Wave intensity analysis in the great arteries – What has been learnt during the last 25 years? Part 1

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Abstract

Wave intensity analysis (WIA) was introduced 25 years ago for the study of arterial wave propagation. The mathematical derivation of the method is complex, but the results are simple to use and WIA has since been established as a valuable technique for investigating the cardio-arterial interaction. WIA has several advantages; the most important of them is that it is a time-domain technique, which enables the direct association between waves and events during the cardiac cycle. Further, WIA allows for the separation of the measured pressure and velocity waveforms, and derived wave intensity, into their forward and backward directions, and also provides a means for the determination of the arrival time of reflected waves to the measurement site. This powerful technique has been used in several locations in the vascular system for investigating a wide range of physiological and clinical questions, but this review will focus on the clinical application of WIA, as demonstrated from in vivo and clinical studies in the aorta, pulmonary arteries and pulmonary veins.

Introduction

Stroke volume ejection into the roots of the aorta and main pulmonary artery at every heart cycle gives rise to inextricably linked blood pressure and flow disturbances that propagate as waves along the flexible-walled vascular tree. The study of wave propagation in the circulation is gaining increasing clinical interest, as it can provide information about the physiological/pathophysiological mechanisms that integrate the various components of the cardiovascular system. Understanding these dynamic mechanisms allows for the derivation of markers that characterise the deterioration that occurs with disease or the improvement accomplished with therapeutic interventions. Such biomarkers provide valuable prognostic, diagnostic and treatment evaluation tools.

Wave intensity analysis (WIA) was introduced 25 years ago for the study of arterial wave travel[1, 2]. This analysis provides a method for the assessment of propagating waves and thereby of cardio-vascular interaction. The theoretical basis of WIA is founded on the solution of Euler's one-dimensional equations of mass and momentum conservation in elastic tubes with Riemann's method of characteristics[3, 4]. Unlike impedance-based methods, which assume that a waveform is synthesised by the superposition of sinusoidal wavetrains, WIA considers a waveform to be composed of the sequential addition of infinitesimal wavefronts[1, 2, 5]. WIA is a time-domain technique, with the results presented as a function of time, therefore enabling the association between wave intensity features and events during the cardiac cycle. It is outside the scope of this review to provide an extensive description of the method and the underpinning theory, but that material is available elsewhere[1, 3, 6-8].

Briefly, WIA relies on the co-localised and simultaneous measurements of blood pressure (P) and flow velocity (U). Net wave intensity dI at any sampling interval is defined as:

$$dI = dP\,dU \quad (1)$$

where dP and dU denote the incremental differences in pressure and flow velocity, respectively, between successive sampling points. Therefore by definition dI is the power per unit area (W/m2) carried by a propagating wavefront[1]. With the dI profile constructed as a time series, the major peaks of the profile correspond to the dominant propagating waves over the course of the cardiac cycle. The area under a peak has units of J/m2 and characterises the energy per unit area transported by the wave. Based on standard convention, positive dI peaks correspond to waves propagating in the same direction as net blood flow (forward-traveling waves, originating from upstream) and negative dI peaks to waves propagating in the opposite direction (backward-traveling waves, originating from downstream). At any particular instant during the cardiac cycle, dI reveals the dominant direction of wave travel, which depends on the relative size and timing of the forward and backward wavefronts that pass from the measuring location.

Waves travel at speeds considerably higher than U. There is a variety of techniques available for the determination of wave speed (c), based on local measurements of P, U, vessel diameter (D) or analogous hemodynamic parameters[9-17].

When wave speed is known, it is possible to decompose the changes in P and U as:

$$dP_{\pm} = \frac{1}{2}(dP \pm \rho\, c\, dU) \quad (2)$$

$$dU_{\pm} = \frac{1}{2}\left(dU \pm \frac{dP}{\rho\, c}\right) \quad (3)$$

where ρ is the density of blood, and '+' and '–' indicate the forward and backward direction of the wave travel, respectively[1].

The dI separated into forward (dI+) and backward (dI-) components can be written as $dI_{\pm} = dP_{\pm} \cdot dU_{\pm}$, which, according to equations (2) and (3), yields:

$$dI_{\pm} = \pm\frac{1}{4\,\rho\, c}(dP \pm \rho\, c\, dU)^2 \quad (4)$$

Apart from their direction of travel, waves can be further categorized based on their nature, according to the blood pressure changes that accompany them. A compression

wave is associated with an increase in pressure, and an expansion wave is associated with a decrease in pressure. Consequently, there are four possible types of waves: forward compression (FCW) and expansion (FEW) waves, and backward compression (BCW) and expansion (BEW) waves. A forward compression wave (FCW) causes flow acceleration, but a backward compression (BCW) wave causes flow deceleration. Conversely, a forward expansion wave (FEW) causes flow deceleration, whilst a backward expansion wave (BEW) causes flow acceleration.

As a consequence of the definition presented above, the value of wave intensity depends on the data acquisition frequency. This poses practical difficulties when a quantitative comparison needs to be made between data collected with different sampling frequencies. To overcome this difficulty, it has been proposed to substitute dP and dU with the corresponding time derivatives, dP/dt and dU/dt, respectively[18]. The resulting dI dimensions ($W/(m^2s^2)$) do not have the straightforward physical explanation facilitated by the original definition. However, the deviation between the original and the time-normalised wave intensity is essentially a scaling factor, with no difference in the physiological meaning or interpretation of the results[7].

The manner in which nonlinear behavior, such as the pressure-dependence of c and other elastic nonlinearities, affect WIA and wave propagation has also received some attention. However, the added value of nonlinear analysis is not unanimously endorsed. Some authors report substantial differences arising when nonlinearities are taken into account[19-21]. Others however state that the differences between the linear and nonlinear treatment of the one-dimensional equations result in quantitative discrepancies of less than 10% and therefore the linear treatment is sufficient for all practical and clinical purposes[22, 23].

Foreseeing the added clinical value that would be imparted by the ability to derive local wave speed, wave intensity and wave separation from non-invasive measurements, equations analogous to those presented above but formulated using vessel diameter (D) and U (instead of P and U) have been recently presented and validated clinically in healthy middle-aged Europeans[15, 24, 25]. The clinical potential of this non-invasive technique is growing, as advances in ultrasound technology make possible the measurement of D and U at more locations and with higher accuracy. Measurements of D and U determined by cardiovascular magnetic resonance imaging (MRI) have been also used for the non-invasive determination of local wave speed and wave intensity in the human aorta[26]. A variation of the non-invasive WIA approach was subsequently presented, based on a vessel cross-sectional area (A) and U formulation of the fundamental equations (rather than D and U), and applied on high temporal resolution, phase-contrast MRI data derived from paediatric patients with single ventricle physiology[27, 28].

Wave intensity wall analysis was developed for application in conjunction with speckle tracking echocardiography and uses the arterial wall deformation changes in the radial and longitudinal directions to derive approximate changes in P and U, respectively[29, 30].

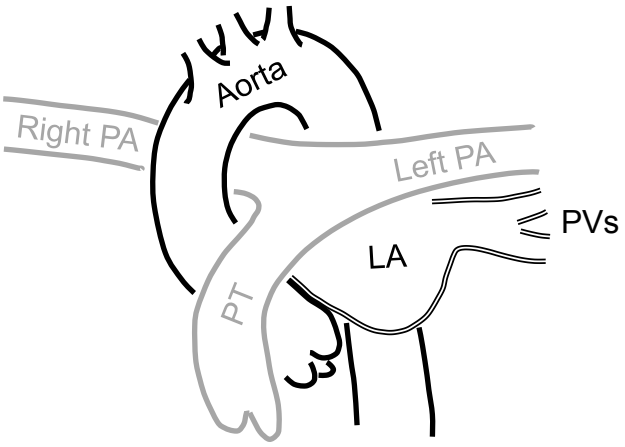

Figure 1: Schematic representation of the major arteries and veins that will be discussed in terms of WIA in this review. PT: Pulmonary trunk; PA: pulmonary artery; PV: pulmonary vein; LA: left atrium.

This review will focus on the clinical usefulness of WIA, as established from in vivo and clinical studies, in the aorta, pulmonary arteries and pulmonary veins (Figure 1). The findings will be presented according to measuring site and are exclusively centred on P-U-based WIA derived from invasive measurements.

Aortic wave intensity

Numerous studies in the aorta have affirmed the reproducibility of the distinct pattern of three dominant wave intensity peaks that was first revealed in 1988, in a pioneering application of WIA in the human aorta[2]. Aortic wave intensity in health is typically characterised by the presence of waves mainly when the aortic valve is open, with little or no wave travel taking place during diastole (Figure 2). During systole, a FCW (FCW_{ao}) associated with a simultaneous upstroke in aortic pressure and flow velocity in early systole is followed by a BCW (BCW_{ao}) that coincides with rising aortic pressure and declining flow in mid-systole, and the wave sequence is concluded in late-systole by a FEW (FEW_{ao}) that is related to both decreasing aortic pressure and flow. A FCW (FCW_{ao_2}) associated with the brief increase in aortic pressure taking place during aortic valve closure (dicrotic notch) might be occasionally discerned in the aortic wave intensity profile as well.

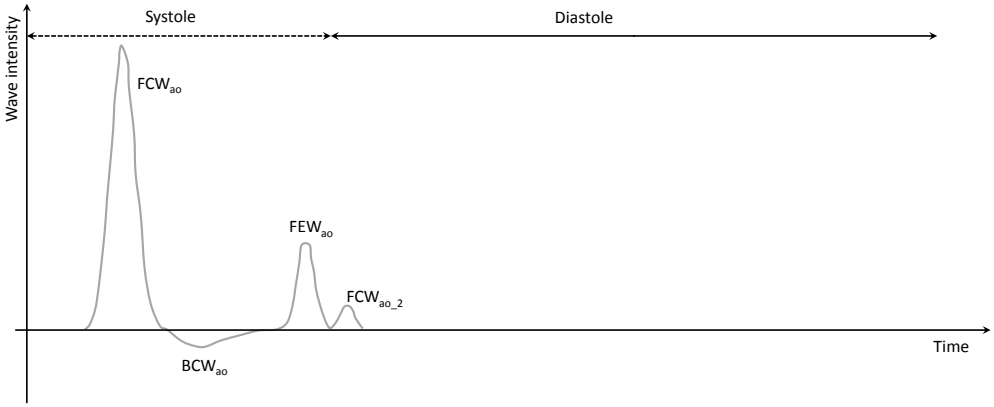

Figure 2: Diagrammatic representation of the aortic wave intensity profile derived from ascending aortic pressure and flow velocity measurements, for one cardiac cycle.

Aortic wave intensity in health

The FCW_{ao} is generated by the contraction of the left ventricle (LV) and is responsible for blood flow acceleration during early systolic ejection, by creating a pushing effect at the proximal end of the aorta[1, 2, 31]. The FEW_{ao} is generated as the rate of myocardial shortening is reduced, and, as it produces a pulling effect at the proximal end of the aorta, it is the main determinant of aortic blood flow deceleration during late systolic ejection and subsequent aortic valve closure. This was a revolutionary finding in the 1990s, that challenged the prevalent belief at that time that wave reflections from the periphery are the main mechanism of aortic flow deceleration[1, 2, 31]. The onset of the FEW_{ao} corresponds well with the time the LV long axis shortening begins to slow down (base and apex moving towards each other at a reduced pace)[32]. It has been shown theoretically that the peak of the FCW_{ao} depends on $(max\ dP/dt)^2\ 1/\rho c$ and the peak of the FEW_{ao} on $\rho c(max(-dU/dt))^2$, where max dP/dt represents the maximum rate of LV pressure increase in early systole and max(-dU/dt) the maximum aortic flow deceleration in late systole[18, 33, 34]. These theoretical derivations consider the LV to be acting as a pressure generator in early systole and a flow generator in late systole.

In contrast to the FCW_{ao} and FEW_{ao} which are both of LV origin, the BCW_{ao} originates distally as the FCW_{ao} is reflected at multiple sites of impedance mismatch along the arterial tree (e.g. bifurcations and locations of change in arterial structure). Thus, the BCW_{ao} is in fact an accumulated reflected wave that is largely determined by vascular properties[35, 36]. The BCW_{ao} produces a pushing effect in the distal aorta, causing aortic pressure rise upon its arrival at the proximal aorta. The arrival time of the BCW_{ao} at the aortic root has been found to be closely related to the time of the inflection point on the systolic aortic pressure upstroke (conventionally thought to signify the arrival of the reflected pressure pulse from the periphery). Also, the magnitude of the BCW showed good agreement with the augmentation index, according to a study conducted in elderly patients with atherosclerosis. The results of the study suggested that the BCW_{ao} provides an alternative means for the assessment of wave reflections, a key phenomenon in cardiovascular research[37]. The importance of wave reflections stems not only from their link to systolic aortic pressure augmentation and consequent hypertension risk, but also from the information they may contain about vascular properties and changes resulting from age, disease or pharmacological interventions. Interestingly, the arrival time of the BCW_{ao} at the aortic root in healthy dogs has been found to coincide with the time that the LV minor axis shortening begins to slow down (septum and free wall moving towards each other at a reduced pace), posing a question about whether the BCW_{ao} does in fact affect LV wall movement speed and thus LV mechanical function[32].

Even though the presence and impact of arterial wave reflections are not doubted, the long-lasting belief that the reflection site lies at a fixed location in the periphery is questioned by recent findings[35]. It might seem straightforward to use aortic wave speed and the time delay between onsets of FCW_{ao} and BCW_{ao}, as observed at a certain measuring location, for estimating the distance to the reflection site, and thereby map it anatomically. However, in vivo studies that involved the progressive movement of the measuring location along the aorta without interfering with the vasculature[35] or, oppositely, maintained the measuring location unchanged while well-defined reflection sites were introduced sequentially through total aortic occlusions along the aorta[36], found a "horizon effect". The summated BCW_{ao} that arrived at the measuring location was not affected in timing or magnitude by contributions from remote reflections (beyond the "horizon"), indicating that the BCW_{ao} is the result of reflections occurring near the measuring location rather than the result of reflections at a fixed anatomical location[35, 36].

Administration of cardioactive and vasoactive agents for the pharmacological manipulation of certain cardiac or vascular mechanisms, and study of the subsequent changes in the aortic wave intensity parameters can provide advanced insight into the dynamics of ventricular-arterial interaction during the cardiac cycle. Dobutamine (positive inotropic effect), propranolol (negative inotropic effect), methoxamine (vasoconstrictor) and nitroglycerin (vasodilator) have been tested in this context in healthy animals[6, 33, 38]. The size of the FCW_{ao} was reduced with propranolol and increased with dobutamine, with no concurrent changes in the FEW_{ao}. This outcome was consistent with the affect these two agents are known to have on cardiac contractility and thus on *max dP/dt*[33]; as mentioned above, *max dP/dt* is a determinant of the FCW_{ao} but not of the FEW_{ao}[34]. Additional observations on the effect of dobutamine have been described by other investigators[38]. Methoxamine also reduced preferentially the size of the FCW_{ao}, a result ascribed primarily to increased afterload[6, 33]. Nitroglycerine caused a decrease in both FCW_{ao} and FEW_{ao}, which was attributed to reduced venous LV filling or preload, and to reduction in wave speed, respectively[33].

Aortic wave intensity in disease and intervention

In the surgical setting, the effect of abdominal aortic clamping on wave travel was investigated in patients undergoing peripheral vascular reconstruction surgery[39]. An increase in the energy carried by the BCWao arriving at the aortic root and evidence of a subsequent rise in LV hydraulic work, presumably triggered by the rise in afterload produced by the BCWao, led to the postulation that the intra-operative impairment of LV function known to occur in this patient population could have been caused by an increase in oxygen demand that was not met by increased supply and thereby provoked ischemia[39]. Aortic malformations, such as an abdominal aneurysm[40] and coarctation[41], have been modelled computationally in the adult circulation and the results revealed a disturbed backward wave intensity pattern in the ascending aorta and the aortic arch, respectively, compared to health.

Aortic WIA during counterpulsation has revealed the presence of additional backward-travelling aortic waves during diastole[42-44]. The energies of these waves are correlated to conventional hemodynamic parameters used for the assessment of counterpulsation benefit.

The reservoir-wave approach

The separation of the P and U waveforms into their forward and backward components using WIA[1] appears to have included two conceptual difficulties. Firstly, the separation exhibits diastolic self-cancelling pressure and flow waves, a phenomenon that is physiologically highly unlikely to occur. The other difficulty is that the separation considers that the measured P is solely due to traveling waves, and does not take into account the pressure changes generated due to the storage during systole and gradual release during diastole of blood volume into the elastic aortic wall.

The reservoir-wave model appears to resolve these two

difficulties, as it essentially assumes that the measured P consists of the reservoir pressure due to the blood volume stored into the aorta (P_r) and an excess pressure associated with wave propagation (P_{excess})[45, 46]. Simultaneous measurements of aortic pressure and LV outflow are required for the separation of these two pressure components. The reservoir-wave model does not produce self-cancelling waves; P_r follows the diastolic exponential decay of P, and P_{excess} follows closely the shape of the flow waveform. The reservoir-wave approach has more recently been extended to calculate P_r from measured pressure alone at an arbitrary location in the arteries, without the need to measure LV outflow[47]. The mechanics underlying the reservoir and excess pressures calculated with the two approaches described above have been investigated theoretically and computationally[48].

When using the reservoir-wave approach, wave intensity can be calculated with P_{excess} and U instead of P and U. Although the shape of the separated curves derived with classical and reservoir-wave WIA is very similar, the intensity of both aortic forward and backward waves is always smaller with the reservoir-wave approach[49]. It has been reported that in the proximal human aorta, peak P- when using the reservoir-wave model accounts for ~6% , whereas it would account for ~30% of total pressure using the classical approach[50]. Analogous findings, comprising a reduction of the BCW_{ao} with the reservoir-wave approach during dramatic physiological manipulations, such as aortic occlusion, have also been reported[49]. Comparable results about the BCW_{ao} are described based on computational and ovine data[51].

Other physiological questions, such as LV filling dynamics[52], wave propagation and reflection in the canine aorta[53], alterations in wave reflection with administration of vasodilators and vasoconstrictors in the canine circulation[54], wave propagation in the venous circulation[55] and the effect of ageing on P_r [56] have also been investigated with reservoir-wave WIA[46].

Pulmonary artery wave intensity

Pulmonary wave intensity in the adult circulation

The wave intensity pattern observed in the main pulmonary artery of healthy animals is qualitatively similar to the typical aortic pattern. An early-systolic FCW (FCW_{pulm}) is generated by the contraction of the RV and exerts a pushing effect at the proximal end of the pulmonary trunk (PT), while a late-systolic FEW (FEW_{pulm}) is produced as the rate of RV contraction begins to decelerate, and with the pulling effect it causes at the proximal end of the PT, it is instrumental in pulmonary blood flow reversal, similarly to the FEWao in the aorta[57-59]. However, the reflection of the FCW_{pulm} that appears in mid-systole is in fact a BEW (BEW_{pulm}), which tends to aid RV ejection by creating a pulling effect downstream of the PT[57, 58]. Although it has been recently advocated that the anatomical site of an “open-end” type reflector that could give rise to such a BEWpulm is not fixed throughout the cardiac cycle[57], it is nonetheless likely located at the proximal portion of the pulmonary tree and gives rise to negative reflections as a result of the immediate and extensive branching of the pulmonary arteries, and the ensuing marked increase in cross-sectional area[57, 58]. A late-systolic BCW that could be the “closed-end” type reflection of the FCW_{pulm} at the terminal arterioles, is also occasionally observed[57].

Human studies have not been performed in the pulmonary artery, however a study related to asthma research was conducted in dogs with hypoxia-induced pulmonary vasoconstriction[59]. An enhanced vasodilatory effect of inhalation of nitric oxide (NO) in He, rather than NO in N_2, was associated with a reduction in the size of the FCW_{pulm}, potentially indicative of the decreased demand for RV contractility for the maintenance of cardiac output[59]. A concurrent drop in wave speed could also be associated with the observed FCW_{pulm} reduction.

Pulmonary wave intensity in the foetal circulation

WIA has been extensively used in studying foetal lamb circulatory physiology. In the foetus, the PT arises from the base of the right ventricle and branches into what is essentially a trifurcation constituted by the left and right pulmonary artery (PA) and the ductus arteriosus (DA). Each PA branches immediately and extensively to form the pulmonary vascular bed, while the DA provides a direct connection between the PT and the descending aorta. Because of its ability to track the origin of propagating waves, WIA is uniquely suited to probe the ventricular-vascular interactions that take place at this junction and that overall result in distinctly different blood flow profiles at each of the daughter and parent vessels involved in the trifurcation[60-62].

The foetal PT wave intensity profile is characterised by the same FCW_{pulm} and FEW_{pulm} that are encountered in the adult PT[63, 64]. Notwithstanding, often the FCW_{pulm} presents a second, mid-systolic peak that might be related to the structural immaturity of the foetal myocardium and the resulting poor coordination between LV and RV systolic function[65]. In addition, the presence of a prominent mid-systolic BCW ($BCW_{pulm\_foet\_PT}$) has been observed in the foetal PT and temporally associated with the onset of the characteristic mid-systolic plateau in PT blood flow [63]. Due to the elimination of the $BCW_{pulm\_foet\_PT}$ upon ligation of the PT proximal to the DA, and taking into consideration the inferred origin of this wave based on wave speed and timing, the $BCW_{pulm\_foet\_PT}$ was attributed to the reflection of the FCW_{pulm} at the distal pulmonary vasculature[63]. The latter was presumed to be acting as a “closed-end” type reflection site in the foetus due to the high vascular resistance of the fluid-filled lungs[63]. Furthermore, it was observed that the magnitude of the $BCW_{pulm\_foet\_PT}$ is larger than that of the foetal and adult BCW_{ao} and also that the BCW ($BCW_{pulm\_foet\_PA}$) of the left PA exceeds in magnitude the FCW_{pulm}. These findings indicated that the $BCW_{pulm\_foet\_PT}$ cannot be accounted for solely by reflections, but most likely mid-systolic impulsive vasoconstriction of the pulmonary microcirculation during each cardiac cycle contributes to its generation[64]. WIA performed in the beats surrounding an ectopic beat, showed that there is a close relationship between the $BCW_{pulm\_foet\_PA}$ and the preceding FCW_{pulm} on a beat-to-beat basis, with matching transient potentiation in both waves after an ectopic beat. This relationship highlighted the possible role of the $BCW_{pulm\_foet\_PA}$ in the regulation of PA and PT hemodynamics[66]. This wave is also transmitted into the DA as a FCW ($FCW_{pulm\_foet\_DA}$) and is responsible for augmentation in DA mid-systolic blood flow, a mechanism that supports foetal right-to-left flow at a period in the cardiac cycle where PT and PA flows are decreasing[67]. The comparative assessment of foetal PT and ascending aortic pressure and flow velocity profiles indicated that the higher mean pressure routinely observed in the PT is entirely due to systolic differences[65]. WIA investigation revealed that these differences were because of a larger FCW_{pulm} than FCW_{ao} and a larger $BCW_{pulm\_foet\_PT}$ than BCW_{ao}, signifying that both ventricular and vascular components are responsible for the augmentation of foetal systolic PT pressure[65].

Pulmonary vein wave intensity

The aetiology of bi-phasic antegrade systolic flow in the pulmonary veins (PVs) has been explored with WIA, in order to establish whether it is predominantly driven by left- or right-sided cardiac events[68]. In patients undergoing elective coronary artery bypass surgery, an early-systolic downstream-originating BEW (BEW_{pulm_vein}) was indicative of suction of blood by the LA as the basis of the first peak in systolic PV flow, while the second peak was temporally associated with a late-systolic upstream-originating FCW (FCW_{pulm_vein}) that actively pushed blood towards the LA[68]. The generation of the FCW_{pulm_vein} has been attributed to the propagation of the FCWpulm across the pulmonary microvascular bed and subsequent transmission to the PVs[68], but mathematical modelling has shown that a contribution from reflected waves cannot be discounted[69].

The late-diastolic retrograde flow observed in the PVs has also been studied with WIA[70]. It was shown that as the LA contracts, it generates a FCW (FCW_{LA}) that travels towards the LV and also a BCW (BCW_{LA}) that travels towards the PVs[70]. The FCWLA tends to accelerate flow into the LV, but gets partially reflected at the mitral orifice, giving rise to a second BCW in the LA (BCW_{LA_2}). Both BCWLA and BCW_{LA_2}, once transmitted into the PVs, tend to decelerate PV flow in late diastole. The size of the reflected wave was augmented as LV stiffness was acutely increased, and resulted in higher retrograde flow through the PVs[70].

Conclusion

Introduced approximately 25 years ago, WIA has proven to be a very useful tool in investigating a wide range of physiological and clinical questions. The technique has a number of features that make it particularly suited to studying ventricular-arterial coupling. The analysis and results are presented in the time domain, where linking WIA features and events during the cardiac cycle is intuitive. WIA also allows for the separation of P, U and wave intensity into their forward and backward components, which originate from upstream and downstream, respectively. Even with the recent introduction of the reservoir-wave approach, WIA remains a useful tool, whether being calculated using the wave pressure or the measured pressure. In this article we reviewed the use of WIA in the great arteries and veins, and in Part II we will review its use in other arterial vessels and in the ventricles.

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