English PhD project description

This is a short description of the PhD project entitled *"Development of Quantitative Magnetic Resonance Imaging (qMRI) Methods for Radiotherapy Response Studies",* enrolled at the Center for Magnetic Resonance at DTU's Department of Electrical Engineering (DTU Elektro) and co-founded by the Danish Cancer Society.

The overall aim of the project is to improve radiotherapy of patients suffering from secondary tumors in the brain by developing and improving MRI methods to reveal and deliver biological information of relevance. With a prevalence of 9-17 % of all cancer cases and an increasing incidence, this is the most common intracranial malignancy in adults, and the efficacy of current standards of therapy needs to be improved.

Tumors are usually inhomogeneous structures. Depending on their primary histology, size and other characteristics, they may be divided into sub-regions based on properties such as cell density, perfusion, cytotoxic and vasogenic edema, hypoxia etc. To seek understanding of the response to treatment on a microscopic level, the first part of the project will concern a voxel-based analysis and tumor tissue segmentation based on existing clinical diffusion weighted MRI data. The results will be used to guide an improvement of acquisition and analysis strategies, involving MRI sequence and protocol design.

In general, the MRI modality forms images of the anatomy and physiological processes in the body and is already widely used in radiology with growing number of applications in oncology. However, the particular method in focus of this project, the novel diffusion weighted qMRI (DW-qMRI), is of relevance as the technique through sensitivity to water motion enables a tissue microstructure probe with real-time insight into the state of the cells. Thus, DW-qMRI is a strong candidate for becoming an imaging biomarker of treatment response in cancer patients receiving radiotherapy and opens the possibility of a day-to-day therapy guidance and monitoring.

Though preliminary investigation the method shows promising potential, however a lot of challenges remains and both sequence optimization and development of robust post-processing methods is necessary. Potential problems to be addressed here may be related to motion, sensitivity, partial volume effects, and suppression of unwanted signals. Nevertheless, the clinical feasibility of the potential remedies to these problems needs to be accentuated. Moreover, measurement of additional parameters such as tissue relaxation properties is expected to add both sensitivity and specificity.

The growing role of MRI in radiotherapy for target definition and potentially in treatment adaptation has recently been manifested with the emerging MRI–linear accelerator hybrid systems (MRLs), of which one will be installed at Odense University Hospital (Denmark). This system enables the mentioned daily adaptation of treatment plans based on biological information acquired with MRI, something not previously feasible. Clinical feasibility however requires that treatment time is not prolonged. Therefore, the development of specialized MRI sequences is tremendously important to allow longitudinal research and clinical implementation of MRI guided radiotherapy. The research of this project will be in close cooperation with Odense University Hospital and the associated radiotherapy and MRL staff, which together with the technical experts at the Center of Magnetic Resonance at DTU will create a multi-disciplinary environment for the PhD student of the project.

The following gives an overview of the main tasks defined to address the overall aim of the project:

- A multi-level differentiation of sub regions in brain metastases by applying a voxel-based approach to existing clinical DW-MRI data, including radiomics.

- A development and simulation of improved clinically feasible DW-qMRI measurements and supplementary quantitative measures as biomarkers for radiotherapy response in human brain metastasis
- A development of dedicated radiotherapy MRI sequences enabling time efficient simultaneous multi-parametric measurements suitable for longitudinal studies in radiotherapy.

Overall, the project is expected to produce valuable prognosis and monitoring methods for patients with brain metastases, which may benefit patients at any hospital with access to MRI. In a broader perspective, results of this study may have impact for MRI guided radiotherapy in general, especially considering the emerging MRL systems which are about to define the beginning of a new era in radiotherapy.