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MRI Susceptibility Mapping Shows Decreased Venous Oxygen Saturation in Sickle Cell Anaemia

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Synopsis

Ischemic stroke is a common and severe occurrence in Sickle Cell Anaemia (SCA) but no accurate screening measures currently exist for adults. Changes in venous oxygen saturation (Y_v) have been suggested as a potential biomarker but measuring Y_v in vivo is challenging. This work explores the potential of MRI susceptibility mapping to measure Y_v in SCA subjects. Susceptibility-mapping-based measures of Y_v were compared between 25 SCA subjects and 15 healthy controls. Significantly lower Y_v was measured in the superior sagittal sinus in the SCA group compared to healthy controls, showing that QSM is sensitive to changes in Y_v in SCA.

Introduction

Sickle Cell Anaemia (SCA) is an inherited red blood cell (erythrocyte) disorder characterized by haemolytic anaemia, cerebral vasculopathy and a high risk of ischemic stroke and silent cerebral infarction (SCI). Transcranial Doppler examinations and SCI presence are currently used to identify children with increased risk of stroke. However, these screening methods lack specificity and are unsuitable in adults. In SCA, ischemic stroke is most frequent in adults aged between 35 and 65[1]. Therefore, there is a clinical need for more accurate screening measures which can identify stroke risk in adults with SCA.

Brain oxygenation imaging is a potential screening measure to investigate stroke risk in SCA. Compromised oxygen delivery leading to stroke results in reduced venous oxygen saturation levels (Yv)[2]. Therefore, reduced Y_v measures may identify tissue regions at increased risk of infarction and stroke. Measuring Y_v in-vivo is challenging and there is not currently a clinically established method[3].

The objective of this work is to assess the potential of MRI Susceptibility Mapping (QSM) to measure Y_v within SCA subjects. Within venous blood, magnetic susceptibility (χ) values are dependent on oxygen saturation as paramagnetic deoxygenated haemoglobin molecules cause a measurable susceptibility shift ($\Delta\chi_{vein\text{-}water}$) relative to surrounding tissue (assuming $\chi_{tissue} \approx \chi_{water}$). Y_v can be calculated from this shift[4]:

$$Y_v = 1 - \frac{\triangle\chi_{vein-water} - \triangle\chi_{oxy-water} \cdot Hct}{\triangle\chi_{do} \cdot Hct} \qquad [1]$$

where Hct is the percentage of erythrocytes in blood, $\Delta\chi_{do}$ is the susceptibility shift between fully oxygenated and de-oxygenated erythrocytes (0.27x4π ppm [SI]) and $\Delta\chi_{oxy\text{-}water}$ is the susceptibility shift between oxygenated erythrocytes and water (-0.03x4π ppm [SI]). Previous work suggests there is no significant susceptibility difference between deoxyhaemoglobin in sickle and normal erythrocytes[5].

QSM was applied in SCA subjects and healthy controls (HCs) to compare Y_v values measured in the Superior Sagittal Sinus (SSS). We hypothesized that Y_v would be reduced in the SCA subjects because haemolytic anaemia reduces global blood oxygen content[6].

Methods

25 SCA subjects (Mean Age: 16.89±3.74 years) and 15 HCs (16.35±5.85 years) were recruited from the Prevention of Morbidity in Sickle Cell (POMS) and Sleep and Asthma Cohort (SAC) clinical studies[7,8].

MRI data were acquired on a 3T Siemens Magnetom Prisma system at Great Ormond Street Hospital, London. Susceptibility maps were calculated from Multi-Echo Gradient-Recalled-Echo (GRE) images. Sequence parameters included: 7 echoes, TE_1/ΔTE/TR: 3ms/4ms/38ms, 1.15mm isotropic resolution, FOV: 180x220x166mm^3. For the SCA subjects, Hct measures were obtained from blood sampled during the clinical study, and for the HCs, Hct was estimated at 0.4[9].

QSM Pipeline: B_0 field maps were obtained from a non-linear fit of complex multi-echo GRE images[10]. Field maps were unwrapped using a Laplacian-based method[11]. Brain masks were segmented using ITK-SNAP[12] ensuring that the entirety of the SSS was within the mask. Background fields were removed using projection onto dipole fields[13]. Field to susceptibility inversion was performed using Tikhonov regularisation[14] with regularization parameter α=0.06, selected using L-Curve methods.

For each subject a single region of interest was segmented in the SSS on T1-weighted images (ROI_{SSS}) using a semi-automated approach in ITK-SNAP[12] (Figure 1). The T1-weighted images were affinely registered to the fourth echo GRE magnitude images using NiftyReg[15], and the corresponding transform was applied to ROI_{SSS} (Figure 2). Mean χ values within ROI_{SSS} were calculated and used to estimate Y_v using Eq.[1].

An independent t-test was used to compare Y_v between the SCA and HC groups.

Results and Discussion

The SCA group had significantly lower SSS Y_v values than the HC group [0.769-0.794, p=0.042] (Figure 3). Therefore, susceptibility-based measures of venous oxygenation are sensitive to the decreased oxygenation present in SCA subjects.

The Y_v values we measured in both SCA and HC groups are larger than the range of Y_v values measured in the SSS of healthy controls using QSM and alternative MRI methods (0.632-0.659)[16,17]. Larger Y_v values may have been caused by inclusion of lower-χ tissue outside the SSS in the ROIs (see Figure 2). Furthermore, the acquisition sequence was not flow compensated which could have led to flow-induced phase errors.

Using automatic vessel segmentation algorithms as well as manual segmentation, future work will examine ROIs beyond the SSS and also close to neurological damage within SCA subjects.

Conclusion

MRI susceptibility mapping measured significantly lower Y_v values in the superior sagittal sinus in an SCA group compared to healthy controls. This work demonstrates the potential of MRI susceptibility mapping to measure venous oxygen saturation in-vivo in the brain of SCA subjects. This provides a platform to investigate the potential of QSM-based measures of Y_v as a screening measure of stroke risk in SCA.

Acknowledgements

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Figures

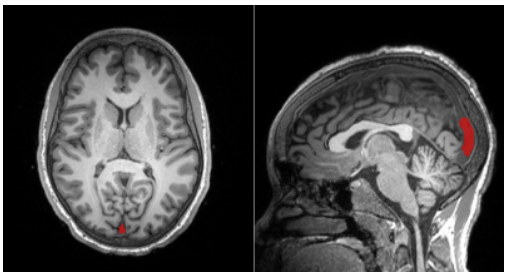

Figure 1: Axial and sagittal views of a T1-weighted image from a representative SCA subject with the superior sagittal sinus region of interest overlaid in red.

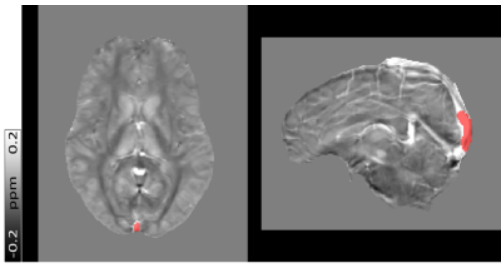

Figure 2: Axial and sagittal views of the susceptibility maps calculated from gradient echo images of the same representative SCA subject shown in Figure 1. The transformed superior sagittal sinus region of interest is overlaid in red.

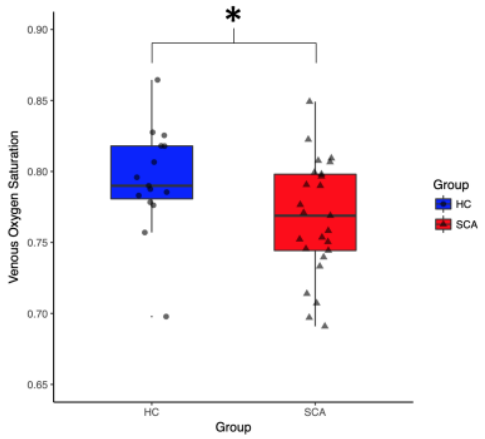

Figure 3: Boxplot showing a comparison of oxygen saturation values (Y_v) measured using QSM in the superior sagittal sinus of sickle cell anaemia (SCA) and healthy control (HC) groups. Significantly lower Y_v were measured in the SCA group. * Indicates p-value significance at the <0.05 level.

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