Deep learning of tumour microstructure using synthetic MRI from realistic tumour simulations

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Introduction

Numerous approaches to quantifying diffusion MRI data from tumours exist, including ADC, IVIM and, more recently, VERDICT [1]. VERDICT is based on a compartmental model, but uses relatively simple geometric forms to represent tumour cells and vasculature. To investigate more complex alternatives, we have used our REANIMATE framework (REAlistic Numerical Image-based Modelling of biologicAl Tissue substratEs), which uses optical imaging data from optically cleared whole-tumour samples as a structural substrate to model realistic tumour microstructure and fluid dynamics [2]. Here, we have extended REANIMATE to synthesise diffusion-MRI data, which were then used to train a deep neural network, and used to quantify *in vivo* diffusion MRI data (**Figure 1**). The aim of this study was to evaluate the feasibility of this approach, and to compare deep learning parameters with parameters from standard analyses.

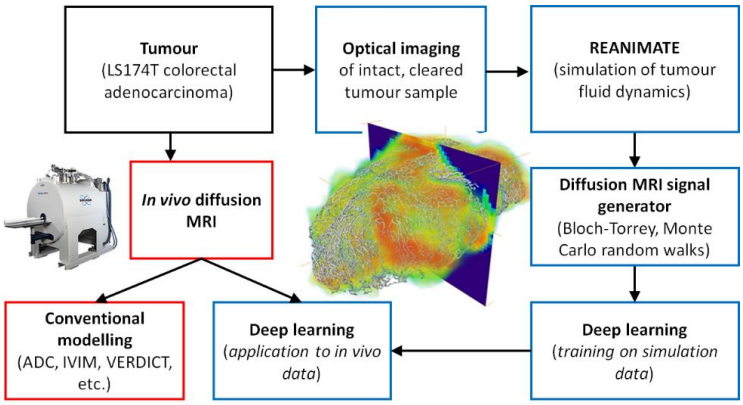

***Figure 1**. Deep learning of simulated tumour data*

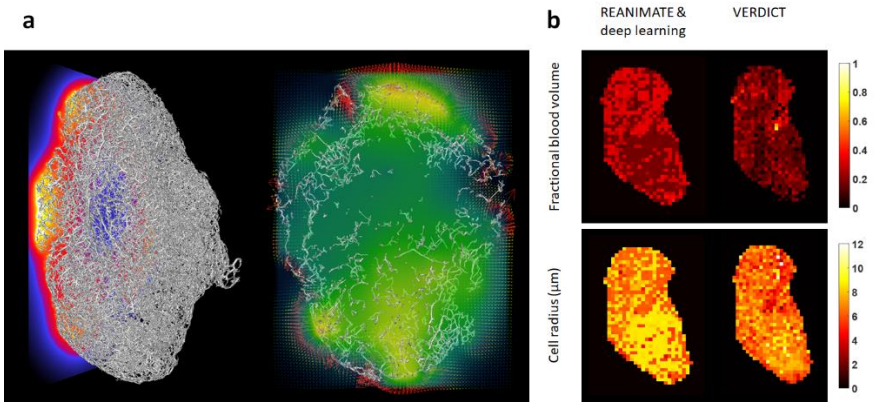

***Figure 2**. a) REANIMATE simulation of an LS174T tumour, showing blood flow and interstitial transport. b) Example parameter maps in cross-section through an LS174T tumour, modelled using deep learning and VERDICT.*

Methods & Materials

Nude mice were injected subcutaneously with LS174T colorectal adenocarcinoma cells in the right flank. After 15 days of growth, diffusion MRI data were acquired using a PGSE sequence (46 diffusion weightings and a 42-direction DTI) on a 9.4T Agilent scanner [1]. Immediately after scanning, mice were administered fluorescent lectin to label blood vessels, tumours were resected and optically cleared. Optical imaging of tumour blood vessels was undertaken with optical projection tomography (OPT). Whole-tumour vascular and interstitial transport were modelled using our REANIMATE framework, using the optical image data as a structural substrate. Diffusion MRI data were generated by performing Monte Carlo random walks and sample magnetisation modelled with the Bloch-Torrey equations. A deep neural network, containing 7 hidden layers (Keras in Python 3.5) was trained on simulation data, and simulation parameters provided as output (blood volume, blood flow, intracellular volume, cell radius, extracellular volume).

Results & Discussion

Training accuracy was 99.5%, following 100,000 epochs. During evaluation on 5,000 simulated data sets, accuracy was 99.3%. Example *in vivo* parameter maps (fractional blood volume and cell radius) in a cross-section through a tumour are shown in **Figure 2**, for VERDICT and deep learning models. As can be seen, both approaches produced heterogeneous parameter distributions, which were of similar orders of magnitude and with similar (but also differing) spatial distributions. This pilot study has therefore demonstrated the ability of deep learning of simulated tumour data to model *in vivo* diffusion MRI data, and produces results that are similar to those produced by VERDICT.

References: [1] E. Panagiotaki et al. Cancer Res. (2014). [2] d'Esposito *et al.* bioArxiv (2017), doi: https://doi.org/10.1101/219865.