#### **Original** article

# Assessment of Inter-modality Spatial Alignment Accuracy in Hybrid Single Photon Emission Computed Tomography in Patients with Hand and Wrist Pain

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### Abstract

Single photon emission computed tomography (SPECT) and computed tomography (CT) integrated in one system (SPECT/CT) is an effective co-registration technique that helps to localize and characterize lesions in the hand and wrist. However, patient motion may cause misalignment between the two modalities leading to potential misdiagnosis. The aim of the present study was to evaluate the hardware-based registration accuracy of multislice SPECT/CT of the hand and wrist and to determine the effect of misalignment errors on diagnostic accuracy. A total of 55 patients who had multislice SPECT/CT of the hand and wrist between July 2008 and January 2010 were included. Two reviewers independently evaluated the fused images for any misalignments with six degrees of freedom: Translation and rotation in the X, Y and Z directions. The results were tested against an automated fusion tool (Syntegra). More than half of the patients had moved during SPECT scanning (Reviewer 1: 29 patients; Reviewer 2: 30 patients) and they all originated in the Y-direction translation (vertical hand motion). Five fused images had significant misalignment errors that could have led to misdiagnosis. The Wilcoxon test indicated statistically non-significant difference (P > 0.05) between reviewers and statistically non-significant difference between the reviewers and software registration. The study also showed high inter-reviewer agreement ( $\kappa = 0.87$ ). Hand movement during the SPECT scan was common, but significant misalignments and subsequent misdiagnosis were infrequent. Future studies should investigate the use of hand and wrist immobilization devices and reductions of scan time to minimize patient motion.

Keywords: Image fusion, registration, single photon emission computed tomography/computed tomography

# **Introduction**

Integrated dual-modality single photon emission computed tomography/computed tomography (SPECT/CT) provides the means to combine imaging modalities for a direct functional and anatomical correlation to precisely localize and characterize abnormalities.<sup>[1-4]</sup> Hybrid SPECT/CT imaging is particularly useful for assessing hand and wrist pain.<sup>[5]</sup> The anatomy of the hand especially

Quick Response Code: Website: www.wjnm.org DOI: 10.4103/1450-1147 136732	Access this article online				
DOI: 10 4103/1450-1147 136732	Quick Response Code:	Website: www.wjnm.org			
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the wrist joint consists of multiple articulating bones and its complex anatomy makes diagnosis and management of hand and wrist pain a challenge.<sup>[6]</sup> This is when radionuclide bone imaging is most valuable. Evidence showed that bone scans are highly sensitive in detecting orthopedic lesions.<sup>[7,8]</sup> Bone scan alone is limited by its poor specificity and inferior image quality, it is often difficult to determine the precise location of the lesion amongst the close association of the carpal bones.<sup>[9]</sup> However, modern hybrid SPECT/CT imaging combines the advantages of both modalities - the underlying CT image allows clinicians to distinguish and evaluate each carpal bone individually, whereas the overlying SPECT image provides the exact location of the metabolic pathology. SPECT/CT has improved specificity and diagnostic confidence; it has shown to be a useful investigation in patients with hand and wrist pain.[10-12]

Address for correspondence: Dr. Cheng Xie, 14 Orion Building, 90 Navigation Street, Birmingham, United Kingdom. E-mail: cheng.xie@hotmail.com The co-registration of images from the hybrid SPECT/CT scanner relies on the common couch to maintain patient position throughout the scanning process. This technique reduces differences in patient positioning, thus limiting misregistration between the two modalities. However, experience from dual modality positron emission tomography (PET)/CT imaging has indicated that misregistration errors were still present in certain situations.<sup>[13-15]</sup> Studies have indicated that patient motion particularly during the long SPECT or PET scanning was the major contributor to the misregistration errors in hybrid systems.<sup>[16-18]</sup>

Over recent years, a series of publications have reported on limitations, artefacts and image distortions of SPECT and CT.<sup>[18-25]</sup> Patient motion was identified as a major contributor to SPECT/CT misregistration. This emphasizes the importance of patient preparation-the need for patient comfort during scanning and reducing scan time to a minimum. Patient motion resulted in misregistration artefacts, most noticeably around the boundaries of the moved limb or organ.

At present, no data is available on the localization accuracy of hybrid SPECT/CT of the hand and wrist. This information is particularly important since a small misalignment between the SPECT and CT images could potentially position the hotspot onto a nearby carpal bone instead of the actual lesion. The result may be misleading and potentially delay appropriate treatment. Therefore, the aim of this study was to evaluate the registration accuracy of hybrid SPECT/CT imaging of the hand and wrist and determine the effect of the misalignment errors on the diagnostic accuracy.

# Materials and Methods

## **Patients**

In this retrospective study, 55 consecutive patients (32 women and 23 men, 22-74 years of age, mean age of 45 years) who had 99mTc-MDP SPECT/CT of the hand and wrist between July 2008 and January 2010 in the Nuclear Medicine Department were included.

## **Imaging protocol**

Dual-phase planar bone scans were performed, followed by SPECT/CT imaging. All the patients received intravenous injections of 750 MBq 99mTc-MDP. 5 min post-injection, blood pool images of the hands (positioned palms down on the camera face) were acquired using a 256 × 256 pixel matrix. At 3 h post-injection, delayed phase images of the hands were acquired in the same manner. SPECT/CT imaging followed straight after.

## **Image acquisition**

For SPECT/CT imaging, patients were placed in the "Superman" position [Figure 1]. Patients lay prone with their head usually turned to one side allowing them to lie as flat as possible. Arms were straightened above the head toward the center of the couch. If only one hand was to be imaged, then only that arm was required above the head. This position limited CT irradiation within the area of interest and minimized irradiation of critical organs such as the head and the eyes. It also optimized the proximity of the gamma camera for better resolution. Pillows and foam blocks were placed under the patients' arms, head and lower legs for support and comfort. When the patient was made as comfortable as possible, their hands were taped palms down flat on a plastic board and finally ready for scan.

Scanning was performed on the dual-head gamma camera SPECT/CT system, the Philips Precedence 16 [Figure 2]. A CT scout view was first used to define the CT and SPECT fields. Next, localization CT was performed on the hands. The settings were 120 kV, 100 mAs/slice, a pitch of 1.188 with 0.75 s rotation time and collimation of  $16 \times 0.75$  mm. The reconstructed images had 0.683 mm transverse pixel size and slice thickness of 1.5 mm. The CT scan took about 1 min to complete.

For SPECT, the emitted gamma rays from the hand were acquired over 360°. Low energy high resolution, parallel hole collimators were used. A total of 128 projections and each with a duration of 20 s. Data were acquired into a  $128 \times 128$  matrix, which resulted in a pixel size of 4.664 mm. The SPECT scan took approximately 25 min.

## **Image analysis**

The raw SPECT data were reconstructed on a Jet Stream Workspace (v3.0, Philips Medical Systems, USA) with filtered back projection and Butterworth filter with cut-off of 0.4 cycle/pixel and order of four. Reconstructed transverse slices were sent to a Philips Extended Brilliance Workstation (EBW) for review of the images fused with the co-registered CT images. The process of defining the co-registration spatial transformation parameters involved scanning a phantom that consists of six point sources visible in both SPECT and CT. The algorithm defined the center of mass for each point source and the spatial transformation parameters that will result in the centroids overlapping on the two modalities. These parameters are saved on the system and consequently applied to all patient data.

Two experienced consultants in Nuclear Medicine were involved in image analysis. They independently evaluated the fused images on EBW using the manufacturer's fusion display tool (Fusion Application Suite V1.2E). This tool provided the reviewers with transverse, coronal and sagittal planes of the fused images for assessment. In each plane, the reviewers went through all the fused slices and if necessary adjusted the linear grey scale and color fusion display to identify anatomical landmarks to help determine the accuracy of alignment. When a reviewer identified a misalignment between the SPECT and CT images, they were able to use the display tool to re-align the images manually across six degrees of freedom: Translation in the X, Y and Z directions, rotation in the X, Y and Z directions [Figure 3a and b]. Any misalignment resulting in spatial displacement of more than 4.66 mm (one pixel size) was defined as a significant misalignment. Misalignment of less than one pixel size was difficult to correct for given the spatial resolution of the SPECT modality and hence regarded as non-significant. In addition to manual re-alignment, the images were analyzed by an automated fusion tool (Syntegra version 2.2). Syntegra was included in the Philips JETStream platform and it performed rigid-body



Figure 1: The "Superman" position for single photon emission computed tomography/computed tomography scanning



**Figure 3a:** The fusion display tool demonstrates misalignments between the single photon emission computed tomography and computed tomography images in the transverse (top left) and sagittal (bottom) planes. The re-alignment box (top right) displays the coordinates in millimeters for six degree of freedom

co-registration with a normalized mutual information algorithm. The spatial transformations required to correct the misalignments were recorded for statistical analysis.

To illustrate the effect that inter-modality misalignment may have had on diagnostic accuracy, the reviewers further evaluated the images that had significant misalignments. They compared fused images before and after misalignment correction to see whether the deviation of the overlying hotspot on the CT image may have resulted in a misdiagnosis.

#### Statistical analysis

All statistical analysis was carried out on Statistical Package for the Social Sciences (SPSS, v17). The level of significance was set at P < 0.05. The Wilcoxon test was used to evaluate the inter-observer reproducibility of this method. This test allowed direct comparison of the two reviewers' misalignment corrections in each of the misalignment directions. Furthermore, the Kappa



Figure 2: The dual-head gamma camera single photon emission computed tomography/computed tomography system – Philips Precedence 16



Figure 3b: The reviewer has re-aligned the single photon emission computed tomography image over the computed tomography image. The re-alignment box displays the misalignment distance of 5.8889 mm in the Y-direction translation

measurement of agreement was used to assess the reviewers' agreement of the misalignments.

#### Manual misalignment corrections performed by the reviewers were also compared with automated correction carried out by the Syntegra software. The Wilcoxon test was used to compare each reviewer's results with those from Syntegra.

# **Results**

### Misalignment analysis

Evaluation of the SPECT/CT fused images revealed that more than half of the patients had moved during SPECT scanning (Reviewer 1: 52%; Reviewer 2: 54%). Most of the misalignments observed were translations along the Y-direction (vertical hand movement) [Table 1] and were evident in the transverse and sagittal planes [Figure 3a]. This indicated that the patients' hands were moving mainly up/down than any other direction during the SPECT scan.

Furthermore, non-rigid body movement was also observed: There were six cases of thumb movement and one case of finger movement [Figure 4]. In these cases, other parts of the hand and wrist were aligned.

#### **Diagnostic accuracy analysis**

Reviewers identified five patients with significant vertical hand motion. The subsequent misalignments of the fused imaged could have led to misdiagnosis if manual misalignment corrections were not performed. Table 2 shows the location of the increased focal uptake of the tracer before and after misalignment correction for these five patients. Figure 5a and b are images of a patient to demonstrate the change in location of the focal tracer uptake after misalignment correction, which could have led to misdiagnosis if corrections did not take place.

#### **Inter-reviewer agreement**

The Wilcoxon test directly compared the two reviewers' misalignment corrections in all six directions and found there was a statistically non-significant difference (P > 0.05) in misalignment measurements in all six directions between the two reviewers. The Kappa value also demonstrated high inter-reviewer agreement (0.87).

The Wilcoxon test was used to directly test the reviewers' manual misalignment corrections against the automated corrections carried out by Syntegra. The results indicated there was a statistically non-significant difference (P > 0.05) between each of the reviewers and Syntegra in correcting for misalignment errors.

## **Discussion**

Recent advances in medical imaging technology have led to the development the hybrid SPECT/CT with multi-detector CT components of fully diagnostic capabilities. This allows fast and effective co-registration of functional and anatomical information. The registration accuracy is particularly important for a confident diagnosis in the hand and wrist due to their complex anatomy. This study was designed to assess the registration accuracy of hybrid SPECT/CT imaging of the hand and wrist and determine the effect of the misalignment errors on the diagnostic accuracy. Our results indicated that approximately half (54%) of the 55 patients had moved between the CT and SPECT scan as determined by the reviewers' reports. Most of the misalignments were translations in the Y-direction. This suggested that the patients' hands were moving mainly up or down than any other direction during the SPECT scan.

Even though more than half of the patients had moved during the SPECT scan or between the CT and SPECT scans, the majority of the subsequent misalignment errors did not interfere with diagnosis. This suggested that hybrid SPECT/CT can be considered to have a good degree of registration accuracy. Among the limited number of published works on this area, the study conducted by Nömayr *et al.* showed agreement with our study findings. Nömayr *et al.* evaluated the anatomical accuracy of hybrid SPECT/CT in 22 patient scans of the lower spine. Two radiologists and an automated fusion tool assessed the images. They reported anatomical inaccuracies below the single pixel width of 4.6 mm and concluded that the hardware approach of SPECT and CT image fusion was "nearly perfect."<sup>[26]</sup>

# Table 1: The number of patients with misalignmentidentified by the reviewers

	Misalignment direction (translation)				
	Х	Y	Z	X, Y, Z	
Reviewer 1	0	29	1	0	
Reviewer 2	1	30	10	0	

Table 2: The location of the increased focal uptakeof tracer before and after manual misalignmentcorrection for five patients who producedsignificant hand movement during imaging

Patient	Location of the focal uptake		
	Before correction	After correction	
A	Soft-tissue overlying the hamate	Hamate	
В	Soft-tissue overlying the trapezium	Cystic lesion of the trapezium	
С	Soft-tissue and radius	Radiocarpal joint	
D	Radiocarpal joint	Between scaphoid and lunate	
E	Soft-tissue overlying first metacarpophalangeal joint	First metacarpophalangeal joint	



Figure 4: Left: The patient's thumb moved during the single photon emission computed tomography (SPECT) scan while all other parts were aligned. Right: The patient's third, fourth and fifth digits moved during the SPECT scan. The misalignment is most visible on the fifth digit



Figure 5a: Images before misalignment correction of patient B. Misalignment between the single photon emission computed tomography and computed tomography images had caused the area of increased focal uptake to be located at the soft-tissues overlying the trapezium



Figure 5b: Images after misalignment correction of patient B. The area of increased focal uptake is correctly positioned over a cystic lesion of the trapezium

Hybrid SPECT/CT may be considered to have a good degree of registration accuracy, but the fact that more than half of the patients in our study did move during scanning and nearly one in five of the patients did produce a significant misalignment suggested that there were factors interfering with the registration accuracy.

One major factor to consider was the long scanning time, which compromised the positioning of the patient during the scan. In this study, the CT scan lasted only about a minute, but the SPECT scan took approximately 25 min to complete. During this long acquisition time, the patient was asked to lie still in the "superman" position. The procedure was made as comfortable as possible with the use of pillows and foam blocks. Yet it was likely that the patient experienced some discomfort or anxiety during the scan and triggered a slight hand movement. In addition, the patients may be already experiencing some pain or discomfort from the hand or wrist injury, which prevented them from lying still for long.

An equally important factor to consider was the immobilization procedures and devices used during scanning. In this study, the protocol was to use tape to fix the patient's hand palm down, flat on a plastic board. First, the tape was effective in fixing the hand and wrist to the plastic board, but the individual fingers and thumb were poorly immobilized onto the board. There was plenty of free space in between the thumb and fingers. This may have contributed to the occasional thumb or finger movements that occurred in this study [Figure 4]. Second, the amount of tape used and the position of the tape on the hand and wrist were variable in between radiographers and these factors could have contributed to the different degree of immobilization.

In this study, we observed that patients' hands were moving mainly along the vertical direction than any other direction during the SPECT scan. Two important contributing factors were identified. The first factor was the immobilization technique used to rest the patient's hand. This has to be firm enough to restrict rigid and affine movement of the object especially under the complexity of the possible degrees of freedom involved in the hand and wrist. According to the radiographers, they have observed that patients can be anxious and stressed during the beginning of the scan (second contributing factor) and sometimes they tense their hand and unknowingly pressed down hard on the board. As the scan progressed, the patients usually relax and their hands on the board sprung back up.

One factor that could have influenced the misalignments was the injury. The severity and timing of the hand or wrist injury could have inflicted more discomfort during the scan and resulted in more movement. We did not explore this relationship, but it would be interesting to examine in our future study.

## **Clinical relevance**

We report that after misalignment correction, 5/55 fused images had demonstrated a change in location of the focal tracer uptake and could have led to misdiagnosis. This indicated that for every 100 patients who had undergone hybrid SPECT/CT scan of the hand and wrist, there is the potential of approximately ten misdiagnosed cases if manual misalignment corrections had not taken place.

## Solutions and future work

In this study, we have identified several causes to patient motion and subsequent misalignment errors. We intend to address these in our future work.

The first practical solution is to implement improved patient immobilization techniques such as the use of a thermoplastic mesh [Figure 6] to immobilize the hand and wrist. The thermoplastic mesh, once submerged in hot water, can be easily molded to fit around each patient's hand. Once cooled, it can immobilize the hand and wrist as well as the individual fingers and thumb. The mesh can be re-used and re-molded for the next patient. It is made from lightweight plastic and will not affect the SPECT or CT images via photon attenuation. We intend to implement the thermoplastic mesh in a prospective study on a sample of patients and assess the registration outcomes.

One of the main causes of patient motion was the duration of the SPECT scan and this is the most challenging obstacle. A trade-off exists between scan time and SPECT image quality. Reducing the scan time would reduce the probability for patient motion, thus minimizing misalignment errors. On the other hand, a reduction in acquisition time would reduce the number of acquired counts and thus increase noise levels. Several published reports on advance image reconstruction methods, such as those incorporating depth-dependent resolution models, have demonstrated promising results in reducing SPECT scan time in



Figure 6: Thermoplastic mesh made from lightweight plastic. It can be individually molded to fit the patient's hand providing better support and immobilization

myocardial perfusion studies by a half to three-quarter of the original time<sup>[27-29]</sup> without compromising image quality or diagnostic accuracy. Thus application of such reconstruction schemes would also be relevant in the context of containing misalignment artefacts due to patient motion.

## **Study limitations**

In this study two reviewers manually assessed all the SPECT/CT images. There was the possibility of subjective errors and inconsistency in between reviewers, which meant that the reproducibility and accuracy of this study method were not absolute. However, results from the Wilcoxon test and the Kappa measurement of agreement did demonstrate a high level of agreement and reproducibility between the two reviewers. Furthermore, there was a statistically non-significant difference when each of the reviewers' results was compared against the automated fusion tool Syntegra when applied to cases of significant misalignments. Therefore, given the subjective nature of observer-based studies the agreement in this case was satisfactory.

Another potential drawback of this study lies within this comparison between the reviewers' manually assessed misalignments and Syntegra's automated fusion results. This comparison was only limited to the images that the reviewers had identified to possess significant misalignments. Only these images were subjected to further analysis on Syntegra. The rest of the images were not processed on Syntegra due to the time consuming nature of performing automated image fusion. As a result, we were unable to assess the rest of the manually corrected images against the automated corrected images. The reliability of this study method would have been more accurately assessed if all 55 SPECT/CT images were analyzed by Syntegra and compared with each reviewer's results.

# **Conclusion**

A dual-modality integrated hybrid SPECT/CT scanner is an efficient and effective co-registration technique that provides direct functional and anatomical correlation to localize and characterize the abnormality in the hand and wrist. Hand movement during the SPECT scan is common, but the degree of movements leading to significant misalignments and subsequently affecting diagnostic accuracy are infrequent. The registration accuracy depends on patient compliance to maintain still during the scan; hence patient comfort during scanning is the prerequisite of an ideal scan.

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How to cite this article: Xie C, Gnanasegaran G, Mohan H, Livieratos L. Assessment of Inter-modality Spatial Alignment Accuracy in Hybrid Single Photon Emission Computed Tomography in Patients with Hand and Wrist Pain. World J Nucl Med 2013;12:87-93.

Source of Support: Nil, Conflict of Interest: None declared