

# Dose-optimization in nuclear cardiac imaging, time for the next step?

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Equilibrium radionuclide angiography (ERNA), also known as multigated acquisition (MUGA), is a well-validated non-invasive test to accurately determine the cardiac function. It is recommended in patients receiving potentially cardiotoxic chemotherapies and it is also used for the evaluation of prognosis in patients with cardiac diseases.<sup>1–3</sup> ERNA is performed by labeling either erythrocytes or human serum albumin (HSA) with technetium-99m-pertechnetate (Tc-99m). After administration of the radioactive tracer, an electrocardiograph (ECG)-triggered planar projection is made of the chest using a gamma camera to determine the volume and contours of both ventricles. Next, a region of interest is drawn over the ventricles in the acquired phase images to calculate the ventricular function parameters using dedicated software.

ERNA was first introduced in the 1970s and rapidly became the standard technique for left ventricular ejection fraction (LVEF) assessment due to its high accuracy.<sup>4</sup> Despite the emerging routine use of gated myocardial perfusion imaging (MPI) SPECT, magnetic resonance imaging and the increased availability of ultrasound, the relatively low operator dependence, low costs, and high reproducibility still make ERNA very valuable in common day practice to assess global heart performance.<sup>3,5</sup>

Although ERNA is widely used to derive the LVEF, it is also associated with a relatively high radiation dose of 3.5–7.4 mSv and protocols for LVEF determination have remained fairly unchanged since the introduction

in the 1970s.<sup>4</sup> This is remarkable, as radiation awareness has increased considerably over the last decades and the performance of the gamma cameras has improved substantially.<sup>6,7</sup> Whereas early studies used 925 MBq (25 mCi) Tc-99m, the dose reference levels are still around 800 MBq (22 mCi) for an ERNA scan and the international guidelines published in 2006 and 2008 still recommend activities of 500–1050 MBq (13–30 mCi).<sup>1,2,4,8</sup>

An alternative to planar-ERNA is ERNA using ECG-gated SPECT. ERNA-SPECT has the possibility to calculate the ejection fraction of both left and right ventricle, to assess the ventricular motion and also to assess wall thickening. Although LVEF measurements using planar and SPECT imaging show a high correlation, ERNA-SPECT results in 7–10 %-point higher values.<sup>9,10</sup> As the evaluation of cardiotoxicity of chemotherapy was originally validated using planar-ERNA, one should therefore be cautious in interchanging the SPECT- and planar-ERNA measurements.

ERNA-SPECT is often performed with conventional Tc-99m activities whereas during the last decades improvements in soft- and hardware resulted in either an increase in image quality or an activity reduction in other nuclear cardiac SPECT studies.<sup>7,11</sup> In terms of software, the routine use of iterative reconstruction and resolution recovery methods and the implementation of noise reduction algorithms enabled activity reductions without compromising image quality. In terms of hardware, especially the dedicated cardiac cadmium zinc telluride (CZT) based SPECT cameras have resulted in major improvements due their inherently high sensitivity and spatial resolution compared to conventional SPECT scanners with sodium-iodide scintillation crystals.<sup>11,12</sup> Duvall et al. reported that reliable LVEF measurements can be obtained using 40% less activity with a CZT-based SPECT camera than with planar-ERNA.<sup>13</sup> Moreover, they also reported that activity reductions of 50% are feasible when increasing the scan time from five to ten minutes. Despite these efforts, there is still a lot to

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gain by transforming fixed protocols into patient-specific activity protocols when comparing it to myocardial perfusion imaging (MPI) with SPECT.<sup>11</sup>

In the current issue of the *Journal of Nuclear Cardiology*, Rydberg et al. studied the influence of patient characteristics such as weight, height, and age on the count rate in ERNA using a CZT-based SPECT camera to derive a patient-specific activity protocol for better radiation dose justification.<sup>14</sup> They retrospectively included 1065 patients who all underwent LVEF determination using ERNA-CZT-SPECT- using 550 MBq Tc-99m-labeled human serum albumin. In their regression analysis they found that body weight explained 68% of the measured count rate. They further showed that their model could be improved to explain 75% of the count rate variation by also including height (4.5%), gender (3.2%), and age (0.7%). Although they did not test their derived protocol in clinical practice, they did derive a patient-specific activity formula incorporating all these variables as a function of the desired count rate.

Although Rydberg et al. made a significant step in improving the acquisition protocol for SPECT-ERNA, the authors used count rate and not the cumulative number of measured counts as the acquisition time solely depended on the number of accepted beats. Although they showed that heart rate did not significantly influence the count rate, it is likely that the heart rate influences the total amount of counts accumulated as a lower heart rate will increase the scan time and, hence, the cumulative number of counts. Yet a higher number of cumulative counts will result, just like for MPI SPECT, in an improved image quality. Duvall et al. showed that an increasing scan time and, hence, increasing count statistics, resulted in a better correlation between planar-ERNA and ERNA-CZT-SPECT LVEF measurements.<sup>13</sup> This seems in line with the current study by Rydberg et al. who showed that also the reproducibility of LVEF measurements was better in patients with higher count rates. It is therefore safe to say that a minimum number of cumulative counts is required to obtain reliable LVEF measurements. Acquiring this minimal number of counts can easily be achieved in all patients by administering a patient-specific activity.

Despite the count rate limitation, Rydberg et al. made an important step towards deriving an optimal patient-specific protocol for ERNA-SPECT and their methodology can also easily be used to derive an optimized activity protocol for planar-SPECT. Yet two additional steps have to be taken prior to clinical adoption, as previously described in a 'hands on approach' by van Dijk et al.<sup>15</sup> The first step is to validate if the derived protocol also results in a constant image quality where the cumulative number of counts could be taken as a

surrogate. The obtained constant number of counts also allows to reduce the average administered activity as current fixed-activity protocols are often aimed to achieve sufficient image quality in all, but especially in heavier patients. Leaner patients often receive an activity which is unnecessarily high using fixed-activity protocols and patient-specific protocols allow to reduce this activity. Hence, the second step is to determine the minimal number of cumulative counts required to obtain accurate and reliable LVEF measurements in all patients. This minimal number of required counts will vary between SPECT cameras and is influenced by reconstruction software and settings. Centers should therefore always test the effects of possible reductions for each new camera set-up before implementing it in clinical practice to ensure sufficient quality.

Besides activity protocol optimization, several other considerations should be made to deliver optimal patient care. First of all, selection of patients undergoing certain diagnostic testing should always be in concordance with the appropriate use criteria.<sup>16</sup> Second, when the newest hard- and software that can cope with lower counting statistics are available, it should be used to further reduce the activity to administer.<sup>7</sup> Third, the acquisition should be performed according to the guidelines using the correct patient positioning and camera angles. Final, as reproducibility of the post-processing of the data varies between centers, especially for ERNA-SPECT,<sup>17</sup> one should be certain that standardized protocols are used to derive reliable and reproducible LVEFs.

In summary, in addition to the existing patient-specific activity protocols commonly used for MPI SPECT, Rydberg et al. demonstrated that patient-specific protocols will presumably also result in constant quality and better radiation dose justification in ERNA using CZT-SPECT. It therefore seems likely that tailored protocols may also result in better quality and activity optimization in other nuclear cardiac examinations such as planar-ERNA. It may therefore not only be time to adopt patient-specific activity protocols in SPECT-MPI and ERNA-SPECT, but also to derive, validate, and adopt patient-tailored protocols in other nuclear procedures.

## Disclosure

*Joris D. van Dijk has nothing to disclose.*

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