Author's response to reviews

Title: Tissue Doppler Imaging of carotid plaque wall motion: a pilot study

Authors:

Dr Kumar V Ramnarine Dr (kumar.ramnarine@uhl-tr.nhs.uk)
Tim Hartshorne Mr (tim.hartshorne@uhl-tr.nhs.uk)
Yvonne Sensier Ms (yvonne-sensier@uhl-tr.nhs.uk)
May Naylor Ms (may.naylor@uhl-tr.nhs.uk)
Joanne Walker Ms (joanne.walker@uhl-tr.nhs.uk)
Ross Naylor Prof. (ross.Naylor@uhl-tr.nhs.uk)
Ronney B Panerai Prof. (rp9@leicester.ac.uk)
David H Evans Prof. (dhe@leicester.ac.uk)

Version: 3 Date: 3 Dec 2003

PDF covering letter
AUTHORS RESPONSE TO COMMENTS FROM REVIEWER 1.

“The presentation of the study population, method of statistical analysis and results are incomplete”
“The Authors don’t report data about the demographic characteristics of the study population (sex differences, mean age, BMI, prevalence of classic cardiovascular risk factors etc.) and they don’t specific statistical methods of analysis.”

Introduction page 6 added text “in the vascular examination”
“The purpose of this study was to investigate the possible clinical value of these recent TDI techniques for AWM imaging in the vascular examination.”

This clarifies a principal aim of the study (the potential of the technique as an extension to the vascular ultrasound examination), and justifies the incorporation of the study population (patients presenting through the vascular clinic) with a wide spectrum of normal and disease vessels.

Additional text has been added to address these comments.

“224 carotid arteries were scanned in 126 patients and volunteers (age 25-88 years, mean 68±11) with a wide spectrum of carotid disease. Patients presenting through the Leicester Royal Infirmary vascular studies unit for carotid artery studies were recruited. Thus, the majority of patients presented with medical conditions including cardiovascular disease (over 90% of subjects) and hypertension (blood pressure greater than 140 mmHg systole or 90 mmHg diastole in approximately 65% of subjects, as measured following ultrasound scan, using an Omron 705CP monitor and cuff over the brachial artery). The 4 volunteers were young and healthy, with no history of cardiovascular disease and no ultrasound evidence of atherosclerotic disease. 70 subjects were male and 56 were female with mean systolic and diastolic blood pressures of 152±24 mmHg and 83±13 mmHg (mean ±1 standard deviation) respectively. In accordance with the Helsinki declaration, informed consent and Ethical approval for the study was obtained. In total, 58 carotid arteries were imaged from patients with no ultrasound evidence of atherosclerotic disease, and 166 arteries imaged with ultrasound evidence of atherosclerotic disease.”

Page 8. End of Data analysis section. Additional text:
“Statistical analysis was performed using the Student’s t-Test to determine if there is a significant difference between the means of two sample populations (p<0.05).”

The clinical impact of their conclusions seems to be not relevant.
Our conclusions highlights the variability and limitations of the TDI AWM technique, clearly demonstrated by the results of the pilot study. It also puts the work in its clinical context, where it is hoped that research in this area may have an important clinical impact- byproviding a more rational basis for referring patients to carotid surgery for example.

“Our pilot study demonstrates that the TDI Arterial Wall Motion imaging technique provides an impressive biomechanical window to atherosclerotic disease. It provides
potentially useful information on the dynamic behavior of normal and diseased carotid arteries. Our initial clinical experience, using a challenging but realistic protocol for imaging carotid plaque wall motion, suggests the use of simple quantitative AWM measures may have limitations due to high variability. The technique must be robust and shown to be clinically useful if it is to play a major role in the vascular examination, where it is hoped that assessment of the mechanical properties of arteries, may help to provide a more rational basis for referring patients to carotid surgery”.

However they don’t explain enough how and why TDI should provide information about carotid wall elasticity.

Page 5. Introduction section. Additional text to address these comments.

“TDI is basically a colour Doppler technique that has been optimised to provide images of tissue motion rather than blood flow, and is capable of high spatial and temporal resolution. The signal processing techniques employed to extract the tissue velocity information from the RF ultrasound data are typically based on time domain cross-correlation techniques [26] or autocorrelation techniques [27]. Clinical applications of TDI of the myocardium, including theoretical, pathophysiological and methodological considerations is reviewed elsewhere [28]. TDI has been applied to image arterial wall motion patterns of the common carotid artery (CCA) and to assess CCA stiffness by calculating distensibility as the change in normalised mean systolic distension relative to the change in blood pressure, and compliance as the change in cross-sectional area relative to pulse pressure [29]”.

There is no mention about some probably interesting characteristics of the plaques (area, homogeneity, soft or hard?) and carotid vessels (intima-media thickness, kinking, stenosis in serie, stenosis of contralateral carotid bifurcation).

These are issues that are being addressed in follow up studies.

Page 12 original text states:

“Pertinent features associated with clinical end points such as plaque development, plaque rupture and stroke are important and will require additional follow up studies.”

Page 16. Discussion section. Additional text has been added:

“There was no gold standard for plaque characterization and the type of plaque in case examples were based on the ultrasound grayscale appearance. Further work and follow-up studies are required to assess interesting characteristics of the plaque (area, homogeneity, histology, composition, mechanical and physical properties) as well as the carotid vessels (intima-media thickness, kinking, stenosis in series, stenosis of contralateral carotid bifurcation)”.

What are the criteria used to define diseased carotid arteries?

Page 7. Methods section. Original text specifies:
“In total, 58 carotid arteries were imaged from patients with no ultrasound evidence of atherosclerotic disease, and 166 arteries imaged with ultrasound evidence of atherosclerotic disease. “

The variability of wall motion indices is wide and it is not surprising that no correlation with severity of stenosis has been reported but a correlation with age could be expected.

Indeed, we have some additional initial data from the CCA 2cm proximal to the bifurcation which is likely to show a clearer correlation with age. However, the challenging imaging protocol used in this paper, the bias towards older patients, the presence of plaque and the simple indices evaluated (i.e. compliance data is not shown), are some reasons why we do not in fact have a clear correlation with age.

The unique significant difference reported about higher spatial gradient value in the plaque region compared to the normal region should be more emphatized.

As the difference is partly due to the methodology, we do not wish to overstate the significance of this.

Page 10 Results text unchanged.

“The significant difference between the maximum and minimum values of the wall dilation within the plaque highlights the inhomogenous wall motion within the plaque, but it is also due to the criteria used to identify the vessel boundaries.”

Page 12 line 7 is Venturi and not venturi.
This has been corrected throughout.

AUTHORS RESPONSE TO COMMENTS FROM REVIEWER 2.

General comments:
A very elegantly illustrated study with a methodologically interesting, although clinically disappointing, approach

Specific constructive comments:

The reader would benefit from a table discussing head to head the theoretical, pathophysiological, and methodological differences between myocardial and arterial tissue Doppler imaging.

We believe such a table, whilst of interest, is outside the scope of this research paper and more suited to a review article. To do justice to such a comparison would extend the introduction section considerably and would be out of proportion to the rest of the text. The introduction has been kept as concise as possible, in accord with the journal’s recommendations to the authors. There are a large number of papers describing the application of TDI to the myocardium, which are not of direct relevance to our application of TDI to image the carotid arteries.
We have referred the reader to an additional review paper addressing the above issues for the myocardium.

“Tissue Doppler Imaging (TDI) is a relatively new commercial technique, originally developed for imaging the myocardium, which has found increasing applications in echocardiography. TDI is basically a colour Doppler technique that has been optimised to provide images of tissue motion rather than blood flow, and is capable of high spatial and temporal resolution. The signal processing techniques employed to extract the tissue velocity information from the RF ultrasound data are typically based on time domain cross-correlation techniques [26] or autocorrelation techniques [27]. Clinical applications of TDI of the myocardium, including theoretical, pathophysiological and methodological considerations are reviewed elsewhere [28]. TDI has been applied to image arterial wall motion patterns of the common carotid artery (CCA) and to assess CCA stiffness by calculating distensibility as the change in normalised mean systolic distension relative to the change in blood pressure, and compliance as the change in cross-sectional area relative to pulse pressure [29].

Revised Abstract
As recommended in the pre-acceptance checklist, the abstract has been shortened in order to keep within 250 words.