Unleashing the power of echocardiography: can we get closer to maximally exploiting all embedded information from the image?

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Ultrasonic imaging has become a widespread clinical tool in almost all medical specialties. While the current generation of equipment provides excellent image quality, the principle of imaging is still very simple: send out an ultrasound pulse, receive the reflections from different tissues, and display the amplitude of the reflected signal on a monitor. In case of echocardiography, this provides high-quality scans of the beating heart, enabling the visual interpretation of morphology and contraction. But what else can we do? Obviously, cardiac ultrasound can also assess (blood and tissue) velocity information using Doppler techniques, but what other information, besides visualization of structures (thus also enabling geometrical measurement), is contained in the image and could be exploited to obtain complementary information?

Recently, there is a lot of attention in analysing the typical speckle patterns present in all ultrasound images, by tracking their displacement over time in order to quantify overall tissue motion and segmental deformation. The clinically available tools that use this approach have shown to provide regional and global deformation assessment, which contains a wealth of information on cardiac mechanics and remodelling.¹

But besides visualization of structures (mainly based on highly reflective boundaries) and tracking speckle patterns for motion/deformation, the power of the reflected ultrasound, from a specific site, should contain complementary information, since the intensity of the signal is determined by the structure and acoustical properties of the tissue that is reflecting it. In the past decades, several authors have attempted to use ultrasound reflectivity for characterizing different tissue types and tissue remodelling and damage in cardiovascular diseases.² While several analysis methodologies have been proposed and assessed, some even embedded in clinical echocardiographic systems, they have proven to be difficult to use and interpret and have not found a place in clinical practice. Why would this be?

To understand this and to know what potential information could be embedded in the reflectivity of cardiac tissue, we have to go back to ultrasound physics and how the image is generated. An ultrasound pulse is generated by the transducer and transmitted into the body. The pulse propagates through the tissue and is reflected by the structure/tissues encountered on its path. These reflected waves travel back to the transducer and are digitized for further processing. Two phenomena play an important role in what the signal will look like when it arrives back at the transducer; first, the alteration the pulse undergoes when travelling to, and returning from, the tissue of interest (mainly attenuation and harmonics generation) and secondly the way the specific tissue reflects the pulse.

The properties of the pulse arriving at the tissue will be predominantly determined by the length of the path and by whether tissues with hugely different reflective properties are encountered. These could be either tissues, such as fat, muscle, lung (with vaguely similar propagation properties), blood (with very low reflectivity and attenuation), or calcified or metal structures (which prohibit further propagation of the pulse). Therefore, in cardiac applications, the predominant determinants of the arriving ultrasound pulse are the depth of the structure and the amount of blood (within heart chambers and large vessels) encountered on the way. This implies, for example, that comparing reflectivity from distal segments in normally sized and in dilated ventricles will be tricky, even if the tissue itself were similar.

Next, the reflectivity from the tissue is determined by its acoustic properties. Here, both the bulk properties and the microstructure play a role. When assessing myocardial properties, its composition and microstructure will be the determinant factor. In this, the extracellular matrix, the presence of interstitial fibrosis or other depositions and the myofibre arrangement will determine how much ultrasound energy will be reflected.³ Given the fact that the myocardium contracts during the cardiac cycle, thus geometrically resizing and rearranging its fibre structure, it is clear that both potential tissue alteration/damage (necrosis, oedema, deposition diseases, etc.) and the amount of regional deformation will determine the properties of the reflected ultrasound wave. In the paper by Kosmala et al.,⁴ the authors used this knowledge to assess fibrosis in patients with metabolic syndrome (MS). They compared ultrasound reflectivity, expressed as calibrated
integrated backscatter (IB) with markers of fibrosis and myocardial deformation.

In the past, IB has been investigated by a lot of authors. It was shown that IB shows a cyclic variation (CV) during the cardiac cycle, with the lowest values at end-systole and the highest at end-diastole. Both the maximal reflectivity and the amplitude and phase of the CV have been shown to change with cardiac disease. It was therefore suggested that IB and its CV could be useful for myocardial tissue characterization.

However, most of this work was performed with scanners with low frame rates (~25 Hz) and before ultrasound deformation imaging was available. When using high frame rate (radiofrequency) imaging and calculating average reflectivity, it becomes clear that the variation in the IB is related to the tissue deformation. Figure 1 shows radial deformation (M-mode thickness) and velocity of a healthy volunteer together with the average IB from 10 healthy volunteers (28 ± 4 years). From this, it becomes clear that with an appropriate frame rate (>100 Hz), the changes in reflectivity closely follow deformation. However, individual IB traces tend to show a higher variability compared with velocities or deformation. This can be explained by the stochastic nature of the speckle patterns in ultrasound.

The absolute IB value, when the muscle is fully relaxed, should represent information from the intrinsic tissue composition. When, for example, fibrosis is present, one would expect increased reflectivity and therefore higher IB values. In normal myocardium, with normal heart rates, this would likely be right before the onset of atrial contraction. Atrial contraction itself stretches ventricular tissue and would change reflectivity. However, relaxation abnormalities and higher heart rates might make onset of atrial contraction not the ideal time period to measure. Therefore, several authors have chosen to work with alternatives such as end-diastole or end-systole (ES), maximal or minimal value or an average of the IB over more cycles (as in ref.4). However, using minimal, ES, or average values will implicitly include IB changes induced by deformation as discussed above. A decrease in deformation, and thus the CV of IB, would increase the ES value and also the average of the IB. Additionally, a change in the timing of deformation (such as induced by the presence of post-systolic thickening) would change the ES value. Thus, both values at specific time points and averages have their disadvantages.

An additional problem with the early equipment, used for reflectivity analysis, was the problem of the absolute value of the measurements. As discussed earlier, the intensity of the reflected wave is directly related to the incident wave. Therefore, larger hearts, chests, muscle, or fat layers will influence the amplitude of the IB potentially much more than changes in the tissue itself. Therefore, normalization by an estimate of the power of the incident wave is crucial. When analysing the posterior wall of the myocardium, using a parasternal window, using the almost specular reflection from the pericardium for this purpose is attractive. Older systems suffered from the problem that this reflection is so powerful that it saturated the electronics, thus clipping its value. Modern, fully digital equipment has a much better dynamic range. When carefully checking that the signal is not saturated, the pericardial reflection can therefore be used to calibrate the reflected power from the nearby myocardium. This is what Kosmala et al.4 used in an attempt to avoid the problems of the path length of the ultrasound.

The study by Kosmala et al. found that IB in the basal septum was the strongest determinant of impaired LV performance, independent of higher procollagen levels, and other remodelling measurement in the MS. Additionally, patients with increased abdominal fat had higher procollagen markers, more dysfunction, and higher IB values.

Interestingly, all changes in deformation and reflectivity occur before changes in global ejection fraction. Additionally, the finding that, in MS, changes occur earlier in the basal septum are similar to what was described in hypertensive patients and relates to differential changes in wall stress in different ventricular segment. This again supports the fact that it is important to do segment-specific evaluation of myocardial diseases, based on the knowledge of the pathophysiological processes involved.

An important finding is that the relation between average reflectivity and deformation is different in subgroups with a different

Figure 1 The comparison of deformation and reflectivity (S, systole; E, early filling; D, diastasis; A, atrial contraction).
amount of circulating fibrosis markers. This suggests that both might have a different relation to fibrosis in the wall. While it is obvious that regional deformation will be influenced by tissue composition, several other factors (as loading and contractility) play a role in how the myocardium deforms. From their findings, it is clear that IB indeed, as discussed above, contains information on both deformation as well as tissue composition and therefore might behave differently in the subgroups. The challenge remains to separate the contributions from tissue and function and a more detailed analysis of the temporal change of the whole IB trace, in relation to deformation, would likely provide more insight compared with working only with the average IB.

When approaches could be developed to extract the complementary information from reflectivity and strain analysis, another, yet unexploited, property of ultrasonic imaging could gain ground in the integrated assessment of cardiac structure, tissue, and function.

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References