September 1, 2014

Study Title: Measurement of Cerebral Blood Flow Using Transcranial Doppler Ultrasound in Children with Sickle Cell Disease NCT: NCT02090881 Protocol ID: 13HH0858

Patients with SCD age 2 to 16 years attending our tertiary paediatric haematology clinic for stroke surveillance were eligible. The study was conducted as part of a higher degree in vascular imaging and hence the study duration was limited to six months. Based on patient numbers within the service, we aimed to study 25 consecutive patients referred to the vascular sciences department for routine TCD scanning. Ethical approval was obtained from the local research ethics committee (ref 13/LO/1503) and IRAS ID 133045) and written informed consent was obtained from legal guardians. A pulsatile flow simulating phantom was used to eliminate patient variability. Study participants were scanned by a single operator with imaging TCCD. Initially a full TCD assessment was performed using the non-portable Philips IU-22 with a S5-1 phased array transducer (5.0-1.0MHz). The measurement was then repeated in every patient in only the MCA on each side of the head using the portable Zonare Z-One scanner with a P4-1C phased array transducer (4.0-1.8MHz). For both examinations, a standardised screening protocol was used recording velocities from the transtemporal windows, a 5mm sample volume size, with no angle correction. Gain was adjusted in order to clearly see the spectral Doppler velocity waveform without the presence of noise in the background. For the purpose of this study, the TAMM velocities were compared because stroke risk categorisation according to the STOP trial was based on TAMM velocity, not peak systolic or end diastolic velocities. Each study was categorised as normal, conditional, abnormal or inadequate according to criteria previously developed by the STOP protocol. The participants were not permitted to sleep during the scan to avoid increase in blood carbon dioxide levels in sleep, which can result in increase in TCD velocities. Methods Patients with SCD age 2 to 16 years attending our tertiary paediatric haematology clinic for stroke surveillance were eligible. The study was conducted as part of a higher degree in vascular imaging and hence the study duration was limited to six months. Based on patient numbers within the service, we aimed to study 25 consecutive patients referred to the vascular sciences department for routine TCD scanning. Ethical approval was obtained from the local research ethics committee (ref 13/LO/1503) and IRAS ID 133045) and written informed consent was obtained from legal guardians.

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Study Title: Measurement of Cerebral Blood Flow Using Transcranial Doppler Ultrasound in Children with Sickle Cell Disease NCT: NCT02090881 Protocol ID: 13HH0858 Statistical Analysis Spearman's Correlation Coefficients were calculated to assess the relationships between different parameters in

order to assess the strength of the association between the two measures. Intra-class Coefficient Correlation (ICC) and 95% confidence intervals were used to provide a measure of the strength of the association between the measurements from both pieces of equipment and therefore the validity of the measurement. It has been stated that ICC >0.75 implies acceptable validity. BlandAltman plots were used to estimates the agreement between TAMM velocity measurements by determining how much the velocity from one machine differs from another. Statistical analyses were performed using SPSS Statistics version 21 (IBM). The level of statistical significance was defined as $p < 0.05$.

Conclusion The purpose of this pilot study was to evaluate the use of a portable ultrasound machine by comparison with an established laboratory-based ultrasound machine. This study demonstrated complete agreement in stroke risk categorisation between the two instruments. As a pilot study, it confirms the feasibility and clinical significance of this investigation. A larger sample size with a greater range in TAMM velocities is needed to further investigate the correlation between different ultrasound machines at extremes of measurement such has very high or very low velocities. Further evidence is needed in order to establish the implications these differences may have on screening