Improved Delineation of Brain Tumour Margins using Whole-brain Track-Density Mapping

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Introduction: Advances in understanding cancerous cell proliferation, combined with the introduction of new drugs, improvement in the delivery of radiotherapy and neurosurgical techniques now make it possible for brain tumours to be rationally treated. Despite these advances, the mortality rate within the first year of diagnosis for high-grade tumours is approximately 80%. A factor contributing to poor outcomes is the limitation of current neuroimaging strategies, which do not reliably establish appropriate therapeutic margins for radiotherapy/resection planning. Anisotropy indices derived from Diffusion Tensor (DT) MRI have shown potential for differentiating tumour boundaries and infiltration within the peritumoural territory (1). However, there are significant limitations of the DT model with regards to resolving complex fibre populations (2). This problem is further exacerbated when tumours compress or compact fibre bundles due to increased mass affects. To address this problem we are investigating the use of HARDI diffusion imaging, utilising *whole-brain track-density* (visitation) maps to improve definition of therapeutic margins. Our hypothesis is that infiltrating tumour, especially within the peritumoral territory will reduce WM connectivity enabling improved depiction of tumour boundaries. To assist in the determination of tumour extent, the 3D visitation maps are anatomically fused to ^{18}F-FDOPA – PET images.

Methods: The study design encompasses serial data acquisition, sMRI / HARDI (60 diffusion encoding directions, b = 3000 mm/s^2, 2.2 mm isotropic resolution, 3T Siemens Trio) and ^{18}F-FDOPA (Philips PET/CT), on patients with high-grade glial neoplasms. preoperatively and at post treatment (1 and 6 months). The fibre orientation distribution was calculated using constrained spherical harmonic deconvolution (2) and probabilistic diffusion tractography was performed using MRtrix (http://www.nitrc.org/projects/mrtrix). Fifty streamlines were seeded for every voxel of the entire brain volume and the resulting 3D visitation maps nonlinearly registered to the contrast enhanced (CE) T1-weighted MRI. Visitation maps were normalised by dividing by the total number of brain voxels. To enable direct comparison of ^{18}F-FDOPA maps with the 3D visitation maps, the PET images were registered to the CET1 via a low dose CT transmission scan.

Results:
Representative preoperative and post treatment data for two patients with high-grade gliomas are given in Figure 1. The whole-brain track density maps, which can be generated in a fully automative process, show high contrast-to-noise ratio and are in agreement with known WM anatomy. In contrast to anisotropy maps generated using the DT model where WM regions exhibiting reduced signal (FA) can correspond to areas of complex crossing WM networks with high anisotropy, the visitation maps show more uniform signal reflecting connectivity of WM pathways. Importantly, when compared with the fused ^{18}F-FDOPA maps, we have found a consistent pattern of reduced connectivity, i.e. streamline density, in WM pathways within the surrounding peritumoral territory that improves delineation of tumour margins.

Discussion: When developing novel diffusion based MRI markers for improved tumour boundary delineation, most studies rely on the use of CET1 images as the gold standard to define tumour margins. Recent reports have shown that PET-MRI fusion technology significantly improves delineation, especially infiltrating tumour within the peritumoral territory (3). Our preliminary ^{18}F-FDOPA - MRI results confirm this finding. Furthermore we report for the first time, that infiltrating tumour delineated on ^{18}F-FDOPA maps that is present outside of the tumour-enhancement boundary defined on CET1 images results in a reduction in WM connectivity or streamline density on corresponding whole-brain track density maps. This has significant implications for surgical and radiation treatment planning. As PET scanning with tumour specific radiotracers is not always available, a combination of CET1 and 3D visitation maps has the potential to provide a useful tumour boundary marker in radiological practise.
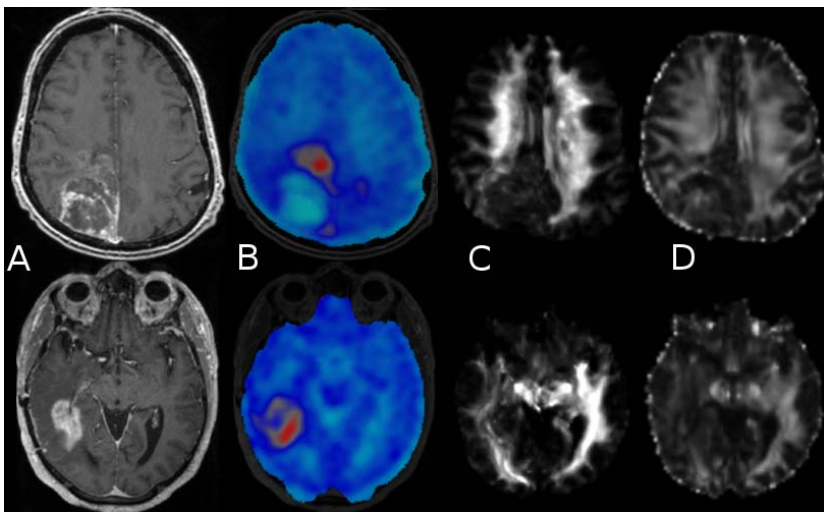

Figure 1.
Representative images for GBM patients preoperatively (top) and 4 weeks after initial post chemoradiation therapy. The maps represent (A) CET1, (B) ^{18}F-FDOPA, (C) visitation map and (D) FA map. In both cases the tumour margins are more clearly depicted on the whole-brain track density maps compared to the FA images due to the improved definition of surrounding WM pathways within the peritumoural territory

References: (1) Ferda J et al., Eur J Radiol 2009; Epub ahead of print; (2) Tournier J-D et al., NeuroImage 2007, 35:1459; (3) Ledezma CL et al., Eur J Radiol 2009;71:242-8