Cardiac atrial metabolism quantitative assessment with analog and digital TOF-PET/CT

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Abstract

Background: Evaluation of left atrial (LA) remodeling is becoming increasingly relevant in understanding several pathological cardiac conditions. While ^{18}F-FDG-PET/CT is currently the gold standard for metabolic evaluation of the left ventricle, it could be extended to LA metabolism evaluation using the latest PET technologies. We sought to perform a phantom study in order to determine the most appropriate advanced reconstruction algorithm in this context.

Methods: The liver, heart cavity and walls of an anthropomorphic phantom were filled with typical patient ^{18}F-FDG activity concentrations. Acquisitions were performed on an analog and on a digital TOF-PET/CT, and reconstructed with and without resolution recovery (RR). For the RR the Richardson-Lucy method was used, either as a post processing of the reconstructed images through a third-party plug-in software, or through the algorithm implemented by the PET/CT manufacturer. Activity recoveries in the atria and ventricles and signal-to-noise ratios were evaluated to rate the reconstructions and identify the best reconstruction and RR parameters. The same methodology was applied on a patient cardiac study to validate the phantom results.

Results: Analog PET/CT with third-party RR cannot improve the activity recovery without markedly degrading the image quality. For the digital PET/CT, the manufacturer RR reconstruction improved LA activity recovery from about 58% to about 70% when using 4 iterations and 15 subsets combined with a 5 RR iterations, while preserving images of diagnostic quality. Similar results were obtained on the SUV values for the patient study.

Conclusions: The digital TOF-PET/CT combined with the manufacturer reconstruction with 4 iterations and 15 subsets together with 5 RR iterations can be used to quantitatively analyze the LA uptake in patient ^{18}F-FDG heart studies while still preserving image reading quality. This may lead to more precise cardiovascular disease status evaluation, especially when atria are concerned.

Background

The prognostic value of the left atrium (LA) remodeling as biomarker of outcome in several cardiovascular diseases, such as atrial fibrillation or heart failure with preserved ejection fraction, is becoming increasingly recognised [1]. Echocardiography, cardiac magnetic resonance or cardiac computed tomography have emerged as interesting non-invasive imaging techniques able to evaluate left atrial remodeling in response to electrical, mechanical or metabolic stressors [2, 3]. On the other hand, LA remodeling can also be characterized from his metabolic changes observed by ^{18}F-FDG imaging with PET/CT [4–6]. In fact, this modality is currently the gold standard for metabolic evaluation of the left ventricle and recently, it has been suggested that, despite the thinness of the LA wall, LA metabolism evaluation is also feasible using the latest PET camera technologies [7, 8].

The last decade has seen the development of PET/CT systems along two axes that leaded to improvement of the spatial resolution. The first one is the strong improvement of the timing resolution from about 650 ps in the first time of flight (TOF)-PET/CT commercialized by Philips [9] to about 300 ps and even less in the last TOF-PET generations [10–12] (partially thanks to the use of digital SiPM detectors). The second one is the improvement of dedicated reconstruction algorithms using TOF and point spread function (PSF) information [10–13].

Consequently, the purpose of this cardiac phantom study was twofold: first, to compare images quality and uptake quantification obtained on an analog (first generation) and on a digital (last generation) LYSO TOF-PET/CT and, secondly, to determine the most appropriate advanced TOF + PSF reconstruction algorithm to quantify the LA uptake. The methodology was also evaluated clinically on one patient imaged with ^{18}F-FDG on both PET systems.

Methods

Phantoms

An anthropomorphic Heart/thorax phantom (Radiology Support Devices, Inc, Long Beach, CA, USA) was used, whose liver, heart cavity and walls were filled with typical ^{18}F-FDG activity concentrations observed in patient studies, i.e., 5, 3.8 and 15 kBq/ml, respectively. The heart part of the phantom has only 2 fillable regions: the cavities (about 284 ml) and the walls (about 183 ml excluding the defects volumes). It also includes 2 unremovable defects of about 14 and 42 ml within the walls. The defect located in the interventricular septum (42 ml) was filled with the same ^{18}F-FDG concentration as the heart walls, while the defect in the lateral wall of the left ventricle (14 ml) was only filled with water.

One bed position acquisitions of 10 minutes were performed, first using the analog camera (Philips Gemini TF64 TOF-PET/CT - Philips Healthcare, Cleveland OH) and then, immediately after, using the digital one (Philips Vereos TOF-PET/CT - Philips Healthcare, Cleveland OH).

Reconstruction

List file data were reconstructed with a 2mm voxel size using standard manufacturer OSEM algorithms with different numbers of iterations and subsets without and with RR. Images were first reconstructed using OSEM algorithms with the recommended manufacturer parameters, i.e. 3 iterations and 33 subsets for the analog camera and 2 iterations and 15 subsets for the digital camera, respectively. As only the digital PET/CT includes a manufacturer PSF RR correction based on the Richardson-Lucy method, a post-reconstruction PSF RR based on the same technique, implemented as a plug-in of the open source ImageJ software [14, 15], was also tested on the reconstructed images of both TOF-PET/CT.

The ImageJ RR plug-in has only one input parameter, i.e. the PSF FWHM that we measured for both PET systems using a ^{18}F point source set at the FOV center. In contrary, the manufacturer RR method includes a spatially variant PSF library and has 2 input parameters: a RR iteration number and a regularization factor [13]. For the digital PET, in addition to the standard manufacturer reconstruction without RR, we performed 3 reconstructions with the PSF RR method by setting the RR iteration parameter equal to 1, 5 and 10. The regularization parameter was not changed and was equal to 6 in all cases.

Activity recovery assessment

Due to the low dose CT scan, as routinely used for patients, jointly to the close HU values of plexiglass and water, automatic drawing of the VOIs based on a threshold was not possible. So volumes of interest (VOI) were manually drawn around the right (RA) and left atria (LA) and ventricles (RLV) on the CT image. Measured ^{18}F-FDG activity concentrations in the atria and ventricles walls were compared to exact values to assess the activity recovery.

These CT VOIs were applied on the PET images to assess the walls activity, whatever the analyzed PET reconstruction (no adaptation of the VOIs to the PET activity was performed) to avoid introduction of a bias in the quantitative comparison between reconstructions with and without RR.

Signal to noise ratio assessment

To evaluate and compare the PET images reading quality, signal to noise ratio (SNR) values were measured from a VOI obtained by using a 9 kBq/ml threshold, i.e. the mean activity concentration of the heart cavity and walls, on the PET original image, i.e. without RR, resulting in a volume including both the atria and ventricles walls. The SNR was evaluated from the VOI by dividing the mean counts value by the standard deviation (SD).

Patient

To validate the phantom results, one patient of the ongoing prospective study TRIATLON (EudraCT number 2019-001813-17) was acquired on both TOF-PET/CT and these data were analyzed similarly to the phantom data. The TRIATLON study was approved by the Institutional Ethics Committee of Brussels Cliniques Universitaires Saint-Luc, and all patients provided written informed consent.

One bed position acquisition of 10 minutes was performed on the Vereos 90 minutes after intravenous injection of about 8 mCi of ^{18}F-FDG, then repeated directly after on the Gemini. Acquisitions were non gated and reconstructed with a 2mm voxel size using 3 iterations and 33 subsets for the Gemini and 4 iterations and 15 subsets for the Vereos acquisition, respectively.

As for a patient the actual uptakes are unknown, the activity recovery and SNR assessments were replaced by the measures of the SUV mean and SD values of the considered VOI.

Results

Phantoms

The PET images of the anthropomorphic phantom acquired on the analog and on the digital PET/CT are depicted on Fig. 1. The reconstructions without RR already clearly show the better image quality (less noise and better delineation of the walls) provided by the digital TOF-PET/CT (Fig. 1D) versus the analog one (Fig. 1A) due to its improved physical characteristics [10, 11]. As expected from deconvolution techniques [16], such as the ImageJ plug-in Richardson-Lucy method [14, 15] (Fig. 1B and 1E), the spatial resolution improvement (characterized by the appearance of a thinner wall) is accompanied by an image noise increase, especially in the case of the analog PET/CT (Fig. 1B). For the digital PET/CT (Fig. 1F), the manufacturer reconstruction RR algorithm which includes the spatially variant PSF, appears to provide, in 5 iterations, a spatial resolution as good as the ImageJ RR method together with a less noisy image appearance.

As seen on Fig. 2, VOIs were manually drawn around the right and left atria and around the ventricles walls of the cardiac phantom. The defect located in the lateral wall of the left ventricle and the remaining air bubbles in the phantom walls were excluded from the VOIs.

As we are looking for the best imaging technique for atrial uptake evaluation, we optimized the reconstruction parameters only for the images obtained with the Vereos digital TOF-PET/CT. The convergence of the LA activity recovery as a function of the reconstruction iteration number is displayed on Fig. 3A. Similar curves are obtained for the RA and RLV activity recoveries with slightly different absolute values (data not shown). For all reconstructions, the convergence of the activity recovery is reached at about 60 OSEM iterations. The maximum LA activity recovery increases from about 58% without RR to about 74% with a 10 iterations RR.

Figure 3B shows that the SNR in the digital PET final image is impacted by both the reconstruction and the RR iteration numbers.

We choose as best reconstruction parameters, 4 iterations x 15 subsets for the OSEM algorithm and of 5 iterations for the manufacturer RR algorithm (we will later discuss this choice).

Table 1
Activity recoveries for the right and left atria and ventricles walls together with the SNR for the standard manufacturer reconstructions on the Gemini and Vereos TOF-PET/CT, without RR, with ImageJ RR and, for the Vereos, with the manufacturer PSF RR.

		Activity recoveries (%)			**SNR**
TOF-PET/CT	Reconstruction	Left atrium	Right atrium	Ventricles	
Gemini	without RR	60	63	74	6.8
3 it x 33 subs	with third party RR	73	71	81	3.9
Vereos	without RR	58	57	72	8.9
4 it x 15 subs	with ImageJ RR	68	66	78	5.1
	with 5 it PSF RR	70	71	80	5.6

Table 1 illustrates the quantitative impact of the RR correction on the activity recoveries in the right and left atria and ventricles walls and on the image quality for both TOF-PET/CT. Standard reconstruction parameters were used for the Gemini while optimum values were selected for the Vereos. As seen on Fig. 1, using a RR method leads to an improved spatial resolution, and as a consequence to an improved activity recovery, whatever the TOF-PET/CT considered. However, the SNR, quantifying the image quality, is already worse in the analog PET image without RR and drops strongly after applying the ImageJ RR. Using the selected optimum set of manufacturer RR reconstruction parameters for the digital TOF-PET/CT provides improved activity recoveries of about 70% for the atria and 80% for the ventricles, i.e. about the same as the ImageJ RR method, but with a drop of only 37% of the SNR versus 43% with the ImageJ RR.

Patient

Figure 4 compares the PET images of one patient FDG cardiac studies on the Gemini and Vereos TOF-PET/CT and reconstructed using OSEM algorithms with the standard 3 iterations and 33 subsets for the Gemini and the optimized 4 iterations and 15 subsets for the Vereos, respectively. Like for the phantom images, the Vereos reconstruction without RR is clearly superior to the Gemini one, as can be seen from the hardly visible left atrium wall and interatrial septum on the Gemini image (Fig. 4A). On the Vereos images, the atria walls become better defined after RR, with the manufacturer spatially variant PSF method providing the best results in terms of image quality (Fig. 4F).

Table 2

provides a quantitative analysis of the patient cardiac PET reconstructions. The RR increases the mean SUV but also the SD, as expected from the phantom results (Table 1). Like for the heart phantom, the manufacturer spatially variant PSF RR reconstruction available on the Vereos TOF-PET/CT provides the best compromise between the atria uptake improvement and the noise level increase, i.e. highest mean SUV associated with SD values similar to the ImageJ RR.

		Left atrium		Right atrium		Left ventricle	
TOF-PET/CT	Reconstruction	Mean SUV	SD SUV	Mean SUV	SD SUV	Mean SUV	SD SUV
Gemini	without RR	2.16	0.87	1.95	0.54	11.84	2.92
3 it x 33 subs	with third party RR	2.26	1.45	2.33	1.01	13.49	4.52
Vereos	without RR	2.13	0.64	2.10	0.59	11.27	2.49
4 it x 15 subs	with ImageJ RR	2.24	1.03	2.37	0.93	12.59	3.68
	with 5 it PSF RR	2.44	0.99	2.50	0.90	13.84	3.71

Table 2: SUV mean and standard deviation (SD) values for the right and left atria and left ventricle walls of a patient cardiac study for the manufacturer reconstructions on the Gemini and Vereos TOF-PET/CT, without RR, with ImageJ RR and, for the Vereos, with the manufacturer PSF RR.

Discussion

To the best of our knowledge, it is the first time that a phantom study is performed to identify the best reconstruction algorithm to compare the LA uptake in patient cardiac FDG studies between an analog and a digital TOF-PET/CT. As the older analog TOF-PET/CT system does not include any RR option in the reconstruction algorithm, a third party post-reconstruction RR based on the Richardson-Lucy method was considered.

While a third party post-reconstruction RR method clearly improves the spatial resolution and cardiac walls activity recoveries by using a constant PSF (see figure 1 and table 1), it is not optimized to the PET image specificities like the manufacturer algorithm that includes a RR that takes into account the variations of the PSF according to the location in the field of view [13]. This results in noisier images, especially in the case of the analog TOF-PET/CT whose original reconstruction is already more impacted by noise (figure 1). Noisier images will result in less reliable activity measurements as very sensitive to the VOIs drawing. It should then be recommended to use the best TOF-PET/CT available to perform this kind of quantitative studies.

Figure 3B shows, for the Vereos TOF-PET/CT, that when no RR or only a light RR (only 1 iteration) is performed, the SNR behaves like an increasing function of the LA activity recovery, while for higher RR iteration numbers, it becomes a decreasing function. This induces that a compromise has to be made between the LA activity recovery and the image reading quality. A post filtering of the image is still possible to make a noisier image more readable. However, one should be careful when pushing the RR algorithms too far (disregarding the SNR) as one might end up with artefactual images that are no more representative of the activity distribution, typically by producing edge artefacts [18,19].

Based on the evaluation of the image quality by our nuclear medicine physicians, we selected as best reconstruction parameters of the OSEM algorithm the values of 4 iterations and 15 subsets as these values correspond to the beginning of the convergence plateau of the activity recovery (see figure 3A), and higher values lead to noisier images. For the manufacturer RR parameters we decided to limit the number of iterations to 5 as the SNR drops quite fast for higher values (see figure 3B). In the present study we did not play with the regularization parameter of the manufacturer RR algorithm that was fixed to the recommended value of 6. Optimizing this parameter, whose function is to drive the image smoothness, might still improve the image quality by reducing the noise level but we do not expect it to alter much the optimized set of parameters found in the present quantitative study. Together these parameters provide a LA activity recovery of about 70%.

The FDG cardiac studies performed on both TOF-PET/CT with the same patient nicely confirmed the results obtained with the phantom. Compared to the phantom the patient heart was about 10 percent larger, but ventricular and atrial wall thicknesses were very similar, with values measured on RMI between 0.9 and 1.5 cm for the LV and between 1 and 3 mm for the LA. The limited spatial resolution of the Gemini PET makes it unfit to study the atria metabolism as the atria walls and interatrial septum are hardly seen on the reconstructed images (see figure 4). On the other hand, these structures are already visible on the Vereos reconstruction without RR, and become sharper when using a RR algorithm. The manufacturer reconstruction including the PSF RR still provide a better image quality compared to post-reconstruction RR (see figure 4 and table 2).

Unlike the cardiac phantom filled in the present study with a homogeneous activity distribution in the walls, patients may suffer from pathologies inducing heterogeneities in RA or LA uptake. However, resolution recovery methods tend to reconcentrate the detected activity in the regions where it originates. If heterogeneities larger than the spatial resolution of the PET system are located in the RA or LA walls, they will still be visible after RR.

One limitation of the present study is that patient motions, like breathing and cardiac motions, were not taken into account. The heart motion impact on the present results is difficult to evaluate. Using cardiac gating acquisition would help the quantification with the RR method applied on each gated bin separately, and afterwards summing together the activities of the bins in order to recover the non-gated statistics. Without gating the RA and LA walls on the PET image are enlarged by the heart motion. The RR cannot correct for that motion but it will still bring back the activity in that enlarged wall, improving the quantification as anyway in that case the VOIs will have to be enlarged too to take the motion blurring into account.

As the reconstruction algorithms with RR, seen as black-boxes by the end user, might strongly differ between manufacturers, the optimized parameters found in this study are only adapted to the Philips Vereos TOF-PET/CT. The observed trends for the activity recovery and for the SNR convergences would probably be similar for other systems but this needs to be checked per TOF-PET/CT system in order to extract the best set of reconstruction parameters.

Conclusions

The Philips Vereos TOF-PET/CT images reconstructed with the manufacturer 4 iterations/15 subsets OSEM algorithm including a PSF RR with 5 iterations/6 regularization can be used to quantitatively analyze the left atrium uptake in patient ^{18}F-FDG heart studies while still preserving image reading quality. This may lead to more precise evaluation of the metabolic cardiac status of cardiovascular disease, especially when atria are concerned.

Abbreviations

LA: Left atrium

RA: Right atrium

RLV: Right and left ventricles

TOF-PET/CT: Time of flight positron emission tomography/computed tomography

PSF: Point spread function

OSEM: Ordered subset expectation maximization

SUV: Standardized uptake value

SD: Standard deviation

FDG: Fluoro-deoxy-glucose

VOI: Volume of interest

Declarations

Ethics approval and consent to participate

All patients provided written informed consent. The TRIATLON study was approved by the Institutional Ethics Committee of Brussels Cliniques Universitaires Saint-Luc.

All methods were carried out in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MH has performed the phantom scans and analysed the corresponding data. SM, BG and VR have managed the patient scans of the TRIATHLON study, and analyzed the patient data. MH and VR have written the article. All authors read and approved the final manuscript.

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Figures

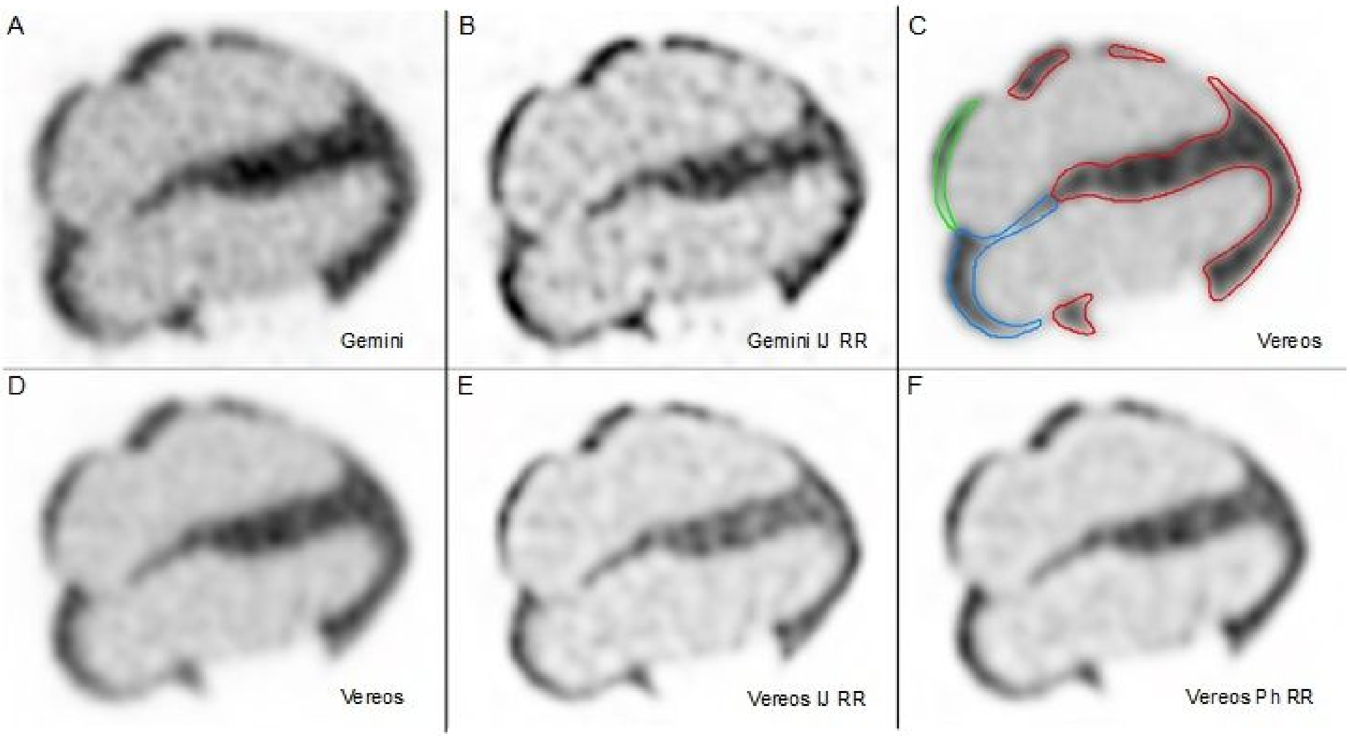

Figure 1

PET reconstructions of the heart insert of the anthropomorphic phantom. A,B: Gemini acquisition; D,E,F: Vereos acquisition. A,D: standard manufacturer reconstructions; B,E: reconstructions with ImageJ (IJ) RR; F: standard manufacturer reconstruction including Philips (Ph) RR with 5 iterations/6 regularization; C: manually drawn VOIs around the left atrium (blue), the right atrium (green) and the ventricles (red) shown on the standard Vereos image

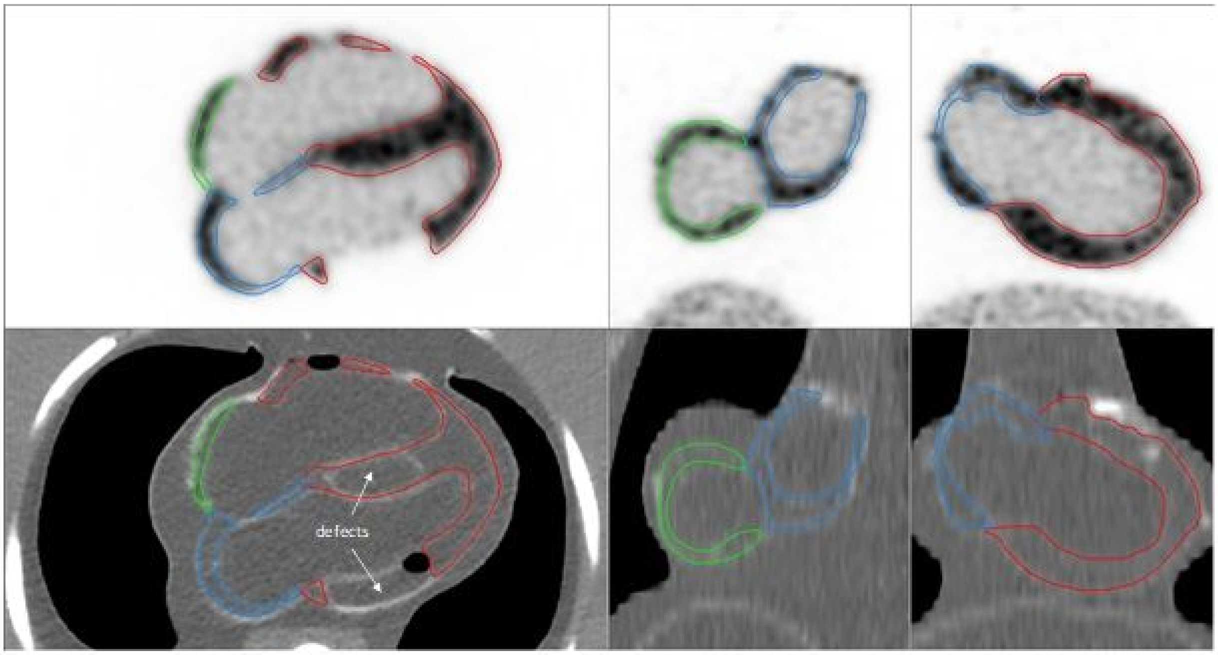

Figure 2

PET reconstructions of a patient FDG cardiac study. A,B: Gemini acquisition; D,E,F: Vereos acquisition. A,D: manufacturer reconstructions; B,E: reconstructions with ImageJ (IJ) RR; F: optimized manufacturer reconstruction including Philips (Ph) RR with 5 iterations/6 regularization; C: manually drawn VOIs around the right (in green) and left (in blue) atria shown on the standard Vereos image

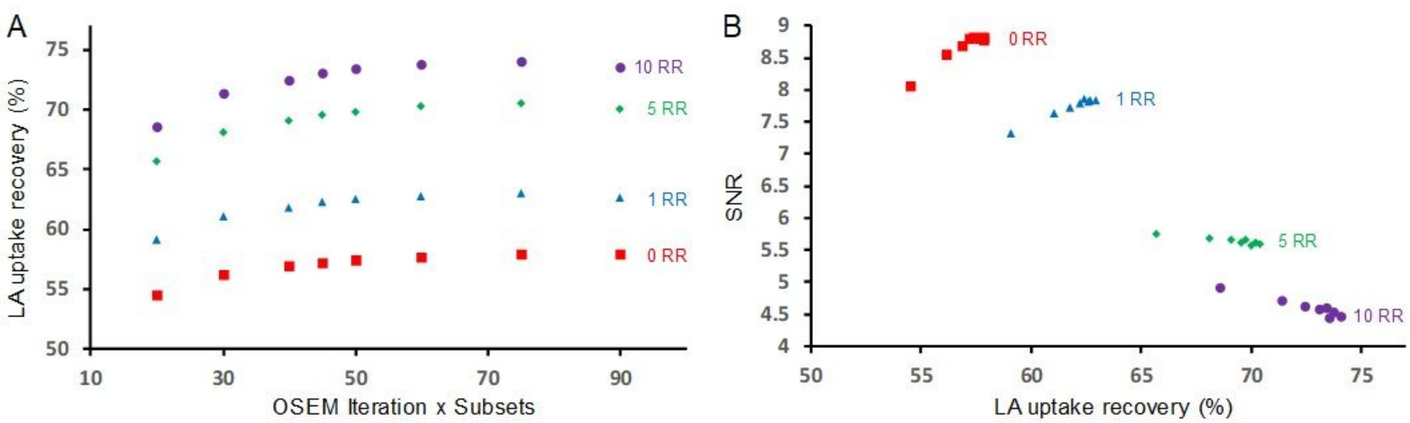

Figure 3

A: Activity recovery values for the left atrium wall as a function of the iteration number of the reconstruction OSEM algorithm for the digital acquisition. B: SNR value with respect to the LA wall activity recovery. Red squares correspond to the reconstruction without RR (0 RR). Blue triangles, green diamonds and purple circle dots correspond to the reconstruction with the manufacturer RR using 1, 5 and 10 RR iterations, respectively

Figure 3B shows that the SNR in the digital PET final image is impacted by both the reconstruction and the RR iteration numbers.

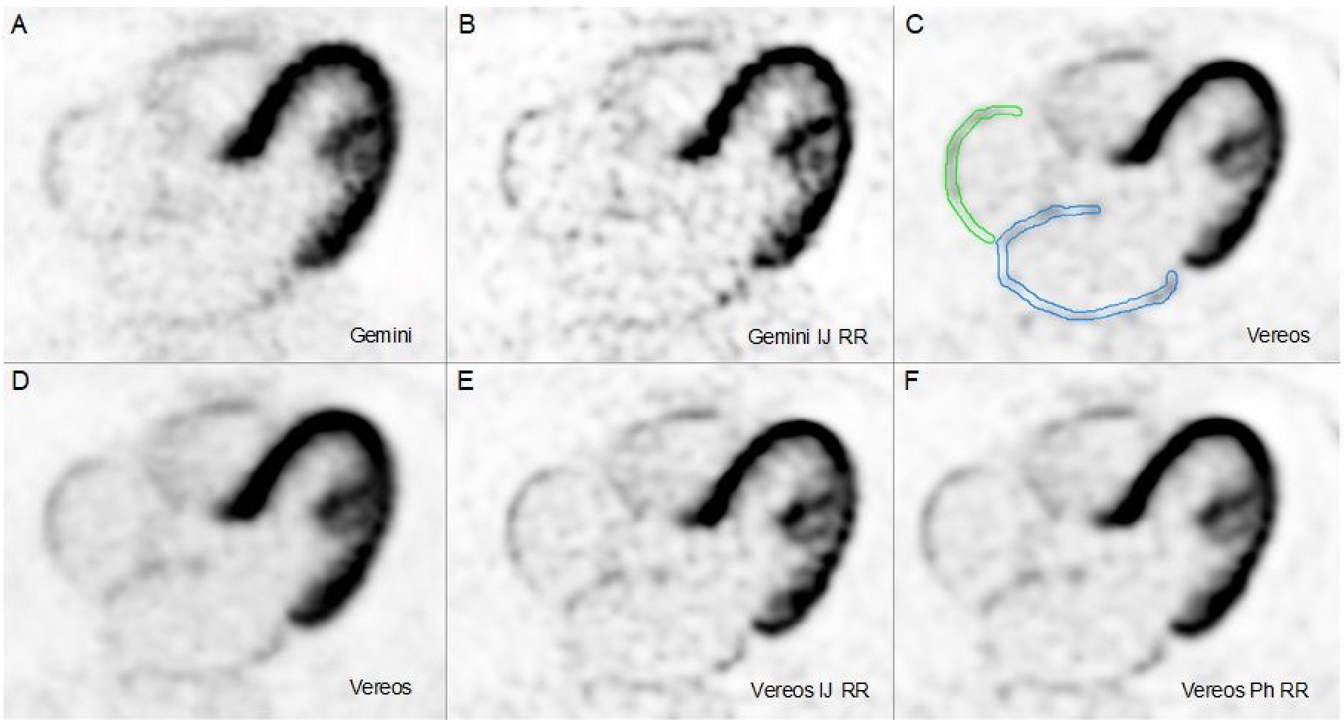

Figure 4

PET reconstructions of a patient FDG cardiac study. A,B: Gemini acquisition; D,E,F: Vereos acquisition. A,D: manufacturer reconstructions; B,E: reconstructions with ImageJ (IJ) RR; F: optimized manufacturer reconstruction including Philips (Ph) RR with 5 iterations/6 regularization; C: manually drawn VOIs around the right (in green) and left (in blue) atria shown on the standard Vereos image