Multiparametric functional MRI for radiotherapy response prediction

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There has been a huge expansion in the use of medical imaging in cancer diagnostics, and treatment evaluation, where particularly magnetic resonance imaging (MRI) is being increasingly used due to the method's ability to provide high-resolution images without the use of ionizing radiation. **Anatomical MRI** is important in the diagnostic work-up in many cancer types, where it allows visualisation of zonal anatomy and detailed evaluation of local disease extent, regional metastasis and general anatomy. Further, **functional MRI** comprises sequences reflecting functional / biological tissue properties, such as tissue structure and cell density (diffusion-weighted MRI), metabolism (MR spectroscopy) and various features of tumour vascularity (dynamic contrast-enhanced (DCE) MRI and dynamic susceptibility contrast (DSC) MRI). These techniques have shown potential to also capture important features of the tumour microenvironment relevant for radiotherapy efficacy. We are investigating how these techniques may be optimally utilised in order to provide pre-treatment measures of whole-tumour radiosensitivity that may be aid planning of individualised radiotherapy strategies. In addition, we are investigation how these techniques may be used both for early monitoring and end-of-therapy evaluation of radiotherapy outcome.

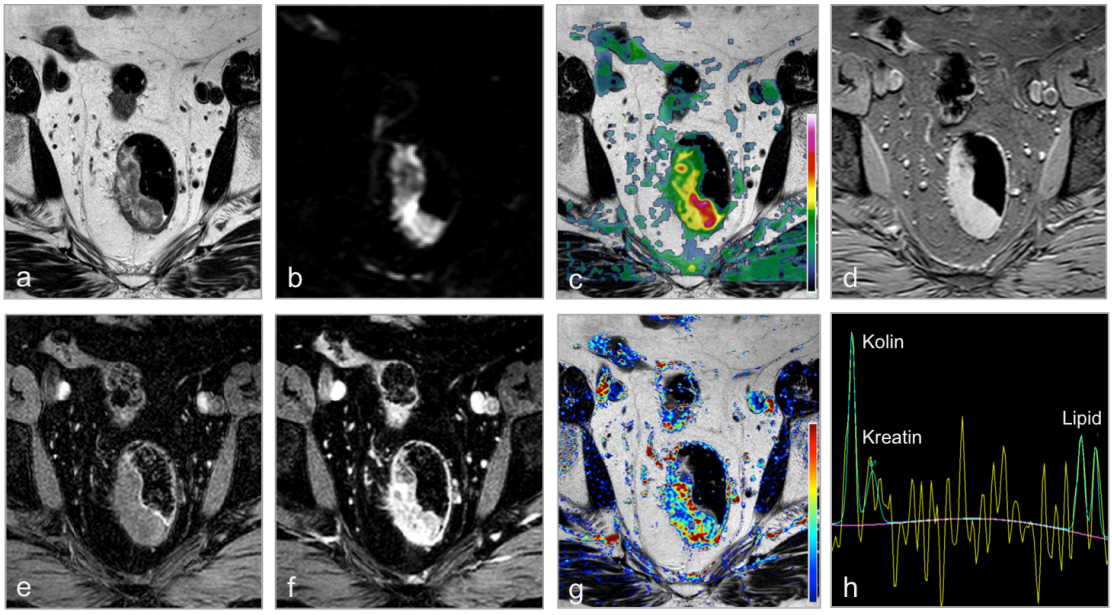

Figure 1: Functional MR images of rectal cancer acquired on a 1.5 T MR scanner. (A) T2-weighted morphologic image, (B) diffusion-weighted (DW) image with b-value of 500 s/mm^2, (C) Parametric b_{max} map from DW image overlaid the T2-weighted image, (D) multi-echo T2-weighted image, (E) T1-weighted image before injection of contrast agent, (F) T1-weighted image after injection of contrast agent, (G) Parametric blood perfusion map from dynamic contrast-enhanced image overlaid the T2-weighted image, (H) Spectra from in vivo MR spectroscopy.*

In a study entitled "OxyTarget – Functional MRI of hypoxia-mediated rectal cancer aggressiveness" a range of functional MR data from 200 patients are collected to investigate whether functional MR images (or a combination of several images – multiparametric MRI) can identify the radiosensitivity of tumours. The study also includes collection of a range of clinicopathologic outcome parameters, radiotherapy plans and patient survival which allows investigation of the predictive and prognostic information contained in the MR images. Example functional MR images from a patient in this study are shown in Figure 1. The data for all patients are available for project- and master theses, and below are presented some suggested proposals. Candidates may also take contact for discussion of alternative proposals.

Proposal 1:

Estimates on tumour blood perfusion is commonly acquired by voxel-wise kinetic modelling of contrast-enhancement curves from T1-weighted DCE MRI, which requires injection of a contrast agent. We have in a small pilot study recently shown that alternative estimates on tumour blood perfusion may be acquired through so-called intravoxel incoherent modelling (IVIM) of diffusion-weighted (DW) MRI data (Bakke et al, 2017), which does not require injection of a contrast agent, and which were shown to both predict radiotherapy response and patient survival.

In the first part of this proposal the candidate will use Matlab (or a similar tool) to estimate blood perfusion parameters from both DW MRI and DCE MRI from the OxyTarget data set. The second part will be to perform a comparison between the different parameters and evaluate their ability to assess tumour radiosensitivity and their ability to predict patient outcome.

Proposal 2:

T2* relaxation refers to decay of transverse magnetisation caused by spin-spin relaxation or magnetic field inhomogeneity. T2*-weighted MR images may be acquired by gradient echo MRI with multiple echo-times (TE) or by DSC MRI. The inverse T2* is R2* and is in theory a measure of the oxygen saturation in the tissue. Oxygen (or oxygen deficiency; hypoxia) is an important determinant for radiotherapy response and outcome in patients with solid cancer.

In this proposal, the candidate is expected to use Matlab (or a similar tool) to estimate R2* tumour maps from both multi-TE MRI and DSC MRI data from the OxyTarget data set. Thereafter, the candidate will evaluate the potential of these measures to assess tumour radiosensitivity and their correlation to tumour hypoxia by comparison with immunohistochemical analysis of tumour hypoxia in tissue. Depending on the candidate's competences and interests the generated MR data may also be further

used to simulate various approaches of delivering radiotherapy based on the R2* tumour maps, for instance through dose-painting or heterogeneous boosting techniques.

Proposal 3:

It is acknowledged that solid tumours are heterogeneous and that mean tumour values of estimated MR parameters do not reflect the heterogeneous information contained in the tumours. One way to capture tumour heterogeneity is through texture analysis. The term texture refers to specific properties of the internal structure of image regions, for example rough versus smooth or oriented versus randomly dispersed (among others). In medical image analysis, texture-based methods are very useful to classify tissue types, typically by first extracting texture features and then feeding these features into a classifier. However, investigations on the potential of texture-based methods of imaging data in the context of radiotherapy is poorly investigated, and particularly the potential value of texture-based analysis of functional imaging data in the context of radiotherapy.

In this proposal, the candidate will use various functional MR images from the OxyTarget data set and explore how texture analysis may prove added value in detection of tumour radiosensitivity and radiotherapy outcome compared to mean parameter values. The candidate will start with lower-order histogram features (such as kurtosis, entropy and skewness) and may proceed to more advanced texture analysis based on for instance local binary patterns (BNP), gray-level co-occurrence matrix (GLCM), filtering approaches (e.g. Gabor filters) and various classifiers and multi-channel visualisation methods.