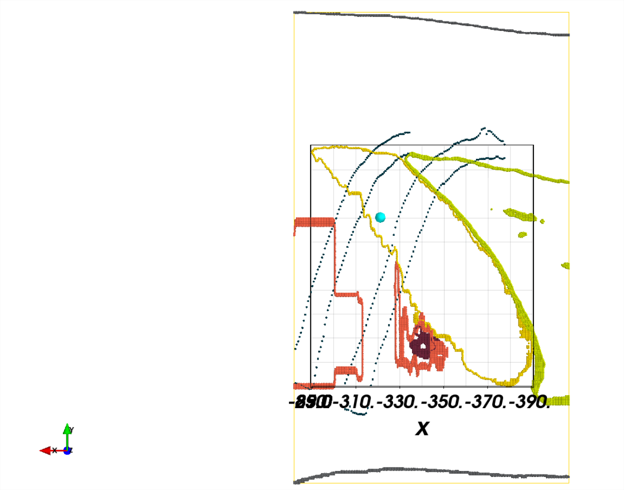


Figure: Image plane in orthogonal plane to the optimized transducer head

Direction for Electronic Steering

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

Visualization of Treatment Plan

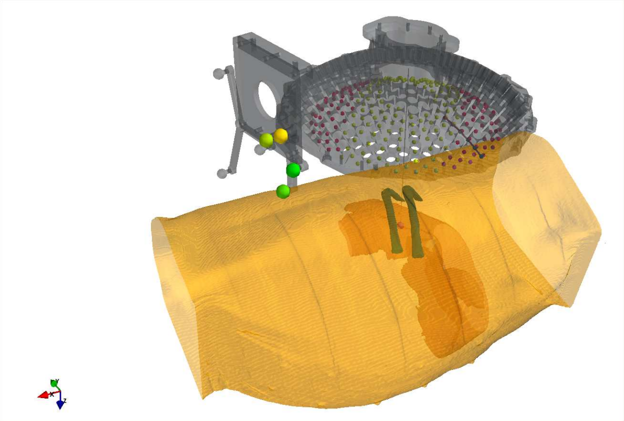


Figure: Optimal location of treatment head with respect to liver, ribs, optical trackers

Optical Registration of Treatment Head

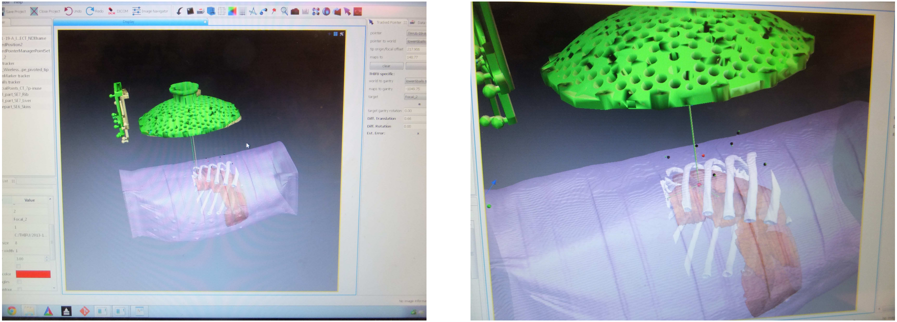


Figure: Optical registration of planned position of transducer head

Results: Skin

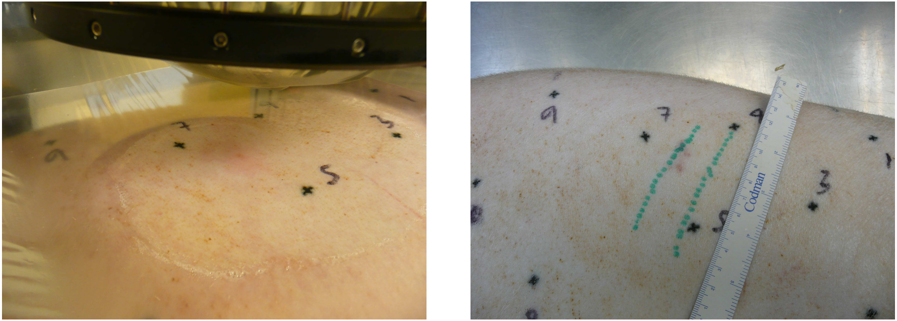


Figure: Slight marking on skin, possibly erythema or burn - samples fixed for histological studies. Note from location of mark relative to the ribs this is not due to reflections on the ribs, but perhaps due to rapid absorption of high-harmonics at skin, generated through large propagation distance through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

Results: Lesioning in Liver

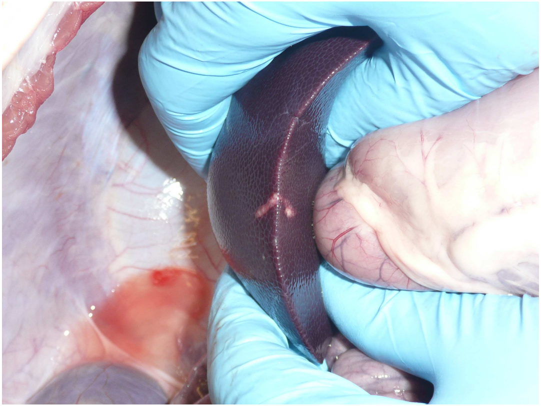


Figure: Lesioning of steered volume from edge of lobe

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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