MRI-enabled noninvasive wave intensity analysis: an exciting tool for cardiovascular (patho)physiology research (in absence of local reflections)

Patrick Segers

Much of our current understanding of cardiovascular physiology and hemodynamics, documented in seminal textbooks [1,2], is based on invasive measurements in mammals and in humans, with pressure and flow (velocity) – measured inside the heart or in the (ascending) aorta or pulmonary artery – and cardiac volumes being the key signals for our analyses. This has provided us with a toolkit of methods, techniques and paradigms that we use for the understanding of (components of) the cardiovascular system and the interaction between the heart and its arterial load.

Impedance analysis, based on pressure and flow (velocity), expands the notion of resistance (the ratio of mean pressure to mean flow) to pulsatile signals and allows us to assess the systemic or pulmonary circulation using a systems dynamics approach (in which one can either adopt a ‘windkessel’ or a wave-based paradigm for the interpretation) [3]. Pressure–volume loops have been and still are the solid gold standard basis of cardiac function assessment, yet the real functional information is only obtained when measurements are performed under altered loading conditions for assessment of functional indices such as the end-systolic pressure–volume relation [4] or preload recruitable stroke work [5].

A more recently introduced technique (yet around the block now for about 30 years) for the analysis and interpretation of hemodynamics is wave intensity analysis (WIA) [6]. In the original formulation, temporal changes in local pressure (dP) and flow velocity (dU) are considered as wavefronts, and their product is the wave intensity, dI = dPdU, representing the energy flux carried by the wavefront. Together with knowledge of the local wave speed (pulse wave velocity (PWV)), waves can be further decomposed into their respective forward and backward components. The technique has the advantage of being applied in the time domain and offers a straightforward and intuitive way to, at each moment in time and for a given location, understand the nature and direction of the waves present. When applied to the aorta, for instance, the standard observed pattern in normal physiology is a sequence of a forward compression wave, generated by cardiac contraction, accelerating blood and increasing pressure; a mid-systolic backward compression wave, indicating the return of wave reflections increasing pressure and decreasing flow velocity; and a forward expansion (also called decompression) wave at end systole generated by the relaxing ventricle and closing aortic valve, decelerating the blood and lowering pressure [7].

The intrinsic drawback of all above described techniques is the necessity of measuring pressure, flow (velocity) and/or volume, limiting the techniques to the research setting or the rather rare clinical setting that warrants invasive monitoring (with high-fidelity instrumentation). In recent years, however, MRI and especially cardiovascular MRI have expanded from an anatomical imaging technique to a technique that also encompasses functional imaging. For the sake of this editorial comment, particularly the feasibility of simultaneous dynamic measurements of flow velocity and arterial diameter/area measurements via phase contrast imaging is relevant. Vulliémoz et al. [8] were among the first to explore the new possibilities offered by this novel imaging modality in assessing the local PWV. Their method, called the Q4 loop method and based on flow, Q, and cross-sectional area, A, is a variant of the so-called PU-loop method (based on pressure P and flow velocity U) introduced by Khir et al. [7]. Feng and Khir [9] also worked out a complete WIA framework not based on pressure and flow velocity but on the arterial diameter (D) and flow velocity, hereby creating a noninvasively applicable alternative for WIA termed nWIA. The method was initially envisioning implementation via ultrasound, but can obviously also be applied to MRI, equally providing access to diameter and flow velocity data.

In this issue of the Journal of Hypertension, Li et al. [10] have applied this nWIA framework on MRI data acquired in 144 healthy individuals, aged 20–77 years for the
as these directly result from heart–arterial interaction, however, important to keep in mind is that nWIA (or WIA) and ln(WIA) decrease in the ventricle’s ability to actively relax. What is, in fact, more modestly influenced by age is local PWV (nWIA analysis, as absolute values are obtained after (n)WIA analysis). The age-related increase in wave speed is also less outspoken than what is found for carotid–femoral PWV. The reference values study indicates an increase in 70% or more (11) or for the thoracic aorta in a transit-time-based MRI study (f 90%) over a more or less comparable age range (12). Whether or not this more modest age-related increase in local PWV is an effective indication that the proximal aorta seemingly stiffens at a slower pace than the aorta as a whole is difficult to assess, as direct comparison with other measures is nontrivial. The immediate local mechanical environment of the proximal aorta is also quite complex, with the mechanical interaction with the heart and complex interference between the axial properties and load on the aorta and its behavior in the circumferential direction which determines its wave speed (13).

Another important methodological factor that can probably never completely be ruled out is the fact that single point local PWV methods are susceptible to the presence of reflections (14–16). The PU, QA and ln(DU) method all rely on the assumption that, in absence of wave reflection, the relationship between P and U or Q and A is linear and the slope is (proportional to) the local wave speed (the water hammer equation). What is not correct, however, is the inverse, that is that linearity of this relation implies absence of wave reflections, as we have demonstrated for the PU loop method (15). Given that reflection has a differential effect on pressure and flow (velocity), reflections of the closed end-type lead to overestimation of local PWV when using the PU-loop method, while they lead to an underestimation of the QA and ln(DU) method (14–16). This basically renders these methods unreliable at sites with known presence of strong local reflections such as the carotid artery (16). Although I would not expect such a strong effect at the level of the aorta, the progressive increase in wave reflection with age may explain the more modest increase in local wave speed as obtained with the ln(DU) loop method. A potential way out may be the use of the Bramwell–Hill formula to calculate local wave speed (in which one may use a pressure recalibration of the area or diameter waveform to get a better estimate of the local pulse pressure (17)).

The study of Li et al. also addresses heart–arterial interaction using nWIA with results that make sense and are anticipated in an ageing population with a decrease in the forward compression wave (what one could link to a decreased contractility in combination with an increased load) and forward expansion wave (what one could link to a decrease in the ventricle’s ability to actively relax). What is, however, important to keep in mind is that nWIA (or WIA) is based on arterial diameter (pressure) and flow velocity. As these directly result from heart–arterial interaction, nWIA by itself does not directly express ventricular function as such. It is therefore hard to comprehend what it effectively means if the magnitude of the forward compression or expansion wave decreases by a factor 4 over the considered age range. How much of this is effectively due to a regressing ventricular systolic and diastolic function, and how much can be ascribed to changes in load? What is the impact in terms of ventricular myocardial energetics or cardiac output? It would therefore be extremely interesting to see the method being applied in future research in conjunction with more traditional/conventional pressure–volume-based methods. As a side note, it should be emphasized that investigators taking up this research should not overly focus on the absolute value of waves obtained after (n)WIA analysis, as absolute values are highly influenced by a.o. sampling rates of signals and filtering steps in postprocessing.

Despite the above side notes, I believe the study of Li et al. is important. It not only shows that the nWIA framework is applicable, but that it leads to more than plausible trends in the evolution of arterial stiffness with age and the impact of age on the compression and expansion waves arising from the interaction of the ventricle and the circulation it sustains. At the same time, one should remain aware of the limitations of the used methodology (particularly in presence of wave reflections), which may have an effect on reported numbers and trends and thus on potential therapeutic decisions if these methods are to make it into the clinic.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES


