



# Noninvasive evaluation of varying pulse pressures *in vivo* using brachial sphygmomanometry, applanation tonometry, and Pulse Wave Ultrasound Manometry



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**Abstract** The routine assessment and monitoring of hypertension may benefit from the evaluation of arterial pulse pressure (PP) at more central locations (e.g. the aorta) rather solely at the brachial artery. Pulse Wave Ultrasound Manometry (PWUM) was previously developed by our group to provide direct, noninvasive aortic PP measurements using ultrasound elasticity imaging. Using PWUM, radial applanation tonometry, and brachial sphygmomanometry, this study investigated the feasibility of noninvasively obtaining direct PP measurements at multiple arterial locations in normotensive, pre-hypertensive, and hypertensive human subjects. Two-way ANOVA indicated a significantly higher aortic PP in the hypertensive subjects, while radial and brachial PP were not significantly different among the subject groups. No strong correlation ( $r^2 < 0.45$ ) was observed between aortic and radial/brachial PP in normal and pre-hypertensive subjects, suggesting that increases in PP throughout the arterial tree may not be uniform in relatively compliant arteries. However, there was a relatively strong positive correlation between aortic PP and both radial and brachial PP in hypertensive subjects ( $r^2 = 0.68$  and  $0.87$ , respectively). PWUM provides a low-cost, non-invasive, and direct means of measuring the pulse pressure in large central arteries such as the aorta. When used in

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conjunction with peripheral measurement devices, PWUM allows for the routine screening of hypertension and monitoring of BP-lowering drugs based on the PP from multiple arterial sites.

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## Introduction

Hypertension is a highly prevalent cardiovascular risk condition that affects nearly 1 billion people globally,<sup>1</sup> increasing the risk of heart disease and stroke by 3–4 times.<sup>2</sup> In current clinical practice, the diagnosis and monitoring of hypertension is based on peripheral blood pressure measurements taken from the brachial artery using a sphygmomanometer. However, the central blood pressure (CBP) near the heart (i.e. in large arteries such as the aorta) has been recognized to play a key role in the pathogenesis of cardiovascular disease.<sup>3–5</sup> The distending pressure in the large elastic arteries is a key determinant of the degenerative changes that characterize accelerated aging and hypertension.<sup>6</sup> Furthermore, it has been demonstrated that different anti-hypertensive pharmacological treatments may have different effects on CBP reduction while maintaining similar brachial BP reduction.<sup>6,7</sup> These findings support the need to account for CBP during hypertension treatment and monitoring.

Pulse pressure (PP), defined as the difference between the systolic and diastolic blood pressures (i.e. the pressure increase required to generate a pulse), has been recognized by several studies as a significant predictor of all-cause cardiovascular mortality and morbidity.<sup>3,8,9</sup> PP arises from the interaction of cardiac ejection (stroke volume) and the properties of the arterial circulation. An increased stiffness of the large arteries leads to an increase in PP due to a reduction in arterial compliance and increased speed of wave reflections.<sup>10</sup> The PP in peripheral arteries is commonly assessed using cuff sphygmomanometry at the brachial site and applanation tonometry at the radial site.<sup>11</sup> However, the PP in large arteries remains challenging to measure clinically, as the only method to obtain a direct measurement of central PP in the clinic is by way of a highly invasive arterial catheter. Many longitudinal clinical research studies<sup>3,12–16</sup> have employed radial applanation tonometry with a generalized transfer function to derive central PP in large populations of patients. However, an indirect method may not be used for evaluation on an individual case-by-case basis.

Pulse Wave Ultrasound Manometry (PWUM) was previously developed by our group<sup>17</sup> as a noninvasive, easy-to-use central PP measurement technique based on the regional pulse wave propagation characteristics obtained using ultrasound elasticity imaging. Initial feasibility studies have demonstrated the reproducibility (~11% average intra-subject variability) of the method and its high correlation ( $0.94 < r^2 < 0.98$ ) with the aortic PP waveforms obtained using radial applanation tonometry and a generalized transfer function in healthy, normotensive subjects.

A block diagram of the PWUM technique on a normal human aorta is shown in Fig. 1. Aortic wall displacements and pulse wave velocity (PWV) are estimated using our established Pulse Wave Imaging (PWI) technique,<sup>18–25</sup> and the incremental distension curve is obtained by subtracting the posterior wall displacements from anterior wall displacements at the central scan line to avoid angle artifacts. The theoretical basis for PWUM is formed by combining the Laplace Law<sup>26</sup> and the Modified Moens–Korteweg Equation,<sup>27–29</sup> thus relating an incremental change in fluid pressure ( $dP$ ) to the PWV, incremental distension ( $dR$ ), fluid density ( $\rho$ ), Poisson's ratio ( $\nu$ ), and lumen radius ( $R$ ).

While PWUM has been tested in healthy, normotensive subjects,<sup>17</sup> it has not yet been used to evaluate patients with elevated blood pressure. This study aims to evaluate the feasibility of a more complete assessment of PP variation throughout the arterial tree by performing direct measurement of PP at three arterial sites using three different instruments – a sphygmomanometer cuff for the left brachial artery, an applanation tonometer for the left radial artery, and PWUM for the infrarenal abdominal aorta.

## Methods & study design

### Study design

This study was approved by the Institutional Review Board (IRB) of Columbia University. Outpatients visiting the Dental Clinic at Columbia University Medical Center for routine dental exams were recruited. Patients who provided informed consent to participate in the study were instructed to lie in the supine position for the duration of the exam. Three brachial blood pressure measurements were performed on the left arm over a 15-minute period using a clinically recommended<sup>30</sup> automatic digital blood pressure monitor (HEM-705CP, Omron Corp., Kyoto, Japan). The first measurement was excluded, and the average of the latter two was used to classify each subject as pre-hypertensive (systolic blood pressure between 120 mmHg and 139 mmHg) or hypertensive (systolic blood pressure >140 mmHg) based on the American Heart Association (AHA) recommendation for blood pressure categorization.<sup>31</sup>

Brachial PP was calculated as the difference between the systolic and diastolic pressures. Because blood pressure is known to fluctuate throughout the day,<sup>32</sup> it was important to perform all measurements as concurrently as possible. In between each brachial cuff measurement, PWUM and radial applanation tonometry were performed to obtain the pulse pressure waveform in the aorta and left radial artery, respectively. Only the subjects who exhibited

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