

DEMONSTRATION OF THE RELATIONSHIP BETWEEN OXYGEN DELIVERY AND CONTRAST AGENT DELIVERY IN HUMAN GLIOMA USING COMBINED OEMRI AND DCE-MRI

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Introduction

Tumour hypoxia has been linked to progression and metastasis and is also known to affect sensitivity to treatment. Oxygen-enhanced MRI (OEMRI) is a proposed non-invasive method to investigate oxygen delivery and consumption in tumour tissue that is based on observing changes in T_1 . Under normoxic conditions, an oxygen gas challenge results in an increase of paramagnetic molecular oxygen dissolved in the blood plasma, leading to a signal change on T_1 -weighted images in arteries and certain tissues, including tumours. Initial clinical results have shown regional correlations between signal changes during OEMRI and those during DCE-MRI in abdominal and pelvic tumours [1]. More recently, pre-clinical results in a glioma model have shown significant R_1 changes in both a positive and negative direction during a normobaric oxygen gas challenge [2]. The aim of this work was to analyse a human glioma dataset that included both OEMRI and DCE-MRI to establish if similar phenomena are apparent in humans and to investigate the oxygen-enhanced R_1 changes and the regional correlations between these and DCE-MRI parameters.

Methods

Patients Ethical approval was granted. 4 patients with glioma were recruited and informed consent was obtained.

Imaging OEMRI: Subjects were scanned on a 3.0 T Achieva scanner (Philips Healthcare, Best, the Netherlands) with an 8 channel SENSE head coil. Subjects sequentially breathed medical air and 100% O_2 (15 l/min) through a non-rebreathing face-mask. 3D T_1 maps were acquired using spoiled gradient echo sequences with the variable flip angle technique [3] ($TE=1.1$ ms, $TR=3.5$ ms; flip angles =2°, 5°, 10°, 16°; matrix 128 x 128 x 25, 1.8 mm x 1.8 mm x 4.2 mm, 4 signal averages): 11 maps during the breathing of air, and then 12 during the breathing of O_2 .

DCE-MRI: Breathing gas was changed back to air, and a baseline 3D T_1 map was acquired, followed by 100 T_1 -weighted spoiled gradient echo volumes ($TE=1.1$ ms, $TR=3.5$ ms; flip angle=15°, matrix 128x128x25, 1.8 mm x 1.8 mm x 4.2 mm). Contrast agent was injected after 10 time points.

Analysis OEMRI Images were registered using the 3D rigid body algorithm in FLIRT [4] to correct for possible patient motion. T_1 values were converted to R_1 , and baseline drift was corrected using a linear regression fit [5]. Maps of mean R_1 and standard deviation were calculated for air and oxygen inhalation, and then ΔR_1 was calculated on a voxel-wise basis. Area under the $O_2 \Delta R_1$ curve (IAUC_{OE}) was calculated. A t-test ($p \leq 0.05$) was carried out to determine voxels with a significant positive or negative ΔR_1 on oxygen. Tumour VOIs were delineated on the initial acquisition and applied to the time series for all subjects. VOIs were then created for regions within the tumour with significant positive or negative ΔR_1 .

DCE-MRI: T_1 -weighted signal intensity was converted to contrast agent concentration. Initial area under the concentration curve up to 120 seconds post-injection (IAUC_{Gd}) was calculated.

Results

Figure 1 shows the R_1 change for regions with significant positive (red) and negative (blue) ΔR_1 during oxygen inhalation averaged over all tumours ($n = 4$). 12 % of voxels in all tumours showed a significant positive ΔR_1 and 34% showed a significant negative ΔR_1 . DCE contrast agent uptake curves for the same regions are shown in figure 2. Figure 3 shows glioma IAUC_{OE} (left) and IAUC_{Gd} (right) maps for a single slice in two subjects.

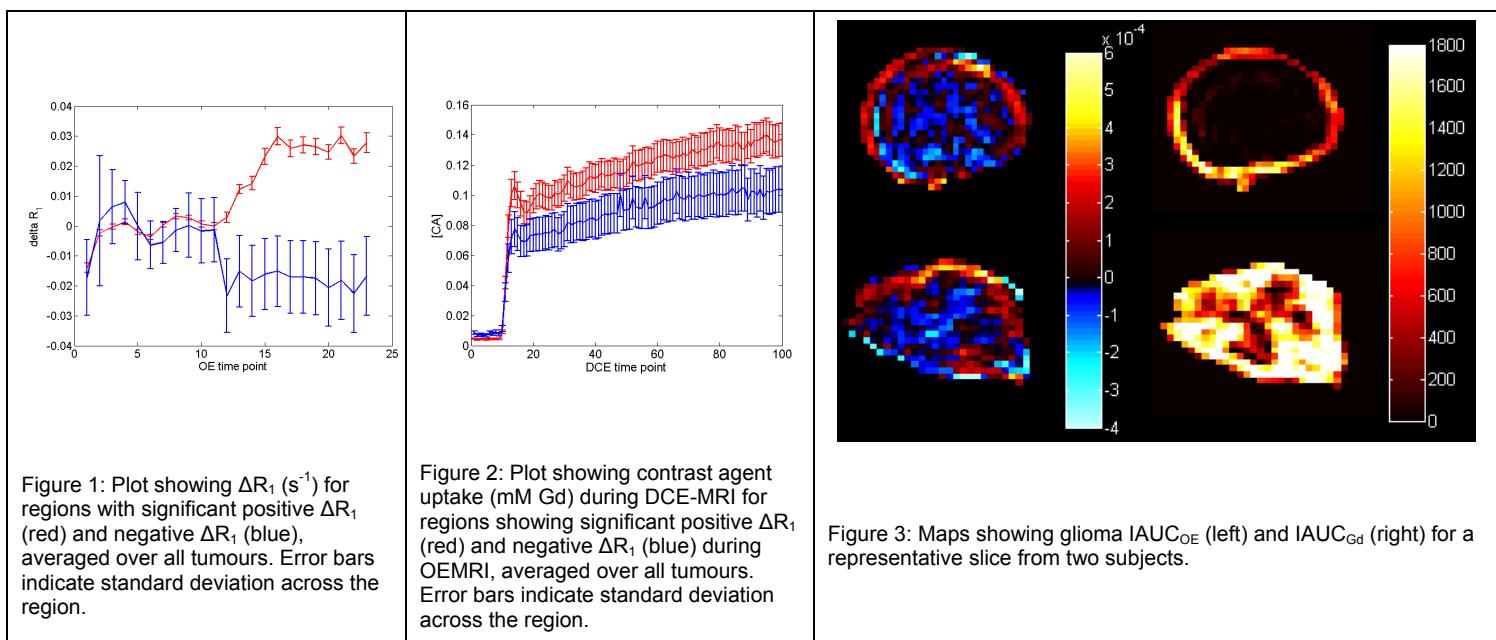


Figure 1: Plot showing ΔR_1 (s^{-1}) for regions with significant positive ΔR_1 (red) and negative ΔR_1 (blue), averaged over all tumours. Error bars indicate standard deviation across the region.

Figure 2: Plot showing contrast agent uptake (mM Gd) during DCE-MRI for regions showing significant positive ΔR_1 (red) and negative ΔR_1 (blue) during OEMRI, averaged over all tumours. Error bars indicate standard deviation across the region.

Figure 3: Maps showing glioma IAUC_{OE} (left) and IAUC_{Gd} (right) for a representative slice from two subjects.

Discussion

We have demonstrated that human gliomas contain regions which show significant positive and negative R_1 change during an oxygen gas challenge, which matches findings in pre-clinical experiments in a glioma model [2]. The contrast agent uptake for these negative-going regions is lower than for positive-going regions, indicating likely lower perfusion. Additionally, the presence in the positive oxygenation ΔR_1 regions of a clear first-pass peak in the DCE time course (Fig 2, red curve) indicates a likely greater blood volume than in the negative oxygenation ΔR_1 regions. It is therefore proposed that the negative-going regions are hypoxic on baseline, and the negative R_1 changes are caused by a decrease in the amount of paramagnetic deoxyhaemoglobin during the oxygen challenge. Positive R_1 changes occur in regions that are well perfused owing to a large increase of oxygen dissolved in the blood plasma, as these are well oxygenated on baseline as well as during the oxygen challenge.

Acknowledgments: Marietta Scott for advice on analysis, AstraZeneca for research funding.

References: 1. O'Connor (2009) *Int J Radiat Onc Biol Phys* **75**: 1209-1215, 2. Linnik (2010) Abstract 4816, *Proc 18th Annual Meeting of ISMRM, Stockholm*, 3. Fram (1987) *Magn Reson Imag* **5**: 201-208, 4. Jenkinson & Smith (2001) *Medical Image Analysis*, **5**(2):143-156, 5. Mills (2009) Abstract 2746, *Proc 17th Annual Meeting of ISMRM, Honolulu*