Ionacoustic imaging for eventual in-vitro and in-vivo dose mapping

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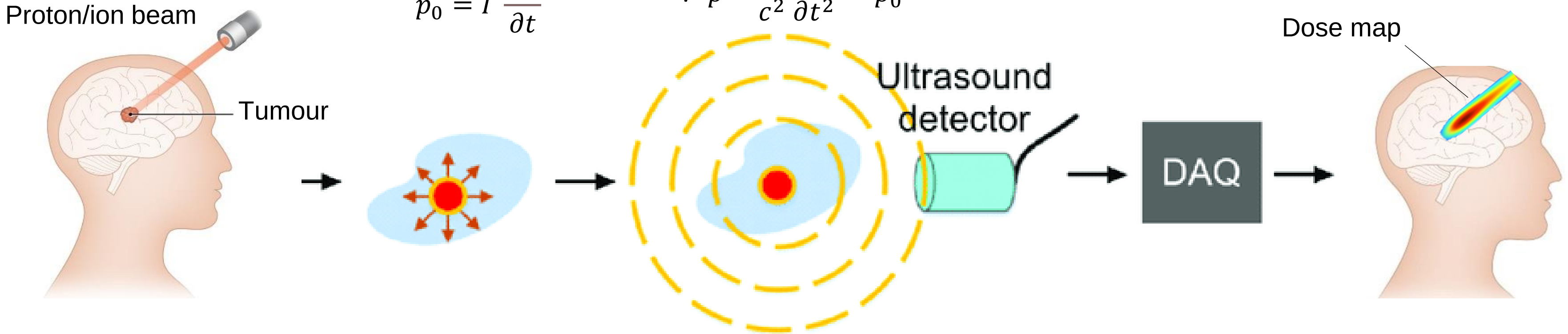
Ionacoustic Process

Proton/ion pulse energy absorption → Transient pressure rise → Acoustic wave propagation → Acoustic wave detection → Data acquisition and image reconstruction

$$p_0 = \Gamma \frac{\partial H}{\partial t}$$

$$\nabla^2 p - \frac{1}{c^2}\frac{\partial^2 p}{\partial t^2} = p_0$$



- Pulses are needed. A constant energy deposition produces no acoustic wave.
- High resolution demands short pulses, e.g., 150 µm requires 100 ns (10 MHz)
- Nearly homogenous dose regions produce very low acoustic frequencies (kHz)
- Nevertheless, success obtained in vitro and in vivo, by various groups

} Extremely wide bandwidth acoustic sensors required

Our ion-acoustic ambition

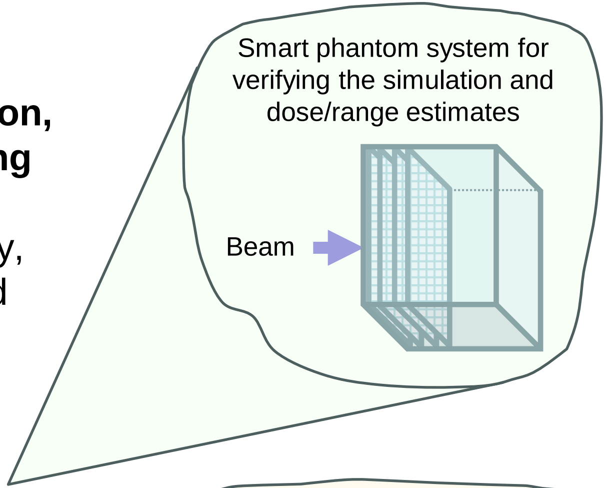
- In-vivo real-time 3D dose localisation and quantitative mapping, for real-time pulse-to-pulse adaptive treatment as the beam is moved around
    - **Localise the Bragg peak** (submillimetre accuracy possible), to avoid damage to healthy tissue and under-dosing of the tumour.
    - **Measure the deposited-energy distribution** in the tissue, preferably on a pulse-by-pulse basis.
    - **Simultaneously image** with ultrasound and photoacoustics, registered to planning CT/MRI - track tissue motion, image anatomy, perfusion, microvasculature, hypoxia, tissue stiffness, speed of sound, molecular biomarkers and dose enhancement distribution from molecularly targeted dose enhancers.
    - **Suitable for organs with acoustic access**: breast, prostate, liver, pancreas, pelvic, head and neck, etc. (perhaps eventually brain).
    - **Enable preclinical radiobiology research** to provide the knowledge needed to take full advantage of the new accelerator, and for its optimal clinical use.
    - **Especially applicable to mini/micro-beam and FLASH** irradiation.

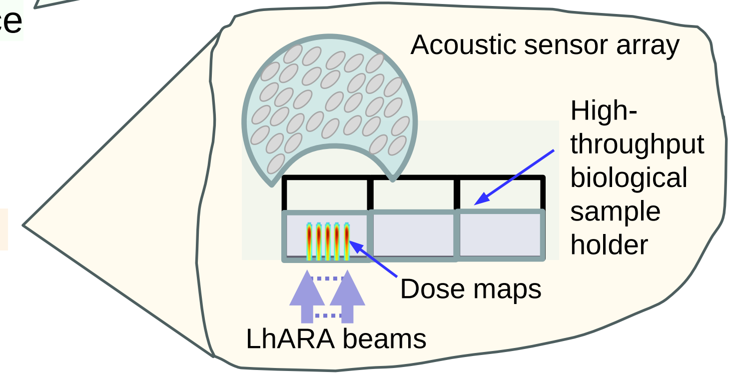
Our main challenges

- **Very weak signals**
  - LhARA technology generates 10 - 40 ns pulses
  - Massively parallel ultrasound electronics and transducer arrays, and front-end compressive sensing
  - Techniques described below will also enhance signal to noise ratio
- **Matching signal frequency content to ultrasound transducers**
  - Novel acoustic beamforming and transducer arrays take advantage of LhARA to adjust the beam size
  - Prior knowledge of expected dose distribution
- **Ultrasound transducers must permit imaging and PB access, without an operator**
  - For some organs (e.g. breast, thyroid, prostate), suitable 3D automated scanning is already used clinically
  - Current work around the world to develop conformable arrays in the form of inter-communicating patches
- **The acoustic properties for which compensation is needed, for spatially accurate and quantitative dose, are patient specific**
  - Speed of sound, attenuation and Grüneisen coefficient imaging are being developed for diagnostic imaging
  - Ultrasound contrast microbubbles can act as beacon signals for aberration and attenuation correction

Our approach

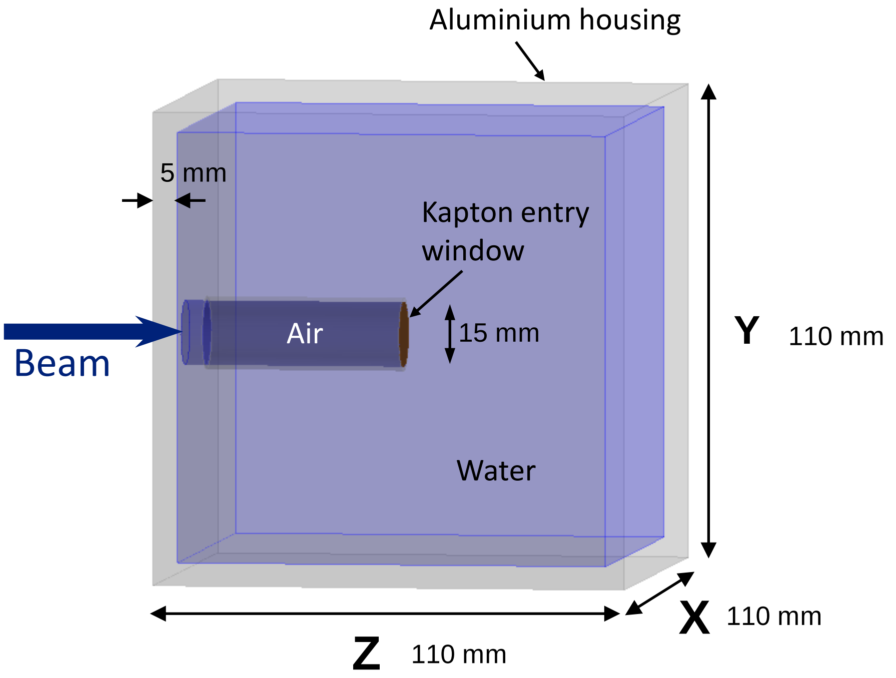
- **Modelling of proton/ion beam, transport, energy deposition, thermoacoustic generation, acoustic propagation, sensing and dose-map reconstruction**
  - study variables (e.g., beam size, pulse length, kinetic energy, particle type, dose per pulse, ultrasound sensor positions and characteristics, reconstruction method)
  => predict dose imaging capabilities
  => define ultrasound sensor and system requirements
- Early experiments to validate the modelling – existing source
- Build prototype preclinical demonstrator system
- Bring together with LhARA prototype
- Conduct preclinical experiments to generate radiobiological knowledge
- Refine and repeat, translate to clinical scale, …



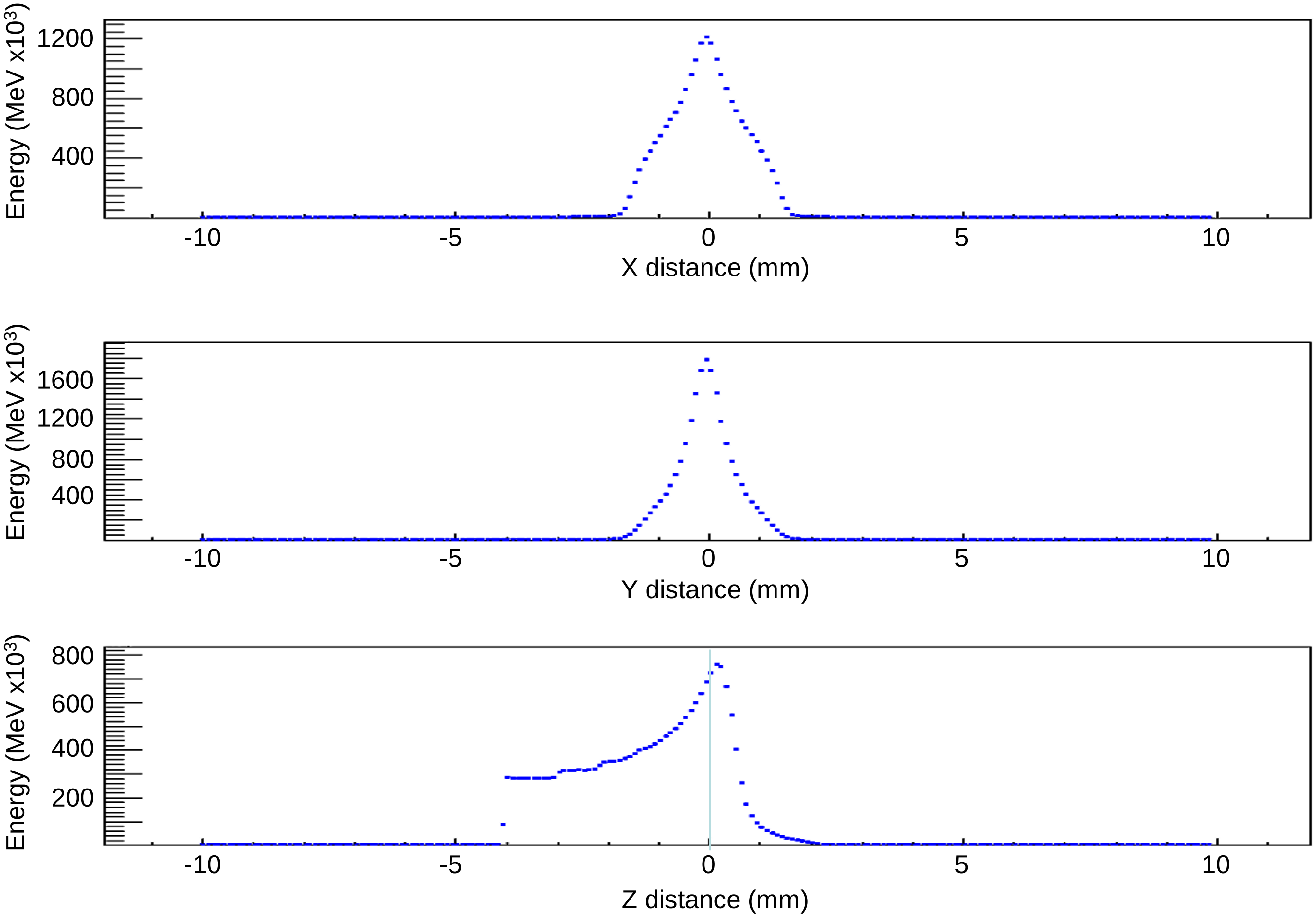


Digital simulation studies

GEANT4 simulation of the water phantom



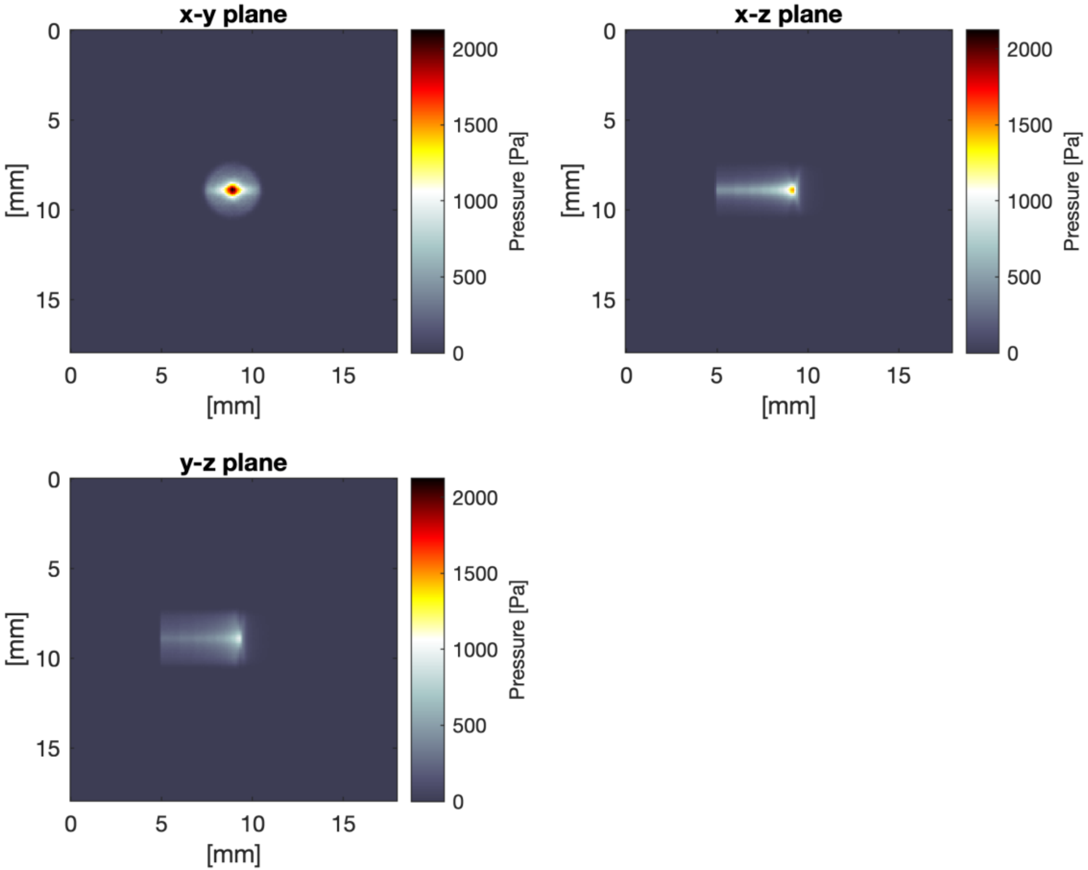
Binned energy deposition profiles



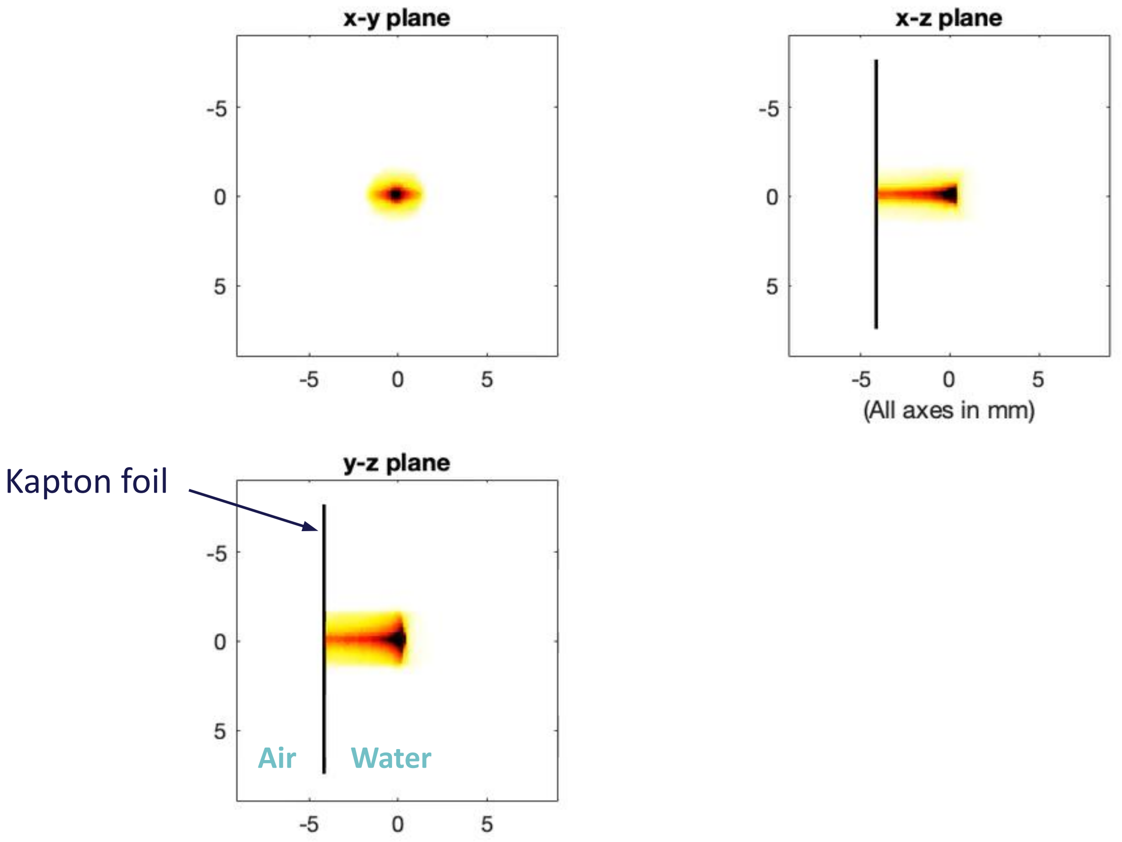
k-Wave simulation - source pressure distribution due to deposited proton energy

A MATLAB toolbox for the time-domain simulation of acoustic wave fields

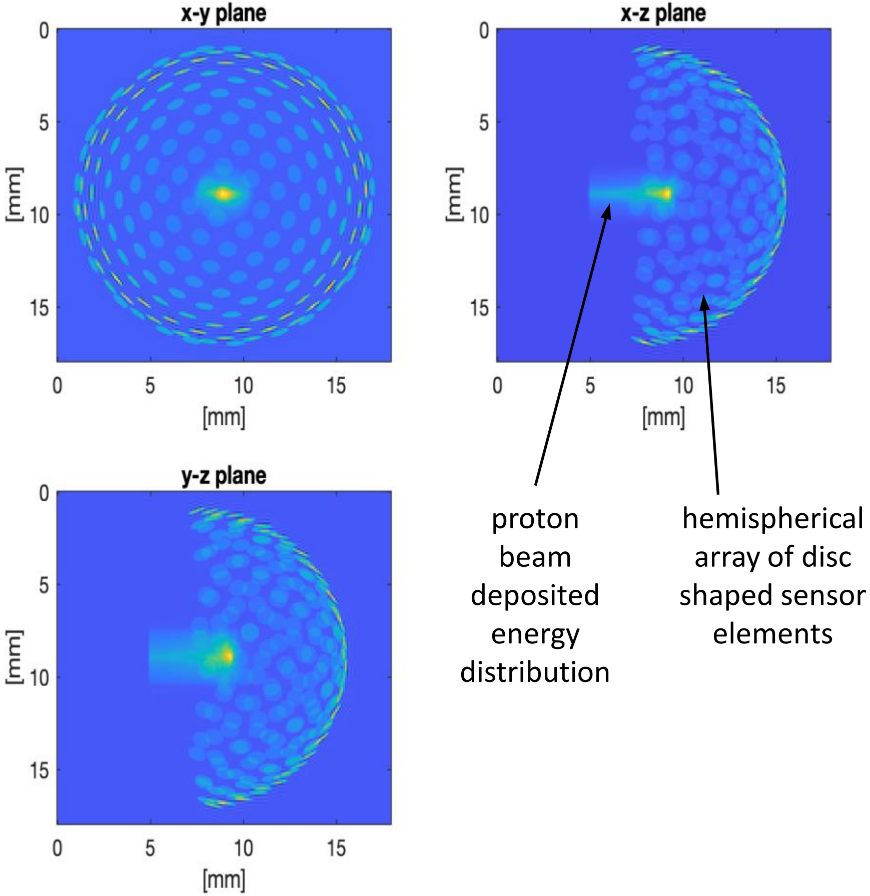
The Institute of Cancer Research



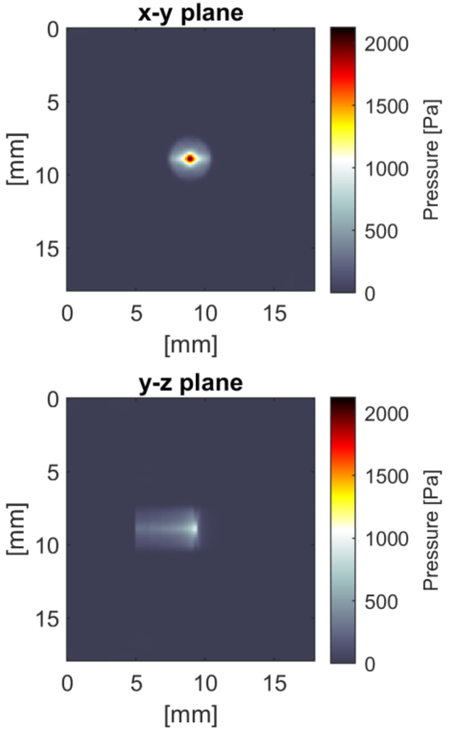
Acoustic Wave Propagation



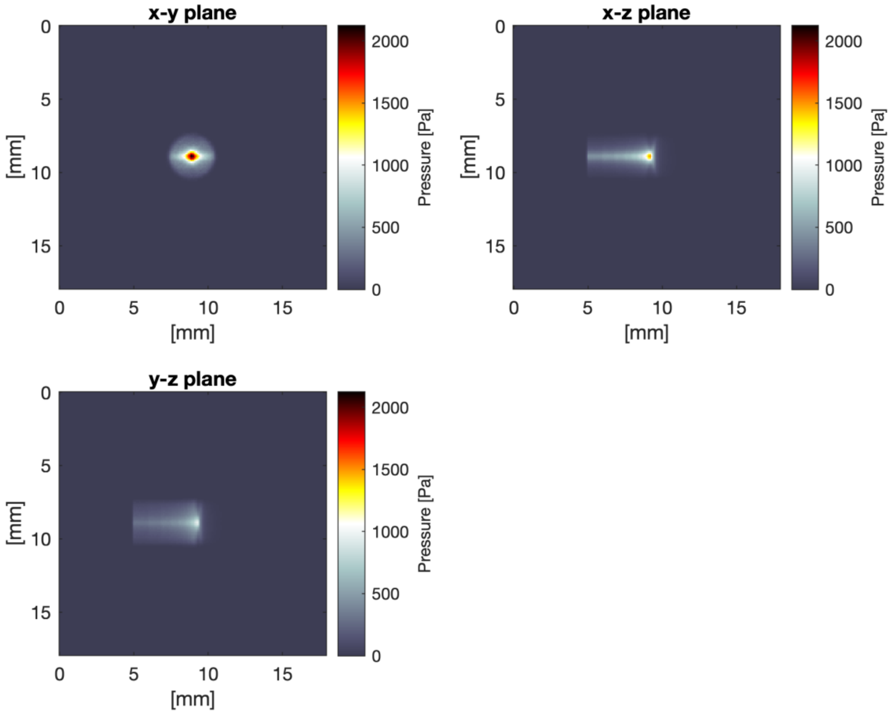
Acoustic sensor geometry and location in relation to the proton energy deposition



Pressure distribution reconstructed using iterative time reversal – comparison with the source pressure

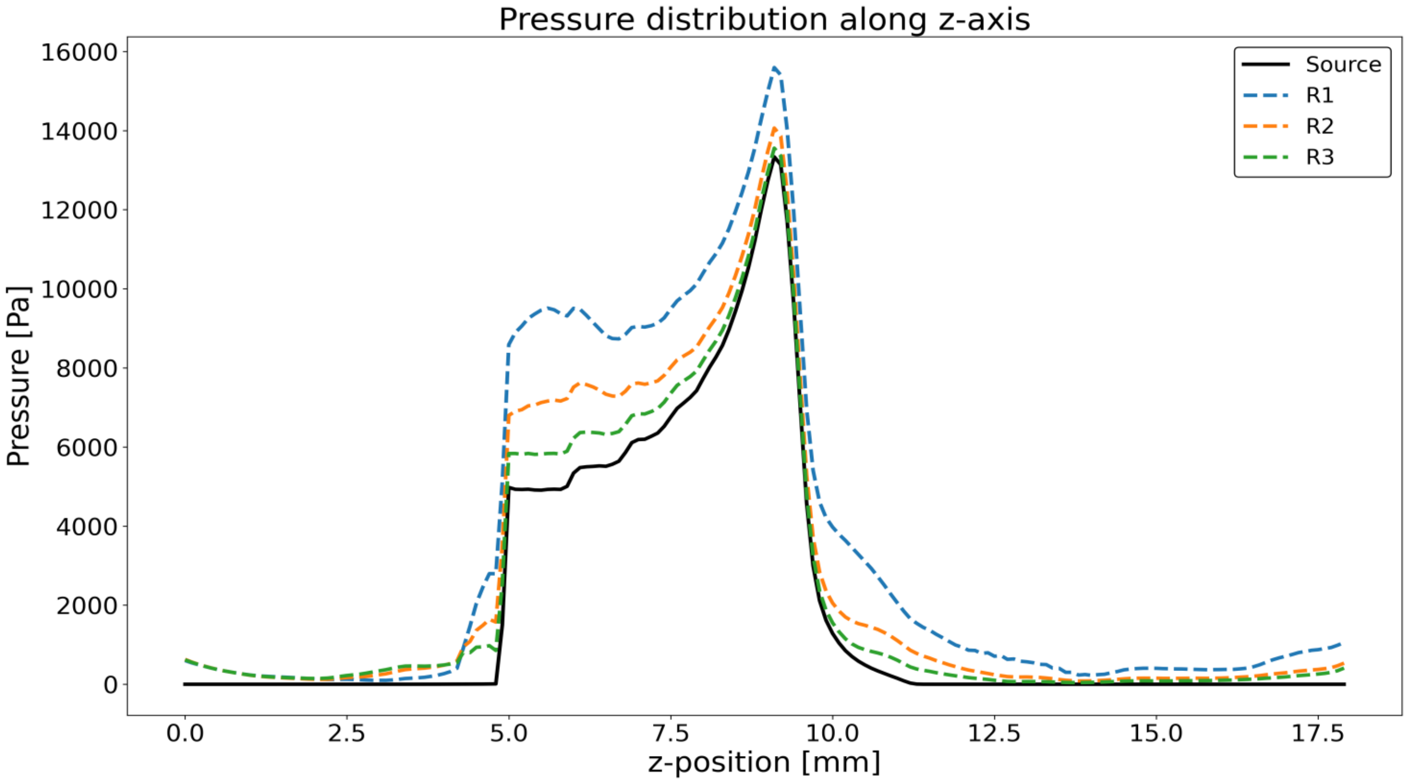


Reconstruction



Source pressure

Axial profile through the reconstructed pressure distribution – iterative time reversal convergence



Experimental simulation studies

Preliminary photoacoustic “experimental simulation”

Monte Carlo simulation

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3-D dose distribution

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Threshold and tessellate 3-D surface

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3-D print to produce mould

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Optically absorbing gel phantom in the shape of the deposited dose distribution

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Image using a photoacoustic system

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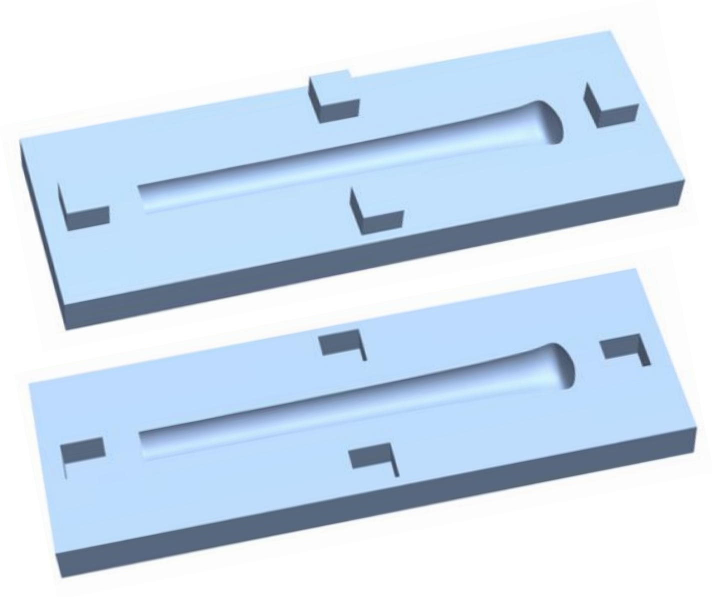
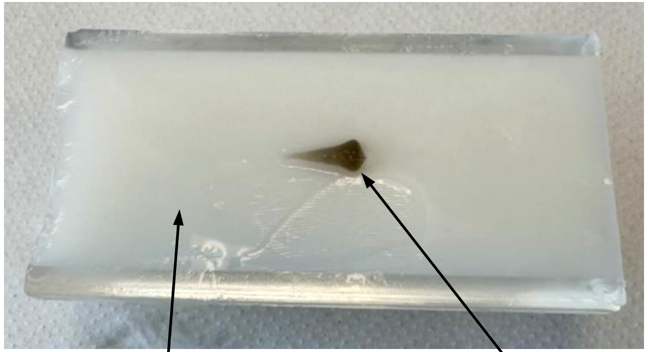
Evaluate received acoustic frequencies and reconstructed images in terms of analytical predictions and compare with k-Wave predictions

Example mould design and final photoacoustic phantom of thresholded simulated dose distribution (70 MeV)

Two halves of mould for deposited dose distribution at 5% threshold



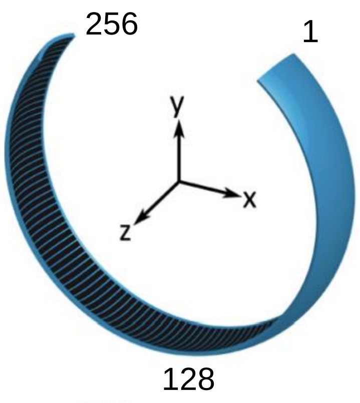
Halve the phantom for deposited dose distribution at 40% threshold



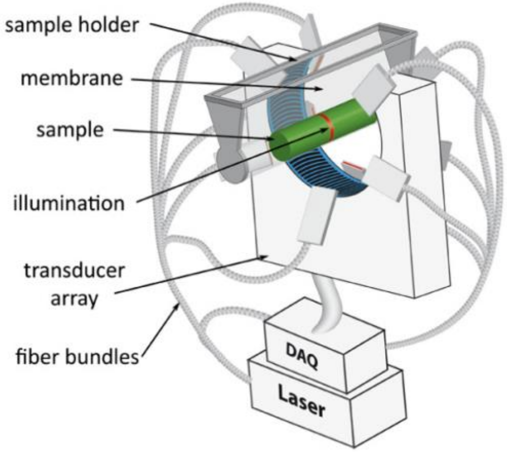
Background (TiO^2 in gelatine)

Beam insert (India ink pigmented)

Photoacoustic imaging system

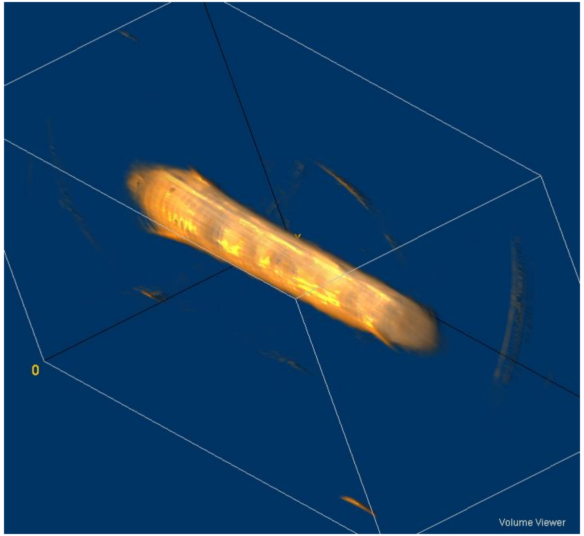


Acoustic sensor elements



Example photoacoustic images (5%)

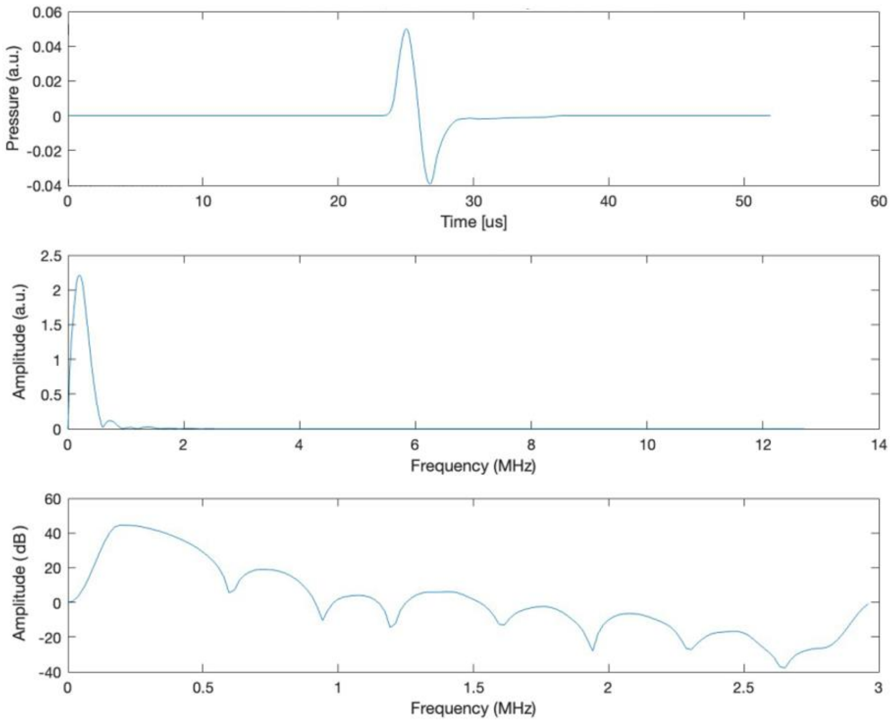
Surface rendering of 3D reconstruction



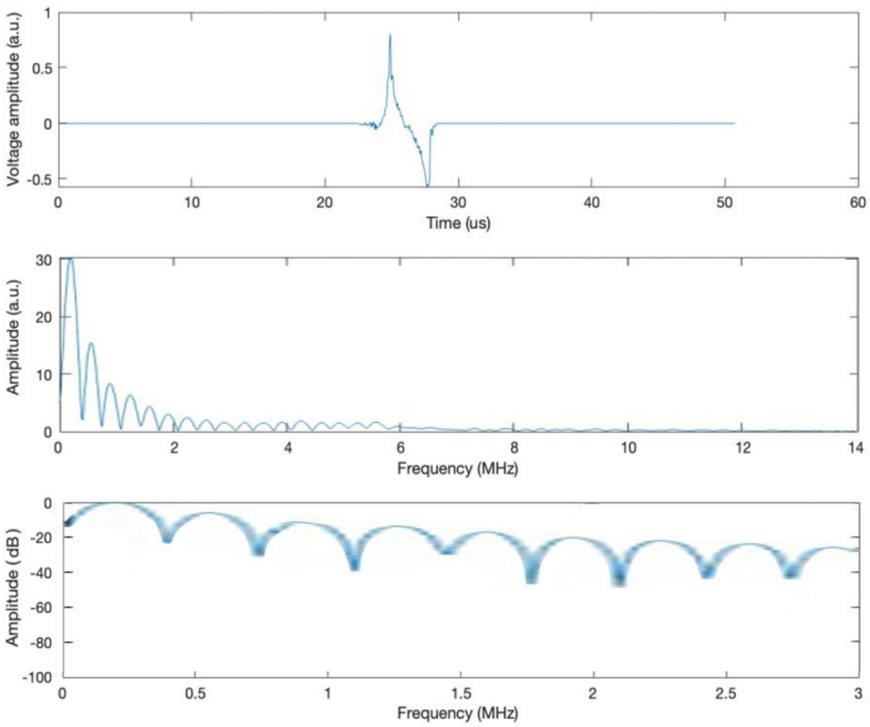
Stack of cross-sectional reconstructions

Radial acoustic signals received from position of the Bragg peak by sensor element 128

Computer (IO) simulation



Experimental (PA) simulation



Conclusion

Simulation appears to be behaving well (analysis ongoing)

The next steps:

1) Validate the simulation against an ionacoustic (rather than photoacoustic) experiment with a pulsed proton source
2) Use the simulation to design the ionacoustic system for preclinical LhARA experiments
3) Build the ionacoustic system, test and demonstrate in a proof-of-principle radiobiological experiment