MULTIMODALITY: PET/CT and PET/MR

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Abstract

In this paper we review the current implementation of modern PET/CT scanners which are composed of composed of a CT (Computed Tomography) imaging system and a PET camera in the same gantry. The advantage of this technology reside in the ability to inherently produce high resolution anatomical images and highly informative functional images of the body at the same session. The use of CT has also showed to improve image quality through lower noise in the attenuation images. More recently, PET/MR scanners have appeared on the market. This paper will review the building characteristic of those devices and describe their current functionality, limitations and usage.

Keywords: PET/CT, PET/MR, attenuation correction, metal artifacts, motion correction.

Resumen

En este artículo se describirá la implementación de scanners PET/CT, los cuales están compuestos de un sistema de imagen CT y una cámara PET, ambos integrados al mismo gantry. La ventaja de este dispositivo reside en la adquisición de imágenes de alta resolución de carácter morfológico y funcional del cuerpo y tomadas en una sola sesión. Recientemente scanners PET/MR han aparecido en

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el mercado; las características de su construcción, su actual funcionalidad, usos y limitaciones, serán discutidos en este trabajo.

Palabras clave: TEP/TC, TEP/RM, corrección por atenuación, artefactos metálicos, corrección por movimiento.

Introduction

From its introduction in the early 2000, PET/CT appeared as a revolution in medical imaging. In effect, the juxtaposition of highly effective and well established technology of Computed Tomography (CT) provided the much needed high resolution anatomical images to functional PET images obtained with ^{18}F-FDG. In the clinical setting, this combination was extremely well received in the clinical community by providing improved guidance in determination of the anatomical localization of the activity. Declared invention of the year in 2000, PET/CT soon received early recognition of its diagnostic capability, so much that from 2003 most of the sales of new PET cameras were in the form of PET/CT.

More recently, PET/MR appeared on the market. If PET/CT created a revolution, PET/CM was more an evolution, although not for being short in promises. Indeed, PET/MR offers improved soft-tissue contrast and provide images without any radiation doses. However, its clinical acceptance is slow and even uncertain, the high price still being a major driving factor. This paper will discuss the implementation PET/CT and PET/MR technology and discuss their functionality and applications.

PET/CT

All current PET/CT scanners are made by the sequential juxtaposition of a CT and PET scanner in the same gantry. This technology allows to image a subject by CT and PET in the same session with little chance for relative motion in between the two imaging modalities. The typical configuration is a CT followed by PET scanners. In this configuration, a patient receive a CT scan,

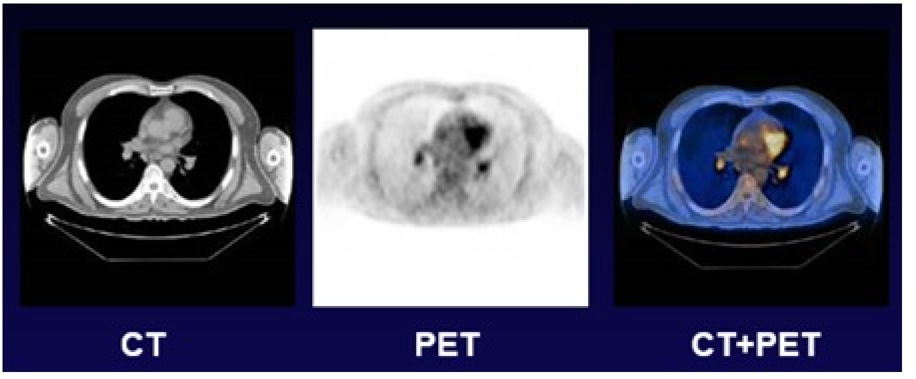

Figure 1. *Example of CT, PET and PET/CT images obtained with 18F-FDG is patient with a mediastinal lesion. Although, not apparent on CT, the lesions appears as highly metabolic on the PT images.*

then the bed pallet moves to the PET position and a PET scan follows. The images being inherently registered by a pre-determined spatial position of the CT and PET field of view (FOV), fused rendering on the three dimensional distribution of the activity distribution can be produced as an overlay of the PET onto the CT images. An example is shown in fig. 1. The CT images are used not only for anatomical localization but also for attenuation and scatter correction.

Attenuation Correction in PET

One of the important hallmark of PET is that of being quantitative. This requires an accurate account of the attenuation or absorption of the annihilation photons by the patient's body. By the nature of PET, sinogram counts are the result of linear integration along lines of response adjoining two individual crystal elements. One important characteristics of PET is that the total attenuation along a line of response is given by a similar line integral of the attenuation coefficient distribution. This is essentially the definition of a CT scanner. Early implementation of attenuation correction in first generation PET scanner was done with the use of rotating ^{68}Ge line sources or ^{137}Cs point source. Attenuation images were then obtained by taking the inverse Radon transform of the ratio of a transmission scan and a previously stored reference blank scan. Good quality attenuation images were obtained only with a 5-10 minutes transmission scan and required segmentation to convert the noisy transmission images into a usable attenuation map, albeit low resolution. X-ray CT offers a much larger photon flux allows for much faster acquisition (typically in less than 1 minute for 1 meter long scan) and the high-resolution CT detector produces exquisite images of the body. The fundamental physics of photon interaction from annihilation photons (511 keV) and CT X-rays (40-140 keV) is similar but the greater absorption by photo-electric effect in CT leads to differences that are worth discussing.

In PET, most of the attenuation is due to the Compton effect while in CT, the attenuation coefficients are determined by the electron density times the sum of Compton and Photo-Electric contributions. The main consequence of this is that the bones (having more elements of higher Z material, notably Calcium and Phosphorous), are seen with much more contrast. This is desirable for visualization of bone lesions but has for consequence that the conversion of CT image intensity into PET attenuation values needs to consider two zones of attenuation: soft-tissue like (fat, muscle, lungs, organs and so on) and bone like tissue.

So, two formulas are employed to scale the CT intensity to PET attenuation values for either soft-tissue like material [1]:

$$\mu_{PET}(511) = (CT + 1000)\frac{\mu_W(511)}{1000} \tag{1}$$

and for bone like materials:

$$\mu_{PET}(511) = \mu_W(511) + CT\frac{\mu_W(70)(\mu_{Bone}(511) - \mu_W(511))}{(\mu_{Bone}(70) - \mu_{Water}(70))} \tag{2}$$

This bi-linear relationship is thus applied by using an empirically determined threshold value of a few hundred HU (Hounsfield units) to discriminate between soft-tissue and bone. Thus, in practice, attenuation correction in PET/CT is done by scaling

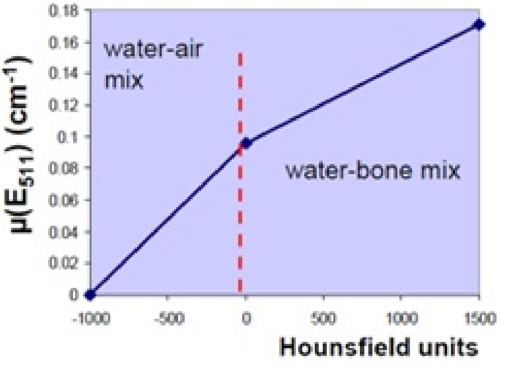

FIGURE 2. *Relationship between PET attenuation coefficient values and CT Hounsfield units.*

the CT images resampled on the PET pixel size by the formulas above. Then the resulting images are forward projected (Radon transformed) to produce the Attenuation Correction factors (ACF) in the form of sinograms that are used multiplicatively with the measured emission sinograms for attenuation correction.

Scatter Correction

Since traditionally, attenuation maps in the form of low-resolution transmission images or CT images were available, the correction for Scatter has been performed since the early days of PET. The most widely adopted technique nowadays is the modeled single scatter correction algorithm [2], [3]. This technique essentially employ an estimate of the activity distribution and the attenuation map (from point/line source transmission or CT images) to perform a calculation of the scatter distribution using the known Compton scattering differential cross-section of Klein-Nishina. The complete algorithm proceeds from a first iteration with an estimate of the activity distribution that includes scatter, and then a second pass from an estimate of the activity distribution using the first pass scatter correction. In practice, just a few iterations are required to reach a stable correction for scatter.

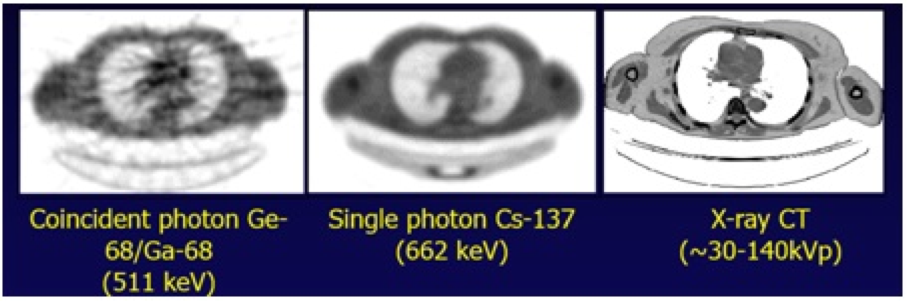

FIGURE 3. *Evolution in attenuation correction maps from left to right, line source ^{68}Ge transmission (5 min/15 cm), ^{137}Cs point source (2 min/15 cm) and CT imaging (1 min/100 cm).*

PET/CT artifacts

Although patient motion is minimized between the two modalities since the patient stay on the same couch for the two examinations, there remains still the motion from normal respiration which can lead to visual mis-alignment of the PET to the CT data. CT imaging can be done very quickly and typically can be done within a single breath. PET however is relatively slow and can take a few minutes per bed position. Difference in breathing phases can lead to mis-registration. Those can be minimized by proper instruction to the patient such as instructing to hold-breath at the end-of expiration during the CT or by using shallow breathing techniques throughout the procedure. Techniques for correcting for motion have been developed for PET/CT and will be discussed later.

A second source of artifact is due to the limitation that the CT FOV is only 50 cm while typical PET FOV is 66 cm or more. This essentially yields to areas of the body not adequately covered by the attenuation correction (namely arms alongside the patient). Vendors now offer extended FOV capabilities for the CT where the area outside the measured 50 cm FOV is extrapolated to 70 cm. This yields to approximate correction for attenuation beyond 50 cm and is a subject where further improvement is required.

Finally, a third source of artifacts is from metal due to prosthesis, dental work of else or other highly attenuating material such as CT contrast media. Metal will essentially attenuated X-ray photons very strongly and lines of response passing through metallic region will have little or no counts. This will yield to streaking artifacts in the CT images and bad scaling to PET attenuation values. The most promising technique is through pre-correction of the CT sinograms. However, the recent commercial introduction of iterative reconstruction for CT will probably provide a definitive solution to this problem. Contrast agents will generate areas overly corrected for attenuation in the PET data. This is due to the fact, that the CT contrast agent will produce highly contrasted images but by the time of the PET, the agent will have dissipated and will no longer present high attenuation. A non-contrast CT is this highly preferred for attenuation correction purposes.

PET/MR

The combination of PET and MRI (Magnetic Resonance Imaging) has recently been made available commercially. The promises of this technology is many fold. This scanner must offer whole-body scanning technology (not just the head) since the main application is oncological body imaging in PET. This requirement demanded putting the PET detectors in the MR field. The conventional photo-multiplier tube used in PET scanner will simply not work in the intense magnetic field of MRI and thus novel PET detectors were needed. Semi-conductors allows for compact detector design. The technology available today is in the form of avalanche photo-diodes (APD) and Si-photomultipliers (Si-PMT). APDs were chosen by Siemens in for their mMR simultaneous PET/MRI scanner, while GE opted for Si-PMT. These two PET/MR scanners use LSO based scintillator couple to either APDs or Si-PMTs.

Many technological hurdles had to be overcome to make this technology possible. First, the scanner needed to use a wide enough bore for whole-body PET scanning. Initial PET/MR were designed limited to animal or Brain imaging but the principal applications of this technology in in body imaging.

This necessitated the PET detectors to have a small size, thus eliminating the option of bulky PMTs, and required to sandwich them between the gradient and the RF coils. In addition, any additional conducting elements placed in the MR field can affect its homogeneity, and conversely the presence of high magnetic can affect the functioning capability of the PET detectors. Indeed, rapidly changing MR fields such as those created by the RF can induce Eddy currents which will affect PET electronics and generate heat. Since APDs and Si-PMTs are very temperature sensitive, highly effective cooling with circulating water had to be implemented.

PET/MR systems combine functional PET imaging with high-resolution anatomical MR imaging. The wide variety of MR sequences allows for various contrast level in the anatomical images allowing to produce images where water, fat, flow or motion is a dominant feature. This is a clear advantage over CT. High quality images can be obtained without contrast agents and does not require high-radiation dose to the patient. This is of particular importance for pediatric patients.

PET/MR also proposes to be truly simultaneous. The inclusion of the PET detectors in the MR field has thus made this possible. This characteristic allows to reduce procedure time but mainly proposes to develop joint imaging protocol from which functional PET, and either anatomical or functional MR images can be acquired. The high speed of MR allows for motion correction due to the absence of radiation dose. This is a very important feature. The main difficulty of PET/MR is for the attenuation correction and this problem still hasn't found a completely satisfactory solution yet. We will discuss this first.

Attenuation correction in PET/MR

Contrary to CT, signal in MR images is not proportional to electron density which is the driving factor governing photon attenuation. MR image intensity is governed by the magnetic properties of nucleus with spin (namely protons are by the fact the most abundant in the body) in their magnetic local environment. Once material is placed within a constant and homogeneous magnetic field, protons will either align along the direction of the magnetic field or in its opposite direction. A slightly larger number of protons will align in the direction of the magnetic field and will create an overall magnetization. The RF coil having for function to tilt the global magnetization, this magnetization will start precessing around the main filed axis at the Larmor frequency. The micro-environment determines the time needed to recover the longitudinal magnetization (T1). In addition, as the global magnetization it tilted by the RF, individual protons will lose coherence in the reference frame of the global magnetization and will lead to dephasing. This micro-environment and local magnetic homogeneity will also determin the time required to return to equilibrium in this tilted reference frame is (T2 or T2*). Also, MR images often suffers from loss of signal intensity away from the MR coil. Therefore, other technique are necessary. The most-widely adopted technique is nowadays the 2-point DIXON sequence which is spin-echo with a short TR and two short TE acquisitions (T1 dominated). This technique exploits the difference in resonance frequencies of proton from water and fat (known as chemical shift). The two echo times are chosen for which the proton in water and fat appear either in-phase or out-of-phase. In the in-phase image, the fat and water signal are additive while in the opposite phase, the signal from fat and water subtract. From those, water and fat dominated images are produced and by segmentation pixels are identified as either from soft-tissue (internal organs, muscle, etc) or fat. These areas are assigned the known attenuation coefficient of 511 keV photons for water (0.096/cm) or fat (0.0854/cm). Subsequently, contouring algorithms are used to delineate the body edges and the internal lungs cavity (0.0224/cm). Soft-tissues, fat and lungs are then segmented at fixed and known attenuation coefficients.

The main limitation of this technique is that bones are segmented as soft-tissue. Protons from bone have very fast T1 values (short

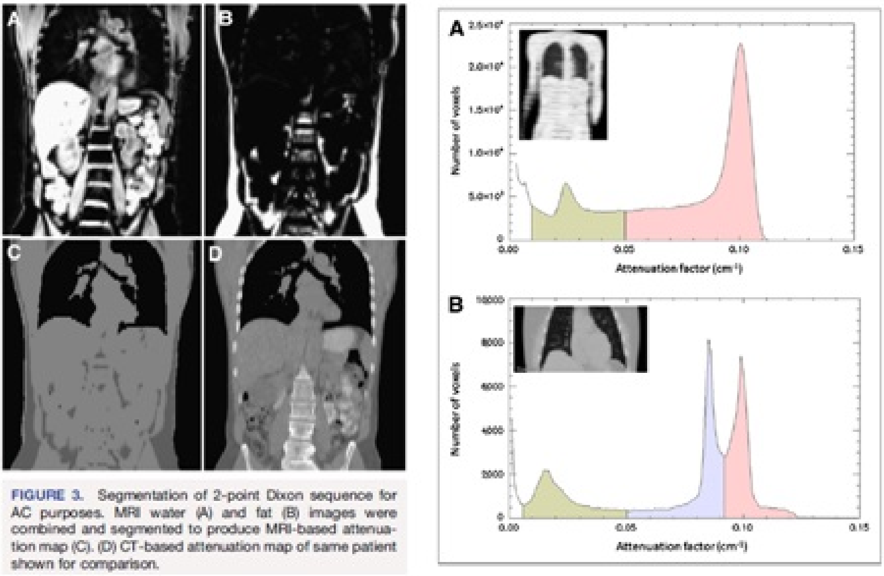

FIGURE 4. *Attenuation correction images (left) and attenuation values histogram (right) from PET transmission point source (right-A) and low dose CT (right-B) [4].*

longitudinal relaxation time) and thus have very little intensity in the MR images despite having the most attenuation for PET photons. The development of techniques for inclusion of bones in the attenuation correction is actively under way and involves the use of UTE (Ultra-short Time of Echo) sequences, T2 imaging and advanced signal processing algorithms. As an alternative to MR imaging, registered CT images can be used. This techniques is however only amenable for the head where the skull offers a rigidly non-deformable structure.

This is essentially the largest point of contention against PET/MR and numerous studies have evaluated the quantitative accuracy of PET/MR against the more established PET/CT. Differences of the order of 2-4 % have been observed in lesion activity in the body while differences of the order of 7-15 % have been observed in the bone lesions. This differences has no consequences in lesion detectability and thus does not limit the clinical utility of

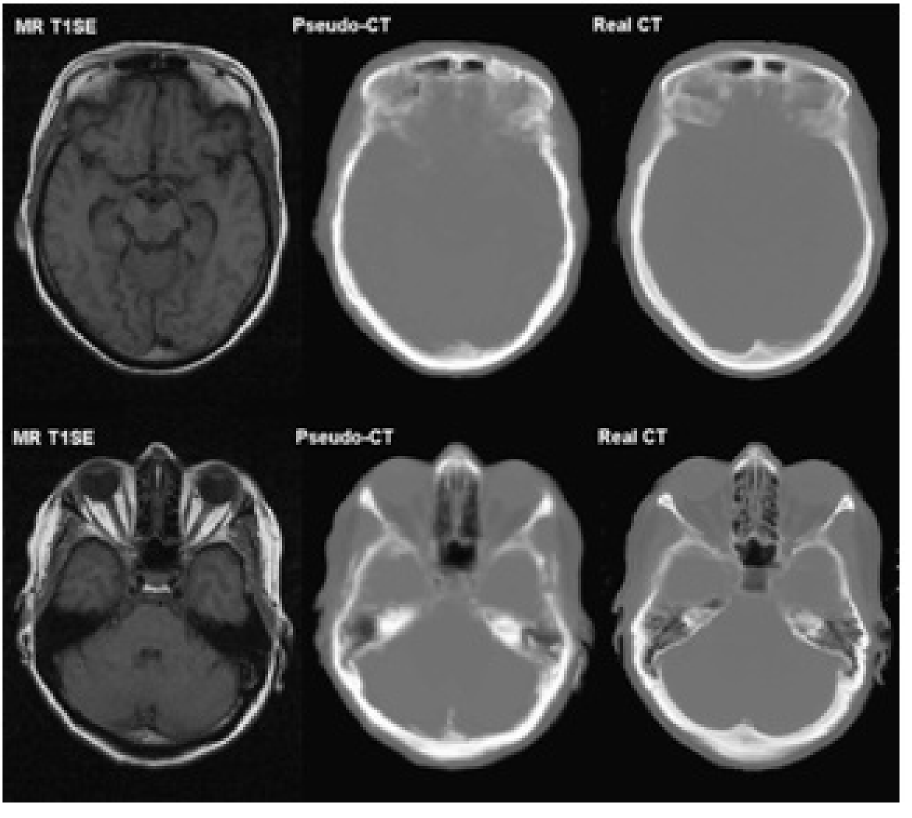

FIGURE 5. *Illustration of the used of registered CT images in lieu of MR-based attenuation correction for accurate bone segmentation in PT/MR.*

PET/MR as compared to PET/CT but has nonetheless prevented PET/MR to have been fully recognized as a clinical modality to this date by the insurance companies in the USA.

Artifacts in PET/MR

The 2-point DIXON is relatively fast (¡20sec) and can easily be done in a single breath. Fig. 6 shows chest attenuation maps obtained at breath hold, either end of expiration or end of expiration and shows substantial difference in the size of the lungs. This difference can have important consequences on the reconstructed PET images. Fig. 7 shows attenuation maps form the DIXON sequence taken at end-of-expiration and illustrate a subtle artifact at the edge of the lungs. Since the PET is acquired free breathing, a relaxed position close to the end-expiration often provides a satisfactory attenuation map and in many cases the patient can be instructed to stop breathing and hold a relaxed position for the duration of the attenuation correction MR sequence. This figure also illustrate another source of artifact in PET/MR due to the limited FOV size in MR. In this figure this is illustrated by a truncation of the arms at the edge of the FOV. This defect can be in part compensated by a joint estimation of the true activity distribution and attenuation media in the image reconstruction. This problem is still in need of a completely satisfactory solution.

Coils not included

By its nature, the measured attenuation maps form the DIXON sequence only provide attenuation information for the subject. All other hardware in the FOV needs to be added to the attenuation by other means. Permanent fixture such as patient couch, spine coil, head coil are typically included as hardware attenuation maps and are stored in the systems. From the known position of the patient couch during acquisition, their attenuation effects can thus be compensation accurately. Other MR coils such as the flexible phased-array coil for body imaging (Fig. 8) or neck

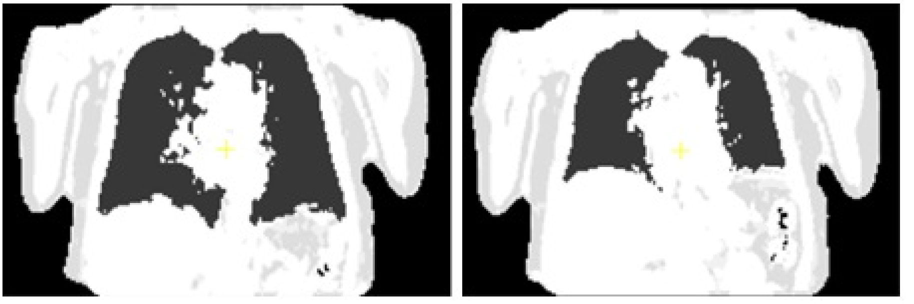

Figure 6. *Attenuation maps takes at breath-hold, either at full inspiration (left) or expiration (right).*

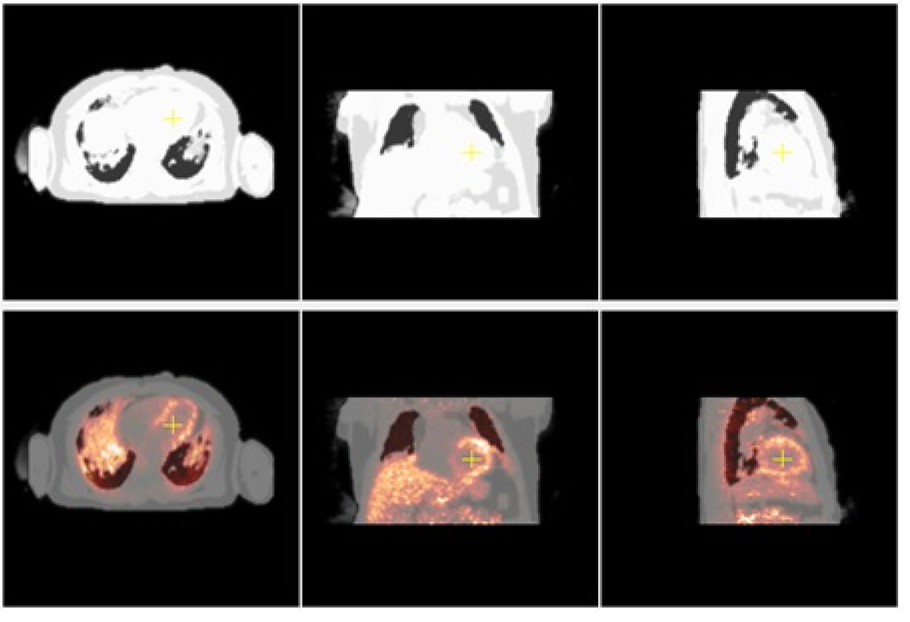

Figure 7. *Attenuation maps (top) and registration to PET) bottom indicating that the attenuation was capture at a stage with lungs slightly deflated with respect to PET.*

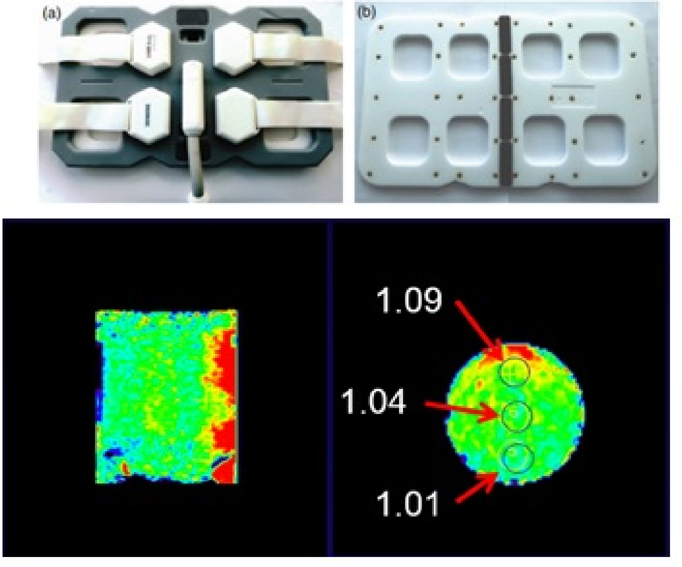

FIGURE 8. *Chest flexible phased0array coil used for body PETMR imaging (top), and effect of these coil of PET accuracy (bottom).*

coil are typically not included in the attenuation correction. The magnitude of their attenuation effect can be minimized by construction with low Z material and by minimizing the size of the electronic components. Despite this, the attenuation form the flexible coils can have a substantial effect. Fig. 8 (bottom) shows a picture of such a phased-array coil and its effect on attenuation. Regional effect of up to 20-30 % have been observed notably at the close vicinity of the coil.

Inclusion of the flexible phase-array coil can be done in post-processing by using a template of the coils (obtained from CT) and a combination of rigid and deformable registration with the help of fiducial markers attached to the coil. Techniques for this have developed and implemented at research institutions but not by the vendors at this time.

Motion Correction in PET

PET/MR allows for correction for motion due to normal respiration with the help of fast MR sequence that can capture the motion of the chest during breathing. In PET/CT, this can be achieved as well but at the cost of high radiation dose to the patient. The PET/CT technique involves capture of a CINE-CT scan which takes pictures of the chest at various phases of the respiration and then uses of a camera to monitor the breathing phase. The respiration-gated PET data can then be matched to the proper respiration phase from CINE-CT. Phase specific attenuation correction is applied and finally, PET phases are merged to a common phase by deformable registration with motion field defined by the CINE-CT.

In PET/MR, similar approached have been developed. For example above, Würslin [5] proposes to use fast MR composed of a stack of 2D-CINE MR in sagittal planes to capture chest motion during respiration. Using phase matching, the technique deforms the attenuation maps to match each phase of the respiratory cycle for accurate attenuation correction. Finally each phase of the gated PET data are merged together by deformable image registration with motion field defined by the CINE-MR. Alternatively, deformation information can be included inside the PET image reconstruction by altering the system matrix using the MR derived deformation fields. More advance approaches using for example self-gated MRI radial acquisition to capture respiratory and cardiac motion have been proposed [6].

Conclusions

Multi-modality imaging despite its limitation provides much superior diagnostic quality and has made its way into routine clinical practice. ^{18}F-FDG PET/CT imaging in particular is now the established standard of care for numerous forms of cancer. PET/MR is without hesitation a wonderful research instrument and offers tremendous possibilities for the development of powerful imaging protocols free of motion artifacts with enormous information about anatomy, material composition, flow, diffusion and many more. If PET/CT has now reached maturity, PET/MR is still undergoing development most notably in the areas of attenuation and motion corrections. Future areas of development will involve the development of imaging protocol that truly exploits the simultaneity and the joint information from the data from each modality. Whether it will remain a research instrument, time will tell.

Acknowledgments

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