EXTRACTS FROM RECENT PUBLICATIONS ON ST+D PULSE WAVE VELOCITY SYSTEM

SUMMARY

This note provides a summary of the research results published and in progress in various studies related to the ST+D Pulse Wave Velocity system. A list of publications and extracts is at the end of this document.

This summary highlights some of the work from the publications, further work is in progress and will be published when available.

OVERVIEW OF PWV MEASUREMENTS

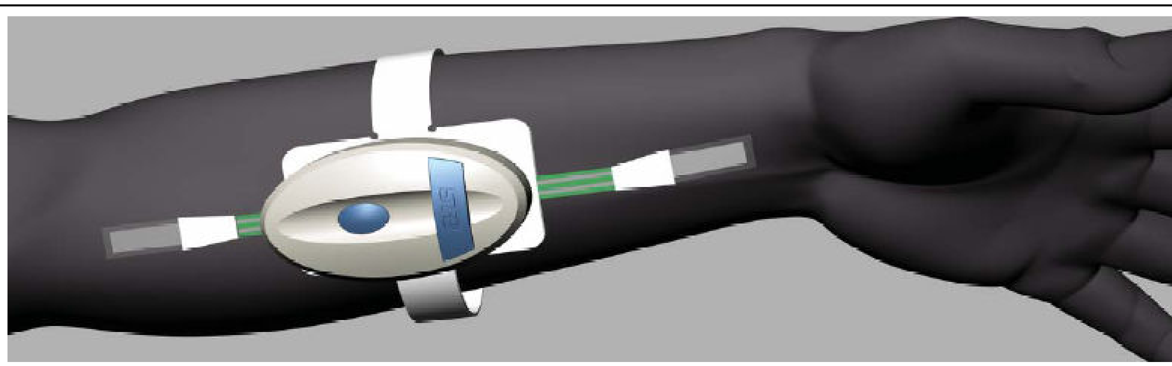
The principle of the PWV measurement is based on simultaneous measurement of two pulse waves at two different positions, such as the radial artery at the wrist and the brachial artery just above the elbow or carotid to heart or femoral to lower leg etc. By determining the pulse transit time between these points and the distance measured between the two locations, pulse wave velocity may then be calculated. The pressure pulse detection is done by using two piezoelectric sensors which generate a measurable voltage at the output contacts if they are mechanically deformed.

Pulse Wave Velocity is a useful index to assess arteriosclerosis and is now regarded as an early warning for cardiac dysfunction. Management of arteriosclerosis is very important to help prevention of cardiovascular diseases.

Most systems use the ECG as a start point meaning the pulse wave passes from main arteries to peripheral arteries flowing through many junctions causing undesired reflections which could lead to false results. The measurement of PWV has previously been cumbersome and slow with results often operator dependant and unrepeatable.

ST+D PWV SYSTEM

The ST+D PWV system is based on two fast response piezoelectric sensors. It can be used on various parts of the body, but is shown in radial/brachial form below.



The system is wireless in order to provide the convenience of no dangling cables.

It is envisaged that ultimately this system will be developed for use in a doctor's surgeries as preventative treatment and monitored along with a blood pressure measurement.

- The ST+D PWV system is repeatable and the operation requires no training
- This PWV system is quick and easy to use and readings can be self-acquired, meaning it could be a home based monitoring system
- The measurement is direct and uses no assumptions
- No ECG taken or blood pressure calibration required
- Direct peripheral artery detection of PWV and wireless communication

PIEZO ELECTRIC SENSORS TO MEASURE PWV

MEASURING TECHNIQUE

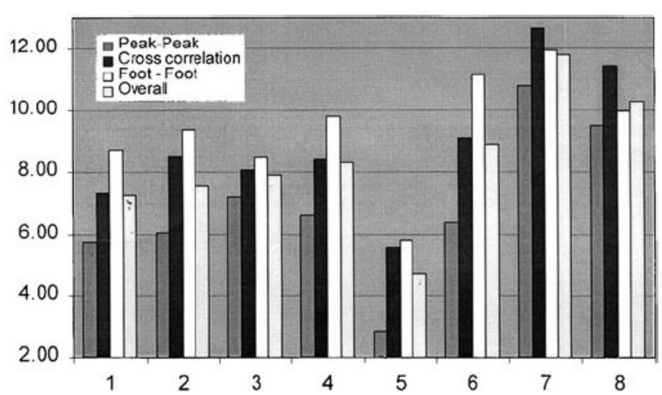
The aim of this work focuses on the development of a fast and easy to use system for the determination of peripheral arterial pulse wave velocity.

Arterial pulse wave velocity (APWV) is a measure of the elasticity (or stiffness) of peripheral arterial blood vessels. The pulse referred to here will be the pressure pulse as opposed to the flow pulse measured by ultrasound Doppler. The pressure pulse velocity varies over the range from about 12m s^{-1} to 15m s^{-1} in stiff peripheral arteries, whereas in normal arteries it has a velocity in the range of 7 to 9m s^{-1}.

The principle of the PWV measurement is based on simultaneous measurement of two pulse waves at two different positions, such as the radial artery at the wrist and the brachial artery just above the elbow. By determining the pulse transit time between these points and the distance measured between the two locations, pulse wave velocity may then be calculated. The pressure pulse detection is done by using two piezoelectric sensors which generate a measurable voltage at the output contacts if they are mechanically deformed.

The deformation produced voltage is first amplified and filtered and then digitalized with a data acquisition system. The analysis of the data obtained from the sensors includes a filtering process, the calculation of the PWV with three different methods - foot-to-foot, cross-correlation and peak-to-peak - and the determination of the arterial pulse rate.

Extensive measurements with human test subjects were carried out to optimize the techniques of data acquisition and analysis. The data analysis was upgraded with an additional software module, which deletes, in effect, outriders or invalid measurements. With the optimized system, a series involving eight test subjects ranging in age from 22 to 32 years was completed (all normotensive). The arterial pulse wave velocities determined covered a range from 6m s^{-1} to 12m s^{-1}, with an average standard deviation of less than 2.5m s^{-1} for individual results. These are slightly higher, but close to published APWV data. The results showed that reproducible results can be obtained with the existing PWV acquirement and analysis system.



Histograms of PWV values for all three calculation methods for all eight subjects.

EFFECT OF EATING AND EXERCISE ON PWV

The effect of acute moderate intensity aerobic exercise on Pulse Wave Velocity and oxidative stress markers following a high-fat meal.

It is postulated that the postprandial impairments in vascular function are mediated via an oxidative stress mechanism. Exercise has been shown to improve this postprandial endothelial dysfunction, the exact mechanism, however, remains elusive. The purpose of this study was to measure and correlate PWV and markers of postprandial oxidative stress before and after an acute bout of moderate intensity exercise.

METHODS

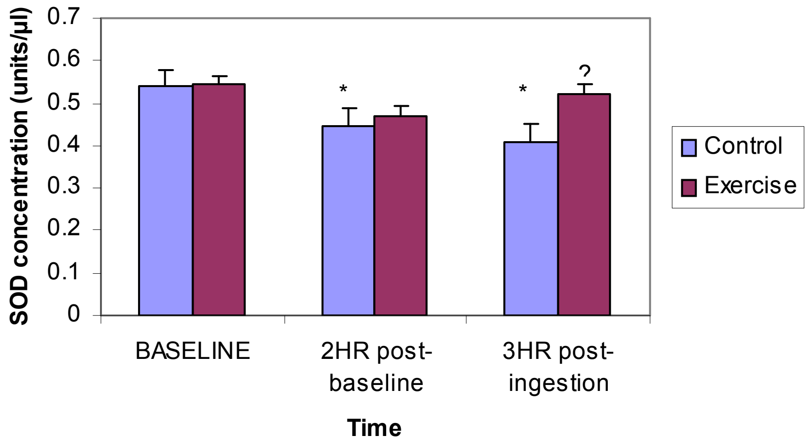
Ten recreationally trained male subjects (age 21.5 ± 2.5 yrs, VO_2 max 58.5 ± 7.1 $ml \cdot kg^{-1} \cdot min^{-1}$) participated in a randomised crossover design: (1) high-fat meal alone (2) high-fat meal followed by a bout of moderate (60%) intensity exercise performed 2 h after meal ingestion. PWV was examined at baseline, 1 h, 2 h, 3 h, and 4 h postprandially. Venous blood samples were taken to measure LOOHs, SOD and other biochemical markers. Comparative analyses were carried out using repeated measures ANOVA and Pearson's correlations.

RESULTS

Mean PWV increased significantly at 1 h (6.49 ± 2.1 m/sec), 2 h (6.94 ± 2.4 m/sec), 3 h (7.25 ± 2.1 m/sec) and 4 h (7.41 ± 2.5 m/sec) respectively, post ingestion in the control trial (P= <0.05). There was no significant change in PWV at 3 h (5.36 ± 1.1 m/sec) and 4 h (5.95 ± 2.3 m/sec) post ingestion in the exercise trial (P= >0.05). Mean serum LOOH levels were significantly decreased at 3 h post ingestion in the exercise trial compared to corresponding serum LOOH levels at 3 h (P = 0.002) and 4 h (P = 0.019) in the control trial. Serum SOD levels were significantly lower at 3 h post ingestion in the control trial compared to 3 h in the exercise trial (0.52 units/µl ± 0.05 vs. 0.41 units/µl ± 0.1; P = 0.012). There was a main effect for time for NO_X levels (P = <0.001). There was a significant positive correlation between PWV and LOOHs levels (*r*=0.226, P=0.04) yet there was a significant negative correlation observed between PWV and serum SOD levels (*r*= -0.383, P= 0.003).

CONCLUSION

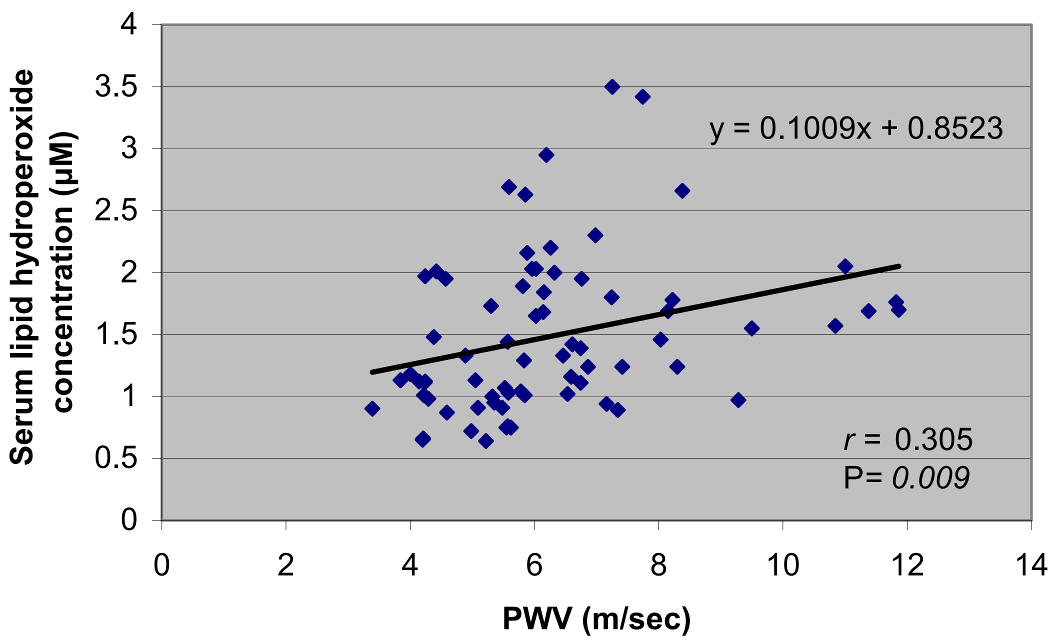
These findings suggest that a single session of aerobic exercise can ameliorate the postprandial impairments in arterial function by reducing oxidative stress levels and by possibly increasing the bioavailability of NO.



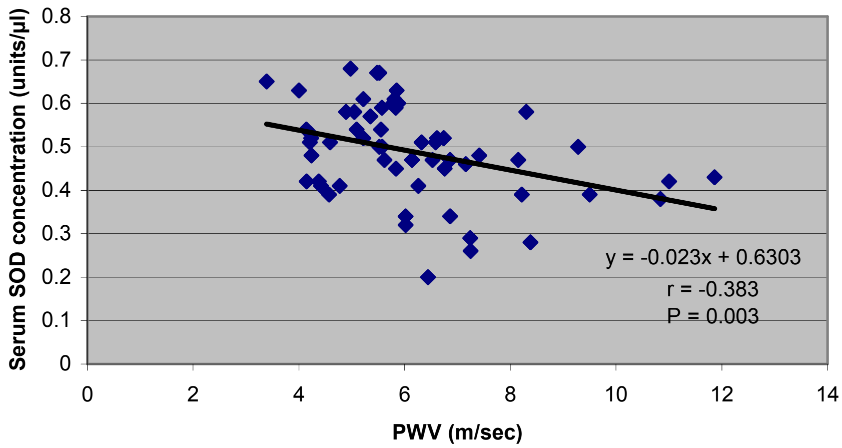
Superoxide dismutase (SOD) concentration over time

* P = < 0.05 vs. baseline control; ‡P = < 0.05 vs. three hour post ingestion control trial

Correlation of PWV and serum lipid hydroperoxides



Correlation of PWV and serum SOD

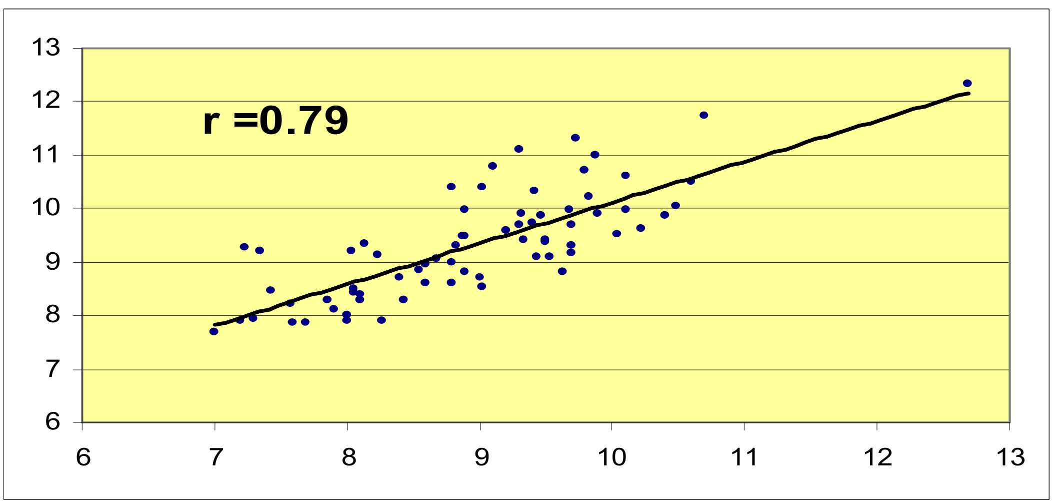


ST+D SYSTEM COMPARED TO THE GOLD STANDARD

Pulse Wave Velocity System (ST+D) as measured against the Sphygmocor PWV gold standard.

The graph below shows a set of PWV readings taken on around 40 patients. Measurements are obtained from the carotid-radial positions and demonstrate a close correlation between PWV measured on the ST+D PWV piezoelectric sensing system and the SphygmoCor golden standard. Following further improvements, additional results will be published shortly.

Pwv0006 vs SphygmoCor



PVDF carotid-radial (ST+D on horizontal axis) vs SphygmoCor carotid-radial (vertical axis).

Positive correlation r = 0.79

IMPACT OF PATIENT POSITIONING

Patient positioning and its impact on local PWV measurement

Pulse wave velocity is an accepted methodology that provides a surrogate marker of arterial stiffness. PWV has been shown to be an independent predictor of cardiovascular events. Many methods exist which assess regional arterial stiffness (carotid-femoral, carotid–radial) but to our knowledge no devices exist to measure local PWV and thereby assess the local mechanical properties of an artery. We sought to assess the reliability of measuring local radial artery PWV using a novel PVDF system. We also sought to assess patient positioning and its impact on local PWV measurements.

METHODS

Local radial pulse wave velocity was measured in 20 healthy volunteers (12 male). Two piezoelectric sensors were placed over the brachial and radial pulses on the right forearm of subjects lying prone after a period of rest. PWV was calculated as the distance between the sensors divided by peak to peak time delay between the two waveforms produced by the sensors. For each reading the mean PWV over a 10 second period was taken as the accepted figure. A total of 126 readings were taken from 20 patients (mean 6.4/patient).

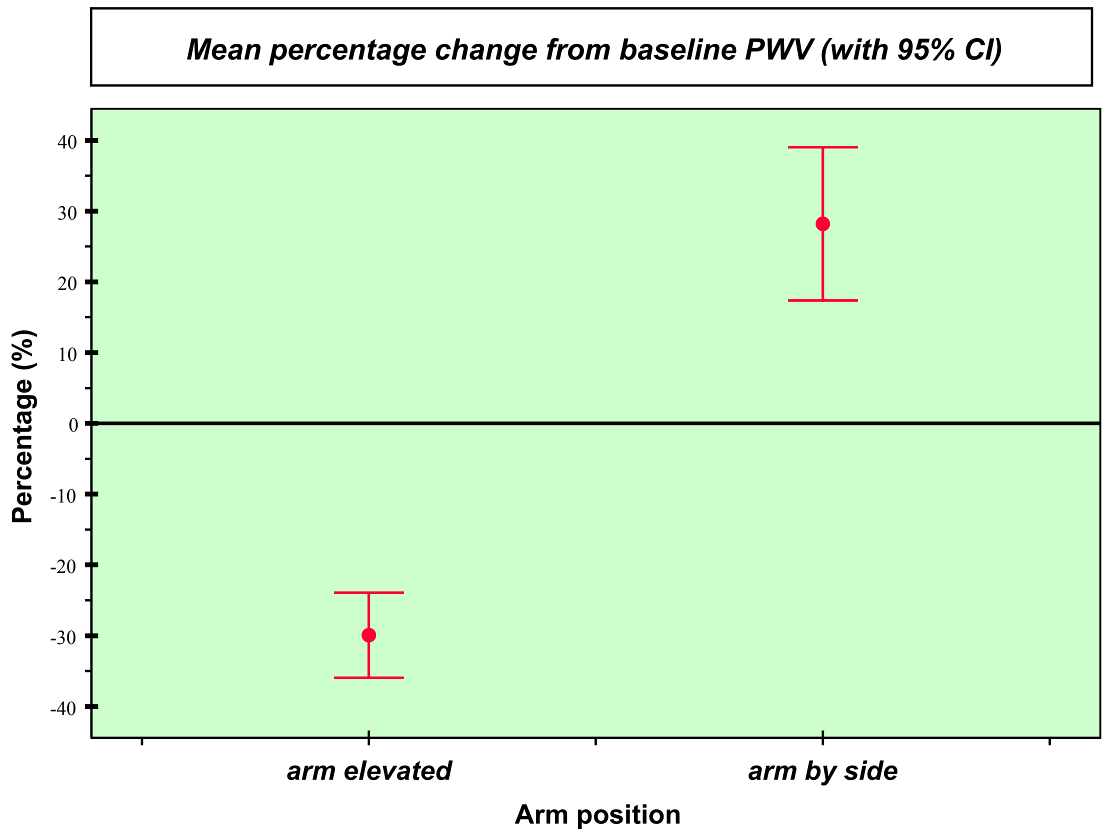
In addition 12 subjects had radial PWV measured with the forearm in a neutral position (i.e sitting with the right forearm resting on a table at the level of the heart). Serial measurements were then taken with the arm raised directly above the head and again with the patient standing with his/her arm relaxed by their side.

RESULTS

Among healthy volunteers mean PWV was 9.8m/sec (range 8.2 – 11.7 m/sec). Intra-subject repeatability was 2.2 m/sec with an inter-subject repeatability of 3.7 m/sec. The interclass correlation coefficient was calculated as 0.65. When assessing for variability in PWV values in response to changes in arm position significant differences were noticed when the arm was both above and below the neutral position. With the arm lifted directly above the head there was a mean change from baseline PWV of -29.9% (95%CI -23.9% - -35.9%). In contrast, with the arm resting by the side of the standing volunteer a mean change from baseline PWV of +29.0% (95% CI 18.7% - 39.0%) was observed. These changes can be explained by passive changes in distending forearm blood pressure in response to deviation of the radial artery relative to the level of the heart.

CONCLUSION

Local PWV can be measured swiftly, accurately and non-invasively using the novel PVDF system. Local PWV is sensitive to changes in blood pressure as evidenced by significant changes noted with the forearm at different levels in relation to the heart. This finding also underlines the importance for standardisation of methodology among investigators when assessing local PWV.

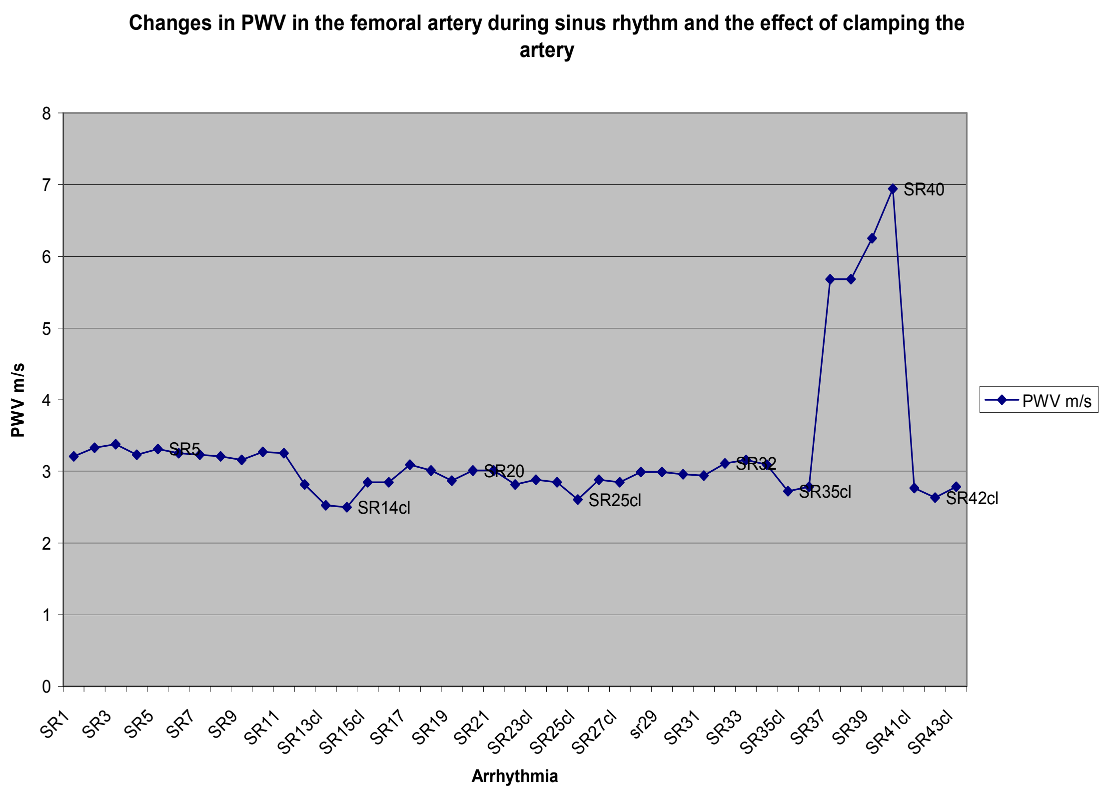

Mean percentage change from baseline PWV (with 95% CI)
40
30
20
10
0
-10
-20
-30
-40
Percentage (%)
arm elevated
arm by side
Arm position

CHANGES IN THE FEMORAL ARTERY DURING SINUS RHYTHM AND THE EFFECT OF CLAMPING THE ARTERY

This work is demonstrating the ability of PWV to be measured a bare artery.

Work is on-going to establish the relationship between PWV and changes in the hearts rhythm and thus establish some important findings associated with arterial stiffness and the working heart.

This graph illustrates the changes in pulse wave velocity prior to, during and following the application of a clamp to the femoral artery. Most noticeably there was a substantial and immediate increase in pulse wave velocity following the removal of the arterial clamp.



PUBLICATION DETAILS

1. J McLaughlin et al 2003 Physiol. Meas. **24** 693-702; Piezoelectric sensor determination of arterial pulse wave velocity

2. Conor M. Mc Clean Æ Jim Mc Laughlin, George Burke Marie H. Murphy, Tom Trinick; Ellie Duly, Gareth W. Davison; The effect of acute aerobic exercise on pulse wave velocity and oxidative stress following postprandial hypertriglyceridemia in healthy men Eur J Appl Physiol DOI 10.1007/s00421-007-0422-y; Eur J Appl Physiol. 2007 Feb 24; [Epub ahead of print]

3. Abstracts to be published at the European Meeting on Hypertension in Milan and the American Society of Hypertension and include: Abstract 1. THE EFFECT OF INCREASING EXTRINSIC PRESSURE ON ARTERIAL PULSE WAVE VELOCITY MEASUREMENTS. *'The Journal of Hypertension'*

4. Abstract 2.LOCAL RADIAL ARTERY PULSE WAVE VELOCITY CAN BE ACCURATELY MEASURED AND IS RESPONSIVE TO CHANGES IN ARM POSITION. The *Journal of Hypertension*