Review Article

My approach to optimize my equipment for the use of ultrasound contrast agents

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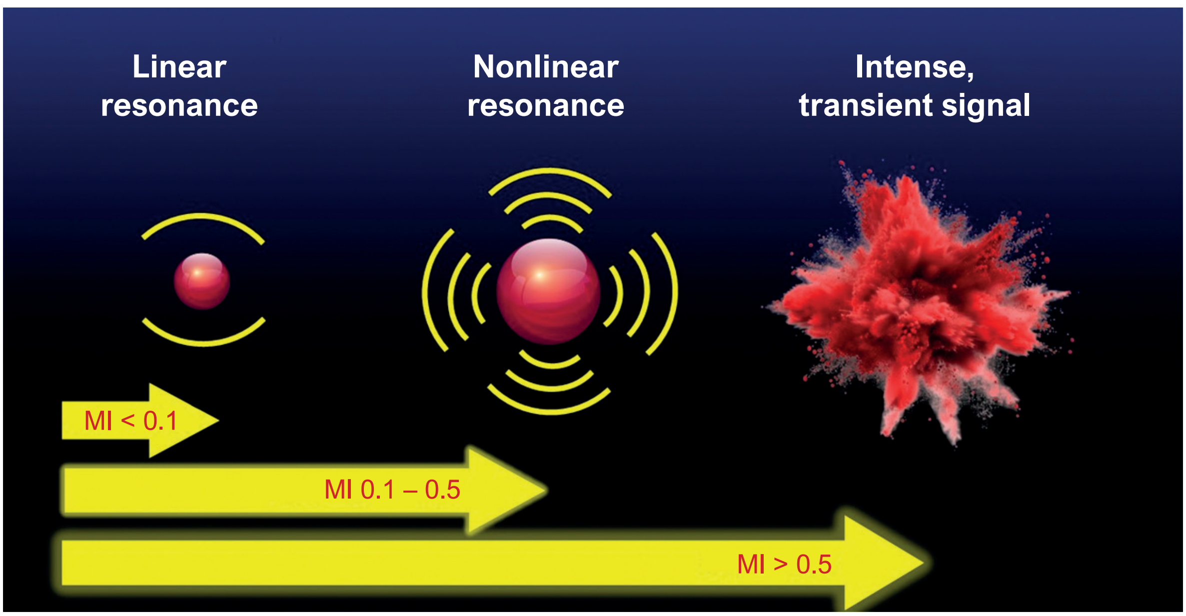
Central Illustration: My approach to optimize my equipment for the use of ultrasound contrast agents



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Resonance of microbubbles in response to the energy transmitted by the echocardiography equipment transducer. MI: mechanical index.

Abstract

Contrast echocardiography, based on ultrasound contrast agents composed of microbubbles, has been increasingly incorporated into echocardiography labs. It involves the infusion of compounds that enhance the visualization of various cardiac and vascular structures. The multiple adjustments required are usually included in pre-configured packages (presets) installed by manufacturers on the equipment. However, it is possible – and sometimes necessary – to make modifications to optimize image generation and, guided by the objective of the echocardiographic study, to achieve the full potential this technique can offer.

Keywords

Echocardiography; Contrast Media; Diagnostic Equipment

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Introduction

Contrast echocardiography (CE) is based on the use of ultrasound contrast agents (UCAs), or echocardiographic contrast, for the purpose of opacifying cardiac structures. It is a safe, cost-effective technique that significantly aids the diagnostic process and, consequently, guides treatment, improving patient outcomes across various clinical scenarios.[1-4]

In this advanced echocardiographic technique, microbubble-based compounds are used – microspheres composed of high molecular weight gas (perfluorocarbon or sulfur hexafluoride) encapsulated by an albumin or lipid shell. In addition to being smaller than red blood cells, this composition gives microbubbles some unique properties. For example, they have lower solubility and diffusibility in blood, meaning greater compound stability, which allows them to cross the pulmonary capillary barrier.[5] Another very important aspect is the rheology of the microbubble when interacting with ultrasound (US) waves. Depending on the amount of transmitted energy, there may be linear or nonlinear radial oscillation, or even microbubble destruction. Therefore, energy adjustment is crucial in CE (Central Figure).

The opacification of structures occurs through the interaction between US waves and microbubbles, generating a powerful reflected signal – approximately 135 times stronger – that is captured by the echocardiography equipment. At this stage, to maximize the effectiveness of the technique, it is essential to optimize the settings of the device being used. The multiple adjustments required are typically included in preconfigured packages provided by manufacturers (presets), and the main variable is the transmitted energy, measured by the so-called Mechanical Index (MI). This adjustment should be guided primarily by the specific objective of the echocardiographic examination being performed.

Ultrasound Contrast Agents and Contrast Echocardiography

The main and most frequent indications for the use of UCAs are:

- Poor acoustic image quality: the use of UCAs can “rescue” exams that would otherwise require additional, more complex and costly imaging methods (Figure 1);[6,8]
- Volume quantification and assessment of left ventricular (LV) systolic function: This estimation shows excellent correlation with cardiac magnetic resonance imaging, improving interobserver reproducibility (Figure 2);[9,10]
- Optimization of Doppler signal for evaluating valvular gradients and estimating pulmonary artery systolic pressure;
- Stress echocardiography: enhances the analysis of segmental wall motion and allows for myocardial perfusion assessment (Figure 3);
- Investigation of thrombi and evaluation of cardiac masses;
- Detection of LV rupture;
- Area delimitation during septal alcoholization for hypertrophic cardiomyopathy.

There are numerous benefits to using UCAs in echocardiographic examinations. Some of the main advantages include:

- They are safe and cost-effective;
- Administration is relatively simple and quick;
- They are non-nephrotoxic;
- They do not accumulate in various tissues;
- They are associated with improved diagnostic accuracy in multiple clinical scenarios and better outcomes in critically ill patients.

Although relatively straightforward, certain steps are essential for the proper administration of UCAs. The key steps are outlined below:

1. A peripheral venous access should be obtained, preferably in the antecubital fossa, with a gauge of at least 20G, along with the installation of a three-way stopcock. This access must be tested for patency to ensure proper infusion.
2. The UCA should be prepared according to the manufacturer’s specifications. Sonovue, an agent approved by ANVISA and authorized for routine use in Brazil, consists of a kit containing a vial with lyophilized microbubbles of sulfur hexafluoride at a

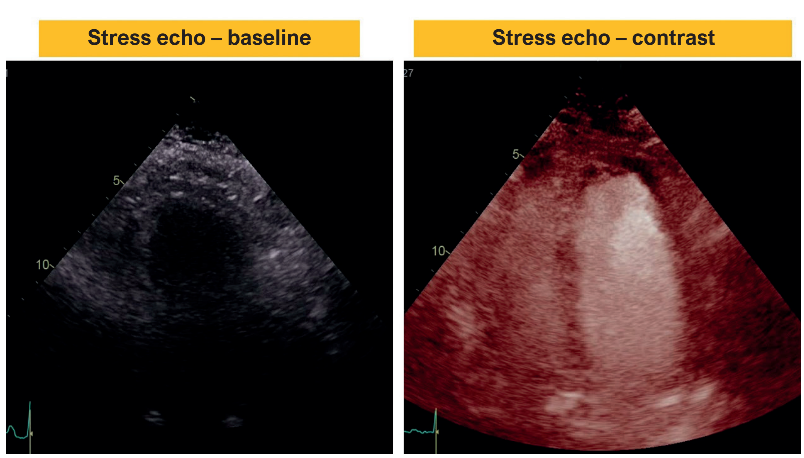

Figure 1 – *Patient with chronic obstructive pulmonary disease and obesity referred for a pharmacological stress echocardiogram using dobutamine. Baseline imaging showed reduced quality. Improvement was observed with the use of an ultrasound contrast agent, allowing the exam to be successfully performed.*

concentration of 8 μL/mL and a syringe with a 0.9% sodium chloride diluent solution. After dilution, the compound should be manually and gently homogenized.

3. Sonovue can be administered in small boluses or, much less frequently, via continuous infusion. Bolus doses typically range from 0.5 to 1.0 mL, followed by a 5 mL flush of 0.9% saline infused over 5 to 10 seconds, or by elevating the limb. It is recommended to use the smallest bolus that ensures adequate opacification, thereby conserving contrast for the entire echocardiographic study. Optimal contrast of the left ventricle is achieved when the cavity is well opacified and the endocardial-cavity interface (endocardial border) is clearly defined. Administering an excessive dose of the contrast agent may result in a "blooming" artifact – an intense apical brightness that distorts adjacent structures – and acoustic shadowing with image attenuation in the basal segments. Conversely, using a lower dose may lead to suboptimal contrast in the apical region, producing a "swirling" appearance, as well as myocardial attenuation that may be generalized or segmental, mimicking perfusion defects.

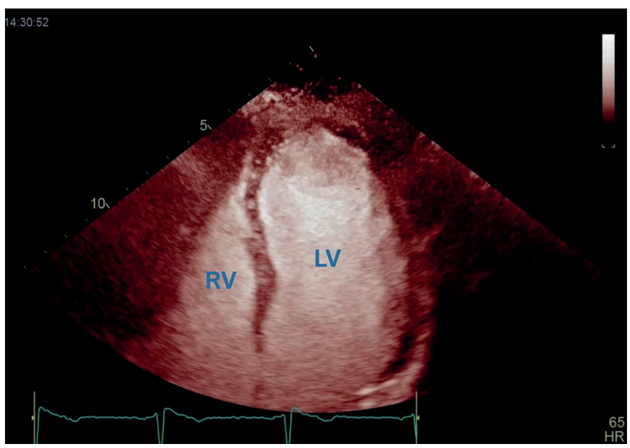

Figure 2 – *Clearer visualization of the borders allows a more accurate measurement of left ventricular volumes and calculation of ejection fraction, reducing interobserver variability. LV: left ventricle; RV: right ventricle.*

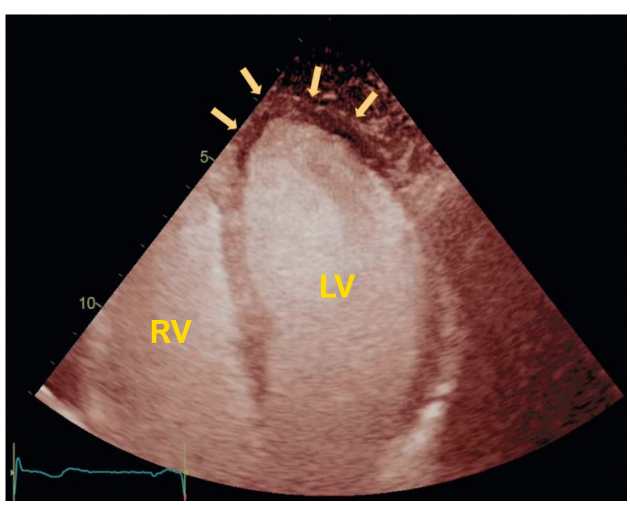

Figure 3 – *A 60-year-old woman underwent contrast echocardiography under pharmacological stress with dobutamine. She experienced chest discomfort and ST-segment depression in the precordial leads on the electrocardiogram. An area of myocardial perfusion deficit was observed at the apex of the left ventricle, associated with localized hypokinesia (arrows). The test was positive for the presence of myocardial ischemia. LV: left ventricle; RV: right ventricle.*

Optimizing my equipment for contrast echocardiography

The rheology of microbubbles and the high reflectivity of US waves are the core of the image opacification technique in CE. The structural composition of the microsphere leads to different bubble behaviors when interacting with US beams at varying levels of transmitted energy.

The MI is a measure that expresses the energy transmitted to tissues, *i.e.*, the acoustic power. Conceptually, it corresponds to the peak negative pressure of the US wave divided by the square root of the central frequency (P- $/\sqrt{f}$), and it is typically greater than 0.8 in most non-contrast images. This is the primary parameter to be adjusted in CE. A very low MI (< 0.2) causes asymmetric and nonlinear radial oscillation of the microbubbles, characterized by greater expansion during the rarefaction phase of the US wave compared to compression at the peak acoustic pressure. This phenomenon is highly relevant in CE, as it not only reflects the fundamental frequency of the US beam transmitted by the transducer but also generates multiple harmonic frequencies – especially the second harmonic.[5] The resulting signal is intense and forms the basis of image opacification in CE. Simultaneously, CE equipment is equipped with specific image cancellation algorithms that filter the received signals. Two of the most common technologies for this purpose are pulse amplitude modulation and pulse inversion, the latter illustrated in Figure 4.

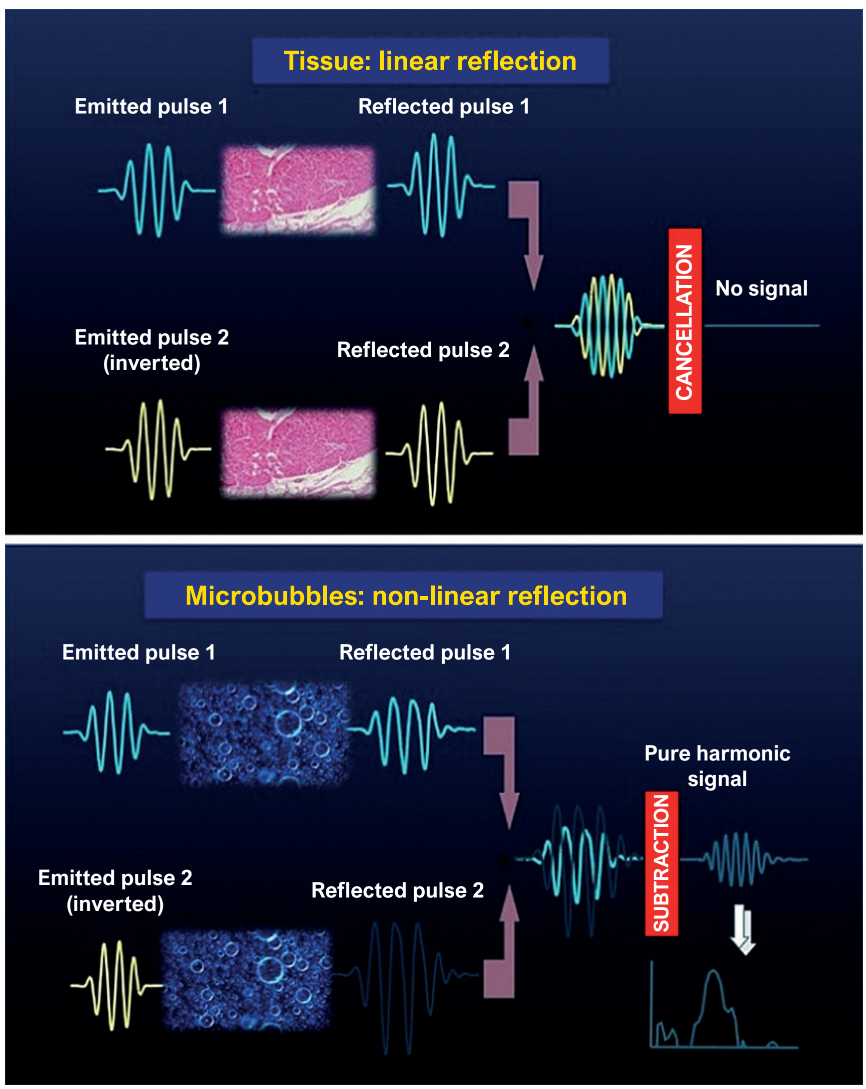

Figure 4 – *Pulse inversion algorithm for image cancellation. Two ultrasound pulses are emitted at the fundamental frequency, one normal and one inverted. Top panel: In tissue, these pulses are reflected similarly (linear reflection). Subtracting the received pulses results in a null signal (no output), leading to image cancellation and reduced brightness in that sector. Bottom panel: The pulses are reflected by microbubbles at both the fundamental and harmonic frequencies. Subtracting these reflected pulses removes the fundamental frequency, resulting in a "pure" harmonic signal, which appears as a bright intensity in the image.*

Another important point is that with the low amount of transmitted energy, there is minimal destruction of microbubbles within the myocardial microvasculature. This allows not only enhanced visualization of the LV cavity but also for the assessment of myocardial perfusion (MP). Following the recommendation to use imaging in fundamental mode (although harmonic mode may also be used), with a very low Mechanical Index (MI < 0.2), an excellent contrast-to-noise ratio is achieved, along with clear delineation of the interface between the myocardium and the LV cavity (endocardial borders), as well as the ability to evaluate MP. Therefore, setting a very low MI (< 0.20) combined with image cancellation algorithm technology represents the optimal parameters for assessing volumes, ejection fraction, segmental contraction, and MP – even in real time, both at rest and under stress.[4,11-13]

Specifically for the assessment of MP, the use of high-energy pulse "flashes" (MI: 0.8–1.2; 5–15 frames) is recommended to destroy microbubbles within the myocardium while preserving opacification within the cardiac chamber. The replenishment time should be less than five seconds at rest and less than two seconds under stress. Typically, this function is already included in the equipment's preset and can be easily activated.

Intermediate MI levels (0.2–0.5) may be used, offering improved image resolution, though at the cost of increased microbubble destruction. MI values above 0.5 should not be used in CE. Situations where this energy level may be appropriate include the investigation of thrombi and masses, as well as the diagnosis of non-compacted cardiomyopathy.

Regarding image generation technology, although harmonic imaging is currently available in CE transducers, the use of nonlinear fundamental frequency is recommended. This approach ensures a better contrast-to-noise ratio, with the frame rate adjusted to approximately 25–35 Hz and the transducer transmission frequency kept below 2.0 MHz.

In patients with a larger body surface area, it may be necessary to adjust to an even lower transmission frequency to allow greater penetration of the ultrasound beam into the tissues. It is possible to use either grayscale imaging or apply color mapping ("chroma"), such as red ruby, to the generated images.

Image depth should be adjusted according to the objective of the examination. If the focus is on LV opacification for volume quantification, systolic function assessment, and delineation of endocardial borders for segmental contraction analysis, the image depth should be set to visualize the mitral valve and approximately 1 to 2 cm of the left atrium.

Image attenuation in the basal segments of the LV may occur, especially when an excessive amount of UCA is used. This can lead to a misdiagnosis of perfusion deficits in these regions. Some strategies can be adopted to improve image definition, such as centering the basal segments in the image – since axial resolution is superior to lateral resolution in the ultrasound field – positioning the focus at the level of the mitral valve, and increasing the gain in this area using the time gain compensation adjustment. An example of these adjustments is illustrated in Figure 5.

If the goal is to investigate a possible apical thrombus, non-compacted cardiomyopathy, or evaluate an apical aneurysm (Figure 6), it is necessary to reduce the image depth and adjust the focus to that specific region. Setting the Mechanical Index (MI) to an intermediate level (2.0–3.0) may help improve spatial resolution, although this comes at the cost of increased microbubble destruction.

Attenuation may also occur in the myocardium of the apical region of the left ventricle, due to higher acoustic power in that area and, occasionally, a higher frame rate, which leads to greater microbubble destruction. Recommended adjustments to optimize the image in these cases include reducing the frame rate and adjusting the gain locally.[4]

Finally, UCAs can also be used to assist in estimating valvular gradients and systolic pressure in the pulmonary

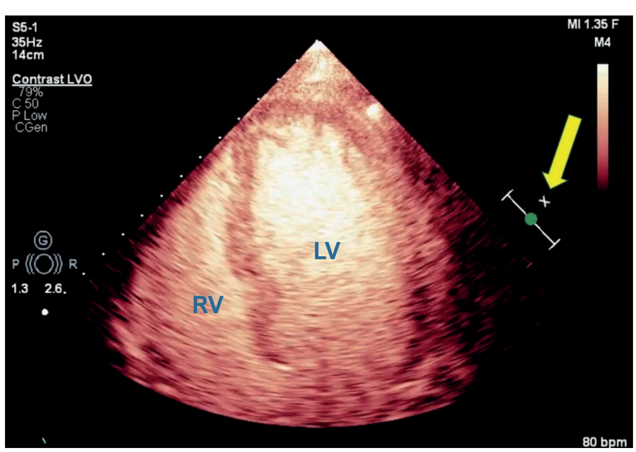

Figure 5 – *Contrast echocardiography. Recommended adjustments to optimize this image include: positioning the focus (yellow arrow) at the level of the mitral valve to improve acoustic resolution of the basal segments and reducing the gain to enhance delineation of the endocardial borders. LV: left ventricle; RV: right ventricle.*

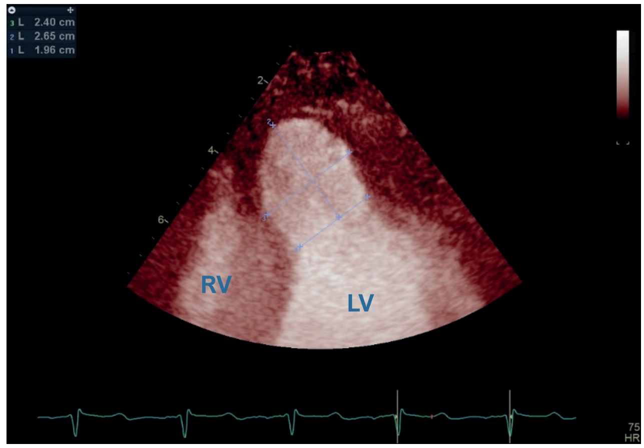

Figure 6 – *Apical aneurysm image better visualized with the use of an ultrasound contrast agent, allowing clear definition of the endocardial borders and more accurate measurement. LV: left ventricle; RV: right ventricle.*

artery. In such cases, the signal (and noise) generated may be intense. The recommendation is to reduce the gain until clear spectral curves with well-defined envelopes are obtained.[4]

Conclusion

CE, based on the opacification of cardiac structures using UCAs composed of microbubbles, has been increasingly adopted across various echocardiography labs. This procedure offers numerous benefits, but to fully achieve its potential, certain equipment adjustments are necessary. Typically, adjustment packages (presets) come pre-configured and installed by manufacturers, and their use is recommended. The primary adjustment involves the level of energy transmitted by the transducer, represented by the MI, which is crucial for minimizing microbubble destruction. This ensures proper opacification of the left ventricle and enables the assessment of MP. Other recommended adjustments include place the image focus at the level of the mitral valve, modifying overall and/or sectoral gain to enhance visualization of apical and basal segments, reducing the frame rate, adjusting the US beam depth, and selecting either fundamental or harmonic imaging modes for image generation.

Author Contributions

Conception and design of the research; Acquisition of data; Analysis and interpretation of the data; Statistical analysis; Writing of the manuscript; Critical revision of the manuscript for intellectual content: Lima MSM.

Potential conflict of interest

I declare no relevant conflict of interest.

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Study association

This study is not affiliated with any graduate programs.

Ethics approval and consent to participate

This article does not contain any studies with human or animal subjects performed by any of the authors.

Use of Artificial Intelligence

The authors did not use artificial intelligence tools in the development of this work.

Data Availability

The underlying content of the research text is contained in the manuscript.

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