EDITORIAL

The long way to dose reduction in myocardial perfusion imaging

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In the last decade, the concerns about radiation in myocardial perfusion imaging (MPI) have propelled the development of high-efficiency cardiac SPECT scanners, innovative collimators and iterative reconstruction algorithms with resolution recovery (IRR) for performing low-dose myocardial perfusion studies.[1] However, the extent to which, using this new technology, the patient dose can be reduced is still unknown today.

Several studies have shown that, using the IRR algorithms, it is possible to reduce the patient dose by half and at the same time, to provide diagnostic results equivalent to conventional reconstruction algorithms, such as ordered subset expectation maximization (OSEM) and filtered back projection (FBP).[2–6] The recommended activities, per single scan, according to the American Society of Nuclear Cardiology (ASNC), may now range from 148 MBq (stress-only protocol, new technology, body mass index (BMI) = 25 kg/m^2) to 1332 MBq (second injection in a one-day stress/rest protocol, GP gamma camera, BMI = 35 kg/m^2), resulting in effective doses of between 1.0 and 10.5 mSv.[7] However, the IRR algorithms have demonstrated the potential to reduce the patient dose below 50% of the reference in an anthropomorphic phantom study[8] and in two clinical studies,[9,10] mostly in the presence of normal-weight patients (between 18.5 and 24.9 kg/m^2 of BMI).

The study of Juan Ramon et al.[11] in this issue of the Journal of Nuclear Cardiology is the first study that investigates the extent to which patient dose can be reduced in cardiac SPECT through the optimization of reconstruction process. The authors simulated different dose levels (from 100 to 12.5% of the standard dose) using cardiac SPECT data modified to contain realistic simulated perfusion defects. The first step of this study is to find the best set-up of the reconstruction parameters for each reconstruction method and for each dose level considered in the study without the comparison with the conventional clinical outcome. The reconstruction methods considered were (1) FBP, (2) OSEM with attenuation, scatter, and resolution corrections and (3) OSEM with scatter and resolution corrections only. For each of these reconstruction strategies and dose level, the authors conducted a receiver operating characteristics (ROC) study based on the total perfusion deficit (TPD) score computed by the Quantitative Perfusion SPECT (QPS) software package. TPD score quantifies the non-uniformity of myocardial perfusion in the left-ventricle polar maps with respect to normal limits derived from a series of reference databases created from normal MPI scans. The authors generated separate reference databases depending on reconstruction strategy (reconstruction method, number of iteration and/or filter parameter) and dose level, optimizing in this way also the automatic quantification process to each specific polar map. The results of the study suggest that, by using OSEM with all the corrections, a reduction of dose level to 25% could be achieved without limiting diagnostic accuracy in relation to full dose FBP. Without attenuation correction, the dose limit should be higher, proximately 40% of the standard.

OPTIMIZATION OF RECONSTRUCTION ALGORITHMS IN PERFUSION DEFECT DETECTION: ROLE OF NUMBER OF ITERATION AND FILTER CUT-OFF FREQUENCY

The reconstruction parameters (number of iterations, number of subsets, and post-filters) have a

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significant impact on image quality. In fact, it is well known that increasing the number of updates (iterations * subsets) will improve the spatial resolution but this is at the expenses of an increased noise in the reconstructed images. Similarly, the use of a post-filter reduces the noise but worsen the resolution down to the one obtained with a conventional FBP reconstruction.[12] A fine tuning of these parameters is usually performed by the manufacturers which produce software packages with default parameters adjusted for specific tasks (bone study, cardiac study, etc.), making the vendor reconstruction parameters the most widely used in clinical practice.

To avoid the introduction of misleading factors, the performance of the IRR algorithms was evaluated in the past by phantom studies using the manufacturers' recommendations.[8,13]

Juan Ramon et al. demonstrated that, for all reconstruction methods considered, high and low values of the reconstruction parameters led to significant decreases in diagnostic performance (perfusion defect detection), emphasizing that optimization of this is essential to achieve maximum dose reduction. For example, when using OSEM with all the corrections, the optimal number of iterations was 12 for the reference dose level and 4 when the dose is reduced by 25%.

However, the optimal values found by Juan Ramon et al. are not directly applicable to all clinical IRR algorithms, firstly, because some of the commercial software are not OSEM type of reconstruction and then, because the regularization of the noise in the images is performed with a different technique than Gaussian post-filter (see Table 1). What is different from conventional low-pass filtering is that the modeling process preserves the original defect contrast, thus making it possible to reduce noise without compromising image contrast.[14] Moreover, it has been recently demonstrated that general purpose collimators may perform better than high-resolution collimators when IRR algorithms are used.[15]

OPTIMIZATION OF RECONSTRUCTION ALGORITHMS IN THE ASSESSMENT OF CARDIAC FUNCTION

Although most of the research was conducted with the aim of determining the lower activity that could be injected into patients undergoing myocardial perfusion studies, actually more than 90% of MPI exams are performed using the ECG-gated techniques with the purpose of studying also left ventricular (LV) function. In this case, a standard SPECT projection is divided into different ECG-dependent projections, each of them receiving just a portion (usually, 1/8 or 1/16) of the counts that are collected in the summed non-gated projection. Thus, the ECG-gated images are more noisy and this has to be taken in account when the reconstruction parameters are chosen and the best reconstruction parameters should be different from that used for non-gated images for perfusion evaluation. Moreover, higher LV ejection fraction (LVEF) values are obtained when measure is performed on high-quality images, such as those of IRR reconstruction, based on the consideration that high contrast images increase the identification of the correct position of endocardium, thus increasing the derived volume of the ventricular cavity and, consequently, rising the LVEF values.

For the study of LV perfusion, the diagnostic accuracy of low-dose studies can be evaluated by realistic simulated perfusion defects or by the outcome of the subsequent coronagraphy. On the contrary, for the study of LVEF, the real values are known as the possible gold-standard techniques (MRI, first pass, contrast ventriculography, blood pool SPECT) have their own

Table 1. Main characteristics of the commercial iterative reconstruction algorithms with resolution recovery and noise regularization

Algorithm	Type	Noise regularization
EfC (GE)	MAPEM	One-step late method with green prior and median root prior at last iteration
Astonish (Philips)	OSEM	Priority filtering (Hanning) of acquired projections and computed projections by forward-projection
Flash3D (Siemens)	OSEM	Gaussian post-filter (6-mm FWHM default value)
WBR (UltraSPECT)	MAPEM	Modification of the quadratic penalty function to model a statistical data distribution with heavier tails than the Gaussian one

EfC, evolution for cardiac; *WBR*, wide beam reconstruction; *MAPEM*, maximum a posteriori expectation maximization; *OSEM*, ordered subset expectation maximization limitations, a most notable one being that their measurements are more dependent on human operation and more susceptible to error than those with ECG-gated MPI.[16] The only way to evaluate the accuracy of LVEF measurement, as a function of the dose level, would be with the use of a calibrated dynamic phantom, but this is difficult to set because dynamic phantoms are complex to build and validate, costly, and not as available as static phantom. Jin et al. were able to reduce the administered activity to a quarter of the reference and still have diagnostic quality images when an algorithm that exploit the temporal correlation among the gated frames is used.[17]

The goal of the optimization of reconstruction strategy of ECG-gated images can be to reproduce the EF values of the 100% dose level and conventional reconstruction, as in this case, the conventional normal limit can be used.

SPECIFIC DATABASE OF NORMALITY FOR THE RECONSTRUCTION STRATEGY AND DOSE LEVEL OF THE STUDY

The perfusion scores, such as TPD, are based on the evaluation of the differences between the patient-specific distribution of myocardial counts and the corresponding mean in normal population as a function of normal variability. Both normal mean and its variability depend on a number of factors, including patient related factors, image reconstruction algorithm and image noise. Thus, a potential limitation of this quantitative approach is the need for system-specific, protocol-specific, dose-specific, and gender-specific databases of normality.[18]

Very recently, different studies have shown that to compare data from the analysis of polar maps across different systems or different configuration of the same system will require the adoption of specific databases of normality, developed for each system and reconstruction method employed.[19,20]

On the contrary, if the database of normality should be specific also for the dose level of the study is still an open question today. With the creation of normal databases that are specific for the low-dose studies, the noise in the normal polar maps and in the patient-specific polar map would be similar and consequently the software would be ''more conservative'' in estimating perfusion abnormalities.[21] However, results from an experimental phantom study found that the regional normalized tracer uptake is maintained across all count densities up to a quarter of a standard study count statistic with conventional gamma cameras and IRR algorithms.[19]

DOSE REDUCTION IN OBESE POPULATION UNDERGOING MPI STUDIES

In obese patients, myocardial perfusion imaging has some drawbacks that are related to the limited physical abilities of the subjects that may limit the sensitivity of the technique and to the artifacts due to attenuating tissue that hampers the detection of gamma photons, limiting its specificity. Although attenuation correction strategies based on X-ray computed tomography is an appealing possibility to overcome this limitation, its use is still controversial[22] and justified, in relation to patient dose, only when a stress-first imaging protocol is scheduled.[23]

To limit the count artifacts in obese patients, the activity have to be injected as a function of the body weight or BMI,[24] resulting in higher doses in the obese population respect to normal-weight subjects (see also Ref. [7]). We recently found that the reduction of the injected activity beyond 50% of the reference were associated with a worsening of the diagnostic judgment of the MPI investigation in overweight or obese patient.[9] We used the same vendor reconstruction parameters and databases of normality for all the dose level of the study and for both normal-weight and overweight groups of patients. An optimization of iterative reconstruction strategy different for normal-weight and obese patients could potentially produce better results. Patients characteristics have to be taken into account in the research studies of the limit of reducing patient doses in MPI studies with general purpose gamma camera and IRR algorithms.

Further investigations are need in relation to the extent to which the patient dose can be reduced using the new technology and in the presence of obese patients.

Disclosures

The authors declare that they have no conflict of interest.

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