PHD STUDENTSHIP PROJECT PROPOSAL: BRC PROJECTS

PROJECT DETAILS

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<th>Project Title:</th>
<th>The development and implementation of Multi-Spectral CT imaging techniques and artificial intelligence methods within stereotactic radiosurgery treatment planning for oligometastases in the brain and intracranial meningiomas</th>
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<td>Short Project Title:</td>
<td>Multi-Spectral CT and artificial intelligence in stereotactic radiosurgery treatment planning for neuro-oncology</td>
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SUPERVISORY TEAM

| Primary Supervisor(s): | Dr Dimitra Darambara  
|                        | Dr Liam Welsh  
|                        | Dr Ben Glocker (Imperial College) |
| Associate Supervisor(s): | Margaret Bidmead |
| Backup Supervisor: | Prof Chris Nutting |
| Lead contact person for the project: | Dr Dimitra Darambara |

DIVISIONAL AFFILIATION

| Primary Division: | Division of Radiotherapy and Imaging |
| Primary Team: | Multimodality Molecular Imaging |

PROJECT PROPOSAL

BACKGROUND TO THE PROJECT

Imaging protocols in neuro-oncology for radiotherapy treatment planning are typically multimodal. Magnetic Resonance (MR) sequences provide the spatial information and soft tissue contrast necessary to enable delineation of Gross Tumour Volumes (GTV) and Organs At Risk (OAR). Electron density data is generated from a corresponding conventional Computed Tomography (CT) image.

These images are combined through a rigid image registration. Uncertainties in this registration can occur from

- patient specific paramagnetic distortions in MR imaging
- spatial imaging distortions introduced through the undesirable use of 3-Tesla MR imaging
- an inferior soft tissue contrast observed in conventional-CT (oligometastases in the Brain can often be invisible)
- temporal and setup uncertainties between the scans

These compound already significant GTV/OAR delineation uncertainties that represent a leading source of error within the radiotherapy workflow [1].
These uncertainties could be reduced by

- implementing a single-modality state-of-the-art imaging technique
- developing and implementing Machine Learning (ML) techniques for GTV/OAR segmentation.

ML, a branch of artificial intelligence (AI), is a rapidly emerging field within the health care profession; applied correctly it could help tackle GTV/OAR edge uncertainty. ML techniques will perform repetitive well defined tasks consistently; reduce clinical interpretation time and discover patterns well beyond human perception.

The use of ML for automatic image segmentation for MR imaging of brain metastases [2] and brain lesions [3] has been reported. However, due to the sub-optimal soft tissue contrast observed in conventional-CT automated image segmentation is problematic. Whereas Dual Energy Computed Tomography (DECT) has been shown to improve soft tissue contrast in comparison to conventional-CT; specifically when utilizing Virtual-Mono-Energetic (VME) post-processing imaging capabilities. VME imaging in combination with a two-step 3D U-net deep learning deep method has been shown to quantitatively and qualitatively improve image OAR segmentation in brain tumour patients compared to ground truth and multi-atlas segmentation [4].

PROJECT AIMS

1. The use of in-house and commercially available test phantoms to assist in the development of state-of-the-art imaging techniques based on DECT that can be clinically implemented into the stereotactic radiosurgery (SRS) treatment planning workflow for neuro-oncology, specifically in regards to oligometastases in the Brain and intracranial meningiomas.

2. The development of a pilot study using DECT-VME imaging for patient SRS treatment planning for oligometastases tumours in the brain has been extensively discussed with Dr. L. Welsh, the Head of Neuro-Oncology at the RMH, who specializes in stereotactic radiotherapy and radiosurgery for brain tumours. It is understood meaningful data will be available within the timeframe of this research study. Recruitment and ethics will be ongoing as the student develops novel imaging and ML techniques for use in neuro-oncology.

3. A Deep learning 3D Convolutional Neural Network (CNN) [3] developed by Dr. Ben Glocker, leader of the Biomedical Image Analysis Group at Imperial College, will be trained with retrospective MR images with metastatic volumes manually segmented by a clinical expert. Following successful training of the ML algorithm, a frontend application, also developed by Imperial College, will be used to run the trained 3D CNN on the RMH system to segment MR sequences of patients with metastatic disease. These segmented metastatic volumes will be registered to their accompanying false-negative conventional-CT images (Aim 4); this will be repeated with DECT-VME images when they become available (Aim 2).

4. ML - Proof of concept – The design and development of ML techniques for the auto segmentation of retrospective CT images (based on the registered MR image segmented volumes from aim 3), for patients treated for oligometastases in the brain who have undergone
multimodal (CT/MR) imaging during their SRS treatment planning. This will be repeated with the DECT-VME / MR image data acquired from the pilot study. These segmented images will be qualitatively and quantitatively evaluated.

5. The use of advanced Geant4 Application for Tomographic Emission (GATE) simulations to evaluate and explore different DECT hardware configurations alongside novel photon counting approaches to establish which techniques could provide the best clinical solutions for the future.

RESEARCH PROPOSAL

A clinical need exists for the development and implementation of novel DECT techniques into the radiotherapy treatment planning workflow. DECT is widely used in diagnostic radiology, whilst its benefits are underutilised in radiotherapy treatment planning. Any imaging techniques developed in neuro-oncology will be highly translatable into other anatomical regions and will set the foundation for the further growth of multi-spectral imaging and photon-counting technologies within radiotherapy and the healthcare system generally. Moreover, DECT is an exceptionally important resource in Proton-beam-therapy [5] due to the proton Bragg-peak and the radiosensitive nature of neurological tissues. The clinical need for ML is growing rapidly and in harmony with the development of state-of-the-art novel imaging techniques there is great potential for real advances in this field.

Expected outcomes:

- develop, test and implement ML techniques for the automatic segmentation of oligometastases of the Brain and OARs in conventional-CT (proof of concept) and DECT-VME imaging.
- develop techniques for the routine use of DECT within the radiotherapy planning workflow
- reduce/eliminate the need for routine Gadolinium contrasted MR imaging in SRS planning.
- reduce the clinical burden on the MR infrastructure
- reduce radiotherapy simulation time pressures.

Rapid advances in DECT hardware have led to the need and development of increasingly more sophisticated post processing algorithms that have in turn led to marked qualitative and quantitative improvements in soft tissue differentiation [6].

DECT has expanded rapidly in recent years and efforts are being made to integrate it into the radiotherapy workflow. DECT scanners are divided into several hardware configurations [7]. A 1st generation hardware approach with sequential axial scans at 80kV and 140kV will be utilised in this study. Sequential DECT scanners can be susceptible to temporal coherence uncertainties in time dependant imaging. However, in non-contrast brain/skull imaging where patient specific immobilization shells are used to limit patient movement this is not an issue.

Material decomposition for the imaging of intracranial meningiomas - Material-specific images can be reconstructed that display concentrations and distributions of specific materials. Particular materials can be virtually eliminated from the image using a material decomposition method. The ability to
effectively decompose a voxel into its material components allows the creation of virtual contrast free and bone subtraction imaging. Meaning, there is no need for a separate contrast free scan in radiotherapy treatment planning and that intracranial vessels which can be difficult to interpret on MR sequences can be seen readily on DECT following a bone subtraction.

Contrast imaging could pose temporal problems while imaging intracranial meningiomas. This could be overcome by imaging the patient post arterial/venous phase, where an Iodine density plateau is temporarily achieved, but there will be an uncertainty. It is therefore of interest to develop a phantom to model patient specific iodine renal clearance to evaluate how image density shifts between sequential DECT scans effects the reconstructed images. From this bespoke clearance models can be developed to correct for renal clearance.

**VME and ML for imaging oligometastases in the Brain** - VME images can be synthesized between 40kV-190kV and are created through a non-linear combination of the opposing kV data sets or via local spatial-frequency filtering. This feature has been shown [8] to improve the Contrast to Noise Ratio (CNR) at low virtual energies, specifically at 40kV where image noise would typically overcome any contrast gains. VME images can be used to optimize brain visualization in non-enhanced scans, specifically to image brain parenchymal; further documented improvements over 120kV conventional-CT in Signal Noise Ratio (SNR) and CNR are noted for supratentorial grey and white matter [9].

The consistency and accuracy of image segmentation is highly dependent on image quality, but it is equally dependant on inter/intra human subjectivity. Auto-contouring software applications aid the outlining process, from a workflow, consistency and accuracy perspective, but further gains are desirable. If DECT-VME images can be optimized to the extent where tissue boundary edges were spatially similar to what is currently achievable on registered CT/MR images then MR may not be required. However, if this study demonstrates multi-modal imaging is needed, an MR/DECT-VME imaging approach would nonetheless

- reduce image registration uncertainty
- reduce GTV/OAR uncertainty
- ease planning/registration time pressures

Processing raw CT data into a 2D image can be reductive. PACS monitors, reconstruction algorithms, room lighting and intra/inter clinician subjectivity all serve to mask the signal. In optimal viewing conditions the human eye can perceive around 1,000 different shades of grey over this entire luminance range; whilst an unprocessed 16-bit image contains 65,536 shades of grey. The signal we need could already be present in the data.

Volumes of oligometastatic tumours in the brain are clearly defined in contrasted MR images but are often poorly defined or even invisible in a corresponding non-contrast conventional-CT image; this gives reason for the current multimodal imaging approach. However, cancerous tissue will inevitably attenuate differently to healthy tissue, even if just on a minute scale, a scale to which the human eye cannot perceive. In this case the signal could be found with ML techniques.
Objectives:

- Evaluate retrospective pairs of MR/CT metastatic brain tumour images.
- An expert neuro-oncologist will contour ‘ground truth’ metastatic volumes on Gadolinium contrasted MR sequences.
- These labelled MR sequences will be used to train a deep learning 3D CNN [3]. It is important to develop this 3D CNN technique 1) To avoid intra/inter clinician subjectivity 2) Time pressures
- Once the algorithm is trained to accurately segment metastatic disease in test MR sequences a front end developed by Imperial College will be tested and developed as it is used to automatically segment a sample of MR sequences of patients with oligometastatic tumours in the brain.
- Register the MR metastatic volumes spatially with their accompanying conventional-CT images.
- Create and develop a ML technique to analyse false-negative labelled conventional-CT images to establish if a signal can be found. Even if no signal is found, the ML proof of concept technique will be ready for implementation with the DECT-VME/MR images obtained from the pilot study.
- Conduct a quantitative assessment of DECT-VME image segmentation using: Dice-Similarity-coefficient, the 95th percentile Hausdorff distance and the centre-of-mass-displacement.

TRANSLATIONAL TRAINING

The student will develop multi-disciplinary skills and knowledge in oncology, radiology, radiotherapy, clinical physiology, novel imaging techniques and analysis, image processing, artificial intelligence, computational simulations and statistics analysis.

The student will be based within the Joint Department of Physics at ICR/RMH but will be expected to work across sites and in collaboration with staff at the ICR, RMH and Imperial College, where the student will establish clinical skills and advanced knowledge on ML/AI. Work will revolve around novel state-of-the-art imaging techniques that aim to improve imaging in neuro-oncology. The student will learn about neuro-anatomy and the importance of imaging quality in the context of image segmentation in SRS planning. As the student develops a quantitative and qualitative understanding of novel imaging techniques he/she should act as an intermediary between clinical, computational and medical physics professionals to aid in and facilitate the design, production and implementation of ML techniques to be used within neuro-oncology for DECT-VME imaging at RMH.

All developed DECT/ML techniques are highly transferable to further radiotherapy treatment planning areas so as to provide an excellent footing for future research and development.

The student will attend training and development courses across all sites and suitable conferences.

LITERATURE REFERENCES

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 in Physics/Engineering (1st/2i) MSc in Physics/Medical Physics/Radiation Physics MPhys in Physics

Intended learning outcomes: The student will obtain:
- Advanced knowledge in cutting edge medical imaging techniques and systems, including dual-energy CT, multi-spectral and photon-counting CT and MRI
- Advanced knowledge of image-guided radiotherapy
- In depth developmental experience in medical image processing and artificial intelligence /machine learning
- Knowledge of Neuro-Oncology
- Advanced computational skills in Monte Carlo codes and statistical analysis
- Multi-disciplinary skills

ADVERTISING DETAILS
| Project suitable for a student with a background in: | □ Biological Sciences  
x Physics or Engineering  
□ Chemistry  
□ Maths, Statistics or Epidemiology  
□ Computer Science  
□ Other (Provide details) |
|---|---|
| Keywords: | 1. multi-spectral x-ray imaging  
2. artificial intelligence  
3. neuro-oncology  
4. image-guided radiotherapy  
5. stereotactic radiosurgery  
6. |