Low-dose gated bloodpool SPECT: Is it time to make the shift?

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Left ventricular radionuclide angiography (RNA) has been extensively used in the past for the assessment of prognosis and therapy in various ischemic and non-ischemic cardiomyopathies. In these indications, however, RNA has been progressively replaced by other cardiac imaging modalities, in particular by echocardiography. From a practical standpoint, most planar RNA are nowadays performed for the serial monitoring of left ventricular ejection fraction (LVEF) in patients with potentially cardiotoxic chemotherapies,¹ even though echocardiography is also the most widely accepted imaging method in this indication.^{2,3}

Notwithstanding, RNA provides a robust, reliable, and cost-effective count-based method of LVEF determination.^{1,4,5} In addition, LVEF remains extensively used in quantifying LV systolic performance with the main limitation being its dependence on loading conditions (i.e., leading to a need for a concomitant monitoring of blood pressure). In current clinical routine, LVEF is much simpler and robust to compute than all other indices of systolic function obtained with invasive methods or through an analysis of segmental strain and contractility.⁴ Furthermore, the need for an accurate determination of LVEF has more than ever become indispensable in numerous therapeutic

algorithms, including for (i) treatment of heart failure with abnormal LVEF, especially for implanted devices (cardioverter-defibrillator, cardiac resynchronization therapy) and for certain medications (mineralocorticoid receptor antagonists, beta-blockers, angiotensin-converting enzyme inhibitor, ivabradine, etc.)⁶ and (ii) as stated above, the monitoring of the growing number of patients treated with potentially cardiotoxic chemotherapeutic drugs.^{2,3}

Regarding the latter, the European and American Societies of Cardiology and of Oncology recommend echocardiography as the primary imaging modality for the monitoring of chemotherapy.^{2,3} This was decided in spite of the fact that planar RNA was shown to detect a subclinical cardiotoxicity of chemotherapy drugs more reliably than echocardiography.^{4,7,8} In fact, echocardiography in its current 2D-mode is limited by a rather low precision for LVEF determination, especially in instances of distorted cavity geometry, and by relatively high intra- and interobserver variabilities.^{4,9,10} Higher levels of reproducibility and accuracy may be achieved with 3D-echography, but with the disadvantage of a decrease in both temporal and spatial resolutions along with a higher proportion of suboptimal quality images, especially in the absence of any contrast injection.^{4,10}

The rationale for the current preference for echocardiography is its high availability, its improved visualization of cardiac structures and, moreover, the absence of any ionizing radiation. However, current RNA investigations are associated with a rather low patient radiation, ranging from 6 to 10 mSv,^{11,12} at a level for which the increase in the risk of further cancer development is likely negligible. Another point of view is that most patients with cancer or heart failure undergo multiple ionizing investigations and/or treatments throughout their life, and therefore, the higher risk levels

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due to this cumulative exposure should be considered.^{13–15}

Lastly, on one hand, while it is true that radiating imaging techniques such as RNA have never been demonstrated to be associated with any significant increase in the risk of cancer development, it must be recognized, on the other hand, that a significant positive impact on patient outcome has yet to be currently demonstrated for the use of RNA instead of or in association with echocardiography (with such demonstration being very difficult to provide from a methodological standpoint). Thus, due to uncertainties on this risk/benefit balance and to the existence of alternative imaging techniques, the medical indications of RNA have decreased over time, whereas there has been continuous growth in the use of cardiac echography and MRI for the same medical indications.

This evolution may be damaging, however, at least for the high number of patients for whom the alternative imaging methods (i.e., echocardiography and MRI) are of suboptimal quality or contraindicated. This may possibly also be the case for patients in whom small

changes in LVEF need to be detected (i.e., patients undergoing potentially cardiotoxic chemotherapies). RNA is indeed poorly impacted by operator experience, patient habits, and implantable electronic devices, and may offer accurate and highly reproducible LVEF measurements.

Furthermore, this decrease in the use of RNA is all the more inopportune given that the level of patient radiation can now be dramatically decreased owing to new collimation systems and reconstruction software and, especially, to high-sensitivity cameras equipped with semiconductor Cadmium Zinc Telluride (CZT) detectors.¹⁶ Several myocardial perfusion studies performed with dedicated cardiac CZT cameras have indeed shown that injected doses can be reduced by a factor of 2 to 3, depending on camera type, with recording times limited to no more than 10 min.^{13,17,18} A similar finding was also recently reported for cardiac bloodpool imaging (Figure 1).^{12,19} As a result of the new collimation systems, the count sensitivity of these CZT cameras is three to sevenfold higher than that of a conventional dual-head gamma camera.¹⁶ This ratio in

Figure 1. Count-based determinations of left ventricular ejection fractions (LVEF) from radionuclide angiographies (RNA) consecutively recorded in the same patient: (1) in a 2D planar mode with a conventional Anger camera (14 min recording time) (far right panels) and (2) in a 3D mode with the high-sensitivity D-SPECT camera (3 min recording time) and with a further correction according to a count calibration process (left panels).¹²

count sensitivity is even twice as high when the comparison is made with the single-head configuration used for planar RNA. This constitutes a dramatic advantage for count-based methods of LVEF determination, albeit with the constraint of a definite shift to a SPECT recording mode.

In the present issue of the Journal of Nuclear Cardiology,¹⁹ a novel approach using gated bloodpool SPECT and a reduced radioactive dose is presented. The underlying rationale is that an integration of all LV short-axis slices in a 2D display, mimicking a left anterior oblique view, will allow reaching high levels of LV counts per pixel as well as high signal-to-noise ratios. Under these conditions, injected doses may be reduced by a factor of 3, with no more than 6 minutes of recording time while maintaining an accurate determination of LV counts. When compared with conventional planar RNA recording, this method has the additional benefit of providing a better separation of the LV from the left atrium, taking advantage of the initial 3D-SPECT views.

This 2D-display method also takes advantage of the lack of any need of a precise 3D segmentation of the LV cavity, contrary to conventional bloodpool SPECT. This segmentation indeed constitutes a point of vulnerability for the accuracy and repeatability by which LVEF may be measured with bloodpool SPECT. This may be explained by complex interactions between the border detection algorithms of the LV cavity and the variable visualization of these borders, depending on a number of anatomical and SPECT imaging factors.

A potential limitation of the 2D-display method is the need for the subtraction of a background count level from acquired LV counts, in a manner similar to planar RNA. This subtraction, which is not required for bloodpool SPECT, is a well-known source of variability and of imprecision for LVEF measurement.

The aforementioned threefold decrease in injected dose was also shown to be feasible in routine bloodpool SPECT imaging performed with another cardiac CZT-SPECT camera and with only a current segmentation of the 3D-SPECT images (i.e., without any additional 2D-reformatting).¹² This method was however shown to require a particular calibration for correcting the upward shift in LVEF within the normal range.¹² It should be noted that this shift is also documented in the present report from Liu et al., together with a certain level of underestimation of the lowest LVEF.¹³ Such count calibrations may be obtained from phantoms, as well as from data provided by a small number of patients imaged with both planar- and SPECT-RNA.^{12,20} Unfortunately, these calibration and correction methods, as well as the possibility of integrating the LV short-axis slices in a 2D display, are not still implemented in the

existing software currently used for measuring LVEF with gated bloodpool SPECT.

It would thus appear high time to make the shift from planar RNA to low-count bloodpool SPECT protocols, bearing advantage of new cameras with improved detectors, enhanced collimation systems, and new SPECT reconstruction software. Such shift is already possible today, with sufficiently high accuracy levels as well as repeatability of LVEF measurements, although the latter would also be rendered much easier by further adaptations of current commercially available software—updated methods for volume calibration, 2D integration of LV slices, etc. Such evolution is definitely warranted, especially given the number of patients for whom echocardiography or MRI is contraindicated or poorly contributive or for whom a precise monitoring of LVEF is otherwise required.

Disclosure

Laetitia Imbert and Pierre-Yves Marie have no conflict of interest related to this manuscript.

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