Potential Utility of Quantitative Magnetisation Transfer Imaging for Detection of Lesion Extent in Glioblastoma Multiforme

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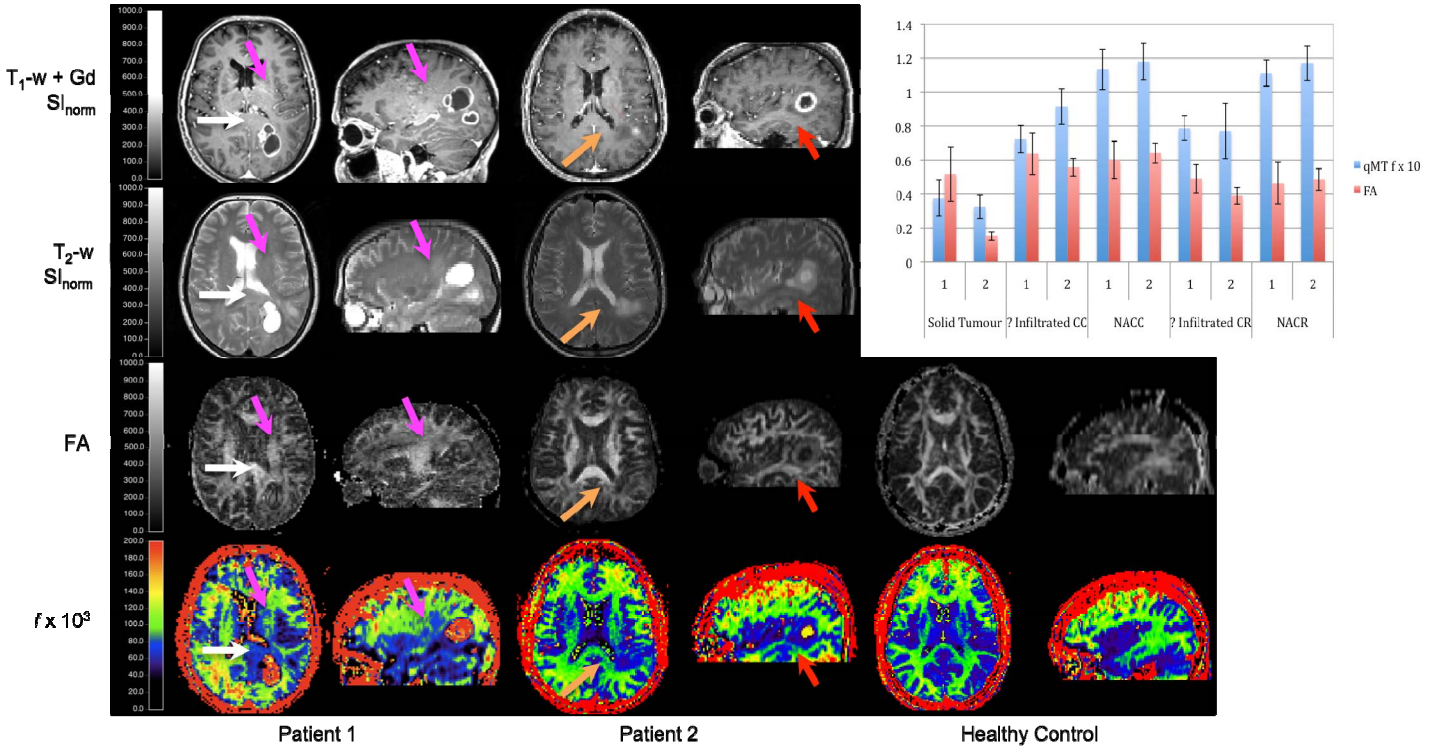
INTRODUCTION: Glioblastoma multiforme (GBM) is a highly invasive primary brain tumour known to infiltrate preferentially along white matter tracts. Tumour cells have been detected histologically at sites distant from the main enhancing tumour at the time of diagnosis, including beyond the T_2-bright oedematous region and in contralateral normal-appearing white matter [1]. Detection of glioblastoma invasion beyond that seen on conventional MR imaging is currently being investigated in order to rationalise radiotherapy and surgical planning, and to detect disease response at the earliest opportunity, without waiting for the appearance of new enhancing lesions. Diffusion tensor imaging (DTI) has, for example, been used to detect gliomatous invasion in white matter [2]. The bound fraction parameter (*f*) derived using quantitative magnetisation transfer (qMT) can provide information about the myelin content of cerebral tissue, and has been used to investigate lesions in demyelinating diseases such as multiple sclerosis [3]. We hypothesise that changes to the white matter myelin content caused by infiltrating glioblastoma may manifest prior to detection of lesion expansion or progression on conventional MRI, or white matter disruption on DTI, and explore this hypothesis with the aid of two case studies.

METHODS: Ethical approval was obtained. Multispectral imaging was carried out on a Philips Achieva 3 T scanner with an 8-channel SENSE head coil (Philips, Best, The Netherlands.) Two patients with GBM underwent pre-operative imaging. An axial T_2-weighted turbo spin echo sequence (TR 3s, TE 80ms, 224x198x120mm FOV, 1x1x3mm voxels), DTI (Philips 15 direction single shot echo planar, no overplus, b=1000, 224x176x120mm FOV, 2x2x2mm voxels) and an in-house optimised qMT sequence (224x176x120mm FOV, 2x2x2mm voxels) [4] were carried out. For qMT analysis, B_1 and T_1 maps of the imaging volume were generated. B_1 efficiency was measured using a magnetisation prepared turbo FLASH sequence with a series of 16 nominal preparation angle acquisitions [5]. T_1 mapping utilised variable flip angle 3D T_1-FFE acquisitions (α = [2° 5° 10° 16°].) A 3D T_1-weighted turbo field echo (T1-TFE; spoiled gradient echo) sequence (TR 9.9ms, TE 4.6ms, 224x176x156mm FOV, 1x1x1mm voxels) was acquired following intravenous administration of gadolinium contrast (Gd-DOTA 0.2mmol/kg, Guerbet, France.)

RESULTS: The figure shows selected axial and coronal slices in T_1-weighted, T_2-weighted, fractional anisotropy (FA) and qMT bound fraction (*f*) images in two patients with GBM. Patient 1 has a left parieto-occipital lesion. The T_2-weighted abnormality can be seen extending medially across the splenium of the corpus callosum (SCC – white arrow) with some superior extension within the corona radiata (CR – purple arrow.) FA is preserved in the CC and CR. The bound fraction (*f*) is lowest in the solid part of the tumour, and is reduced in each region of interest beyond that seen in the T_2-weighted abnormality. In addition, low FA is seen in the occipital pole despite normal bound fraction (blue arrow.) Patient 2 presented with a smaller lesion in a similar anatomical position to patient 1. A halo of T_2-weighted high signal (oedema) is seen adjacent to the posterior horn of the left lateral ventricle. FA is preserved in the SCC (orange arrow) and temporal stem (red arrow) beyond this region. Again, the bound fraction map shows reduction in these regions beyond the boundary of the T_2-bright region. A healthy control is included for visual comparison of FA and *f* in the regions described. The mean±standard deviation of *f* and FA for regions of interest in enhancing tumour, potentially infiltrated CC, normal appearing (NA) CC, potentially infiltrated CR and normal appearing CR are shown in the figure inset.



DISCUSSION: These preliminary data suggest that the qMT parameter bound fraction (*f*) may detect GBM pathological change in white matter beyond that visible with conventional MR imaging, and complementary to changes in DTI-derived FA. Areas are seen outwith the T_2-weighted abnormality which possess near normal FA and low *f*, possibly indicating preserved axonal integrity despite the presence of tumour infiltration. Further transverse and longitudinal imaging is required to describe the changes in this parameter during GBM growth and progression.

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