The Institute of Cancer Research

PHD STUDENTSHIP PROJECT PROPOSAL: ESR7 (UCOM)

PROJECT DETAILS	
Project Title:	Development of clinically relevant acousto-thermal tissue mimics(ESR7)
Short Project Title:	**Acousto-thermal tissue phantoms**

SUPERVISORY TEAM	
Primary Supervisor:	Gail ter Haar
Associate Supervisor:	Ian Rivens
Backup Supervisor:	Dimitra Darambara
Lead contact person for the project:	Gail ter Haar

DIVISIONAL AFFILIATION	
Primary Division:	Division of Radiotherapy and Imaging
Primary Team:	Therapeutic Ultrasound

PROJECT PROPOSAL

BACKGROUND TO THE PROJECT

The ICR is a member of an exciting new EU funded innovative training network (ITN) which aims to exploit EU wide experience of industrial and biomedical ultrasound cavitation and sonochemistry. This ambitious overall programme will take a systematic approach towards understanding ultrasound cavitation better using a combination of experiments and simulations. The ITN includes academic and non-academic partners from the EU, Switzerland and Singapore, and beneficiaries and partners from medical/biomedical fields.

From the experimental point of view, the research programme focuses on the onset of cavitation in tissue and tissue mimicking materials, ultrasound assisted drug delivery techniques, bubble cleaning, fundamental bubble dynamics and shock tube tests.

At a theoretical/numerical level, the focus is placed on developing, improving and validating new state-of-the-art tools for ultrasound cavitation modelling in tissue and tissue mimics, heterogeneous bubble nucleation at walls, shock wave/bubble interaction (including deformable surfaces/cell membranes) and chemical reactions inside collapsing bubbles.

The proposed work will provide a unique training opportunity for the student who will gain knowledge, skills and expertise through state-of-the-art experimental and simulation methods, alongside gaining experience at the premises of internationally renowned universities, biomedical research institutes and industry, and core studies at their host institution.

The therapeutic ultrasound team at the ICR has a world-leading reputation as a result of its extensive experience in developing and implementing ultrasound based therapeutic approaches to cancer treatment. Most recently, we have been looking at a therapeutic approach that exploits ultrasound cavitation using pulsed exposures, often referred to as histotripsy.

Applications are invited for a 4 year PhD studentship (aka Early Stage Researcher or ESR position). The first 3 years are EU funded and the 4th year is funded by the ICR. The preferred state date for the projects is June 2019.

Applicants must be able to demonstrate that they have spent fewer than 12 months working in the UK in the last 3 years, and should have a minimum of a BSc, but preferably an MSc, in a relevant physical science or engineering subject, and be able to demonstrate strong experimental and mathematical modelling capabilities.

For more information please contact Professor Gail ter Haar: gail.terhaar@icr.ac.uk.

If you wish to apply, please do so via: https://euraxess.ec.europa.eu/jobs/326464 (ICR projects are listed as ESR7 and ESR8).

PROJECT AIMS

- **Acoustic, mechanical and thermal characterisation of a range of tissues (e.g. adipose tissue, kidney tissue, blood vessels etc.)**
- **Development and characterisation of mimics for these tissues**
- **Design of phantom to allow simulation of cavitation enhanced drug delivery**

RESEARCH PROPOSAL

After undertaking an exhaustive Literature survey of tissue and tissue mimicking material properties. The appointed PhD student (ESR9) will undertake experiments to perform a comprehensive characterisation of clinically relevant tissues such as skin, fat, muscle, major organs (liver, kidney, etc), brain. Measurements will be made of acoustic properties including, but not restricted to: attenuation coefficient, absorption coefficient, speed of sound and non-linearity parameter (B/A). Measurements will be made at a range of temperatures relevant to therapeutic applications of ultrasound. In addition, measurements of mechanical properties (density and strength and elasticity related factors) will be made with this knowledge extended to the derivation and calibration of material strength models, based on material composition. Extrapolation of the models for the prediction of tissue properties will be the next target.

While many of the techniques for acoustic (attenuation, sound speed and non-linearity) and thermal (specific heat capacity and thermal conductivity) property measurements are already available at the ICR, it will also be necessary to develop and implement methods for measuring additional properties.

Once a comprehensive list of tissue properties has been compiled, a range of tissue mimicking materials will need to be fabricated and comprehensively measured for the same properties as the tissue study detailed above.

Knowledge of these properties and tissue mimic fabrication processes will be shared with the UCOM consortium so that ESRs in other establishments can investigate their fluid dynamics, cavitation and chemical properties by numerically and experimentally. Ultimately this will allow tissue mimics to be used in studies for shock wave device design, allowing further studies of dependence on pulse type, mechanisms of damage and the importance of heating effects, as well as studies aimed at controlling the stochastic nature of cavitation.

The measurement aspect of this project will be exploited through mathematically modelling of ultrasound cavitation enhanced drug delivery. The modelling will be validated by designing, building and evaluating a

phantom in which to simulate ultrasound enhanced drug delivery.

Outcomes:

1. Development of methods for characterising tissues/tissue mimics
2. Comprehensive list of acoustic, mechanical and thermal properties of biological materials
3. Identification of a comprehensive list of tissue mimicking materials
4. Fabrication of a range of tissue mimics
5. Comprehensive list of acoustic, mechanical and thermal properties of tissue mimics
6. Derivation and calibration of material strength models for tissue mimics
7. Shortlist of tissue mimics for ESR10 (another ICR PhD student) to study the acoustic cavitation nucleation properties of
8. Provision of comprehensive characterisation data and tissue mimic fabrication details to other consortium members (ESRs).
9. Design, fabrication and demonstration of a phantom for validating ESR8's mathematical model of cavitation enhanced drug delivery

LITERATURE REFERENCES

HILL, BAMBER, TER HAAR (Ed) Physical Principles Of Medical Ultrasonics, Ed (Second Edn) Pub. John Wiley & Sons, 2004

BROWNE, J. E., RAMNARINE, K. V., WATSON, A. J. & HOSKINS, P. R. 2003. Assessment of the acoustic properties of common tissue-mimicking test phantoms. *Ultrasound in Medicine & Biology,* 29**,** 1053-1060.

DUCK, F. 1990. Ultrasonic Attenuation, absorption, scatter. *Physical Properties of tissue.* Academic Press P100-115

EL-BRAWANY, M. A., NASSIRI, D. K., TERHAAR, G., SHAW, A., RIVENS, I. & LOZHKEN, K. 2009. Measurement of thermal and ultrasonic properties of some biological tissues. *J Med Eng Technol,* 33**,** 249-56.

TER HAAR, G., SINNETT, D. & RIVENS, I. 1989. High intensity focused ultrasound--a surgical technique for the treatment of discrete liver tumours. *Phys Med Biol,* 34**,** 1743-50.

VLAISAVLJEVICH, E., KIM, Y., OWENS, G., ROBERTS, W., CAIN, C. & XU, Z. 2014. Effects of tissue mechanical properties on susceptibility to histotripsy-induced tissue damage. *Physics in Medicine and Biology,* 59**,** 253-270.

CANDIDATE PROFILE

Note: the ICR's standard minimum entry requirement is a relevant undergraduate Honours degree (First or 2:1)

Pre-requisite qualifications of applicants: e.g. BSc or equivalent in specific subject area(s)	BSc is essential, MSc desirable
Intended learning outcomes: Please provide a bullet point list (maximum of seven) of the knowledge and skills you expect the student to have attained on completion of the project.	Characterisation methodology Data analysis techniques Scientific rigor Mathematical modelling Phantom design and fabrication Experimental design Scientific writing and publication

ADVERTISING DETAILS

Project suitable for a student with a background	☐ Biological Sciences

in: (Please tick all categories that apply – your project will be advertised under all selected categories)	☒ Physics or Engineering ☐ Chemistry ☐ Maths, Statistics or Epidemiology ☐ Computer Science ☐ Other (provide details)
Keywords: Please provide 4-6 words/short phrases that potential students may type into search engines (e.g. Google) to search for PhDs similar to yours – e.g. 'cancer predisposition genes', 'physics PhD London' etc.	**1. Therapeutic ultrasound cavitation** **2. Ultrasound enhanced drug delivery** **3. Tissue characterisation** **4. Tissue mimic phantom design and fabrication** **5. Mathematical modelling and validation**

FUNDING (only complete this section if this project already has full/partial funding)	
☒ This project is fully funded	*Full-funding details (this must include stipend, fees and consumables) including the source of funding:* ***UCOM EU funded ITN full funds first 3 years, ICR underwrote the costs of the 4th year at the time of application***