

REVIEW ARTICLE

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# A Systematic Review of Wave Speed and Wave Intensity Measures in the Human Carotid Arteries

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## Abstract

Wave intensity and wave speed are measures used to assess the dynamic properties of the arteries and travelling waves within the circulation. Wave intensity and wave speed measured in the carotid artery have the potential to provide hemodynamic and biophysical insights that can advance our understanding of the physiology of cerebral circulation. However, whilst studies have been performed in different patient cohorts exploring different methodological implementations of wave intensity analysis (WIA), to date little work has been done to unify wave measures or provide reference ranges on which to build the field of research and inform clinical practice. This review thus focuses on wave speed and wave intensity in the carotid artery in man with the aim to summarise the current knowledge of the field. From this review, the different methods of measurement and the disparity of the reported values currently hinder efforts to construct reference ranges for a comparator or intervention to be assessed.

**Keywords** Internal carotid artery, Common carotid artery, Wave intensity analysis, Wave speed, Cerebral blood flow

## 1 Introduction

Wave intensity is the rate of energy transport in a longitudinal wavefront per unit area. Wave intensity analysis (WIA) provides a quantitative measure of the incremental net energy flux density of travelling waves within the circulation or the power carried by the wave per cross-sectional area. The work done by the wave comprises kinetic energy associated with the velocity of flow and potential energy associated with the expansion of the arterial wall [1]. Wave speed or pulse wave velocity (i.e. the velocity at which the blood pressure pulse propagates

in an artery or system of arteries) is often, but by no means invariably, calculated as part of wave intensity analysis. Wave speed is generally evaluated in early systole and is related to the distensibility of the artery as shown by the Moens–Korteweg equation [2, 3], i.e. wave speed is inversely proportional to the square root of distensibility.

So far, little work has focused on the use of WIA for understanding the cerebral circulation, or the impact of the energy transfer from the extracranial to the intracranial vessels, even though WIA has often been measured in the common carotid artery. This is an important area of translational and clinical research. For instance, people with hypertension are more likely to suffer small vessel disease and have poorer cerebral perfusion [4, 5], and increased arterial pressure may heighten the risk of aneurysm formation and rupture at the circle of Willis [6–8]. Understanding wave travel could potentially provide a better understanding of such pathology and the analysis is increasingly showing promise in this context. A recent

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study, for example, found that the forward compression wave intensity in mid-to-late life predicted faster cognitive decline independent of other cardiovascular risk factors as well as markers of carotid structure and stiffness [9]. At present, however, there are very limited direct measurements of the intrinsic mechanical properties of the intracerebral arteries in vivo [10].

Let us consider the setting for this physiological problem. Blood flow to the cerebral circulation arrives through two artery pairs: the left and right internal carotid arteries, which largely supply the anterior circulation of the brain, and the left and right vertebral arteries, responsible mainly for the posterior circulation [11]. The vertebral arteries converge over the brainstem to form the basilar artery. The basilar artery together with the internal carotid arteries form a ring-like anastomosis known as the Circle of Willis. The basic anatomy is shown in Fig. 1, although variants are common [12]. This organisation allows for the re-distribution of blood based on demand, can compensate for resistance such as stenosis, and may therefore represent a collateral system to protect against hypoperfusion. The anastomotic nature of the cerebral arterial anatomy also enables a range of shunt and steal phenomena [13] as illustrated by subclavian steal syndrome [14], reversed Robin Hood syndrome [15], and luxury perfusion syndrome [16, 17].

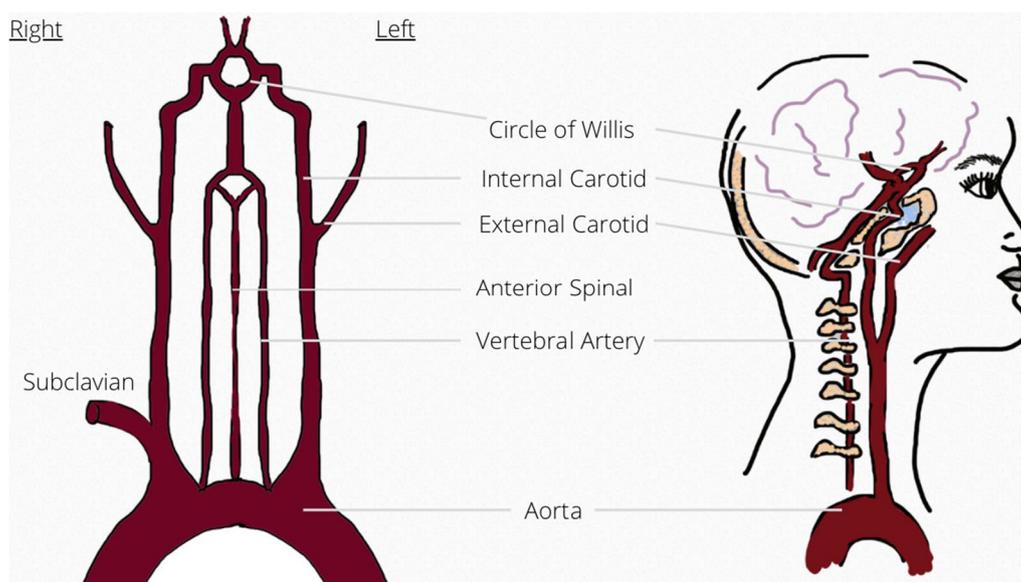
From a biophysics perspective, the cerebral circulation is unique. Various constraints, which are set out by the Monroe-Kellie doctrine [18], are assumed to hold true for the perfusion of the brain to be maintained within physiological boundaries. Imbalances and breaches of these

assumptions are considered to cause marked pathophysiological disturbances, such as Cushing's triad, ischaemic haemorrhage, or syncope. The first constraint is that the cerebral circulation is encased in the isovolumetric container of the skull. The inlets and outlets (including the cerebrospinal fluid space) are generally through non-compressible bone, which limits the ability for pulsatile movement and hypertrophy at these junctures. Second, the pressure within the skull must be maintained within relatively narrow boundaries to avoid percussion of the brain tissue against the bone [19]. Third, the adaption to the systolic pressure wave must be sufficient to move blood against gravity in the upright position [20], whilst tolerating the orthostatic changes to the supine position and even inversions (such as handstands and other oddities humans master).

In this context, we aim to review current knowledge on wave speed and wave intensity measures in the carotid artery in man. The review will summarise the effect of interventions and any other comparisons made within each study but will not aim to compare interventions between reports.

### 1.1 What is the wave speed measure?

Wave speed ( $c$ ) is the speed at which a disturbance travels through a medium [21]; in this case, energy through arteries.  $c$  is dependent on the viscosity of blood and the mechanical and geometric properties of the vessel [21, 22].  $c$  is an indicator of arterial stiffness (or its inverse distensibility [23]), with higher wave speed indicating a stiffer, less distensible vessel.



**Fig. 1** Anatomy of the cerebral circulation. Left diagram shows coronal view; Right diagram shows sagittal view

Whilst aortic wave speed is often measured clinically by femoral-carotid pulse wave velocity, this is a weighted average over the arterial pathlength and does not account for more local variation in arterial vessel mechanics and geometry [24]. Regional, or local, wave speed can be estimated by single-point methods derived from the slope of the loop of two measured variables such as pressure (P) and velocity (U), or flow (Q) and cross-sectional area (A). Specifically, these methods are known as the PU-loop [25], QA-loop [26], ln(D)U-loop [27], and ln(A)U-loop [28] methods. Alternative formulations based on the knowledge of P and U at a single point in the cardiac cycle includes the sum of the squares methods (see [29]). This method has the advantage of being independent of the period of unidirectional waves required for the loop methods but has a larger margin of error when applied to measures taken close to a reflection site.

The linearity between pressure and diameter over the cardiac cycle has been demonstrated using invasive pressure measurements in the carotid artery [30]. However, Kowalski et al. (2017) suggested that the wave reflections may cause an underestimation of  $c$  by  $-36.9\%$  ( $\pm 6.7\%$ ) in the carotid artery [31]. Furthermore, it has been shown that reflected waves [32] and the proximity of the measurement to the reflection site [32–34] significantly influence the measured wave speed. Using the diameter-velocity loop method, Borlotti et al. [35] showed that proximity to the reflection site affects the measured wave speed so that a positive reflection coefficient leads to an underestimation of wave speed, whilst a negative reflection coefficient leads to an overestimation of wave speed. This is particularly important in the carotid artery given its geometry and anatomy; namely the carotid bifurcation in the neck, the curvature of the internal carotid siphon and the juncture at the Circle of Willis. The degree to which the pressure and flow (or velocity) changes are affected by reflections and the convective contribution is assumed to be negligible in the early part of systole when measurements of  $c$  are typically made. The linearity of elasticity of the vessel wall over the physiological pressure range is a necessary assumption, however, there is not sufficient evidence at present to demonstrate the absolute validity of this assumption.

When comparing the theoretical local wave speed to that measured experimentally, discrepancies are observed [36, 37]. Namely, based on theoretical grounds from its composition and on experimental studies the relationship between stress and strain in arteries is known to be non-linear [38]. Nonetheless, the assumption of a unique elastic modulus (incremental elastic modulus) may be approximately valid within the pressure range of the cardiac cycle, however, differences in operating pressure may be relevant when comparing measures of  $c$  between

individuals (e.g. between normotensive and hypertensive individuals) [39]. Extrinsic factors, the tethering of the vessel, and the compressibility of the surrounding tissue have also been suggested to affect  $c$  [40].

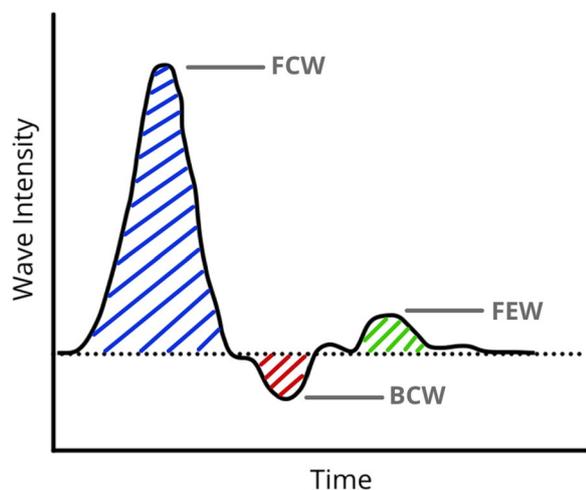
Therefore, given the special limitations of the cerebral circulation suggested above, and the internal carotid artery in particular, measuring wave speed in this artery experimentally is of particular future interest.

## 1.2 What is wave intensity analysis?

Unlike wave speed, which is measured in m/s, the units of wave intensity depend on the method of measurement and introduces the variable of local distensibility [41] (e.g. if derived from pressure and velocity, it is commonly reported in  $W/m^2$  or  $mmHg \cdot m \cdot s^{-3}$ , whereas if derived from diameter and velocity it is commonly reported in  $m^2/s$ ). Despite the variability of units, the measures are essentially equivalent although not interchangeable, and related to each other through the tube law which describes the relationship between the pressure and the area (or diameter) of the artery.

The original method for analysing wave intensity ( $dI = dPdU$ ) describes the use of pressure and velocity to calculate wave intensity, defined as the maximum value of the composite waves, and wave energy, defined as the integral of the wave intensity over time. Other approaches, such as using a logarithm of the area and velocity, have since been proposed [28, 34]. A large subset of studies report wave intensity using the time-corrected formula,  $dP/dt \times dU/dt$ . This carries the advantage of being able to compare data acquired with different sampling rates, but with the disadvantage that the resulting units are complex and unintuitive to interpret ( $mmHg \cdot m \cdot s^{-3}$ ) [42]. An alternative approach where  $dI$  is expressed per cardiac cycle and which preserves its interpretability has been proposed [43].

The net wave intensity can be separated into its component forward and backward waves if the wave speed is known [47]. Net wave intensity is a result of the algebraic sum of the forward and backwards travelling waves [44, 45]. Compression waves are associated with a rise in pressure, whilst decompression waves are associated with a fall in pressure. Whilst there are many reflections and re-reflections [46], wave intensity in most large elastic arteries is commonly described in terms of three major wave components. The first is a forward compression wave (FCW) which carries most of the energy over the cardiac cycle and is a measure of the rate of forward wave energy density propagation in early systole due to ventricular ejection. This is followed by a smaller backward compression wave (BCW) which, outside the coronary circulation, represents backward travelling waves (reflections) from



**Fig. 2** Illustration of wave intensity (peaks) and wave energy (shaded areas). Blue; FCW Forward Compression Wave, Red; BCW Backward Compression Wave, Green; FEW Forward Decompression (Expansion) Wave. NB: the latter part of the diastolic period of the cycle has been omitted for clarity

various sites of impedance mismatching, such as those due to branching, confluences and changes in cross-sectional areas and/or material properties of the arteries [48]. Finally at the end of systole (protodiastole), a forward decompression wave (also known as the forward expansion wave, FEW) decelerating systolic flow in the arteries is observed. This is caused by the slowing of ventricular contraction which creates a suction effect preceding and contributing to aortic valve closure [49, 50]. It has also been proposed that the end-systolic FEW is caused by the inertial effects of the negative reflection of the BCW [49]. Figure 2 illustrates the various wave components.

A strong correlation between the energy of the BCW and FCW has been shown in the common carotid artery of healthy volunteers, suggesting that the forward wave energy generated by the left ventricle is a predictor of the amplitude of the reflected wave [45]. Anti-hypertensive treatment, which effectively lowers blood pressure, increases the FCW and decreases the BCW [51]. In a virtual population of 2000 subjects, it was shown that wave intensity analysis may prove useful in the diagnostics and treatment of people with heart failure [52].

Interestingly, in the carotid artery, another forward decompression wave in mid-systole has been reported [42, 49, 53]. This wave is reported to have a variable size. Hughes et al. [53] saw that this augmentation in the carotid artery was associated with a larger second forward decompression wave, suggesting a possible relationship between the additional wave and inertial or re-reflection effects.

## 2 Methods

This systematic review follows the PRISMA-P guidelines for systematic reviews [54]. The inclusion criteria were original research articles measuring local wave speed or wave intensity in the human carotid artery. Studies reporting any of the measures (i.e. wave speed, wave intensity, forward compression wave energy, forward decompression wave energy, backward compression wave energy) were included regardless of whether they reported only a subset of the measures. Articles were included if they had full-text versions available in English and were published between 1990 and January 1st 2023. Review articles, meta-analyses, studies in non-human species and in silico models were excluded.

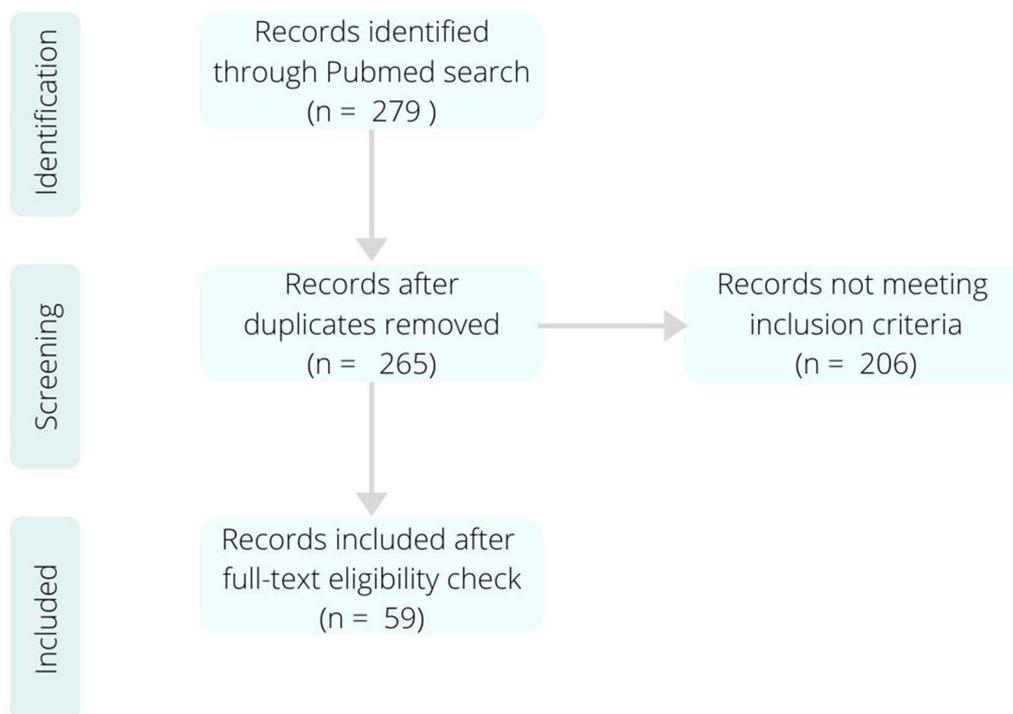
The following PubMed searches were run on the 15th of April 2020, repeated on the 1st of April 2021, and on the 12th February 2023 with the following terms: (1.) carotid artery + wave speed, (2.) carotid artery + wave intensity analysis, (3.) internal carotid artery + wave speed, (4.) internal carotid artery + wave intensity analysis.

Data extracted were directly from the articles and checked by the second investigator independently. The data extracted was: (1) Wave speed, (2) Net wave intensity or energy, (3) forward compression wave intensity or energy, (4) forward decompression wave intensity or energy, and (5) backward compression wave intensity or energy.

Risk of bias was not assessed as the bias domains [55] were not considered relevant to the particular type of studies available in the literature. For example, selection, performance and detection bias require the blinding of outcome assessment, which was not a feasible objective. Further, attrition bias, reporting bias and other biases are better assessed against a standard convention of reporting which is not available at the present time for wave speed or wave intensity analysis in the carotid artery. Instead, data are presented with the details of the population studies in each case, as well as the method of measurement.

## 3 Results

The search yielded a total of 279 articles, of which 14 were duplicates, resulting in a total of 265 articles that were screened based on abstract content. In total, 59 articles were ultimately included. These contained either wave intensity analysis in the carotid artery, wave speed measurements in the carotid artery, or both. PRISMA flow diagram is shown in Fig. 3.



**Fig. 3** PRISMA flow diagram of the records identified, screened and included

### 3.1 Wave speed in the common carotid artery and its branches

Only two studies measured wave speed in the internal carotid artery experimentally [56, 57]. Neumann et al. found wave speeds around 1–1.5 m/s in the internal carotid artery using the lnA-U loop method. Ayadi et al. used two methods of wave speed estimation, i.e. the foot-to-foot method ( $c = \frac{\Delta z}{\Delta t}$ , where  $\Delta z$  represents the distance between two anatomical cross sections, and  $\Delta t$  is the time interval between the feet of two waves) and a mathematical modification of the foot-to-foot model (summarised as  $(c = \frac{2L}{t_0}$ , where  $L$  is the distance between the measurement point and reflection area and  $t_0$  is the arrival time of the first reflected wave). Using the traditional foot-to-foot method, the authors reported a similar wave speed of  $2.6 \pm 0.2$  m/s in the young ( $n = 11$ , 0 men,  $29.4 \pm 6.8$  years), and  $3.3 \pm 0.3$  m/s in the older group ( $n = 11$ , 8 men,  $66 \pm 14.9$  years). However, using the new mathematical model which corrects for the temporal inaccuracy of the foot-to-foot method, the authors reported wave speeds of  $5.2 \pm 0.5$  m/s in the young, and  $6.3 \pm 0.4$  m/s in the older group, suggesting more traditional methods may underestimate wave speed in the internal carotid artery [56].

All other studies report wave speed in the common carotid artery. The measurements in the human carotid artery are summarised in Table 1.

The average wave speed ( $\pm$  standard deviation) reported in healthy volunteers (regardless of method) was  $5.58 \pm 2.1$  m/s, with the median wave speed at 5.38 m/s. The minimum average speed was reported in endurance-trained men (0.8 m/s, age  $27 \pm 4$  years) using the lnDU loop method [58] and the maximum was reported in healthy volunteers (14.2 m/s,  $60 \pm 9$  years) using the PU loop method [59].

Whilst it is known that wave speed increases with age [60], this accounts for 2–3 m/s of the variability and, therefore, the range of values reported in the literature cannot be accounted for by age alone. Interestingly, it was not possible to determine a bias to yield a higher or lower wave speed value based on the method used.

One study reported wave speed in the left and the right common carotid separately, using three different methods of measurement, and found that wave speed was consistently higher in the right compared to the left CCA [61].

Wave speed is consistently reported as marginally higher in men compared to women [45, 62].

### 3.2 Wave intensity in the carotid artery

Wave intensity in the internal carotid artery was assessed in two studies only [56, 90], while several studies have assessed wave intensity in the common carotid

**Table 1** Wave speed in human common carotid artery

Method of measurement	Wave speed (m/s)	Population	References
PU	4.0 (left CCA) 7.8 (right CCA)	Healthy volunteers ( $n=8$ , 8 men, age range 23–31 years)	[61]
Wave component $p$ & $u$	3.5 (left CCA) 6.7 (right CCA)		
Sum of the squares ( $c\Sigma^2$ )	3.9 (left CCA) 7.0 (right CCA)		
PU (Bramwell Hill)	6.17 ± 1.34	Volunteers ( $n=22$ , 13 men, 49 ± 17 years)	[63]
PU loop	7.53 (± 2.85)	Healthy volunteers ( $n=37$ , 17 Men, 47.2 ± 5.4 years) obtained from the Asklepios population study [64]	[32]
QA loop	3.4 ± 1.1		
PU1-5 (harmonic-based correction)	4.99 ± 0.87		
PU loop (Median)	8.7	Placebo, ASCOT substudy ( $n=62$ , 57 male, 64 ± 7 years)	[65]
	8.1	Atorvastatin, ASCOT substudy ( $n=78$ , 70 male, 64 ± 8 years)	
PU loop	8.5 ± 3.1	Amlodipine-based regimen, ASCOT substudy ( $n=122$ , 99 men, 64.3 ± 7.1 years)	[66]
	9.0 ± 5.4	Atenolol-based regimen, ASCOT substudy ( $n=138$ , 119 men, 63.3 ± 7.6 years)	
PU loop	14.2 ± 1.4	Healthy volunteers ( $n=29$ , 13 men, 60 ± 9 years)	[59]
	14.0 ± 0.9	Compensated systolic heart failure patients on medication ( $n=67$ , 42 men, 66 ± 10 years)	
PU loop	7.5 ± 2.4	Hypertensive, treated, volunteers ( $n=12$ , 12 men, 63 ± 9 years)	[67]
PU loop	5.40 (± 0.34*)	Healthy volunteers ( $n=21$ , 14 men, 44 ± 6 years)	[42]
In(D)P loop [31]	3.9 ± 0.5	Ex pre-term ( $n=76$ , 40 men age 18.2 ± 1.3 years,)	[68]
	3.9 ± 0.5	Control ( $n=42$ , age 18.6 ± 0.9, 16 men)	
In(D)P loop	3.49 ± 0.45	Control group ( $n=42$ , 15 male, median age 19 years)	[68]
	3.71 ± 0.50	Coarctation Patients ( $n=43$ , 21 male, median age 25 years)	
InDU loop	8.4 ± 1.9	Healthy volunteers ( $n=12$ , 6 men, aged 27 ± 2 years)	[69]
	10.2 ± 3.4	Rest Day 1	
	7.9 ± 2.6	Exercise 1	
	9.3 ± 3.2	Rest Day 2	
	10.6	Exercise Day 2	
InDU loop	10.6	Healthy volunteer ( $n=1$ )	[70]
InDU loop	♀ 3.71 (± 1.21) ♂ 4.16 (± 1.58)	Volunteer, subgroup of Asklepios population study [64]s ( $n=70$ , 35 men, age range 35–55 years)	[62]
InDU loop ± (1/2) ( $dU_{\pm} / d\ln D_{\pm}$ )	4.03 ± 1.64	Volunteers, subgroup of Asklepios population study [64] ( $n=1774$ , 840 men, mean age 45.8 ± 6 years)	[24]
InDU loop ± (1/2) ( $dU_{\pm} / d\ln D_{\pm}$ )	4.45 ± 0.73	Volunteers free of major cardiovascular events ( $n=47$ , 59% men, mean age 24 ± 5 years)	[71]
	5.58 ± 1.12	Volunteers free of major cardiovascular events ( $n=78$ , 53% men, mean age 51 ± 6 years)	
	6.49 ± 1.50	Volunteers free of major cardiovascular events ( $n=78$ , 68% men, mean age 67 ± 5 years)	
InDU loop	6.9	Hypertensive patient ( $n=1$ )	[27]
InDU loop	0.8 ± 0.2	Endurance trained volunteers ( $n=8$ , 8 men, aged 27 ± 4 years)	[58]
DU; Bramwell–Hill equation based on distension curve	8.9 ± 1.8	Type 2 diabetics ( $n=191$ , 148 men, aged 65 ± 7 years)	[72]
	7.9 ± 1.5	Non-diabetics ( $n=94$ , 66 men, aged 62 ± 8 years)	
( $dP/dU$ )/ $\rho$	3.10 ± 1.3	Healthy volunteers, baseline ( $n=55$ , 12 men, 22 ± 5 years)	[73]
	4.00 ± 1.9	After exercise	
One-point carotid PWV $\beta$ (m/s)	4.08 ± 0.51	Baseline, healthy volunteers ( $n=55$ , 12 men, 22 ± 5 years)	
	4.44 ± 1.20	Post high-intensity cycling, healthy volunteers	

**Table 1** (continued)

Method of measurement	Wave speed (m/s)	Population	References
$(dP/dU)/\rho$	6.8 ± 1.1	Normotensive volunteers ( $n = 20$ , 13 men, 56 ± 4 years)	[74]
	7.8 ± 1.0	Hypertensive volunteers ( $n = 21$ , 14 men, 58 ± 8 years)	
	7.5 ± 1.4	Hypertensive volunteers after 3 months of barnidipine therapy	
	7.5 ± 1.7	Hypertensive volunteers after 6 months of barnidipine therapy	
$(dP/dU)/\rho$	3.5 ± 4.9	Children of African American descend ( $n = 154$ , 66% male, 10.3 ± 0.9 years)	[75]
	3.3 ± 1.3	Children of white descend ( $n = 115$ , 64% male, 10.6 ± 0.9 years)	
$(dP/dU) \times 1/\rho$	5.7 (Median)	Healthy men ( $n = 57$ men, 47 ± 13 years)	[45]
	6.2 (Median)	Healthy women ( $n = 49$ men, 45 ± 12 years)	
$dP/(\rho \times dU)$	4.0 ± 0.6	Healthy volunteers ( $n = 10$ , 5 men, 42 ± 13 years)	[76]
	3.7 ± 0.3	Control group (60 min)	
	3.7 ± 0.3	Caffeine group (baseline) ( $n = 17$ , 8 men, 42 ± 13 years)	
	4.5 ± 0.4	Caffeine group (60 min)	
$(dP/dU) \times \rho$	4.28 ± 1.0	Healthy volunteers, Baseline ( $n = 22$ , 22 male, 21.7 ± 1.4 years)	[77]
	5.58 ± 1.68	Cold Pressor Test	
$(dP/dU) \times \rho$	3.3 ± 1.4	Healthy volunteers, before exercise ( $n = 16$ , 16 men, 26 ± 6 years)	[78]
	4.6 ± 1.3	After exercise	
$PWV = (P_s - P_d)/2 * \ln(P_s/P_d)/[(D_s - D_d)/D_d]$	4.03 ± 0.19	Healthy volunteers ( $n = 191$ , 50 men) $N = 28$ (aged 20–30)	[60]
	5.16 ± 0.31	$N = 15$ (aged 30–40)	
	6.20 ± 0.17	$N = 34$ (aged 40–50)	
	6.36 ± 0.12	$N = 73$ (aged 50–60)	
	6.92 ± 1.17	$N = 34$ (aged 60–70)	
PWV $\ln((P_s/P_d)/(D_s/D_d) - 1) \times P_d / 2 \rho)^{1/2}$	3.90 ± 0.8	Control ( $n = 20$ , 12 male, 13.4 ± 6.0 years)	[79]
	3.56 ± 0.10	Fontan ( $n = 34$ , 16 male, 11.5 ± 8.6 years)	
One-point carotid $PWV\beta$ (m/s)	6.8 ± 1.5	Survivors of patients with congestive heart failure and reduced ejection fraction ( $n = 39$ , 69.6 ± 12.7)	[80]
	6.6 ± 1.7	Non-survivors of patients with congestive heart failure and reduced ejection fraction ( $n = 23$ , 69.1 ± 9.2)	
One-point carotid $PWV\beta$ (m/s)	5.35 ± 1.2	Male healthy volunteers ( $n = 388$ , 43.0 ± 17.4)	[81]
	5.48 ± 1.3	Female healthy volunteers ( $n = 292$ , 44.8 ± 17.7 years)	
One-point carotid $PWV\beta$ (m/s)	5.42 ± 1.0	Normotensive ( $n = 145$ , 91 men, 50 ± 10.1 years)	[82]
	6.5 ± 1.6	Hypertensive ( $n = 145$ , 96 men, 51.9 ± 12.1 years)	
$PWV\beta$ (m/s) where $\beta = \ln(P_s/P_d)/[(D_s - D_d)/D_d]$	5.3 ± 1.0	Young men, $n = 53$ , 39 ± 9 years	[83]
	4.6 ± 1.0	Young/premenopausal women, $n = 62$ , 37 ± 10 years	
	6.2 ± 1.3	Older men, $n = 78$ , 65 ± 7 years	
	6.2 ± 1.2	Older/post-menopausal women, $n = 70$ , 65 ± 7 years	
$PWV = \sqrt{\beta \times P / 2 \rho}$	4.2 ± 0.2	Healthy volunteers ( $n = 18$ , 18 men, 22 ± 1 years)	[84]
$PP/(2 \times \beta)$ where $PP$ is local carotid pulse pressure	3.7 ± 0.7	Controls ( $n = 26$ , 15 men, 19 ± 2 years)	[85]
	4.3 ± 0.4	Type 1 diabetics ( $n = 16$ , 11 men, age 18 ± 2 years)	
$PWV\beta = \sqrt{\beta \times DBP/2 \times \rho}$	6.13 ± 1.68	Control ( $n = 30$ , 23 men, 47.0 ± 14.5 years)	[86]
	6.99 ± 1.77	Nasopharyngeal carcinoma patients with IMT < 1.0 mm ( $n = 37$ , 28 men, 48.9 ± 17.3 years)	
	7.84 ± 1.99	Nasopharyngeal carcinoma patients with 1.0 mm ≤ IMT ≤ 1.5 mm ( $n = 30$ , 23 men, 47.6 ± 16.0 years)	
$PWVWI = \sqrt{WI \times DBP/2 \times \rho}$	7.82 ± 2.67	Control ( $n = 30$ , 23 men, 47.0 ± 14.5 years)	[86]
	8.47 ± 2.51	Nasopharyngeal carcinoma patients with IMT < 1.0 mm ( $n = 37$ , 28 men, 48.9 ± 17.3 years)	
	10.19 ± 3.89	Nasopharyngeal carcinoma patients with 1.0 mm ≤ IMT ≤ 1.5 mm ( $n = 30$ , 23 men, 47.6 ± 16.0 years)	

**Table 1** (continued)

Method of measurement	Wave speed (m/s)	Population	References
$(\beta P/2\rho)^{1/2}$	7.4±0.2	Healthy volunteers, control, baseline (n= 18, 18 men, range 19–28 years)	[87]
	7.4±0.2	seated 10 min	
	7.3±0.2	seated 20 min	
	7.1±0.2	seated 30 min	
	7.1±0.1	Resistance exercise baseline	
	8.1±0.2	10 min post exercise	
	7.6±0.1	20 min post exercise	
	7.3±0.1	30 min post exercise	
Carotid wall displacement	8.3±1.6	Type 2 Diabetics (n= 133, 88 men, 57±4 years)	[88]
Phased-tracking method	6.23±0.6	Healthy volunteers (n= 3, 3 men, 28±8 years)	[89]

Wave speeds presented as mean ± standard deviation unless otherwise stated

\*Denotes standard error

artery. Wave intensity has been assessed during exercise [69], caffeine and tobacco consumption [76], hot water bathing [91], chronic heart failure [59], and in patients with a Fontan circulation [79]. Wave intensity and wave energy measures are summarised in Table 2.

In examining the effect of gender on wave intensity in the common carotid artery, the peak amplitude and the net energy of FCW and BCW were higher in men [45]. However, when normalized for the amplitude of the forward-travelling waves, the difference in BCW was abolished [45]. Rakebrandt et al. (2009) further showed an inverse correlation with age, diastolic blood pressure, local wave speed, beta stiffness index and augmentation index for both the FCW and BCW.

Importantly, Chiesa et al. (2019) reported on a large longitudinal study showing that increased carotid FCW in mid- to late-life was associated with greater 10-year cognitive decline [9]. Higher wave reflection index (a measure relating the magnitude of the BCW to the FCW) and lower FCW has been associated with an increased risk of cardiovascular events [80, 92]. In the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), it was shown that in the group treated with amlodipine the wave reflection index was significantly attenuated compared to the group treated with atenolol [66]. Manisty et al. also looked at the effect of atorvastatin versus placebo and found that whilst there was evidence of reduced augmentation index and greater wave reflection from the body, there was no significant change in wave speed or wave energy [65].

From Table 2 below, it is clear the measures of wave intensity and wave energy cannot easily be compared between methods. However, looking only at the most common method i.e.  $(dP/dt) \times (dU/dt)$ , and removing

the outliers reporting a vastly different range of values [73, 78, 79, 83, 87], the mean (± standard deviation) FCW intensity was  $9520 \pm 2258.7$  mmHg m/s<sup>3</sup> (median 9308 mmHg m/s<sup>3</sup>; minimum (reported average) 5750 mmHg m/s<sup>3</sup>, maximum (reported average) 14,700). The mean BCW energy was  $322 \pm 1484.5$  mmHg m/s<sup>2</sup> (median 29 mmHg m/s<sup>2</sup>; (minimum (reported average) 18 mmHg m/s<sup>2</sup>, maximum (reported average) 7600 mmHg m/s<sup>2</sup>). And finally, the mean FEW intensity was  $2039 \pm 581.6$  mmHg m/s<sup>3</sup> (median 1900 mmHg m/s<sup>3</sup>; (minimum (reported average) 1070 mmHg m/s<sup>3</sup>, maximum (reported average) 3220 mmHg m/s<sup>3</sup>).

#### 4 Discussion

Wave speed and wave intensity analysis present an opportunity to better our understanding of the physiology of cerebral circulation. At present, a relatively large body of work has been carried out assessing wave speed and wave intensity in the common carotid artery. However, little work has focused on intracranial blood flow or cerebral haemodynamics. When looking at the reports within studies, it is clear that various health conditions and physiological manipulations (such as hot baths, stress tests, exercise and more) are able to modify wave speed and wave intensity suggesting the measures are sensitive to change.

Local wave speed in an artery is intrinsically interesting because of its effect on arterial haemodynamics and because it is a measure of the distensibility of the artery. The separation of the net wave intensity into its forward and backward components requires knowledge of the local wave speed. The disparity in the number of studies that report separated wave intensity results and those that report wave speeds indicates that many studies that

**Table 2** Peak amplitude of wave intensity and wave energy in the common carotid

Method	Units	FCW intensity	BCW intensity	FEW intensity	Units	FCW energy	BCW energy	FEW energy	Population	References
dPaU NB: Median values	W/m <sup>2</sup>	9.6	- 1.8	2.0	W/m <sup>2</sup>	403	- 99	58	Healthy women (n = 49, age 45 ± 12)	[45]
		8.7	- 1.5	1.4		315	- 80	50	Healthy men (n = 57, age 47 ± 13)	
dPaU scaled by the excess pressure with an assumed peak aortic flow velocity of 1 m s <sup>-1</sup>	Wm <sup>-2</sup> s <sup>-2</sup> × 10 <sup>4</sup>	224 ± 76	13 ± 9	61 ± 24					Framingham volunteers (n = 1617, age 66 ± 9 years, 814 men)	[93]
dPaU scaled by the excess pressure with the measured peak aortic flow in each individual		212 ± 88	12 ± 10	58 ± 24						
dPaU scaled by the excess pressure with an assumed peak aortic flow velocity of 1 m s <sup>-1</sup>	Wm <sup>-2</sup> s <sup>-2</sup> × 10 <sup>4</sup>	222 ± 73	13 ± 9	61 ± 25					Framingham volunteers; healthy individuals (n = 1344)	
		232 ± 83	12 ± 13	62 ± 24					Framingham volunteers; individuals with Cardiovascular Disease (n = 192)	
		242 ± 103	11 ± 8	61 ± 25					Framingham volunteers; individuals with only Valvular Disease (n = 81)	
		236 ± 91	9 ± 8	65 ± 21					Framingham volunteers; individuals with CHF (n = 18)	
dPaU	W/m <sup>2</sup>	16.8 ± 1.5*	2.2 ± 0.4*	2.1 ± 0.2*	mJ/m <sup>2</sup>	616.9 ± 55.0	108.9 ± 15.9	75.7 ± 5.0	Healthy volunteers (n = 21, 14 men, 44 ± 6 years)	[42]
dPaU	W/m <sup>2</sup>	13.8 ± 7.3	1.4 ± 0.8	2.9 ± 1.3					Hypertensive, treated, volunteers (n = 12, 12 men, 63 ± 9 years)	[67]

**Table 2** (continued)

Method	Units	FCW intensity	BCW intensity	FEW intensity	Units	FCW energy	BCW energy	FEW energy	Population	References
dPeU	W/m <sup>2</sup>	335±174	108±63	59±27					Normotensive volunteers (n=20, 13 men, 56±4 years)	[74]
		376±129	87±43	73±32					Hypertensive volunteers (n=21, 14 men, 58±8 years)	
		486±148	123±74	87±45					Hypertensive volunteers after 3 months of barnidipine therapy	
		414±147	98±47	5±33					Hypertensive volunteers after 6 months of barnidipine therapy	
dPeU Tonometry	W m <sup>-2</sup>	2.22±1.11	0.15±0.13	0.20±0.27					(n=22, 13 men, aged 49±17 years)	[63]
dPeU Linear US-derived	W m <sup>-2</sup>	1.17±0.43	0.28±0.19	0.12±0.07					(n=22, 13 men, aged 49±17 years)	
dPeU Exponential US-derived	W m <sup>-2</sup>	1.35±0.47	0.42±0.26	0.18±0.10					(n=22, 13 men, aged 49±17 years)	
dPeU Accelerometric	W m <sup>-2</sup>	1.79±0.98	0.19±0.17	0.24±0.27					(n=22, 13 men, aged 49±17 years)	
dPeU Median					J/m <sup>2</sup>	0.69		0.16	Placebo (n=62, 57 male, age 64±7 years)	[65]
								0.16	Atorvastatin (n=78, 70 male, age 64±8 years)	

**Table 2** (continued)

Method	Units	FCW intensity	BCW intensity	FEW intensity	Units	FCW energy	BCW energy	FEW energy	Population	References
dPaU	W m <sup>-2</sup>	19.6±9.0	1.8*	4.3±2.1	mJ/m <sup>-2</sup>	701±201	114±76	167±83	Amlodipine-based regimen, ASCOT substudy (n = 122, 99 men, 64.3 ± 7.1 years)	[66]
dPaU		18.7±8.3	1.9*	4.0±1.9		694±295	126±65	162±79	Atenolol-based regimen, ASCOT sub-study (n = 138, 119 men, 63.3 ± 7.6 years)	
dPaU					mJ/ m <sup>2</sup>	745±46	75±13	149±16	Healthy volunteers (n = 29, 13 men, age 60 ± 9 years)	[59]
dDaU	m <sup>2</sup> /s	2.60±1.41·10 <sup>-7</sup>	0.22±0.14			467±29	73±8	144±11	Compensated systolic heart failure patients on medication (n = 67, 42 men, age 66 ± 10 years)	
dDaU	10 <sup>-6</sup> m <sup>2</sup> /s	0.16±0.06	-0.05±0.02	0.04±0.01	10 <sup>-9</sup> m <sup>2</sup>	4.83±1.76	-1.52±0.70	0.60±0.21	(n = 1774, 840 men, age 45.8 ± 6 years)	[24]
dP/dt×dU/dt	mmHg x m x s <sup>-3</sup> × 10 <sup>-3</sup>	0.39±0.16 0.15±0.10 0.39±0.23 31.0±2.6	-0.13±0.08 -0.05±0.02 -0.13±0.07	0.06±0.02 0.03±0.01 0.06±0.02 5.24±0.79		9.66±3.56 4.50±2.32 9.53±5.0	2.85±1.61 1.50±0.65 2.97±1.77	1.13±0.41 0.56±0.21 1.17±0.46	Healthy volunteers (n = 12, 6 men, 27 ± 2 years) Rest Day 1 Exercise 1 Rest Day 2 Exercise Day 2	[69]
		48.1±4.4		3.00±0.55					Control (n = 20, 12 men, age 13.4 ± 6.0 years) Fontan (n = 34, 16 men, age 11.5 ± 8.6 years)	[79]

**Table 2** (continued)

Method	Units	FCW intensity	BCW intensity	FEW intensity	Units	FCW energy	BCW energy	FEW energy	Population	References
$dP/dt \times dU/dt$	$\times 10^3 \text{ mmHg m/}$ $s^3$	$7.1 \pm 2.6$		$1.9 \pm 1.1$					Control group ( $n=21$ , 7 men, age $58 \pm 13$ years)	[94]
		$25.0 \pm 19.8$		$2.4 \pm 1.6$					Control group at peak exercise	
		$10.3 \pm 4.2$		$2.2 \pm 1.1$					Hypertensives ( $n=21$ , 10 men, age $71 \pm 6$ years)	
		$19.9 \pm 12.3$		$3.3 \pm 1.9$					Hypertensive group at peak exercise	
$dP/dt \times dU/dt$	mmHg $m/s^3$	$6951 \pm 4119$		$1950 \pm 1006$					Survivors of patients with conges- tive heart failure and reduced ejec- tion fraction ( $n=39$ , age $69.6 \pm 12.7$ )	[80]
		$5748 \pm 3891$		$1117 \pm 708$					Non-survivors of patients with conges- tive heart failure and reduced ejec- tion fraction ( $n=23$ , age $69.1 \pm 9.2$ )	
$dP/dt \times dU/dt$	mmHg $m/s^3$	$12.37 \pm 6.89 \times 10^3$		$3.22 \pm 1.81 \times 10^3$					Male healthy volun- teers ( $n=388$ , age $43.0 \pm 17.4$ )	[81]
		$9.75 \pm 4.88 \times 10^3$		$2.98 \pm 1.69 \times 10^3$					Female healthy volunteers ( $n=292$ , age $44.8 \pm 17.7$ )	
$dP/dt \times dU/dt$	mmHg $m/s^3$	$9308 \pm 4675$		$2995 \pm 1868$					Normotensive ( $n=145$ , 91 men, age $50 \pm 10.1$ )	[82]
		$13,646 \pm 7368$		$4289 \pm 2017$					Hypertensive ( $n=145$ , 96 men, age $51.9 \pm 12.1$ )	

**Table 2** (continued)

Method	Units	FCW intensity	BCW intensity	FEW intensity	Units	FCW energy	BCW energy	FEW energy	Population	References
$dP/dt \times dU/dt$	$10^3 \text{ mmHg m/s}^3$	$9.36 \pm 4.70$		$1.89 \pm 1.06$	$\text{mmHg m/s}^2$		$43.33 \pm 22.07$		Healthy volunteers ( $n=80$ , 34 men, age $34.5 \pm 10.6$ age range 17–57 years)	[95]
$dP/dt \times dU/dt$	$/10^3 \text{ mmHg m/s}^3$	$21.95 \pm 12.08$		$2.39 \pm 1.61$			$77.90 \pm 51.32$		Hyperthyroid ( $n=86$ , 33 men, age $37.4 \pm 10.5$ years, age range 18–57 years)	
$dP/dt \times dU/dt$	$\text{mmHg m/s}^3$	$14.7 \pm 7.1$		$1.9 \pm 1.2$					$N=22$ (22 men, age $21.7 \pm 1.4$ years)	[96]
$dP/dt \times dU/dt$	$\text{mmHg m/s}^3$	$9.1 \pm 4.3 \times 10^3$		$1.5 \pm 0.7 \times 10^3$	$\text{mmHg m/s}^2$		$21 \pm 9$		Healthy volunteers ( $n=13$ , 9 men, age $47 \pm 10$ )	[97]
$dP/dt \times dU/dt$	$\text{mmHg m s}^{-3}$ (log x)	$0.96 \pm 0.2$	$1.53 \pm 0.3$	$0.28 \pm 0.3$					Healthy volunteers, before exercise ( $n=55$ , 12 men, age $22 \pm 5$ )	[73]
$dP/dt \times dU/dt$	$\text{mmHg m s}^{-3}$ (log x)	$1.55 \pm 0.2$	$2.39 \pm 0.7$	$0.04 \pm 0.5$					After exercise	
$dP/dt \times dU/dt$	$\text{mmHg m s}^{-3}$ (log x)	$0.88 \pm 0.3$	$1.43 \pm 0.4$						Healthy volunteers, baseline ( $n=16$ , 16 men, age $26 \pm 6$ )	[78]
$dP/dt \times dU/dt$	$\text{mmHg m s}^{-3}$	$1.66 \pm 0.3$	$2.51 \pm 0.55$						Post exercise	
			<i>NB BCW presented as: Ln(X)</i>						Healthy volunteers ( $n=18$ , 18 men, age $22 \pm 1$ )	[87]
		$9.39 \pm 0.84$	$3.25 \pm 0.45$						(control, baseline)	
		$10.65 \pm 1.25$	$3.58 \pm 0.3$						(seated 10 min)	
		$9.66 \pm 1.24$	$3.47 \pm 0.23$						(seated 20 min)	
		$9.13 \pm 0.80$	$3.27 \pm 0.28$						(seated 30 min)	
		$9.31 \pm 0.97$	$3.85 \pm 0.35$						Resistance Exercise	
		$16.61 \pm 2.04$	$4.89 \pm 0.47$						[10 min post exercise]	
		$13.51 \pm 1.45$	$4.22 \pm 0.42$						[20 min post exercise]	
		$11.71 \pm 1.31$	$3.22 \pm 0.47$						[30 min post exercise]	

**Table 2** (continued)

Method	Units	FCW intensity	BCW intensity	FEW intensity	Units	FCW energy	BCW energy	FEW energy	Population	References
$dP/dt \times dU/dt$	mmHg/m s <sup>-1</sup>	7.9 ± 0.9	38.7 ± 7.8	2.5 ± 0.6					Healthy volunteers (n = 10, 5 men, age 42 ± 13 years)	[76]
		8.7 ± 1.3	32.6 ± 6.1	1.6 ± 0.2					Control group (60 min)	
		8.6 ± 1.1	36.8 ± 9.4	1.8 ± 0.3					Caffeine group (baseline) (n = 17, 8 men, age 42 ± 13 years)	
$dP/dt \times dU/dt$	mmHg ms <sup>-3</sup>	10.5 ± 1.1	46.0 ± 6.9	10.5 ± 1.1					Caffeine group (60 min)	
		9060 ± 330*		1763 ± 330*					Healthy volunteers (n = 170)	[98]
		4,320 ± 420*							Dilated cardiomyopathy (n = 36)	
$dP/dt \times dU/dt$	mmHg ms <sup>-3</sup>			875 ± 98*					Hypertrophic cardiomyopathy (n = 27)	
				140 ± 130*					Mitral regurgitation, before surgery (n = 11)	
				1090 ± 580*					Mitral regurgitation, after surgery (n = 11)	
$dP/dt \times dU/dt$	mmHg ms <sup>-3</sup>	9.1 ± 4.3 × 10 <sup>3</sup> *							Healthy volunteers (n = 13, 9 men, 47 ± 10 years)	
		12.3 ± 5.5 × 10 <sup>3</sup> *							Baseline	
		9.2 ± 5.1		9.0 ± 4.1	mmHg/m/s <sup>2</sup>		71.3 ± 49.2		After sublingual nitroglycerin	
$dP/dt \times dU/dt$	mmHg ms <sup>-3</sup>	2.1 ± 1.2		2.2 ± 1.3					Children of African American descent (n = 154, 66% male, 10.3 ± 0.9 years)	[75]
									Children of white descent (n = 115, 64% male, 10.6 ± 0.9 years)	

**Table 2** (continued)

Method	Units	FCW intensity	BCW intensity	FEW intensity	Units	FCW energy	BCW energy	FEW energy	Population	References
$dP/dt \times dU/dt$	mmHg ms <sup>-3</sup>	7.3 ± 3.2		1.6 ± 1.0	mmHg ms <sup>-2</sup>		32.9 ± 19.1		Young men, n = 53, 39 ± 9 years	[83]
		5.3 ± 2.2		1.5 ± 0.9			28.4 ± 16.3		Young/premenopausal women, n = 62, 37 ± 10 years	
		6.7 ± 3.0		1.8 ± 0.8			26.3 ± 15.8		Older men, n = 78, 65 ± 7 years	
		6.2 ± 3.2		1.7 ± 1.1			23.5 ± 14.0		Older/post-menopausal women, n = 70, 65 ± 7 years	
$dP/dt \times dU/dt$	mmHg ms <sup>-3</sup>	7.4 ± 6.5			mmHg/m/s <sup>2</sup>		30.4 ± 26.5		Normotensives (n = 30, 16 men, 56 ± 6 years) pre-exercise	[99]
		9.2 ± 5.4					34.5 ± 21.5		Normotensives, post-exercise	
		6.8 ± 3.0					23.2 ± 10.4		Hypertensive volunteers (n = 30, 16 men, 56 ± 6 years) pre-exercise	
		8.8 ± 4.8					26.6 ± 14.6		Hypertensive, post-exercise	
$dP/dt \times dU/dt$	mmHg ms <sup>-3</sup>	9.4 ± 0.8		3.2 ± 0.5	mmHg x m x s <sup>2</sup>		47.9 ± 12.9		Healthy volunteers (n = 18, 18 men, 22 ± 1 years)	[84]

**Table 2** (continued)

Method	Units	FCW intensity	BCW intensity	FEW intensity	Units	FCW energy	BCW energy	FEW energy	Population	References
$dP/dt \times dU/dt$	mmHg ms <sup>-3</sup>	12,490 ± 4380		2400 ± 870	mmHg m/s <sup>2</sup>	37 ± 14	37 ± 14		Under 25 y, male, n = 12	[100]
		9990 ± 1660		1657 ± 660		33 ± 15	33 ± 15		Under 25 y, female, n = 10	
		8590 ± 2130		2080 ± 1080		36 ± 10	36 ± 10		26–35 years, male, n = 12	
		7520 ± 2450		1270 ± 380		18 ± 8	18 ± 8		26–35 years, female, n = 11	
		9740 ± 3920		1790 ± 710		28 ± 8	28 ± 8		36–45 years, male, n = 17	
		5750 ± 2100		1070 ± 390		20 ± 5	20 ± 5		36–45 years, female, n = 10	
		8400 ± 4860		1960 ± 603		25 ± 9	25 ± 9		46–55 years, male, n = 10	
		6300 ± 1680		1540 ± 540		19 ± 5	19 ± 5		46–55 years, female, n = 9	
		9980 ± 3770		2640 ± 1420		34 ± 17	34 ± 17		56–66 years, male, n = 11	
		9710 ± 4030		2190 ± 900		24 ± 12	24 ± 12		56–66 years, female, n = 12	
		8220 ± 3020		1590 ± 430		22 ± 17	22 ± 17		Over 66 years, male, n = 12	
		8570 ± 4260		1800 ± 970		28 ± 17	28 ± 17		Over 66 years, female, n = 9	
		$dP/dt \times dU/dt$	$\times 10^3$ mm Hg m/s <sup>3</sup>	8.5 ± 3.6		1.9 ± 0.8				
10.7 ± 5.7				0.8 ± 0.6					Mitral Regurgitation patients, before surgery (n = 98, 60 men, 52 ± 14 years)	
		8.3 ± 3.7		2.4 ± 1.0					Mitral Regurgitation patients, after surgery (n = 98, 60 men, 52 ± 14 years)	

**Table 2** (continued)

Method	Units	FCW intensity	BCW intensity	FEW intensity	Units	FCW energy	BCW energy	FEW energy	Population	References
$(dP/dt) \times (dU/dt)$	mmHg·m·s <sup>-3</sup>	9782 ± 6096		2118 ± 1306	mmHg·m·s <sup>-2</sup>		54 ± 15		Healthy volunteers, Pre-Low-heat stress (n = 11, 11 men, 22 ± 3 years)	[102]
		11,545 ± 8315		1455 ± 905			57 ± 21		Post- Low-heat stress	
		9873 ± 5849		1773 ± 714			55 ± 36		Pre- Moderate-heat stress	
		11,936 ± 6683		2336 ± 1507			50 ± 30		Post- Moderate-heat stress	
$(dP/dt) \times (dU/dt)$	mmHg m/s <sup>3</sup>	7170 ± 4180		1550 ± 590					Chronic heart failure with normal ejection fraction (n = 16, 10 men, 59 ± 13 years)	[103]
$(dP_e/dt)^2 - (dP/dt)^2 / \rho c$	mmHg ms <sup>-3</sup>	14,250 ± 5872			DU		43.0 ± 27.1		Healthy volunteers (n = 10, 10 men)	[104]
$(dP/dt) \times (dU/dt)$	mmHg m/s <sup>3</sup>				mmHg m/s <sup>2</sup>				Hypertensive patients:	[105]
		12,470 ± 6618.6		3141 ± 2260.7			48.41 ± 38.6		Normal con-figuration group (n = 27, 17 men, 49.8 ± 9.2 years)	
		9721 ± 5003.6		2398 ± 1602.5			35.43 ± 1.0		Concentric remodeling (n = 42, 22 men, 50.4 ± 11.8 years)	
		9613 ± 5065.1		2268 ± 1636.5			39.6 ± 20.3		Concentric hypertrophy (n = 62, 32 men, 49.21 ± 12.46 years)	
		9275 ± 6190.0		2367 ± 1921.2			32.2 ± 28.3		Eccentric hypertrophy (n = 24, 16 men, 58.3 ± 11.4 years)	

**Table 2** (continued)

Method	Units	FCW intensity	BCW intensity	FEW intensity	Units	FCW energy	BCW energy	FEW energy	Population	References
$(dP/dt) \times (dU/dt)$	mmHg ms <sup>-3</sup>	$7.01 \pm 3.62 \times 10^3$		$1.65 \pm 0.96 \times 10^3$	mmHg ms <sup>-3</sup>		$31.7 \pm 23.1$		Control group (n = 37, 24 men, 52.3 ± 13.1 years)	[106]
		$11.83 \pm 7.85 \times 10^3$		$0.85 \pm 0.87 \times 10^3$			$34.2 \pm 13.0$		Non-obstructive cardiomyopathy (n = 19, 11 men, 57.3 ± 16.6 years)	
		$13.67 \pm 13.49 \times 10^3$		$2.31 \pm 1.39 \times 10^3$			$57.6 \pm 57.8$		Left ventricular hypertrophy secondary to systemic arterial hypertension (n = 34, 25 men, 56.4 ± 14.6 years)	
$(dP/dt) \times (dU/dt)$					W/m <sup>2</sup> /s × 10 <sup>4</sup>	$2.18 \pm 0.85$	$0.76 \pm 0.27$	$0.33 \pm 0.18$	Control (n = 42, age 18.6 ± 0.9, 16 men)	[68]
						$2.45 \pm 1.11$	$0.84 \pm 0.34$	$0.34 \pm 0.23$	Ex pre-term (n = 76, age 18.2 ± 1.3 years, 40 men)	
$(dP/dt) \times (dU/dt)$ Median (25th, 75th Percentiles)					W/m <sup>2</sup> /s × 10 <sup>4</sup>	$1.68 (1.28, 2.78)$	$-0.84 (-1.23, -0.65)$	$0.76 (0.56, 1.14)$	Control group (n = 42, 15 male, median age 19)	[68]
						$3.18 (2.27, 4.11)$	$-1.32 (-1.96, -0.89)$	$0.33 (0.20, 0.58)$	Coarctation Patients, (n = 43, 21 male, median age 25 years)	
$(1/D) (dD/dt)$ $(dU/dt)$	m/s <sup>3</sup>	$24.9 \pm 10.6$							Healthy volunteers (n = 25, 35 men, 20.8 ± 1.2 years)	[107]

Waves reported after wave separation unless otherwise stated

\*SEM

measure or estimate wave speeds do not report them. We recommend that any future study that measures local wave speeds should report their results.

With regard to wave speed calculations, a large variability exists between studies and methods. These differences are not obviously explained by method, age, gender or population; however, the current review did not undertake meta-regression to understand the contributions of confounding or modifying factors. Nevertheless, it is clear that, for wave speed to be clinically and scientifically useful for the understanding of the cerebral circulation, a consensus on the reference range for normal wave speed is needed. To obtain this, large-scale studies investigating the contribution and differences in methods as well as the reliability and reproducibility will be necessary.

Wave speed in the extracranial common carotid, as opposed to the intracranial internal carotid, has been extensively reported. It is interesting that whilst the mean wave speed is in line with the systemic circulation at approximately 5 m/s, the range is wide and appears biologically improbable, at least at the lower end (minimum 0.8 m/s and maximum 14 m/s). In the intracranial internal carotid artery, traditional wave speed estimation suggested a greatly reduced speed at 2-3 m/s. This must be interpreted with caution given the limited number of observations but could suggest that the internal carotid, and by extension the intracranial circulation, behaves differently to the systemic pressure/velocity wave associations, or that corrections must be applied to the measures to account for the limited resolution in this space. There is evidence that intracranial arteries undergo cyclic distension but the distensibility appears much reduced compared with extracranial arteries [10]. On that basis, the wave speed is likely to be higher albeit not infinite.

A similar limitation exists for wave intensity. Indeed, the axial distension wave as assumed for the analysis of wave intensity may be absent or much reduced under the isovolumetric constraints of the cranial cavity. Nonetheless, with the limited number of observations in the internal carotid artery and no studies directly comparing the dynamics between the internal and the external segment of the carotid artery, we are limited to the interpretation of each in isolation.

Here, a further complication comes from the inconsistent reporting both in terms of the measurement and calculations presented, that is, whether the peak amplitude or the area under the curve is reported, but also in terms of the variation in units of measurements, making it challenging to directly compare between studies. A consensus on a standardisation of units, e.g. to be reported as Standard International units for future studies would be useful. Whilst the conversion between units is relatively trivial, comparing results of different measures and

different methodologies is not. In addition, wave intensity varies across the cardiac cycle. However, the temporal variation is commonly ignored as only the peak systolic intensity or the total energy across the cardiac cycle is usually reported.

From a methodological perspective, it is worth mentioning that the estimate of velocity using pulsed Doppler use peak velocity since this is what the US device typically provides. Other devices (e.g. ALOKA) which use Colour Doppler calculate average velocity. This could introduce substantial differences in estimates of both wave speed and WI.

Despite a substantial body of research spanning 30 years, both on the theoretical side but also on clinical applications relating specifically to the carotid artery and clinically important scenarios such as hypertension, the use of wave intensity analysis is still not widespread in clinical practice. There are examples of ultrasound machines that can yield wave intensity values as part of the cardiovascular analytics [108] but consensus on units and prognostic value of wave intensity indices, in addition to reference ranges, is required to establish this indicator as a useful clinical variable.

It is interesting to note that, despite the clear implications of wave speed and energy on cerebral haemodynamics and the potential development of therapeutic markers of cerebrovascular health, no study has, to our knowledge, assessed the direct impact of wave energy or wave speed on the cerebral circulation by means of functional or perfusion imaging. It should of course be noted that a limitation of the measurements in the common carotid is the bifurcation of this artery into the external and internal carotid artery of which only the internal carotid branch is relevant for the cerebral circulation. Also, an investigation of the impact of wave energy and wave speed on the carotid sinus baroreceptor, a homeostatic sensor of blood pressure, has not been performed. Importantly, the internal carotid arteries supply the anterior circulation of the cerebrum and as such the posterior circulation as supplied by the vertebral arteries are neglected, largely due to the limitations of the current imaging resolution and the high risk of invasive measurements in these arteries.

Overall, despite over thirty years of research and – to some degree – implementation of the analysis, some points remain to be resolved, for carotid analysis and wave analysis in the vasculature in general:

- Consistency around nomenclature would be beneficial: this includes terms such as ‘wave’ (which often needs to be defined due to its many meanings) and terminology such as decompression vs. expansion (for the protodiastolic wave); the former also relates

to the theoretical importance of framing the analysis based on successive wave fronts vs. sinusoidal waves, potentially posing theoretical complications, such as discussing the arrival time of a sinusoidal wave which theoretically has no beginning or end. Usually, this is overcome by utilising phase differences, however, this approach is not universally applied at present.

- Consistency with respect to the use of FCW, BCW and FEW from wave separation as opposed to net wave intensity.
- Consistency around symbols: as different formulations can be adopted, particularly (P, U) formulation vs. (A, U) or (D, U) formulations, clarity around symbols would be helpful.
- Consistency around the formulation itself, with consensus about the use of differences or differentials, i.e.  $dI = dPdU$  vs.  $dI/dt = dP/dt dU/dt$ , which in turn would raise the questions of  $I = dPdU$  vs.  $dI = dPdU$ .
- Systematic identification of wave intensity peaks could be beneficial particularly when considering clinical implementation, analogous to ECG peaks identification.

#### 4.1 Outlook

Wave intensity and the measurement of wave speed are accepted techniques in the field of vascular physiology and arterial research. Here, we propose that wave speed and wave intensity may be useful non-invasive measures to better our understanding of cerebral haemodynamic mechanisms. We suggest further work is needed to understand the reported variability of the measures across studies and to evaluate relevant reference values for wave speed and the wave components in the healthy human artery.

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#### Author contributions

SN has contributed to the conception and design of the work; the acquisition, analysis, and interpretation of data and have drafted the work, edited revisions of the manuscript and have approved the submitted version. GB has contributed to the conception and design of the work; the acquisition, analysis, and interpretation of data and have drafted the work, edited revisions of the manuscript and have approved the submitted version. KP has contributed to the conception and interpretation of data, provided revisions of the manuscript and have approved the submitted version. AH has contributed to the conception and interpretation of data, provided revisions of the manuscript and have approved the submitted version.

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## Declarations

#### Conflict of interest

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