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● *Original Contribution*

COMMON CAROTID ARTERY DIAMETER, BLOOD FLOW VELOCITY AND WAVE INTENSITY RESPONSES AT REST AND DURING EXERCISE IN YOUNG HEALTHY HUMANS: A REPRODUCIBILITY STUDY

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Abstract—The aim of this study was to assess the reproducibility of non-invasive, ultrasound-derived wave intensity (WI) in humans at the common carotid artery. Common carotid artery diameter and blood velocity of 12 healthy young participants were recorded at rest and during mild cycling, to assess peak diameter, change in diameter, peak velocity, change in velocity, time derivatives, non-invasive wave speed and WI. Diameter, velocity and WI parameters were fairly reproducible. Diameter variables exhibited higher reproducibility than corresponding velocity variables (intra-class correlation coefficient [ICC] = 0.79 vs. 0.73) and lower dispersion (coefficient of variation [CV] = 5% vs. 9%). Wave speed had fair reproducibility (ICC = 0.6, CV = 16%). WI energy variables exhibited higher reproducibility than corresponding peaks (ICC = 0.78 vs. 0.74) and lower dispersion (CV = 16% vs. 18%). The majority of variables had higher ICCs and lower CVs during exercise. We conclude that non-invasive WI analysis is reliable both at rest and during exercise. (E-mail: ashraf.khir@brunel.ac.uk)

Key Words: **Ultrasound, Non-invasive, Wave intensity analysis, Wave speed, lnDU loop.**

INTRODUCTION

The temporal changes in pressure and flow generated during every cardiac cycle are inextricably linked and propagate as waves along the vascular tree. Waves contain embedded information about both their origin and the tissue through which they propagate or are reflected, thereby providing insight into the dynamic interactions among the various components of the cardiovascular system. Since antiquity, the study of the arterial pulse has played a key role in the understanding of human circulation (Karamanou et al. 2015), but recent mathematical and computational developments have opened new windows for advancing our knowledge and understanding of cardiovascular mechanics and hemodynamics. Wave propagation along the vascular tree can be studied with wave intensity analysis (WIA), a powerful tool first developed by Parker and Jones (1990), involving the decomposition of pulsatile flow into its wave components (Bleasdale et al. 2003; Hughes et al. 2008; Parker 2009; Ramsey and Sugawara 1997; Sen et al. 2014; Sugawara et al. 2009).

The common carotid artery (CCA) lends itself to non-invasive investigation because of its anatomic location (Magda et al. 2013). Several carotid WIA studies have been conducted based on non-invasive CCA blood pressure and flow velocity (U) measurements, with the former derived from either CCA diameter (D) measurements (Carbone et al. 2010; Niki et al. 2002; Rakebrandt et al. 2009) or applanation tonometry, after calibration for the derivation of blood pressure-equivalent waveforms (Curtis et al. 2007). The CCA forward waves arrive from the aorta, whereas backward reflected waves return from

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the distal microvasculature (Bleasdale et al. 2003). A forward compression wave (FCW) is created by left ventricular contraction and appears in the peripheral circulation as an early-systolic wave, whereas a mid-systolic backward compression wave (BCW) results from the distal reflection of this wave at the active vascular bed, and, in the case of measurements taken at the carotid artery, the cerebral vasculature (Manisty et al. 2009a, 2009b). The advent of WIA has facilitated the investigation of various physiologic perturbations, both in healthy patients—for example, for the study of the cardiac and/or cerebral hemodynamic effects of nicotine and caffeine (Swampillai et al. 2006), heat therapy (Hatano et al. 2002) and hypercapnia (Bleasdale et al. 2003)—and in patients for the study of pathologies such as mitral valve regurgitation (Niki et al. 1999), chronic heart failure (Curtis et al. 2007; Wen et al. 2010), hyperthyroidism (Zhang et al. 2010) and Fontan circulation (Saiki et al. 2014).

As described above, surrogate signals (computed by the analysis of distally recorded blood pressure waves) require calibration to derive a blood pressure-equivalent waveform, and this inevitably gives rise to inaccuracies (Curtis et al. 2007; Meinders and Hoeks 2004; Van Bortel et al. 2001; Zambanini et al. 2005). To circumvent this problem, recent theoretical work yielded an algorithm incorporating non-invasive D (instead of arterial blood pressure) and U measurements when determining local wave speeds and when implementing WIA (Feng and Khir 2010). This progress paralleled technological developments that led to a new generation of ultrasound machines with the capacity for direct and simultaneous non-invasive measurements of arterial D and U, through echo-tracking and Doppler ultrasound, respectively. A simple physiologic perturbation that may provide a substantial challenge to the implementation of this methodology is exercise. However, unlike other local techniques, WIA applied in the CCA may be uniquely qualified to investigate the cardiac–cerebrovascular interaction under this complex physiologic perturbation. For this endeavour to be successful, the ability to obtain reproducible CCA D and U measurements during rest and exercise is vital.

The aim of this study was to assess the reproducibility of non-invasive ultrasound measurements of CCA D and U, and of derived wave intensity parameters, obtained from young healthy participants at rest and during submaximal exercise. To the best of our knowledge, no studies exist on WIA reproducibility when derived from arterial diameter and velocity waveforms. Establishing WIA reproducibility will pave the way for more detailed exploration of the cardiac–cerebrovascular interaction and cerebral vascular resistance responses during exercise in humans.

METHODS

Study group

The study was approved by the Brunel University London Research Ethics Committee and complied with the guidelines of the Declaration of Helsinki. Twelve healthy volunteers (aged 27 ± 2 y, 6 females, body mass: 66.9 ± 5.7 kg, height: 1.69 ± 0.1 m, body mass index: 23.3 ± 1.2 kg/m^2) participated in the study after providing informed written consent. All participants were familiar with cycling, but none was a trained athlete. The participants' average daily physical activity levels were within the normal range for a sedentary to moderately active population (Sallis et al. 1985).

Instrumentation and measurements

An SSD-5500 ultrasound system (Aloka, Tokyo, Japan) equipped with a 7.5-MHz linear array vascular probe was used. The ultrasound echo tracking subsystem measured D with a resolution of 0.013 mm, whereas the Doppler subsystem measured U with a resolution of 0.012 m/s. The scans were performed in the longitudinal view, obtaining therefore images of the longitudinal section of the artery, approximately 2 cm proximal to the bifurcation. The images were optimised to ensure that the depth was as shallow as possible and the vessel walls well delineated (clear discrimination amongst the lumen, media–intima and adventitia). The gates were positioned manually in B-mode between the media and intima of the anterior and posterior walls, and parallel to them. The Doppler gate was positioned at the centre of the vessel, parallel to the walls, ensuring that the insonation angle was always between 58° and 60°. The B- and M-modes were then simultaneously displayed on a split screen, and the D waveform was calculated as the distance between the two walls over time obtained from the M-mode tracing. The U waveform was obtained from the pulsed-wave Doppler mode. Both D and U were sampled at 1000 Hz (Fig. 1a). Every measurement consisted of the simultaneous recording of D and U signals for at least 6 s. A supine bicycle ergometer, mounted on a bed and equipped with a power control box, was used to perform the exercise protocol (Angio, Lode, Groningen, Netherlands) (Fig. 1b).

Protocol

The participants were tested twice over two consecutive days and at the same time of the day. Temperature and humidity in the laboratory did not differ between the 2 d (*i.e.*, ~20°C and ~40%, respectively). Volunteers were asked to refrain from vigorous exercise and caffeine consumption for 24 h and 12 h, respectively, before the laboratory visits and to maintain the same diet on the 2 d of testing. The tests were conducted with the participants in a reclined position and their upper bodies in the