MAGNETIC RESONANCE IMAGING IN PRE-CLINICAL AND CLINICAL CANCER RESEARCH

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Magnetic Resonance Imaging (MRI) is arguably the most versatile medical imaging technology. Its non-invasive character and the availability of the multitude of different types of contrast makes MRI particularly well suited for pre-clinical and clinical bio-medical applications. The first part of this presentation provides a review of selected applications of MRI in pre-clinical cancer research. In the second part a novel approach to prostate cancer diagnosis with MRI will be presented.

MRI in pre-clinical cancer research:
Tumour microenvironment is significantly different than that of normal tissue, and it is characterized by unbalanced blood supply, perfusion heterogeneity, transient and chronic hypoxia and acidic pH. A number of MRI techniques allow studying various elements of the tumour microenvironment.

Tissue perfusion is commonly studied using Dynamic Contrast Enhanced (DCE) MRI. This technique involves rapid acquisition of a series of T1-weighted images following intravenous injection of a low molecular weight contrast agent (typically Gd-DTPA). Two compartment model of tracer kinetics is often used to estimate the contrast agent’s volume transfer constant, and the fractional volumes of the leakage and plasma spaces. Arterial Input Function (i.e. contrast agent concentration in blood plasma) is required for accurate modelling; however AIF is often difficult to measure in pre-clinical models due to requirements for very high spatial and temporal resolution. A novel technique for measuring AIF with 100 ms temporal resolution is described. The technique estimates Gd concentration from the phase of the MRI signal, and the high temporal resolution is achieved by acquiring projections rather than 2D images. Preliminary results from the mouse tail artery are presented [1].

Vessel Size Imaging (VSI) is a technique that measures a weighted average of blood vessel radius. It involves intravenous injection of a USPIO (Ultra-small Super-Paramagnetic Iron-Oxide) contrast agent to introduce a magnetic susceptibility difference between tissue and the vascular network. This susceptibility difference results in the signal loss in the spin-echo and gradient-echo images, and allows estimation of the vessels radii. The application of this technique in studying hormonal dependence of the vascular changes in a murine mammary carcinoma mouse model is presented [2].

Hypoxic tumours are typically more aggressive and show significant resistance to radio- and chemo-therapy, thus in vivo measurements of pO2 levels in tumours may improve therapeutic efficacy. 19F NMR relaxation measurement of perfluorocarbons (PFC) is one of the few techniques that allow longitudinal monitoring of tumour pO2 levels in vivo. Application of the 19F MRI T1 measurements of 15-Crown-5-Ether to studies of the hormonal dependence of the tumour hypoxia in a mouse model is presented [3].

1H NMR T1 values are also sensitive to pO2. Fatty tissue shows particularly large effects due to high oxygen solubility in fat. A novel technique for fat T1 mapping is described. The technique is a combination of the extended 2 points Dixon method for fat and water separation and Look-Locker T1 mapping technique. Preliminary results from phantom and mouse in vivo experiments are presented [4].

Recently multi-modal imaging, where a combination of different imaging modalities are used simultaneously or sequentially in bio-medical applications, have gained significant interest. Particularly prominent is a combination of MRI with Positron Emission Tomography (PET), which allows combining very high sensitivity functional PET images with high spatial resolution anatomical and functional MRI images. Recently we have started a collaborative project to develop and build an MRI compatible PET insert for a pre-clinical 7 Tesla MRI scanner. The PET insert is equipped with the Silicon Photomultiplier (SiPM) detectors. Preliminary results of the performance evaluation of the SiPM detector inside the 7 T magnet are presented [5].
Multi-parametric MRI in prostate cancer diagnosis:
Prostate cancer remains the most common noncutaneous malignancy in North American males and second leading cause of cancer related deaths in men. Owing to the widespread use of screening tests many more prostate tumours are being detected, many of which are less advanced, localized, lower risk cancers. This prompted increased interest in focal therapy as an alternative to the traditional therapies of radical prostatectomy and radiation therapy. The ultimate success of focal therapy relies on proper patient selection and adequate characterization of the tumour’s location, extent and histological grade. Our results presented here demonstrate multi-parametric MRI capability of accurate characterization of prostate tumours [6].

Patients with a high clinical suspicion for prostate adenocarcinoma due to an elevated prostate specific antigen (PSA) and/or palpable prostatic nodule, with no prior treatment, underwent combined DTI/DCE MRI examination on a 3 T MRI scanner prior to transrectal ultrasound (TRUS)-guided biopsies. MRI parameters (ADC, FA, K\text{\scriptsize{\text{trans}}}, v_c, v_p) were correlated with the biopsy and prostatectomy results. Logistic Regression (LR) and Support Vector Machines (SVM) analyses were used to estimate the diagnostic accuracy of the combined MRI techniques and to predict the location, extent and pathological grade (Gleason score) of the tumours. Both LR [7] and SVM [8] analyses showed that the combination of DTI and DCE MRI has significantly better accuracy in prostate cancer diagnosis than either technique alone, with the area under the ROC curve reaching 0.96 for the combined MRI parameters. Spearman’s rho rank correlation test showed statistically significant correlation between the Gleason score and the ADC (\text{rho} = -0.661, p = 0.0005), and FA (\text{rho} = -0.551, p = 0.0036), with the LR analysis showing statistically significant dependence between the Gleason score and the MRI parameters (p < 0.0001 for the model).

SVM analysis generated cancer probability maps that accurately predicted the location of a dominant lesion, as verified by histology sections [8]. The cancer probability also correlated with the Gleason score. The accuracy of predicting tumour volume by the cancer probability increased with the Gleason score of the tumour.

Magnetic Resonance Elastography (MRE) is a novel technique that allows to measure non-invasively mechanical properties of tissue. In this technique, a mechanical vibrator is used to generate shear waves throughout the tissue and the resulting displacement is measured with MRI. Quantitative maps of tissue stiffness (elastograms) can be calculated by local inversion of the linear viscoelastic 3D wave equation. A transperineal MRE system is presented, which allows data acquisition for generating elasticity maps of human prostate in vivo [9]. Preliminary MRE data for the prostate cancer detection in vivo [10] and ex vivo [11] are also shown.

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