INTRODUCTION
Conventional risk factors are unable to fully predict those individuals at increased risk from cardiovascular disease. Thus alternative, non-invasive, methods of assessment, which can reliably assess cardiovascular risk, are desirable. It has been demonstrated that impaired flow-mediated dilatation assessed by ultrasound correlates with vascular risk factors and future vascular risk.1 Compliance of the arterial tree is associated with cardiovascular risk and may be a reflection of atherosclerotic burden. Aortic compliance is reduced in adults who are at increased risk of premature vascular disease.2 Aortic compliance is rarely measured in clinical practice because direct measurement is invasive. However, compliance can be measured non-invasively with ultrasound3 or magnetic resonance4 imaging, although clinical utility of these techniques are limited. The most commonly utilized method of assessing compliance is to measure pulse wave velocity (pulse...
wave velocity is higher in non-compliant blood vessels). This method requires the placement of sensors over the carotid and femoral arteries so that the delay between the 2 signals can be measured.

The wideband external pulse device (WEP) has been developed to allow quick, simple and non-invasive measurement of aortic compliance, and from the compliance data, to allow the calculation of other physiological parameters such as stroke volume and cardiac output.

The WEP device consists of a piezoelectric sensor that is placed over the brachial artery underneath a standard automated blood pressure cuff. The sensor is connected to a computer which records signals (with the cuff inflated to suprasystolic pressures) that correspond to pulse wave reflections from the aortic tree (Figure 1). The relative amplitude of these waves, SS1 and SS2, provide a measure of aortic compliance.5

### AIM

The aim of this study was to establish the test-retest reproducibility of the WEP device under standard conditions, and to compare WEP derived measurements of stroke volume to a validated method (echocardiographic measurement of stroke volume).

### METHODS

Twenty-six healthy volunteers were recruited from staff and students at the University of Auckland. All studies were carried out in the Cardiovascular Research Laboratory, Department of Medicine, University of Auckland, New Zealand. Subjects provided written informed consent and the University of Auckland Ethics Committee approved the study protocol.

Subjects fasted for 8 hours prior to each of the 2 examinations. Both examinations were carried out at the same time and on the same day.

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**Table 1. Demographic Data for Study Participants**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
</tr>
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<tbody>
<tr>
<td>Male (n,% )</td>
<td>11 (44)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>24.8</td>
<td>4.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.1</td>
<td>3.4</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>122/74</td>
<td>11/7</td>
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<tr>
<td>Fasting glucose (mmol/L)</td>
<td>4.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.6</td>
<td>0.8</td>
</tr>
</tbody>
</table>

BMI body mass index

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**Table 2. Stroke Volume Assessed by Echo and WEP on Two Different Visits**

<table>
<thead>
<tr>
<th></th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Pooled average</th>
<th>Difference</th>
<th>P (difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WEP</strong></td>
<td></td>
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<tr>
<td>C (intraday)</td>
<td>1.59 (0.30)</td>
<td>1.53 (0.36)</td>
<td>1.56 (0.32)</td>
<td>0.06 (0.19)</td>
<td>0.12</td>
</tr>
<tr>
<td>C (interday)</td>
<td>1.58 (0.33)</td>
<td>1.56 (0.30)</td>
<td>1.59 (0.28)</td>
<td>0.02 (0.29)</td>
<td>0.77</td>
</tr>
<tr>
<td>SV (intraday)</td>
<td>72.0 (15.7)</td>
<td>72.1 (20.4)</td>
<td>72.1 (15.9)</td>
<td>0.1 (17.9)</td>
<td>0.98</td>
</tr>
<tr>
<td>SV (interday)</td>
<td>72.0 (15.7)</td>
<td>74.7 (22.6)</td>
<td>73.4 (15.9)</td>
<td>2.7 (22.2)</td>
<td>0.54</td>
</tr>
<tr>
<td><strong>Echocardiography</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV (interday)</td>
<td>88.0 (16.1)</td>
<td>86.1 (16.9)</td>
<td>87.1 (15.9)</td>
<td>1.8 (8.4)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

*Values are mean (SD). SV indicates stroke volume (mL); SS1, Incident wave; SS2, first reflected wave; and C, compliance.
time of day. Subjects rested in a quiet, temperature controlled room in a semi-recumbent position. Blood pressure was established as the mean of 3 readings using the automated Dynamap sphygmomanometer. After ensuring that an adequate signal could be obtained, careful note of the position of the WEP device was made. The WEP device (Ilixir Ltd, Auckland, New Zealand) was fitted on the same arm for each study and care was taken to ensure that the electrode was placed at the same height above the antecubital fossa on each occasion. Three baseline WEP recordings were made. The subject was then rested for 5 minutes and a further 3 recordings were made.

**Technique for Measuring Compliance**

Suprasystolic recordings from the sensor were passed through an analogue signal pre-conditioning filter and digitized. The digital data was displayed on a PC using software written in Java by Ilixir Limited (Auckland, NZ). The waveform was then analyzed using Matlab Software (Mathworks Inc., Natick, Mass, USA). The amplitude of the SS1 and SS2 waves were measured and compliance (C) was calculated using the formula $C = 1.018 \left( \frac{SS1}{SS2} \right)^{0.257}$. This formula has been derived from preliminary data obtained from a small number of patients. Stroke volume (SV) was calculated using the formula $SV = C \times PP$ where PP is the pulse pressure measured non-invasively using a Dynamap.

A transthoracic echocardiogram (see below) was performed after which an additional set of WEP recordings were made.

All data from the WEP device was stored on a laptop computer. At the conclusion of the data collection phase all WEP data was analyzed in random order in a blinded fashion by Andrew Lowe. For each recording the largest contiguous interval of the signal collected, when the cuff pressure was above 15 mmHg higher than the systolic pressure, was identified. The interval was then segmented where each waveform segment corresponded to an individual

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*Figure 1.* Idealized suprasystolic waveforms.

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SS1 indicates the arterial pulse wave; SS2, reflectance wave from the abdominal aorta; and SS3, a reflectance wave from the peripheral circulation (occurs at the beginning of diastole).
heartbeat. These waveform segments were time-shifted, such that the maxima (peaks) of the SS1 waves were aligned. The mean signal level at each point in time of the aligned waveform segments was then calculated and this generated a mean beat.

The amplitudes of the SS1 and SS2 waves within the mean beat were taken as the amplitude difference between the peak of the wave and the following trough.

**Echocardiographic Methods**

Standard 2-D and m-mode images of the left ventricle were obtained using a Phillips HDi5000 ultrasound machine and 3.5 MHz transducer and measurements of left ventricular size and function made (Philips, Bothell, Wash, USA). Measurement of stroke volume was performed using Doppler and 2D data (SV= cross sectional area x velocity time integral). The LVOT diameter was measured from a frozen mid-systolic frame and measured using the leading-edge methodology. Pulsed wave Doppler was used to measure the time-velocity integral of the LVOT blood flow, with the sample volume placed immediately below the aortic annulus.7

All echo images were digitally acquired and analyzed off-line using a dedicated cardiac measurement package. Each echo variable was measured in triplicate and the average value used for the analysis.

At the conclusion of one of the study visits subjects had blood specimens drawn to measure fasting blood glucose and lipids. These were assayed by a commercial laboratory (Diagnostic Medlab, Auckland, New Zealand) using standard laboratory techniques.

**Statistics**

The methods of Bland and Altman8 were used to calculate the limits of agreement for WEP and echocardiographically defined measurements and the coefficient of repeatability (magnitude of test-retest repeatability). Paired data were plotted, and least squares regression lines fitted, to ensure consistency of agreement or repeatability over the entire range of values.

**RESULTS**

One patient had a bicuspid aortic valve identified on transthoracic echocardiogram and was subsequently excluded from the analysis. Demographic data for the study population are presented in Table 1.

Compliance and SV assessed by WEP are similar when assessed on 2 dif-
different occasions on the same day (intra-
day) and on separate days (interday) (Table 2). Pooled interday echocardiographic stroke volume is on average 15 mL greater than WEP stroke volume.

Limits of agreement\(^8\) were calculated comparing WEP measurements on the same day (Figure 2), and on different days (Figure 3). Interday limits of agreement for compliance measured by WEP are ±0.6 with a coefficient of variation (CV) of 26%, however, interday WEP stroke volume measurements are broader (±44 mL), CV 32% meaning that for any given stroke volume measured by WEP, the true value may be as much as 44 mL above or below the measured value. The least squares regression line slopes downward, suggesting that the error is greater at lower measured stroke volumes. Conversely the interday limits of agreement for echocardiographic stroke volume are less (±16 mL), CV 6.9% and the least squares regression line is horizontal, suggesting similar accuracy at all values of stroke volume measured.

DISCUSSION

The WEP device has been developed as a novel technique to non-invasively assess the compliance of blood vessels. Compliance data are then translated into the clinically useful parameters of SV and CO. This study has demonstrated that the average performance of
WEP derived SV between 2 studies (either 2 studies on the same day or on different days) was similar, but inferior to echocardiography. Importantly, the limits of agreement of the WEP-derived SV are more than twice as great as those of SV derived by echocardiography. Reproducible echocardiography is dependent on multiple variables including operator experience, patient body habitus, and heart rate; despite these factors the test-retest reproducibility and CV for echocardiographically derived stroke volume was clinically acceptable in this study, and in keeping with other published data. It is disappointing that the limits of agreement using the WEP technique for measurement of SV are wide. One factor that may explain this is the fact that calculation of SV from the WEP device depends on the reproducibility of 2 measurements, these being the reproducibility of the compliance measurement and secondly the reproducibility of the blood pressure measurements used to calculate pulse pressure. It is known that blood pressure even under controlled conditions can fluctuate significantly, and non-invasive measurement itself involves a significant random inaccuracy. Figure 3 illustrates the fact that the addition of pulse pressure measured non-invasively results in a less precise measurement (limits of agreement for compliance are tighter than limits of agreement for SV measured by WEP). Additionally the formula applied for the calculation of SV from C and PP is simplistic and does not represent well the actual physics involved. The formula assumes a closed, fully elastic, statically linear system, whereas in practice the system under consideration is somewhat more complex.

WEP derived SV was consistently lower than echocardiographically derived SV. This may reflect relative inaccuracy of the formula used to derive compliance with the WEP technique. This device remains investigational and the formula used is based on correlations with hemodynamic data in a small number of cases. Accuracy of compliance data is likely to be improved as larger numbers of subjects are studied and the formula for calculating compliance refined.

Other techniques, such as flow mediated dilatation of an artery, are also relatively imprecise in individual patients, but have proved useful for research purposes in large groups. Further research and development of this device may validate its role in this area, and potentially improve clinical applicability.

**CONCLUSION**

Although the average performance of the WEP device is reasonable, particularly for compliance measurements, WEP derived stroke volume measurements based on non-invasive pulse pressure measurement have poor test-retest reproducibility in normal individuals under standard conditions. Limits of agreement are at least twice as wide as those for echocardiographically derived stroke volume. Clinical application of this technology in individual patients at this stage is likely to be limited, however it may emerge as a promising technique for compliance measurement.

**REFERENCES**

4. Mohiaddin RH, Underwood SR, Bogren HG, et al. Regional aortic compliance studied by magnetic resonance imaging: the effects of


