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Joint Reconstruction of rest/stress Myocardial Perfusion SPECT

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Abstract

Myocardial perfusion imaging (MPI) using rest/stress single photon emission computed tomography (SPECT) allows non-invasive assessment of reversible cardiac perfusion defects. Conventionally, reversible defects are identified using a difference image, called reversible map, obtained by subtracting the stress image from the rest image after registration and normalization of the two images. The identification of reversible defects using the conventional subtraction method is however limited by noise. We propose to jointly reconstruct rest and stress projection data to directly obtain the reversible map in a single reconstruction framework to improve the detectability of reversible defects. To evaluate the performance of the proposed method, we performed phantom studies to mimic reversible defects with different levels of severity and doses. As compared to the conventional subtraction method, the joint method yielded reversible maps with much lower noise and improved defect detectability. At a normal clinical dose level, the joint method improved the signal to noise ratio (SNR) of defect contrast in reversible maps from 13.2 to 66.4, 9.7 to 35.0, 6.1 to 13.2, and 3.1 to 6.5, for defect to normal myocardium concentration ratios of 0%, 25%, 50%, and 75%, respectively. The SNRs obtained using the joint method were improved from 6.1 to 13.2, 3.9 to 9.4, 3.0 to 8.0, and 2.1 to 7.1, for 100%, 75%, 50%, and 25% of the normal clinical dose as compared to the conventional subtraction method. To access clinical feasibility, we applied the joint method to a rest/stress SPECT MPI patient study. The joint method yielded a reversible map with much lower noise, translating into a much higher defect detectability as compared to the conventional subtraction method. Our results indicate that the joint method has the potential to improve radiologists' performance for assessing defects in rest/stress SPECT MPI. In addition, the joint method can be used to reduce dose or imaging time.

Keywords

joint reconstruction; reversible defects; rest/stress SPECT; myocardial perfusion imaging

1. Introduction

Coronary artery disease (CAD) is the most common type of heart diseases and the leading cause of death worldwide. Myocardial perfusion imaging (MPI) using single photon emission computed tomography (SPECT) allows non-invasive evaluation of CAD by detecting flow-limiting defects. Although MPI acquisition protocols have evolved in recent years, rest/stress MPI remains the standard practice [1]. In a standard rest/stress protocol, a patient is imaged twice: once at rest and the other after the patient is stressed either by

exercise or by pharmacological stimulation. The main advantage of acquiring both rest and stress images is that it allows differentiating ischemic (reversible defect) from scarred (non-reversible defect) myocardial tissue. Such differentiation plays an important role in clinical decision-making because reversible defects can recover their function following coronary revascularization, whereas non-reversible defects do not [2]. Reversible defects typically show perfusion deficits in stress images but not in rest ones. To improve the detectability of reversible defects, radiologists commonly use a difference image, called reversible map, which is obtained by subtracting the stress image from the rest image after registration and normalization of the two images [3, 4, 5]. However, such method, denoted conventional subtraction method in this paper, leads to amplified noise level and degraded defect detectability in the difference image.

Extending our previous works on dual-radionuclide SPECT [6, 7, 8] and joint reconstruction of ictal/inter-ictal SPECT [9], we propose to jointly reconstruct rest/stress projection data to directly obtain the difference image. This joint reconstruction approach circumvents the need to subtract stress from rest images and allows one to preserve Poisson noise modeling in the projection space, which is critical to the image quality of the reconstructed difference images. In this paper, we evaluated the performance of our joint reconstruction method as compared to the conventional subtraction method using both phantom and patient studies.

2. Materials and Methods

2.1. Conventional Subtraction

The conventional subtraction method (illustrated in Fig. 1) consists of three steps. First, rest and stress projection data are reconstructed separately to obtain rest and stress image volumes, respectively, using ordered subset expectation maximization (OSEM). Second, the difference image volume, $\hat{\mathbf{x}}^{(D)}$, is computed using:

$$\hat{\mathbf{x}}^{(D)} = \alpha \hat{\mathbf{x}}^{(R)} - \mathbf{R} \hat{\mathbf{x}}^{(S)}, \quad (1)$$

where $\hat{\mathbf{x}}^{(R)}$ and $\hat{\mathbf{x}}^{(S)}$ are the reconstructed rest and stress image volumes, respectively, α is the normalization factor between the two volumes, and $\mathbf{R}$ is the transformation matrix that registers $\hat{\mathbf{x}}^{(S)}$ to $\hat{\mathbf{x}}^{(R)}$ using Demons non-rigid image registration algorithm [10, 11, 12, 13].

2.2. Joint reconstruction

For the joint method (illustrated in Fig. 1), both the stress and the difference image volumes are estimated directly from rest and stress projection data in a single reconstruction step. The forward model is given by:

$$\bar{\mathbf{y}} = \begin{bmatrix} \bar{\mathbf{y}}^{(R)} \\ \bar{\mathbf{y}}^{(S)} \end{bmatrix} = \begin{bmatrix} \beta \mathbf{A}^{(R)}, & \beta \mathbf{A}^{(R)} \\ 0, & \mathbf{A}^{(S)} \mathbf{R} \end{bmatrix} \begin{bmatrix} \mathbf{x}^{(D)} \\ \mathbf{x}^{(S)} \end{bmatrix}. \quad (2)$$

The joint Poisson noise model is given by:

$$P(\mathbf{y} | \mathbf{x}) = P(\mathbf{y}^{(S)}, \mathbf{y}^{(R)} | \mathbf{x}^{(D)}, \mathbf{x}^{(S)}) \quad (3)$$

$$= \prod_i^I \exp(-\bar{y}_i^{(S)}) \frac{(\bar{y}_i^{(S)})^{y_i^{(S)}}}{y_i^{(S)}!} \times \prod_i^I \exp(-\bar{y}_i^{(R)}) \frac{(\bar{y}_i^{(R)})^{y_i^{(R)}}}{y_i^{(R)}!}.$$

In Eqs. 2 and 3, $\mathbf{x} = [\mathbf{x}^{(D)}, \mathbf{x}^{(S)}]^T$; $\mathbf{x}^{(S)}$ is the stress image; $\mathbf{x}^{(D)}$ is the difference image; $\mathbf{y}^{(S)}$, $\mathbf{y}^{(R)}$ and $\mathbf{y}^{(R)}$ are the estimated stress, measured stress, estimated rest, and measured rest projections, respectively; $\mathbf{y} = [\mathbf{y}^{(D)}, \mathbf{y}^{(S)}]^T$; β is the reciprocal of the scale factor in Eq. 1, *i.e.*, $\frac{1}{\alpha}$; $\mathbf{R}$ is the transformation matrix, the same as the one in Eq. 1; $\mathbf{A}^{(R)}$ and $\mathbf{A}^{(S)}$ are the system response matrices for rest and stress studies, respectively. An element of system matrix $\mathbf{A}^{(R)}$ or $\mathbf{A}^{(S)}$ represents the probability that a photon emitted from a voxel is detected at a pixel in the absence of scatter. The system matrix includes the detector point spread function (PSF) and the attenuation in the imaging object if attenuation correction is applied. The PSF is a 2-dimensional projection pixel matrix. The projection pixel matrix for the detector PSF consists of 31×31 pixels. The detector PSFs were simulated by using a point source in air for 32 distances from the collimator (32 bins from 0.4 to 63.6 cm) [6]. All the physical processes in the detector materials, including penetration and scatter in the collimator, the NaI(Tl) crystal, and in the materials behind the crystal, were modeled. PSF can be different if the rest and stress studies are performed in two different scanners. Also, if attenuation correction is applied, the attenuation could be different because of patient motion. For this work, because both rest and stress studies were performed on the same scanner and no attenuation correction is applied, the system matrices of the rest and stress studies are the same.

The joint stress image, $\hat{\mathbf{x}}^{(S)}$, and difference image, $\hat{\mathbf{x}}^{(D)}$ are estimated using

$$[\hat{\mathbf{x}}^{(D)}, \hat{\mathbf{x}}^{(S)}]^T = \underset{[\mathbf{x}^{(D)}, \mathbf{x}^{(S)}]^T}{\operatorname{argmax}} \{ \log [P(\mathbf{y} | \mathbf{x})] \}, \quad (4)$$

where $\hat{\mathbf{x}}^{(S)}$ and $\hat{\mathbf{x}}^{(D)}$ are the same as in Eq. 3

We used OSEM to iteratively find the solution for Eq. 4:

$$\hat{\mathbf{x}}^{(S), n+1} = \frac{\hat{\mathbf{x}}^{(S), n}}{\beta(\mathbf{A}^{(R)})^T \mathbf{1} + \mathbf{R}^T(\mathbf{A}^{(S)})^T \mathbf{1}} \left[(\mathbf{A}^{(R)})^T \frac{\mathbf{y}^{(R)}}{\mathbf{A}^{(R)}(\hat{\mathbf{x}}^{(S), n} + \hat{\mathbf{x}}^{(D), n})} + \mathbf{R}^T(\mathbf{A}^{(S)})^T \frac{\mathbf{y}^{(S)}}{\mathbf{A}^{(S)}\mathbf{R}\hat{\mathbf{x}}^{(S), n}} \right] \quad (5)$$

$$\hat{\mathbf{x}}^{(D),n+1} = \frac{\hat{\mathbf{x}}^{(D),n}}{\beta(\mathbf{A}^{(R)})^T \mathbf{1}} \left[(\mathbf{A}^{(R)})^T \frac{\mathbf{y}^{(R)}}{\mathbf{A}^{(R)}(\hat{\mathbf{x}}^{(S),n} + \hat{\mathbf{x}}^{(D),n})} \right]. \quad (6)$$

In Eqs. 5 and 6, $\mathbf{1}$ is a vector consisting of 1s, $\hat{\mathbf{x}}^{(S),n}$ and $\hat{\mathbf{x}}^{(D),n}$ are the jointly estimated stress and difference images, respectively, at the n^{th} iteration.

For all the studies, we used 5 and 20 iterations for the conventional subtraction method and the joint method, respectively. More iterations were used in the joint method because the joint method yielded slower convergence than the conventional subtraction method (See Fig. 3). Eight subsets were used for all the cases.

2.3. Phantom Studies

We used a dual-head Symbia SPECT scanner in a 90° detector configuration. The camera was equipped with low energy high resolution collimator (LEHR) and operated in a standard non-circular step-and-shoot cardiac protocol, in which the gantry was adjusted according to the contour of the imaging object so that the detectors were positioned as close as possible to the object. Both detectors collected projection data in an energy window of 129–150 keV and rotated 90° with 32 steps. The projection data included a total of 64 views of 64×64 matrices with a pixel size of $6.6 \times 6.6 \text{ mm}^2$.

We used an anthropomorphic torso phantom (Data Spectrum Corporation, Hillsborough, NC), which consists of eight compartments: myocardium, myocardial defect (3.8 mL volume), ventricle cavity, left/right lungs, liver, soft-tissue background, and a non-fillable spine. We acquired two virtually “noise-free” projection data sets, denoted P_1 and P_2 , at the exact same bed position:

1. The myocardial defect was filled with 6.45 mCi $^{99\text{m}}\text{Tc}$ while all other compartments were filled with “cold” water. About 18 million counts were collected.
2. The myocardial defect was filled with “cold” water, while the myocardium, ventricle cavity, left/right lungs, liver, and soft-tissue background were filled with 0.86, 0.04, 0.68/0.76, 4.41, and 6.60 mCi $^{99\text{m}}\text{Tc}$, respectively. The resulting concentration ratios between all the compartments and the soft-tissue background are consistent with those found in a typical patient study [14]. About 203 million counts were collected. The number of counts in the heart region are 50 and 17 times as many as counts acquired in a standard clinical rest and stress studies, respectively

We mimicked realistic rest and stress studies from these two acquired data sets using the following steps:

1. We scaled P_1 so that the concentration in the defect region was the same as that in the myocardium from P_2 . Afterwards, we generated a “noise-free” rest study by combining the scaled P_1 and P_2 .

2. We scaled P_1 so that the concentration ratios (i.e., Def/Myo) between the defect and the myocardium (in P_2) became 0%, 25%, 50%, and 75%. We then combined the scaled data sets 1 and 2 to generate corresponding “noise-free” stress studies.
3. We scaled the combined rest projection data sets obtained from step 1 so that the total counts in the heart region was equivalent to 25%, 50%, 75%, and 100% of what is found in a typical rest cardiac patient study with injection dose of 10 mCi. Similarly, we scaled the combined stress projection data with Def/Myo (Stress) = 50% so that total number of counts in the heart region was equivalent to 25%, 50%, 75%, and 100% of what is found in a typical stress cardiac patient study (injection dose 30 mCi). For stress projection data sets with other Def/Myo (Stress) ratios, we only scaled them to 100% of the clinical injection dose, i.e., the full dose.
4. We generated 64 noise realizations by adding Poisson noise to each scaled projection data set obtained in step 3.

We assessed the performance of both the conventional subtraction method and the joint method by comparing the defect contrast. For both the conventional and joint methods, we defined the contrast of the i^{th} noise realization as:

$$C_i = 1 - \frac{c_i^{(B)}}{c_i^{(D)}}, \quad (7)$$

where $c_i^{(D)}$ is the counts in an ROI with a volume of $3 \times 3 \times 3$ voxels covering the defect, and the $c_i^{(B)}$ is the number of counts in the normal myocardium region with the same volume. Both $c_i^{(D)}$ and $c_i^{(B)}$ were computed using the difference image.

The mean ($\bar{C}$), standard deviation (σ), and signal to noise ration (SNR) of contrast were calculated across 64 realizations using:

$$\bar{C} = \frac{1}{n} \sum_i C_i \quad (8)$$

$$\sigma = \sqrt{\frac{\sum_i (C_i - \bar{C})^2}{n - 1}} \quad (9)$$

$$SNR = \frac{\bar{C}}{\sigma}, \quad (10)$$

where n is the total number of noise realizations, *i.e.*, 64.

In order to assess the impact of registration errors on defect detectability, we deliberately introduced a displacement ranging from 0 to 6.4 mm between the rest and stress phantom locations and computed the contrast using the difference images obtained by both the conventional and joint approaches.

2.4. Patient studies

A patient rest/stress projection data set was collected under the approval of the Institutional Review Board (IRB) at Massachusetts General Hospital (MGH). The patient, who was known to have a reversible cardiac defect in the myocardium, was administered 11 and 37 mCi Sestamibi ^{99m}Tc for the rest and stress scans, respectively. The same camera and acquisition protocol as described in the phantom studies were used. Imaging time was about 10 minutes for each scan. We reconstructed rest/stress projection data to obtain difference images using both the conventional subtraction and joint methods.

3. Results

3.1. Phantom Studies

For one of the noise realizations generated using the full dose data (30 and 10 mCi for stress and rest, respectively) and Def/Myo (Stress) ratio=0%, Fig. 2 shows the same short-axis myocardium slice through rest (top-left) and stress (top-middle) image volumes reconstructed using the standard OSEM, difference image volumes without (bottom-left) and with (bottom-middle) negative filtering using the conventional subtraction method, and stress (top-right) and difference (bottom-right) image volumes using the joint method. The joint method yielded much less noisy difference image, improving defect localization compared to the conventional subtraction method. Fig. 3 shows mean contrast and standard deviation (STD) versus iteration number computed across all the noise realizations for Def/Myo (Stress) =0% and the full dose. Although the joint method depicts slower defect contrast recovery as compared to the conventional subtraction method, both methods yielded almost the same contrast after sufficient iterations. On the other hand, the joint method yielded much less STD than the conventional subtraction method for every iteration.

For the full dose and Def/Myo (Stress) ratios of 0%, 25%, 50%, and 75%, Fig. 4 shows the same slice from difference image volumes obtained using the conventional subtraction (with non-negative filtering) and joint methods. Similar to Fig. 2, the joint method yielded lower noise and better defect localization for all the Def/Myo ratios. For both methods, the defect becomes more difficult to identify as Def/Myo (Stress) ratio increases. Fig. 5 shows SNRs computed across the 64 noise realizations obtained for each Def/Myo ratio. As expected, SNR decreases as Def/Myo ratio increases. For all the Def/Myo ratios, the joint method yields much higher SNR than the conventional subtraction method. Therefore, the joint method greatly enhances the detectability of defects.

For results generated using 100%, 75%, 50%, and 25% of the full dose and Def/Myo ratio=50%, Fig. 6 shows the same slice from the difference image volumes obtained using the conventional subtraction (with non-negative filtering) method and the joint method. For

all the dose levels, the joint method yielded less noise and better defect detectability. When the dose = 25%, it becomes difficult to localize the defect visually given the high background noise in the difference image obtained using the conventional method, while the defect could still be easily identified using the joint method. Fig. 7 shows the SNR computed across all the noise realizations obtained for each dose level. As expected, SNR decreases as dose decreases. For all the dose levels, the joint method yielded much higher SNR than the conventional subtraction method. SNR of the 25% dose using the joint method is even higher than the ones of the full dose using the conventional method.

Fig. 8 shows the same slice of the difference image for different displacements introduced, *i.e.*, registration errors. As expected, registration errors degrade the image quality for both methods. Fig. 9 shows that the contrast of defect decreases as the registration error increases. However, the joint method appears less sensitive than the conventional subtraction method as shown in both Figs. 8 and 9.

3.2. Patient studies

For the patient study, Fig. 10 shows the same difference image slice for both the conventional subtraction and joint methods. For the subtraction method, the top-left and top-middle panels show the same myocardium slice through the rest and stress image volumes, respectively; the bottom-left and bottom-middle panels show the same slice of the difference images obtained without and with negative filtering, respectively. For the joint method, the top-right and bottom-right panels show the same slice through the stress and difference image volumes, respectively. Similar to the phantom studies, the joint method yields lower noise and therefore higher defect detectability in the difference image than the subtraction method.

4. Discussion

In this paper, we applied a joint reconstruction method to rest/stress MPI to obtain a difference image volume directly from measured rest/stress projection data. Compared to the conventional subtraction method, the joint method, which accurately models noise properties of the projection data, yields lower variance, and therefore improved defect detectability, in the reversible map.

The joint method is characterized by several properties. One is that contrast convergence for the joint method is slower than that of the conventional subtraction method (See Fig. 3). Therefore, sufficient number of iterations are needed for the joint method. The other is that the residues in the background region caused by early termination of reconstruction (20th iteration) to limit the noise level will affect the detectability of the reversible defect, especially minor defects (high Def/Myo ratios). More careful and comprehensive studies are needed to provide guidance on how to select the optimal number of iterations for different scenarios. Nevertheless, because the joint method yields much lower variance than the conventional method, we can use high iteration number for the joint method without comprising the performance of defect detection.

Both the conventional subtraction and joint methods require accurate image registration between rest and stress images. Because of poor spatial resolution and high noise levels, non-rigid registration using SPECT images can be challenging, which may introduce errors in the estimated difference images. As shown in Figs. 8 and 9, registration errors can distort image quality and reduce defect detectability. The joint method appears to be less sensitive to registration errors than the conventional subtraction method. For rest/stress SPECT studies performed in a single imaging session, in which a pharmacologic stress is used, such registration naturally becomes much easier to perform. Also, if SPECT-CT studies are used for both rest and stress studies where attenuation correction (AC)-CT scans are available, one can use the AC-CT images to perform image registration to reduce the likelihood of registration errors.

The two phantom data sets, one with only the defect filled with activity and the other with all the compartments other than the defect filled with activity, allow us to mimic different Def/Myo (Stress) ratios. These two “noise-free” data sets also make it possible to mimic different dose levels and to generate multiple noise realizations. As shown in Figs. 4 and 5, the joint method yields much higher SNRs than the conventional method for all the Def/Myo (stress) ratios. The SNR for Def/Myo (Stress) = 75% using the joint method was found to be higher than that of the conventional subtraction method for Def/Myo (Stress) = 50%. Therefore, we believe that the joint method can potentially help improve the detection of minor perfusion defects in clinical practice. As shown in Figs. 6 and 7, the joint method yields much higher SNRs than the conventional method for all the dose levels. The SNR for 25% dose using the joint method was comparable to that of the conventional subtraction method for the full dose. Therefore, the joint method has the potential to reduce dose or imaging time in rest/stress SPECT MPI.

Because SPECT images typically have poor spatial resolution and high noise levels, it is sometimes challenging for radiologists to detect reversible defects in a rest/stress MPI study, especially minor defects. As shown in Fig. 4, the joint method makes reversible defects much easier to identify in the difference image compared to the conventional subtraction method. We therefore believe that if radiologists are provided with the difference image obtained using the joint method in addition to the standard rest/stress images, their performance for detecting reversible defects can be potentially improved. We will evaluate this hypothesis in our future studies using human observer studies and ROC analyses with large number of patient studies. Besides further cardiac SPECT imaging studies, our approach can be extended to rest/stress MPI using positron emission tomography (PET) [15, 16].

5. Conclusion

In this paper, we jointly reconstructed rest/stress SPECT projection data in a single reconstruction framework to directly obtain a difference image volume in which reversible defects can be identified. The results obtained in phantom and patient studies show that defect detectability is much higher than what is obtained using the conventional subtraction method for different Def/Myo (Stress) ratios and dose levels. The joint method has the

potential to enhance the detection of minor defects and to reduce dose or imaging time in rest/stress SPECT MPI.

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Figure 1.
Flow chart for both the conventional subtraction method and the joint method.

Figure 2.

Phantom images obtained using the full dose (30 and 10 mCi for stress and rest, respectively) and Def/Myo (Stress) ratio = 0%. The same short-axis myocardium slice through rest (top-left) and stress (top-middle) image volumes reconstructed using standard OSEM at 5th iteration, difference image volumes without (bottom-left) and with (bottom-middle) negative filtering using the conventional subtraction method, and stress (top-right) and difference (bottom-right) image volumes reconstructed using the joint method at the 20th iteration, are shown.

Figure 3. Contrast and standard deviation (STD) vs iteration using the full dose data (30 and 10 mCi for stress and rest, respectively) and Def/Myo (Stress) ratio=0%.

Figure 4. Difference images with various Def/Myo (Stress) ratios and the full dose. The conventional subtraction and joint methods used images reconstructed at 5th iteration and 20th iteration, respectively.

Figure 5.
SNRs of defect contrast with various Def/Myo (Stress) ratios and the full dose.

Figure 6.

Difference images at various dose levels. The difference images for 100%, 75%, 50%, 25% of the full dose and Def/Myo (Stress)=50%. The conventional subtraction and joint methods used images reconstructed at 5th iteration and 20th iteration, respectively.

Figure 7.
SNRs of defect contrast for various dose levels and Def/Myo (Stress) = 50%

Figure 8. Difference images for different displacements introduced between the rest and stress phantom locations, *i.e.*, registration errors. The full dose and Def/Myo=50% were used.

Figure 9. Defect contrast versus registration error. The x-axis is the displacement deliberately introduced between the rest and stress phantom locations.

Figure 10.

Patient images obtained using the conventional subtraction method and the joint method. The same myocardium slice through rest (top-left) and stress (top-middle) image volumes reconstructed using the standard OSEM at 5th iteration, difference image volumes without (bottom-left) and with (bottom-middle) negative filtering using the conventional subtraction method, and stress (top-right) and difference (bottom-right) image volumes using the joint method at the 20th iteration, are shown.