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Patterns and Prevalence of Misregistration in ^{18}F-FDG PET/CT

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Abstract
Objectives: in PET/CT, the fusion of form (CT) and function (PET) provides high accuracy in staging, restaging and assessing response to therapy in oncology. Precise alignment between ct and pet components of the study is a prerequisite for accurate fusion. However, misregistration in pet/ct is not uncommon and, when present, may compromise image interpretation, resulting in lesion mislocalization and inaccurate suv quantitation. The purpose of this study was to evaluate patterns and prevalence of misregistration in pet/ct. Methods: true whole-body fdg-pet/ct scans, covering from the top of skull to the bottom of the feet, of 100 patients were retrospectively reviewed in nuclear medicine radiology department, saint louis university. Images were acquired on a PET/CT scanner (phillips medical systems) 60 minutes after an intravenous injection of a weight-adjusted dose of 0.14 mCi/kg FDG. A log was kept to measure and record cases of misfusions between the pet and the ct portions as detected on the pet/ct fused images. Six anatomic locations were selected to evaluate for significant Misfusion: arms, head and neck, heart, diaphragm, pelvis and legs. Misregistration was also categorized into non-preventable (ex. Breathing) and preventable (ex. Patient motion). In the current study, misregistration was consi-derd significant if more than 5 mm, the spatial resolution of current pet/ct scanners.
Results: Of 100 consecutive scans reviewed, significant misfusion: in85% the arms (mean=11.50 mm), the head and neck in 67% (mean=8.36 mm), the heart in 88% (mean=8.11 mm), the diaphragm in 68 % (mean=8.36 mm), the pelvis in 98 % (m=14.52 mm), the legs in 86 % (mean=15.02 mm).
Conclusions: Significant misregistration was encountered and measurable in 100% of PET/CT studies. It is important to be aware of misregistration in PET/CT resulting from spatial and temporal misalignment between the CT and the PET portions in order to avoid false interpretations of the PET/CT exam.
Keywords: PET/CT, FDG-PET, Misregistration, Artifacts

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Introduction

Positron emission tomography (PET) using fluorine-18-2-deoxy-D-glucose (^{18}F-FDG) for diagnosis, in many cancers an accuracy ranging from 80-90% and is often better than anatomical imaging[1]. Since the introduction of PET/CT, numerous studies showed that this whole-body (WB) dual-modality imaging is better than PET or CT alone for staging and restaging most cancers[2]. The clinical performance of a combined PET/CT system in 204 cancer patients showed that PET/CT provided additional information over the separate interpretation of PET and CT in 49% of patients with various types of cancers[3]. Another study in 260 cancer patients revealed that PET/CT is significantly accurate (86%) in tumor staging than CT alone (63%), PET alone (64%), and side-by-side PET + CT (76%) (4). Consequently, by 2006, the major vendors no longer offered PET-only systems, and by mid-2008, over 3000 combined PET/CT systems were in clinical operation worldwide[5]. The improvement in accuracy, coupled with the convenience of presenting anatomical and functional information to physicians, has rendered PET/CT imaging as the most important cancer imaging modality at the present time [6].

The use of CT for attenuation correction (CTAC) has become the standard of care in current PET/CT scanners. The use of CTAC not only eliminated the need for a separate lengthy PET transmission scan but also reduced the whole-body scan times by more than 40% at the same time of providing noiseless AC factors compared with those from standard PET transmission measurements with external radionuclide sources. Although the benefits of CT-based AC are well known and documented, several challenges have emerged as we gain more experience with PET/CT studies [7,8]. A disadvantage of the use of CT for AC in PET/CT is the potential for misregistration of emission. The physics of positron emission impose limitations on spatial, temporal, and contrast resolution that can be attained in PET/CT. Any misregistration higher than the spatial resolution of current PET/CT scanners (5 mm) may result in an interpretation dilemma. For example, spatial coregistration throughout the extended coaxial imaging range is compromised by voluntary or involuntary patient motion during the combined examination.

Because the CT and PET images are obtained sequentially, misregistration of the emission (PET) and transmission (CT) scan can occur, resulting in misfusion in the PET/CT images. In this study, our objective was to quantitatively and systematically evaluate pattern and frequency of these misregistration errors in true whole-body FDG PET/CT studies in our PET center.

Materials and Methods

True Whole-Body FDG-PET/CT scans, covering from the top of the skull to the bottom of the feet, of 100 patients were retrospectively viewed. The study was conducted in nuclear medicine, Saint Louis University.

PET/CT scanning

Patients fasted at least 4 hours before the tracer injection and received an intravenous injection of approximately 5.18 MBq/Kg (0.14 mCi/Kg) of 18F-FDG, with a maximum of 444 MBq (12 mCi). Blood glucose level was measured immediately prior to FDG injection and was < 200 mg in all studied cases. Patients were instructed to sit in a quiet injection room without talking during the subsequent 4 –60 min of the FDG uptake phase and were allowed to breathe normally during image acquisition without specific instructions. All scans were acquired using a Gemini TF PET/CT scanner (Philips Medical Systems) with an

axial co-scan range of 193 cm enabling a head-to-toe (TWB) imaging in one sweep.

CT scanning

The CT scan of the PET/CT scanner consisted of a 64 slice multi-detector helical CT. Gantry allows for a patient port of 70 cm. Parameters were as follows for 12–13 bed acquisitions (from the top of the head through the bottom of the feet): 120–140 KV and 33–100 mAs (based on body mass index), 0.5 second per CT rotation, pitch of 0.829 and 512 × 512 matrix. CT acquisition was performed before emission acquisition. CT data were used for image fusion and the generation of the CT transmission map. No oral or IV contrast was used.

PET scanning and image processing

Emission data was acquired for 18-22 bed positions (193 cm coverage, identical to the CT protocol). Emission scans were acquired at 1 – 3 minutes per bed position, dependent on the body mass index (BMI). The FOV was from the top of the head to the bottom of the feet in all patients. The 3-dimentional (3D) TWB acquisition parameters consisted of a 128 x 128 matrix and an 18 cm FOV with a 50% overlap. Processing consisted of the 3D Row Action Maximum Likelihood Algorithm (RAMLA) method [9].

Image analysis

Six anatomic locations were selected to evaluate for significant miss-fusion on the PET/CT images: Arms, Head and Neck, Heart, Diaphragm, Pelvis and Legs. These areas were selected to represent misregistration in multiple regions covering all of the extended coaxial imaging field of view in true whole-body PET/CT scan. Misregistration was considered significant if greater than 5mm, the spatial resolution of our PET/CT scanner. A log was kept to measure and record cases of misregistration between the PET and CT portions as detected on the PET/CT fused images. The best view to detect and measure misfusion was done by reviewing all generated PET/CT views: axial (for dorsal/ventral misregistration), coronal (for cephalad/ caudal misregistration) and sagittal (for left/right misregistration). All measurements were done by the same reviewer to insure reproducibility and avoid inter-observer variability. For each anatomical region, the frequency and the range of misfusion was measured. Misregistration was also categorized into preventable (arms, legs, head and neck) and non-preventable (heart, diaphragm and pelvis). Such categorization was done by consensus.

Results

Table 1 shows summary of the more than 5 mm misregistration results in 100 consequative PET/CT scans. In the head and neck region, the range of misregistration was 1.00 to 53.80mm with mean of 6.31 mm and frequency of 67% **(Figure 1).** The misregistration at the heart region ranged from 1.30-25.90 mm with a mean of 8.11 mm and frequency of 88% **(Figure 2).** The range of the misregistration at the diaphragm was 1.10 to 56.00 mm with mean of 9.36 mm and frequency of 86% **(Figure 3).** In the arms, there was misregistration ranging from 0.10 to 96.00 mm with mean of 11.5 mm and frequency of 85%. The bladder was used as a surrogate for evaluating misfusion in the pelvic region, and misregistration range was 2.90-36.50 mm with mean 14.52 mm and frequency of 98% **(Figure 4).** In The legs region, it was 0.50 to -80.40 mm misregistration range with mean of 15.02 mm and frequency of 86% **(Figure 5).**

Of the 6 areas analyzed, misregistration in the bladder, due to the temporal separation between the CT with bladder empty and PET with bladder relatively extended with urine, was the most common cause of non-preventable misfusion in the pelvic region.

Leg motion was the most common cause of preventable misregistration in PET/CT. The frequency of preventable type of misregistration was 97% versus 100% for the non-preventable type.

Table 1: Misregistration results in 100 PET/CT scans

Location	Frequency	Range (mm)	Mean (mm)
Head & Neck	0.67	1.00-53.80	6.31
Heart	0.88	1.30-25.90	8.11
Diaphragm	0.86	1.10-56.00	8.36
Arms	0.85	0.10-96.00	11.5
Pelvic area (Bladder)	0.98	2.90-36.50	14.52
Legs	0.86	0.50-80.40	15.02

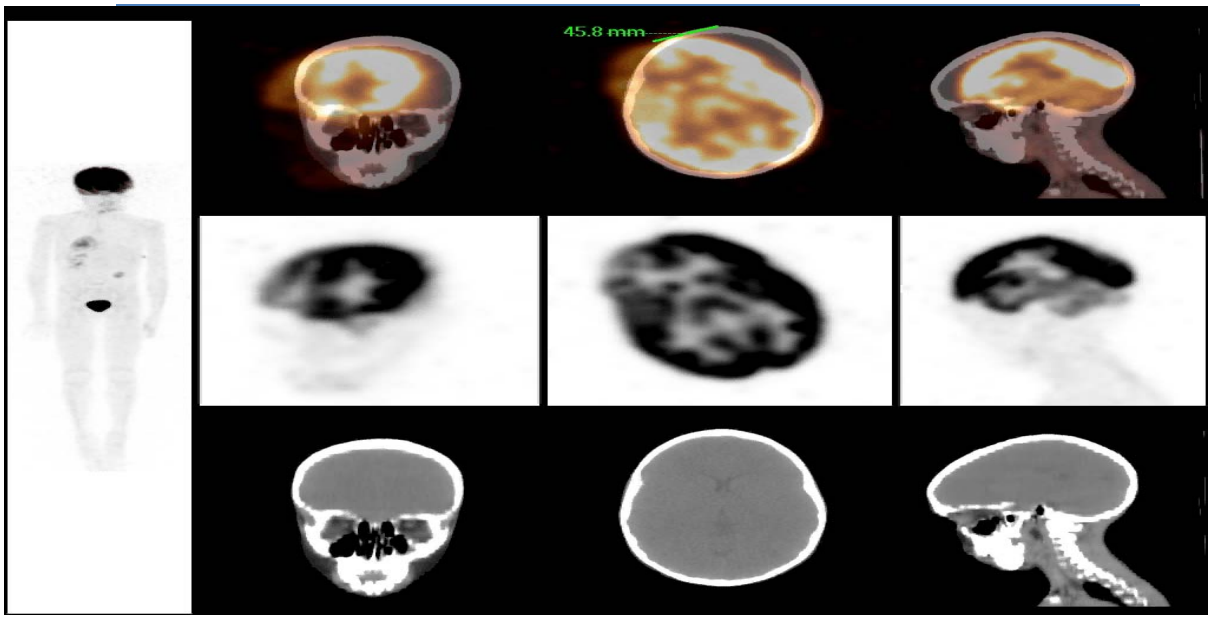

Figure 1: 8 year old male with Wilms' tumor of the right kidney. This is an example of preventable misregistration in the head and neck region. The patient rotated his head between the two scans resulting in a significant misregistration of 45.8 mm.

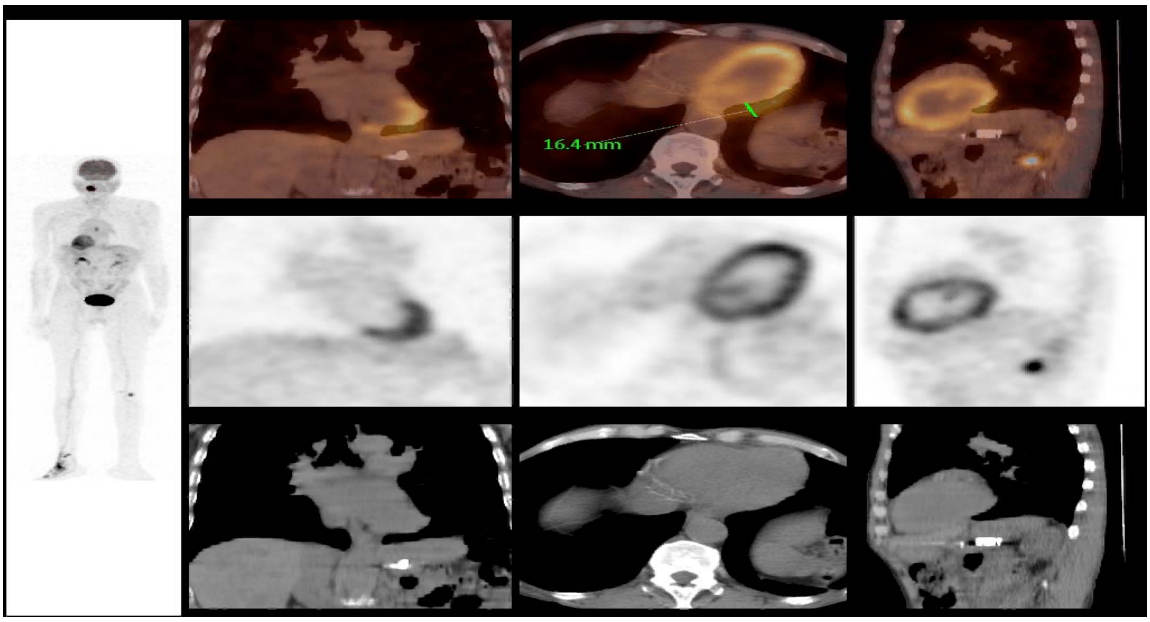

Figure 2: 62 year old male with moderately differentiated squamous cell carcinoma of the left tonsil. There is 16.4 mm misregistration in heart. as an example of non-preventable misregistration due to heart contractility and diaphragmatic movement.

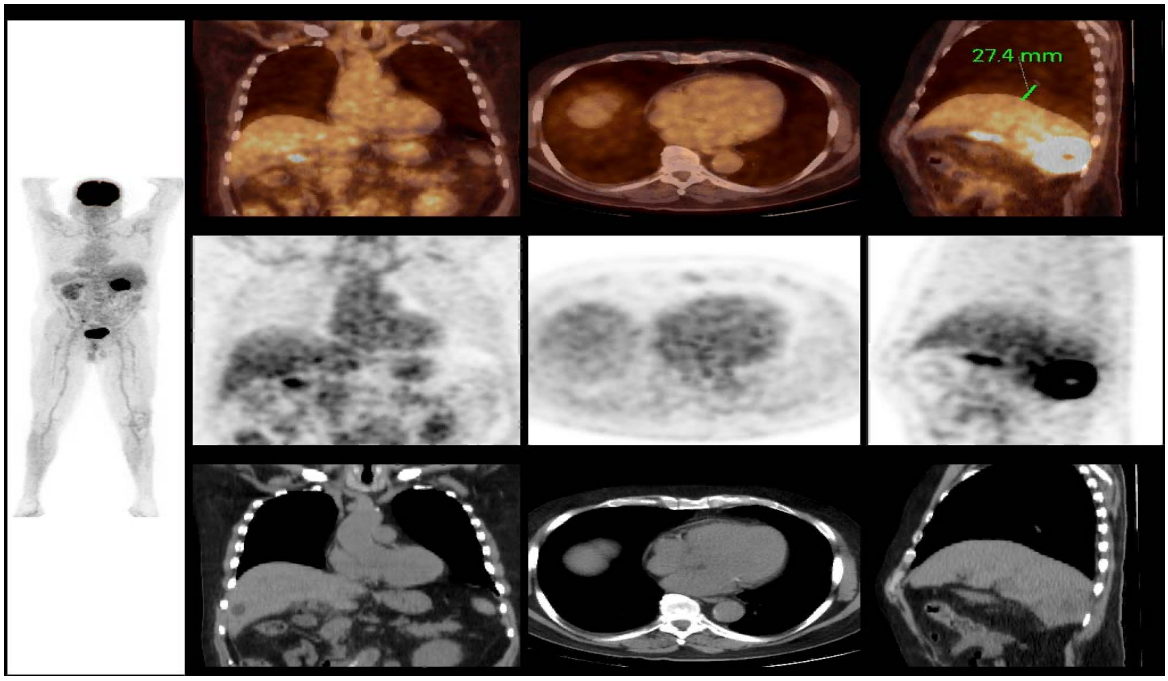

Figure 3: 79 year old male with renal cell carcinoma. This is an example of non-preventable misregistration of 27.4mm in the thoracic cavity due to the physiological movement of the diaphragm during respiration.

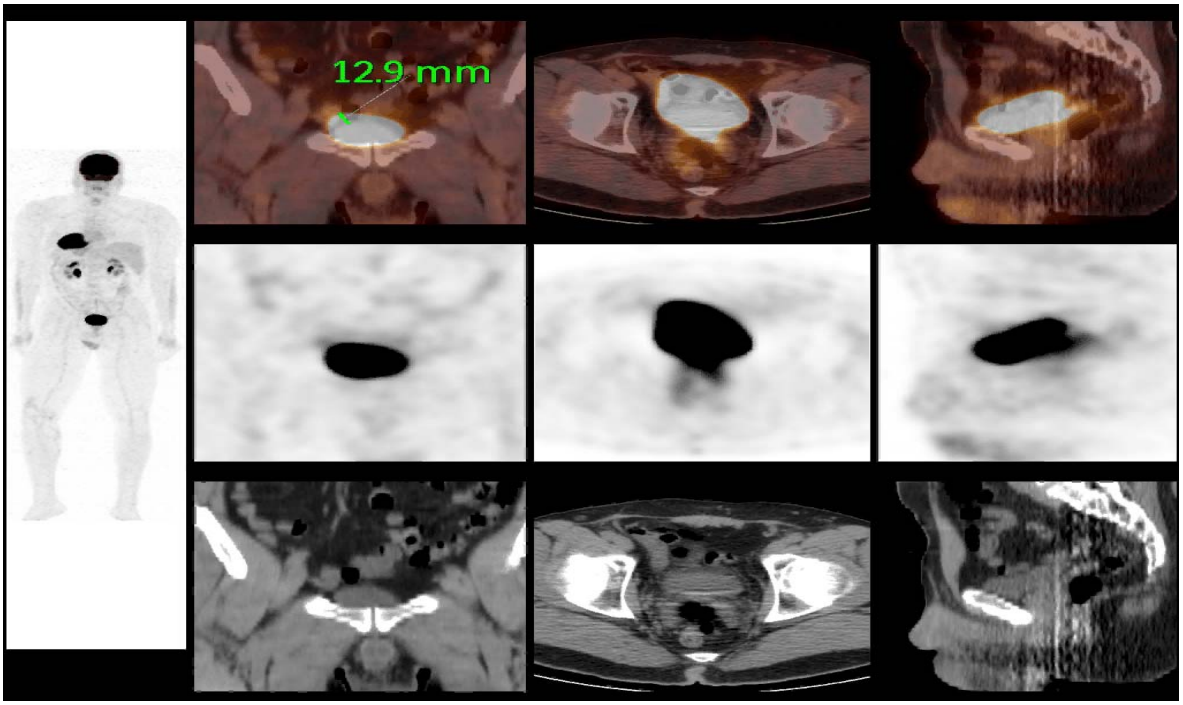

Figure 4: 54 year old male with restless leg syndrome. This is an example of non-preventable misregistration of 12.9 mm in the bladder, due to variable filling time interval between the CT Transmission and PET Emission scans.

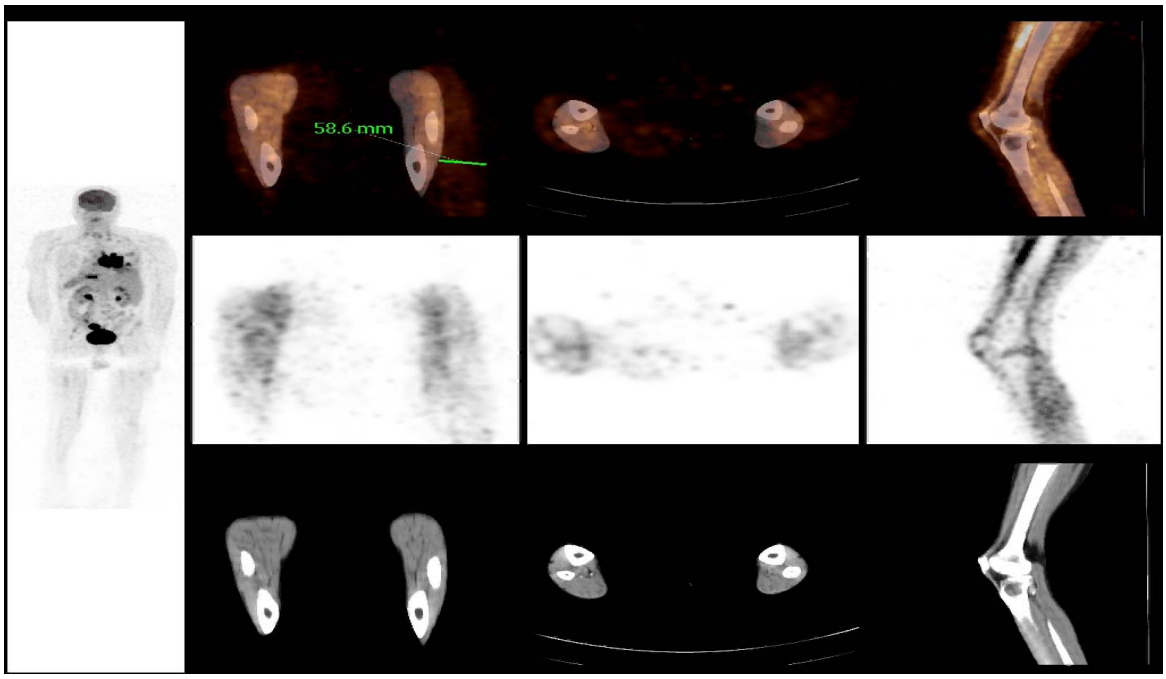

Figure 5: 73 year old Male with lung carcinoma. This is an example of preventable misregistration in the leg, 58.6 mm. The patient moved his leg twice during PET image acquisition (note the multiple legs seen in the transaxial PET view)

Discussion

PET and CT improves diagnostic accuracy, PET/CT scanners have brought their own specific pitfalls and artifacts. The artifacts that can be generated on PET images due to the use of CT data transformed into attenuation maps are related to the use of concentrated CT contrast agents, CT beam-hardening artifacts due to metallic implants, and physiologic motion[10]. Misregistration artifact caused by motion can occur at many sites either as non-preventable misregistration due to physiological motion, such as diaphragmatic motion and cardiac motion, or preventable due to nonphysiological patient movement between PET and CT studies. Misregistration between the PET and CT portions as detected on the PET/CT fused were previously evaluated in a particular anatomic location (ex. lung, diaphragm) but has not been systematically evaluated in true whole-body PET/CT covering from the top of the skull to the bottom of the feet. In this study, many patients had significant misregistration that is larger than the spatial resolution of most current PET/CT scanners.

Involuntary patient motion may also be due to relaxation of muscles during the combined examination, which takes about 20–35 min for a whole-body (WB) acquisition[11,12]. The likelihood of muscle relaxation increases with scanning time; therefore, body regions such as the head and neck, with the largest time differences between the CT and the PET portions, are prone to misregistration.

Accurate fusion is of paramount importance in evaluating head and neck cancer cases where differentiation between FDG avid lesion from normal physiologic FDG avid muscle and lymphoid tissues can be challenging. In our study, mean misregistration in the head and neck area was 6.31 mm and occurred in 67% of the studies (Figure 1). Average motion in Although hardware image fusion between unrestrained subjects during WB PET/CT examinations can be reduced by use of rigid head and neck positioning aids, such as foam molds, or vacum bean bags. Such positioning aids can reduce misfusion to 2 mm, which is less than the full width at half maximum (13). In addition, a recent study showed that routine use of a head holder may reduce the frequency of mis-fusion in the head and neck area to 1% [14].

In cardiac PET/CT, misregistration artifacts in AC myocardial perfusion images (AC-MPI) are more frequent and severe when CT is used for AC than for radionuclide-based transmission maps, in part because of the slower acquisition time of the latter, which averages the attenuation values during breathing cycle. Clearly, mismatches associated with CT-AC are potentially more serious for cardiac studies than they are for oncology. A relatively recent study showed that up to 40% of cardiac PET/CT studies could be affected by misregistration.[15]. This is not only because of respiratory motion but also due to contractile cardiac motion. In our study, accuracy of registration in the heart was measured from FDG PET/CT studies done for evaluation of cancer and not for cardiac evaluation. However, the misregistration at the cardiac region ranged from 1.30-25.90 mm with a mean of 8.11 mm and frequency of 88% (Figure 2).

Respiratory motion artifact (RMA) is probably the most frequently studied misregistration artifact in the PET/CT literature. RMA typically causes curvilinear cold (i.e undercorrected) artifacts paralleling the dome of the diaphragm at the lung/diaphragm interface. In earlier PET/CT design, RMA has been noted on 84% of PET-CT image acquisitions and were not seen on the 68 Germanium-corrected images; however, these artifacts were infrequently severe and were not diagnostically problematic in most cases [16].

The same study reported RMA with an average width of 14–16 mm as an indicator of respiration-induced mismat-ches of CT and emission activity distribution in the area of the diaphragm for normal-breathing protocols. The clinical significance of respiratory artifacts has been studied in a series of 300 patients showing that such artifacts resulted in lesion mislocalization in 2% of patients studies[17]. Consequently, different respiratory protocols, with or without gating, were advocated to be used in PET/CT; however, shallow breathing is probably the most widely used protocol[18]. Arguably, it is frequently difficult to coach cancer patients into any breathing protocol. Therefore, normal breathing is the standard of care in our PET center. In this study, misregistration at the diaphragm ranged from 1.10 to 56.00 mm with mean of 9.36 mm and frequency of 86% (Figure 3). Of note, the frequency of the RMA and related problems are much reduced for the faster higher-performance CT scanners. Indeed, we are experiencing less RMA in our 64-slice PET/CT scanner compared to prior older designs.

Misfusion in PET/CT may not only result from spatial misregistraion but also can be temporal in origin, such as internal organ motion between the CT and PET image acquisition. For example, physiological bowel motion may result in attenuation differences and subsequent differences in SUVs when CT is used for AC[19]. Protocols of PET/CT imaging have not yet been standardized, and the method of performing PET/CT scan variety among cancer centers and clinical sites. It is safe to assume, however, that emptying the bladder before image acquisition is a standard routine in all PET sites. The bladder is typically mostly empty during CT image acquisition; however, continue to expand with radioactive urine during the PET image acquisition. It is that continued filling, due to the time difference between the fast transmission and the slow emission that causes the size of the bladder to appear larger in PET than it is in CT. In our study, the bladder was used as a surrogate for evaluating misfusion in the pelvic region, and misregistration ranged from 2.90 to 36.50 mm with mean 14.52 mm and frequency of 98% (Figure 4).

In oncology, WB PET/CT is typically performed from the head to the pelvic floor[20]. The use of the term WB is misleading since the most commonly used field of view (FOV) for the arms-up PET/CT WB protocols only includes the base of skull to upper thighs, and does not include the brain, skull, and significant portions of both upper and lower extremities. In this study, however, images were acquired from the top of the skull to the bottom of the feet including both upper and lower extremeties. Acquiring true whole-body not only requires additional 10-15 minutes of image acquisition but also may increase the frequency of patient motion. In the current study, misregistration ranging from 0.10 to 96.00 mm with mean of 11.5 mm and frequency of 85% was noted in the arms. Also, misregistration in the legs was the most frequently (86%) noted example of preventable misfusion in PET/CT. It ranged from 0.50 to 80.40 mm with a mean of 15.02 mm (Figure 5).

In summary, combined PET/CT technology cannot resolve all issues associated with accurate alignment of two modalities[21]. However, advances in the technology have resolved some of the problems, and new strategies have been developed that address many of the outstanding issues including creative patient positioning and gating techniques. It is important to note that misregistration related artifacts are less

noticeable in new generations of PET/CT scanners. Furthermore, new promising PET hybrid imaging technology may hypothetically eliminate misregistration artifacts. In hybrid PET/MRI for example, the misregistration artifacts are not expected, as concurrent PET-MRI acquisition within a single scanning system will eliminate errors due to image mismatches caused by a patient being in differing positions in separate scanners [22].

The scope of this study did not aim at performing a comprehensive analysis of the diagnostic impact of misregistration in PET/CT; however, we attempted to quantify patterns and prevalence of misregistration resulting from using the CT for AC. In so doing, the importance of adequate patient positioning and added patient support becomes obvious.

Conclusion

We conclude that at least one form of significant misregistration, more than the spatial resolution of the PET, was present in 100% of studied PET/CT cases. However, misregistration related artifacts are less noticeable in new generations of PET/CT scanners. Advances in the PET/CT technology including creative patient positioning and gating techniques would significantly minimize the frequency of misregistration in PET/CT.

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