The impact of transmission-emission misregistration on the interpretation of SPET/CT myocardial perfusion studies and the value of misregistration correction

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Abstract

Objective: Previous studies indicate that the quality of single photon emission tomography/computed tomography (SPET/CT) myocardial perfusion imaging (MPI) is degraded by even mild transmission-emission misregistrations. The purpose of the current study was to investigate the impact of SPET/CT misalignment on the interpretation of MPI and examine the value of a commercial software application for registration correction. **Subjects and Methods**: A total of 255 technetium-99m (^{99m}Tc)-tetrofosmin stress/rest MPI examinations in 150 patients were reviewed for SPET/CT misalignment. After registration correction by the software, images were reassessed for interpretation differences from the misregistered study. The diagnostic benefit of reregistration was determined by taking into account the non-attenuation compensated image pattern, combined stress-rest evaluation, gated-SPET data and patient's history. In a phantom experiment and in 3 representative clinical cases, SPET/CT misalignment was purposely created by the software by sequential slice shifts and its effect was evaluated quantitatively. **Results**: Misregistration ≥1 pixel in at least one direction was observed in 24% of studies. Interpretation of MPI changed after registration correction in 11% of cases with misalignment <1 pixel, in 18% with 1-2 and in 73% with ≥2 pixels. The diagnostic information seemed to improve after registration correction in 58% of studies irrespective of the degree of misregistration. Software-simulated misregistration had dissimilar effects in the phantom and the 3 selected clinical cases. **Conclusion**: The impact of SPET/CT misregistration on MPI interpretation although influenced by the degree and direction of slice misplacement, it is also case-specific and hardly predictable. Registration restoration by the software seems worthwhile regardless of misregistration magnitude.

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Introduction

Attenuation correction via transmission maps has long been an integral part of positron emission tomography (PET) and is also pursued for single photon emission tomography (SPET) studies particularly after the introduction of hybrid SPET/computed tomography (CT) systems [1]. As regards myocardial perfusion imaging (MPI), the main benefit from attenuation compensation is a considerable improvement in specificity [2-4]. Accurate coregistration of emission and transmission datasets is critical for proper implementation of the correction algorithm. As emission and transmission images are acquired sequentially rather than simultaneously, alignment errors can appear as a result of patient movement or a change in the breathing pattern between acquisitions, flexing of the examining table as it moves inside the gantry and upward creeping of the heart after the cessation of vigorous stress [5].

Transmission-emission misregistration is quite common in MPI studies with reported frequencies up to 73% [6-9]. It affects regional tracer distribution in the myocardium and may give rise to artificial perfusion defects in both PET/CT [10-12] and SPET/CT MPI [7-9, 13-16] although the latter seems to be less severely affected [17]. The presence, severity and location of these false positive abnormalities relates to the magnitude and direction of misregistration. The effect is more prominent when, in fused transmission-emission images, part of the myocardium appears to superimpose on tissues of low attenuation such as the lung or mediastinal fat [5, 9]. The questions that arise in everyday practice are how serious the problem is from a diagnostic point of view and what the

threshold, if any, over which misalignment is considered significant; clinically relevant misregistration should be repaired if possible, otherwise the attenuation corrected study should be ignored. Some studies in phantoms and humans have demonstrated that even slight (1-pixel) SPET/CT misregistration can introduce artifacts in certain areas of the myocardium which may be mistaken for true perfusion defects [13, 15, 16]. These data raise concern about the specificity of attenuation-corrected SPET and contradict the favorable results obtained so far [18]. Other investigators have considered misalignment of more than 2 pixels to be clinically important, particularly when it occurs in the dorso-cranial direction (y-axis) [9]. Software tools for manual emission-transmission registration have been developed by gamma-camera manufacturers. After registration restoration a reduction in the number and size of artificial defects has been reported [7, 15, 16]. However, the correction procedure relies on visual evaluation of coregistration, is fairly reproducible and has not been adequately validated [7].

The purpose of the current study was to investigate the impact of transmission-emission misalignment in the interpretation of SPET/CT MPI and examine the value of a commercial software application for registration correction.

Subjects and Methods

Clinical series

Over a period of 4 months 160 consecutive gated-SPET/CT stress-rest ^{99m}Tc-tetrofosmin MPI studies were retrospectively evaluated. Ten studies were excluded due to motion during SPET acquisition at both stress and rest (n=5), CT truncation (n=3) or serious CT artifacts (n=2). The final study population included 112 males and 38 females (age=61.4±12.0 years, body mass index=28.6±5.7kg/cm2). The patients had been referred to our department for the evaluation of suspected or known coronary artery disease (CAD). Twenty-five percent of patients had a history of known CAD and 15% had suffered a prior myocardial infarction. All patients were subjected to adenosine stress (140μg/kg/min for 6min). One-day stress-rest protocol was followed. Technetium-99m (^{99m}Tc)-tetrofosmin was administered in the mid of adenosine infusion at a dose of 300-370MBq, while 925-1110MBq were injected at rest. Imaging took place approximately one hour post-injection. Forty-five patients had stress-only studies. In all cases, acquisition was performed with a single hybrid SPET/CT system (Infinia™ Hawkeye™ 4, GE Healthcare). The gamma camera heads were equipped with low-energy all-purpose collimators and were positioned in "L" configuration. A standard acquisition protocol was followed for gated-SPET: 60 projections (20sec/projection at stress and 15sec at rest) over an 180^0 body-contour orbit, 64x64 matrix, 1.3 zoom, 140±10% keV photopeak energy window, 120±5% keV scatter energy window, 8 frames per cardiac cycle and ±20% heart rate acceptance. The pixel size for these settings was 6.8mm. Settings for CT were: helical rotation, pitch 1.9, interval 3.40mm; voltage 140KpV; current 2.5mA; rotational velocity 20rpm. Reconstruction of SPET slice was carried out by an iterative algorithm (OSEM, 2 iterations, 10 subsets) which incorporated scatter and attenuation correction, followed by Butterworth post-filtering (0.40 frequency cut-off for stress, 0.45 for rest, order 10). Study interpretation relied on visual inspection of 3-plane slices and myocardial wall motion information. Perfusion data were summarized in 17-segment polar maps. Also, semi-quantitative evaluation included summed stress and rest score (SSS, SRS) calculation by means of a 5-point scale according to the percentage of maximum activity in each segment as follows: >70%=0, 60-69%=1, 50-59%=2; 40-49%=3, <40%=4.

One properly trained physicist (M.G. of the authors) visually examined the coregistration of SPET and CT components via a specific software tool (ACQC tool; GE Healthcare, USA). She manually corrected all misregistered images, recorded the shifts needed for registration restoration in each axis and direction (in mm) and printed out MPI results before and after reregistration. The SSS or SRS difference between the two datasets was also recorded. The shifts were converted from mm to pixels and were classified as being 0, 0-1, 1-2, 2-3 and >3 pixels. Fifty studies randomly selected from the whole series were also processed by a second observer, a technologist from the laboratory staff, and the results were compared. Paired printouts of MPI reports before and after reregistration were randomized and handed to two experienced nuclear medicine physicians (D.J.A and C.A.S. of the authors) for visual assessment. Duplicate images of studies without misregistration were also included in these 255 pairs. The goal of visual evaluation was twofold: First, the observers were asked to detect differences between the two image sets and decide if these could alter the diagnosis with respect to study normalcy, but also to the number, location, extent and severity of perfusion abnormalities. The interpreters were independent to each other and blind as to patient characteristics, clinical information, stress or rest condition, and to the existence and degree of misregistration. The second evaluation aimed at determining the benefit of registration correction, namely its effectiveness in recovering diagnostic information. This time observers had access to non-attenuation corrected images, stress- rest image pair, gated-SPET results, as well as all other relevant information from the patient's record (patient characteristics, symptoms, history, pre-test probability of CAD, etc) and reached a final diagnosis for each MPI study. Misregistered and reregistered datasets showing significant interpretation differences between each other were compared with reference to the final diagnosis. Observers were blind to the degree of misregistration and whether a given image represented the original or the reregistered study.

Phantom experiment

In order to further elucidate the effects of misregistration under experimental conditions, SPET/CT misalignment was purposely introduced by the software in a phantom and in 3 representative clinical cases which originally exhibited excellent coregistration. The cardiac phantom was placed inside an anthropomorphic torso simulation (ECT/CAR/I and ECT/TOR/P, Data Spectrum Corporation, Hillsborough, North Carolina, USA). The torso phantom consisted of a

large body-shaped cylinder with lung, liver and spine inserts. The cylinder (7.4lt), liver insert (1.2lt) and heart chambers ("cavity" 60mL, "wall" 120mL) were filled with water. Then 3.7MBq of Tc-99m were injected into the cardiac "wall", 35MBq in the torso cylinder and 30MBq in the liver insert. No activity was inserted in the cavity of the cardiac insert or in the lungs. Imaging was performed with Infinia Hawkey-4 using the same stress acquisition settings and reconstruction parameters as in the clinical series. Total, maximum and average counts, as well as the standard deviation (SD) of count distribution in the entire polar map were recorded. The uniformity of tracer distribution in the polar map was expressed by the coefficient of variation: CV% = SD/average x 100. Myocardial segments were grouped into anterior, lateral, inferior wall and apex. Average activity of each segment and each wall was expressed as a percentage of the maximum polar map activity.

Misregistration was introduced by sequential CT slice shifts in various directions: X-axis lateral/medial, Y-axis ventral/dorsal, Z-axis caudal/cranial. The ACQC tool allows for rotational shifts as well, but this kind of movement was not included in this evaluation. The shifts measured 0.5, 1, 1.5, 2, 3, 4 and 5 pixels (3.4-34mm). Afterwards, combined multiaxial shifts were created initially by 0.5x0.5x0.5 pixels, then by 1x0.5x0.5 pixels in all possible combinations and then by 1x1x1, 2x2x2 pixels and so on, up to 5x5x5 pixels. The effect of slice misalignment was evaluated quantitatively and visually in terms of changes in polar map counts and uniformity as well as differences in relative uptake across myocardial segments and walls for each translational step with reference to the original image.

The same procedure of simulated misregistration and image processing was followed in the 3 representative clinical studies and the results were compared. The coregistered images of the first study belonged to a male patient and showed a mild perfusion defect in the basal inferior wall; the second case was a female with normal myocardial perfusion and the third a male with a large defect in the anterior wall and the apex.

Statistics

Continuous variables were expressed as mean±SD, while nominal data as percentages. Inter-observer variability was assessed by kappa statistics. Correlation between continues variables was tested by the Pearson's or the Spearman's method. Multivariable logistic regression was implemented to discover independent predictors of a binary outcome. Statistical significance was signified by $P<0.05$.

Results

Clinical series

The MPI findings in the cohort of 150 patients were as follows: 45% normal, 7% equivocal, 23% reversible, 11% fixed and 13% mixed perfusion defects.

Correct slice registration was noted in 34 out of 255 studies (13%) while mild misregistration (i.e. <1 pixel in all axes and directions) in 62%. Misalignment greater than 1 pixel in at least one axis occurred in 24% and >2 pixels in 4% (Table 1).

Table 1. *Frequency of observed misregistration in the patient series. Maximum as well as the sum of multi-dimensional pixel shifts needed for registration correction are presented*

	Magnitude of misregistration (pixels)				
	0	<1	1-2	2-3	>3
Max of XYZ	34 (13)	159 (62)	51 (20)	5 (2)	6 (2)
Sum of XYZ	34 (13)	87 (34)	93 (36)	29 (11)	12 (5)
2-axis	34 (13)	212 (83)	8 (3)	1 (0.4)	0
3-axis	34 (13)	221 (87)	0	0	0

Numbers in parentheses are percentages

Inter-observer variability in correcting misregistration was assessed in 50 studies, as mentioned before. With respect to the pixel shifts needed to restore slice registration in each axis the variability was moderate, as shown by the kappa statistics presented in Table 2. The repeatability was somewhat higher when the maximum or the sum of multi-axial pixel shifts was considered (κ=0.486 and 0.444. respectively). As regards polar map scoring (SSS or SRS) of reregistered images, the inter-observer agreement was very good (κ=0.755). By visual analysis in only 3 out of 50 reregistered studies (6%) there was a different diagnostic result.

As regards interpretational differences between misregistered and reregistered images in the whole series of 255 studies, the inter-observer agreement was good (κ=0.558, Table 2). Differences between raters were resolved by consensus. Accordingly, 40 of 221 (18%) misregistered studies exhibited significant diagnostic differences when compared with the restored images. Changes in interpretation were related to the magnitude of misregistration as shown in Figure 1. These changes were noted in only a minority of studies showing a maximum shift less than 2 pixels or a summed multi-axial shift, less than 3 pixels.

In logistic regression analysis only x- and y-axis translations were independent predictors of a significant diagnostic difference and more specifically CT misplacement in the medial and the dorsal direction. In the multivariable regression model which also included patients' sex, age and body mass index, post-stress versus rest status and MPI findings (normal versus abnormal), significant interpretational differences were predicted by MPI results in the sense that normal MPI studies were less prone to diagnostic changes compared to abnormal ones.

The difference in summed score (either SSS or SRS) between misregistered and reregistered images ranged from -10 to 15 (average±SD=1.70±1.90). Absolute SSS/SRS differences greater than 1 unit were detected in 41% of all misregistered cases, in 37% of those with <1 pixel and in 52% of those with ≥1 pixel maximum misregistration in any direction. The SSS/SRS difference correlated weakly with the

Table 2. *Inter-observer variability in correcting slice registration and determining diagnostic differences between misregistered and reregistered images*

	Observed agreement (%)	Expected agreement (%)	kappa	Standard error	P
X-axis shift	68.0	53.4	0.314	0.094	0.0004
Y-axis shift	82.0	70.1	0.398	0.106	0.0001
Z-axis shift	84.0	73.5	0.397	0.113	0.0002
Max of XYZ shifts	68.0	37.7	0.486	0.091	<0.0001
Sum of XYZ shifts	58.0	24.4	0.444	0.078	<0.0001
SSS/SRS of reregistered images	81.6	25.0	0.755	0.0773	<0.0001
Effect of registration correction					
Interpretational differences	87.0	70.7	0.558	0.076	<0.0001
Restoration of diagnostic information	87.8	78.7	0.430	0.045	<0.0001

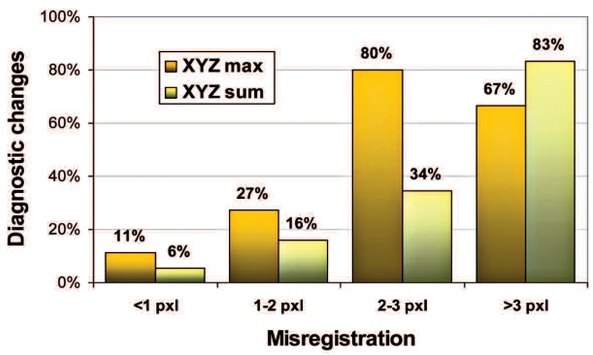

Figure 1. Interpretational changes between misaligned and corrected images for different degrees of misregistration. Maximum (XYZ max) and summed multi-axial (XYZ sum) pixel shifts needed to achieve correct SPET/CT registration are presented.

maximum and the sum of shifted pixels (Spearman's rho=0.30 and 0.28 respectively, P<0.0001). In studies with no interpretational changes on visual assessment the mean of absolute SSS/SRS difference between misregistered and corrected images was 1.19±1.11 (range 0-5) while in those with changes it was 4.03±2.80 (range 1-15).

In determining the efficacy of slice realignment in restoring diagnostic information the outcome was expressed as improvement, deterioration or uncertain. The inter-rater agreement for this assessment was fair (κ=0.43, Table 2). Consensual results are depicted as bar-graphs in Figure 2. After registration correction the diagnostic information seemed to improve in 23 of 40 cases (57.5%). No clear correlation of improvement with the degree of misregistration was evident. In twelve cases (30%) no conclusion could be reached while the deterioration rate was low (12.5%).

Phantom experiment

Total and average polar map activity changes correlated linearly with the degree of single-axis CT slice displacement (Pearson's r = 0.99, -0.96, 0.99 for X, Y, and Z axes) but the slope of the linear regression was different for each direction (X, 4.4; Y, -2.4; Z, 3.2) with x-axis causing the most pronounced alterations (e.g. 14% decrease and 11% increase at 3-pixel medial and lateral shifts respectively). As regards multi-plane translation, the regression pattern was not linear. Misplacement at the medio-dorso-caudal direction yielded the largest count decrease (14% for 1x1x1 pixel shift,

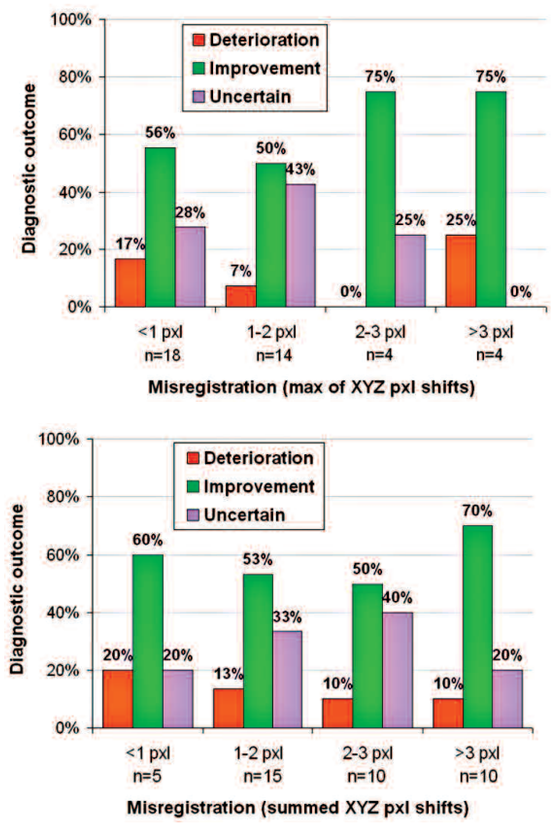

Figure 2. Efficacy of the registration correction in restoring diagnostic information in studies with interpretation differences between misregistered and recovered images. Results are expressed as improvement, deterioration or uncertain and plotted against different degrees of misregistration as described by the maximum (left graph) and the sum of multi-axial pixel shifts (right graph).

nearly equal to the 3-pixel single-axis medial shift) and the latero-ventro-cranial shift resulted in the largest increase (8% for 1x1x1 and 33% for 3x3x3 pixel shifts). Polar map uniformity followed a different pattern, with the single-axis cranial and the multi-axial latero-ventro-cranial translation causing the most conspicuous inhomogeneity (25.4% for 3-pixel and 27.6% for 3x3x3 pixel shifts respectively), compared to 21.7% of the original image.

Fluctuations in relative myocardial wall activity are shown in Figure 3. The lateral and the anterior wall were mostly af-

fected by medial CT shifts, the septum and the inferior wall by dorsal and cranial, and the apex by cranial shifts. The effect of multi-axial shifts was complex; usually uptake changes were propagated but this did not occur in all XYZ combinations (Figure 3). Segmental defects were not visually apparent up to 1.5 pixel single-axis shifts. Multi-axis translation by 0.5x0.5x0.5 pixels had minimal impact on image interpretation but 1x1x1 and even 1x0.5x0.5 shifts in certain directions caused visible defects as illustrated in Figure 4.

In comparing the results obtained in the phantom and the three clinical cases, significant differences were detected regarding the degree of count variation across myocardial walls. Figure 5 graphically demonstrates these differences for 3-pixel singe-axis misregistrations in various directions. The pattern of activity changes was generally similar but there were a few exceptions. The most prominent decrease in relative uptake was observed in the anterior wall of patient 1 after a caudal shift (-21%), in the lateral wall of patient 2 after a ventral shift (-22%), in the inferior wall of patient 3 after a cranial shift (-14%), and in the septum of patient 2 after a ventral shift (-15%). Anatomical variations responsible for a dissimilar degree of overlap of the heart with neighboring tissues, particularly the lung, probably accounted for, but not fully explained the different effect of SPET/CT misregistration in these cases. Figure 6 exemplifies this issue. A 3-pixel ventral shift (Figure 6b) resulted in relatively small polar map changes in the phantom and patient 1 where the heart-lung overlap was minimal while it produced sizeable artifactual defects in the lateral wall of the other two patients in whom significant heart-lung overlap was manifested. On the other hand, a 3-pixel medial shift (Figure 6c) had no effect on patient 2 despite considerable overlap of the left ventricular contour with the lung; dramatic changes were

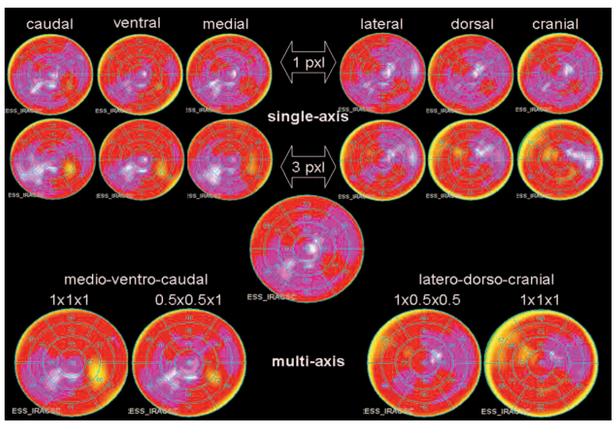

Figure 4. Phantom experiment: Effect of single- and multi-axial misregistration on polar map appearance. Upper 2 rows: Single-axis misregistration by 1 and 3 pixels in various directions. Lower row: Multi-axial misregistration by1x0.5x0.5 and 1x1x1 pixels in two selected directional combinations. The polar map of the correctly registered study is shown in the middle. In this example, the effect of mild multi-plane almost equals that of severe (3-pixel) single-plane misregistration.

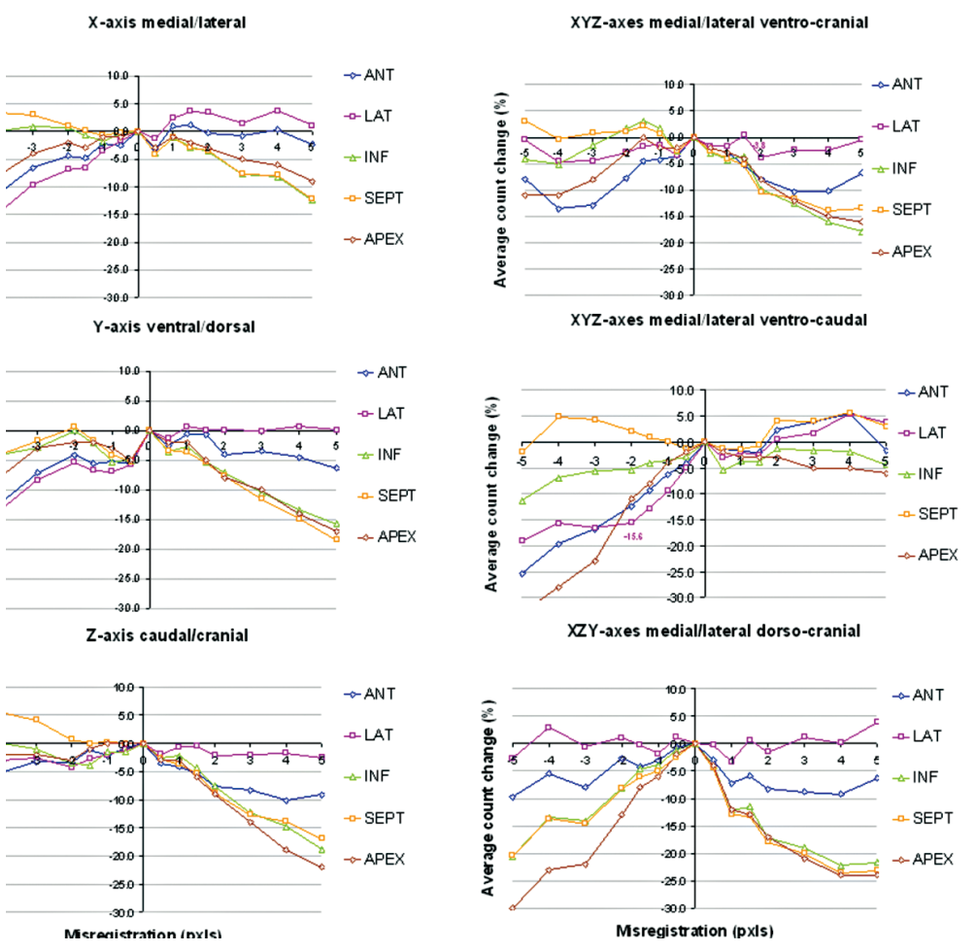

Figure 3. Changes in relative wall activity produced by sequential CT shifts. Single-axis misplacements are shown on the left and three combinations of multi-axial misplacements on the right.

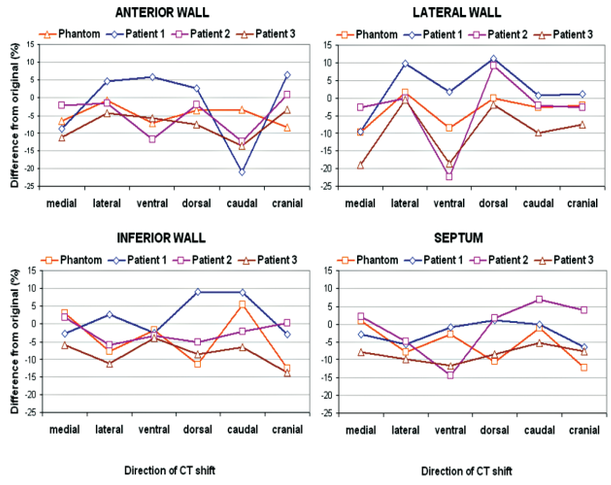

Figure 5. The effect of 3-pixel misregistration on myocardial wall activity in three different patients and the phantom. Changes of relative tracer uptake with reference to the original (correctly registered) image are in the ordinate and the direction of misregistration in the abscissa. Obvious differences in the degree of uptake changes between the 4 studies are evident.

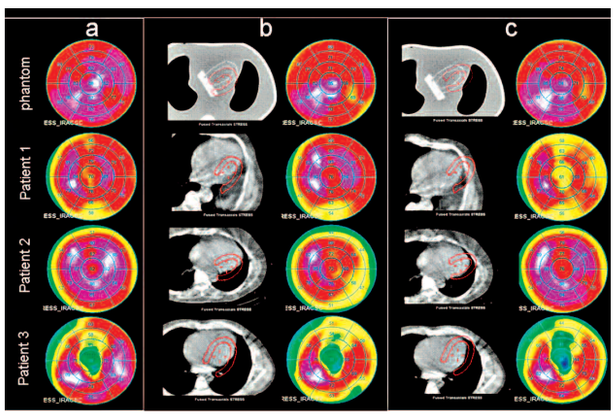

Figure 6. Effect of 3-pixel CT shifts on the polar maps of 3 different patients and the phantom. The original (correctly registered) studies are displayed in (a) and the polar maps after CT displacements in the ventral and medial direction in (b) and (c) respectively. Misregistration effects are apparently case-specific.

evident in patient 2 where there was substantial overlap with the thoracic wall but minimal with the lung. Other factors, such as the presence and the extent of perfusion defects and perhaps the count density of the original (correctly registered) study possibly contributed to the final outcome of misregistration. The phantom and patient 2 had originally uniform tracer distribution across the myocardium and higher count density compared to the two other patients.

Discussion

To our knowledge, this is the first study in the literature thus far to demonstrate the clinical relevance of emission-transmission misregistration in SPET/CT MPI. Previous studies in phantoms and patients have mainly focused on the quan-

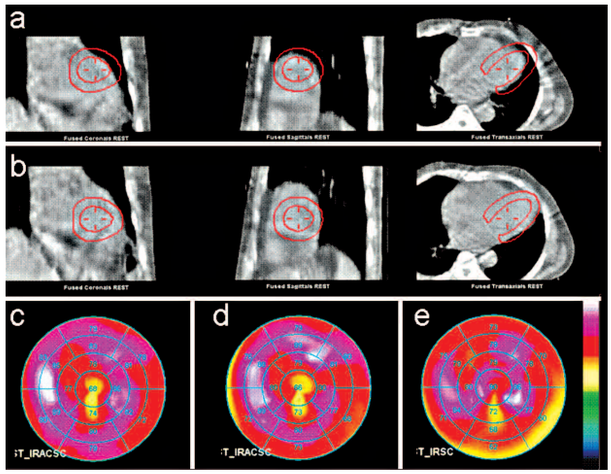

Figure 7. The rest study of a male patient: a) misregistered and b) corrected SPET/CT slopes. The maximum CT shifts needed for registration restoration was 4.9 pixels to the lateral direction and the sum of shifts in all directions was 5.1 pixels. The polar map of misregistered study is shown in (c), of the realigned study in (d) and of the non-attenuation compensated study in (d). The effect of registration correction on the diagnostic information of the study was minimal.

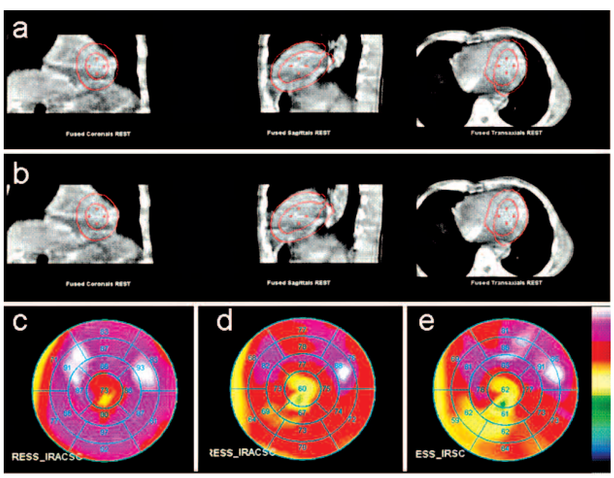

Figure 8. The stress study of a male patient is displayed (a-e) with the same image arrangement as in figure 7. The maximum CT shifts needed for registration restoration was 0.62 pixels to the cranial direction and the sum of shifts in all directions was 0.79 pixels. Despite the mild registration error (a), significant differences between the misregistered (c) and reregistered (d) study are shown in the corresponding polar maps.

titative effects of single-axis misregistration in tracer distribution across myocardial segments or walls and have also correlated the location and severity of artificial defects with the magnitude and the direction of misregistration. In this respect, most of our findings are in line with previous knowledge [5, 8, 9, 13, 14]. However, misregistration in clinical practice is usually multi-axial, each direction affects different areas of the myocardium with different severity and the net effect is complex. We have demonstrated in the phantom that some combinations of 3-plane translations propagate image artifacts (Figure 4). Moreover, for a given magnitude and direction of misregistration the effect is quite variable from patient to patient [13]; present results, summarized in Figures 5 and 6, corroborate this notion. Rotational move-

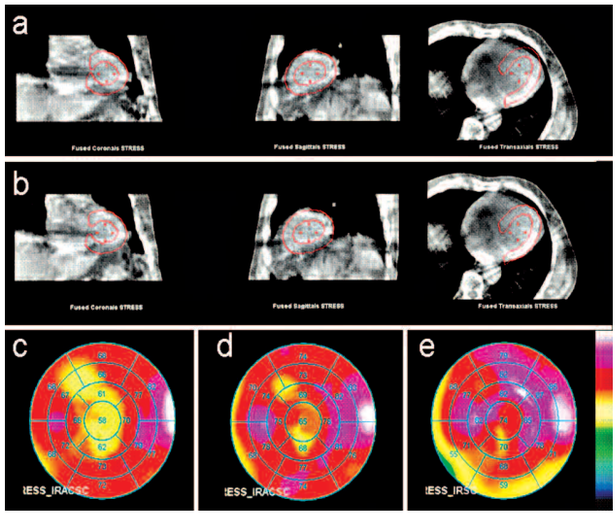

Figure 9. The stress study of a 43 years old male with low probability of CAD is displayed. Image arrangement (a-e) is the same as in Figures 7 and 8. The maximum CT shifts needed for registration restoration was 1.12 pixels in the ventral direction and the sum of shifts in all directions was 1.24 pixels. The misregistered study (c) shows large perfusion defects in the anteroseptal wall and the apex. These defects are not evident in the non-attenuation corrected study (e) in which only an attenuation artifact in the basal inferior wall is demonstrated. After misregistration correction (d) the false positive anteroseptal and apical defects appear substantially milder and smaller while the attenuation artifact of inferior wall is removed.

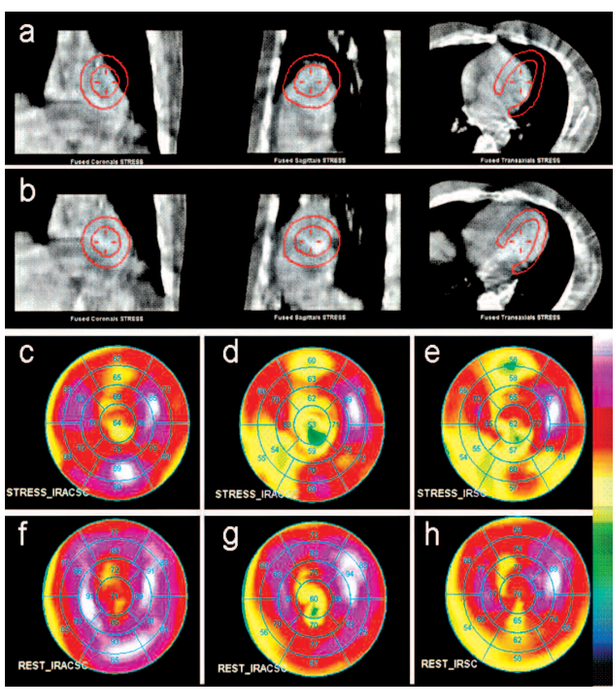

Figure 10. Significant misregistration is detected in the original stress study (a) of this male patient. Reregistration (b) required 5.62 pixels cranial, 0.68 lateral and 0.15 dorsal shifts. Prominent differences are noted in the polar maps of misregistered (c) and reregistered (d) studies. The polar map of the non-attenuation compensated stress study is shown in (e). Corresponding polar maps of the rest study (also with registration error) are depicted in the lower row (f, g and h). The reregistered stress study seems to restore the diagnostic information, namely by disclosing extensive perfusion defects in the anterior wall, the septum and the apex which appear as partly reversible at rest.

ments, which were not examined here, may also be involved and complicate the situation further. However, in one study rotational registration errors were less important than translational ones [5].

Count alterations across myocardial segments or walls do not translate directly or uniformly into differences in image interpretation. For example, a 10% count decrease or increase could be important if it turned a certain segment from normal to abnormal or vise versa but would prove insignificant for an already grossly abnormal segment. The same holds true for SSS or SRS differences. In some of our cases with high SSS values, a SSS difference between misregistered and corrected images up to 5 units had minimal or no impact on study interpretation. On the contrary, there were other cases where a SSS change of only 1 unit altered the final diagnosis.

The main finding of the present study is that the impact of SPET/CT misregistration on the diagnostic accuracy of MPI, although dependent on the magnitude of misregistration, is also case-specific and hardly predictable. Mild and moderate misalignment is usually of no importance. Seventy-three percent of studies suffering from a maximum single-axis misalignment between 1 and 2 pixels did not change substantially after reregistration (Figure 1). Alignment errors exceeding 2 pixels in at least one direction still did not affect 27% of cases. Figure 7 depicts a case in which significant misregistration had minimal impact on image interpretation. On the other hand, 11% of those with less severe (<1 pixel maximum) misalignment had important diagnostic changes after registration correction. Such a case is illustrated in Figure 8.

Another issue addressed herein is whether registration correction by the software restores diagnostic information or not. The procedure of manual reregistration is operator dependent and fairly reproducible as shown by current (Table 2) and previous results [7]. However, we found that the impact of inter-observer differences on the diagnostic outcome was quite small. The outcome of slice realignment can be decided subjectively by comparison with non- attenuation corrected images; the latter are prone to attenuation artifacts and cannot be considered as a gold reference standard, though. However, by taking into consideration expected sites of attenuation artifacts, paired stress-rest evaluation, regional wall motion and relevant information from history, a conclusion could be reached in the majority of cases. For example, one can rely on the normal appearance of myocardial segments in the non-attenuation corrected images and consider this as standard. Similarly, segments with reversible perfusion defects or akinetic segments with fixed defects in the non-corrected stress-rest image pair should maintain the reversibility pattern after proper attenuation compensation, although the severity and the extent of abnormalities may differ. Mild to moderate non-reversible defects with normal kinesis in patients with low pre-test probability of CAD are considered to represent attenuation artifacts and should be removed after attenuation correction; failure to eliminate the artifact indicates an erroneous correction procedure (e.g. because of SPET/CT misregistration). Some uncertain results are inevitable of

course. In the present series 58% of studies exhibiting substantial differences between misregistered and reregistered images seemed to improve after registration restoration. Two typical examples are illustrated in Figures 9 and 10. Improvement did not correlate with the magnitude of misregistration (Figure 2). In a small number of cases (n=5) images seemed to deteriorate after registration correction; this was probably due either to erroneous reregistration or to misinterpretation. Assuming that cases with uncertain results (30%) potentially represented unconfirmed improvements, the improvement rate would rise to 88%. These findings support the realignment procedure regardless of the magnitude of misregistration. In case of mild misregistration, a significant change is unlikely but cannot be excluded.

The main difference of this from previous studies is the frequency of observed misregistration. In the series of Goetze et al. (2007) [7] and Kennedy et al. (2009) [9] misregistration greater than 1 pixel in at least one direction was detected in 64%-73% of cases and >2 pixels in 7%-23%; these rates are considerably higher than the respective 24% and 4% of ours. The reason for this discrepancy is not clear. Probably it is associated, partly at least, with the SPET/CT system and CT acquisition mode. Both aforementioned authors used the Hawkeye-1 system coupled either with the Millennium VG or the Infinia gamma-camera, whereas we exclusively implemented Infinia Hawkeye-4. The helical CT mode of acquisition and the shorter acquisition times of Hawkeye-4 may have played a role in reducing SPET/CT registration errors. Slice misalignement in the ventro-dorsal direction attributed mainly to table sagging was quite frequent both in the previous and the current study. Perhaps the degree of table flexion differs between gamma-cameras. In their study, Kennedy et al. (2009) used both camera models mentioned above but they did not comment on such differences [9].

Conclusion

Mild (<1 pixel in all directions) and moderate (1-2 pixels in at least one directions) SPET/CT misalignment usually does not affect MPI interpretation. However, the impact of misregistration is case-specific and hardly predictable. Occasionally, mild misalignment produces diagnostic errors whereas significant misalignment does not. Manual misregistration correction by means of a software tool seems to restore diagnostic information in the majority of cases regardless of misregistration magnitude and is therefore worthwhile in clinical practice.

The authors declare that they have no conflicts of interest.

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