Title of Study - Method validation of an ultrasound (US) approach to assess velocity profile as a marker of atherosclerotic burden

Background.
Cardiovascular disease (CVD) accounted for 27% of all deaths in the UK in 2014 [1]. CVD is associated with modifiable risk factors (dyslipidaemia, hypertension and diabetes) and treating each of these factors lowers the risk of CVD [2, 3]. It is impossible to estimate the benefit of risk factor modification in the individual patient and extrapolating data from multiple trials is difficult. It would be useful to have a marker of risk that accurately estimates real time risk by measuring blood flow factors associated with the pathogenesis of atheroma. The aim of this preliminary study is to validate a low-cost measurement technique for estimating blood flow velocity profiles and assess whether any of the measured / calculated factors known to be associated with atheroma was associated with coronary heart disease (CHD), thus establishing its feasibility and acceptability as a clinical tool and suggesting areas for future research (incl. sample size etc.).

Methods.
The study was designed to recruit ≥ 52 patients (final recruitment: 30 without CHD, 27 with CHD) in order to 1) optimise non-invasive vascular imaging, 2) establish flow velocity profiles and 3) determine if any factors likely to be associated with atherosclerotic process were associated with CHD. The left-common carotid artery (L-CCA) was chosen as the measurement site. For each subject the velocity was measured at between 10-12 equi-spaced points across the L-CCA. Heart rate (HR), Peak Systolic (PS) and End of Diastole (ED) velocities were recorded. A Bezier curve was fitted through the measured velocity points for a normalised diameter. This velocity profile was then correlated against a number of computational fluid dynamics (CFD) outputs (see Results) such as wall shear stress (WSS, [4, 5]). We looked for differences in US data and CFD outputs between the two patients groups via unpaired t-tests. Associations between any significant US measures found above and CFD outputs was studied via multiple regression with factorised patient groups included in the models.

Results.
PS velocity was associated with CHD (without CHD, mean (SD): 62.8 (16.1) cm/s, with CHD, mean (SD): 53.6 (17.3) cm/s, $p=0.042$). None of the other factors was statistically different between the patient groups. Multiple regression showed that PS velocity was associated with the following CFD outputs: average pressure drop in the carotid bulb ($p<0.001$), area of average WSS in the location of the bulb less than 1 Pa ($p=0.016$), area of average WSS in the location of the bulb less than 2 Pa ($p=0.006$), area of average WSS in the location of the bulb less than 3 Pa ($p=0.001$) and area of average WSS upstream of the bulb less than 3 Pa ($p=0.017$).

Discussion.
The results suggest that PS velocity may be an area of interest. Even with a small number of subjects a significant difference was observed. Many other factors of interest were associated with PS velocity and these associations must be studied in detail in a larger cohort stratified by treatment(s), age, gender, vascular pathology etc. It is apparent that current US technology lacks the resolution for optimal estimation of L-CCA velocity profile. However, newer technology entering the market promises to provide direct and more accurate velocity profile measurements.

Conclusion.
This preliminary study with a small cohort suggests that further work using larger, more defined patient groups with better technology may ultimately lead to development of a non-invasive method of indicating real time CHD risk.

Key references. In alphabetical order, numbered.

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