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MR-based Motion Correction for PET Imaging

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Abstract

PET image quality is limited by patient motion. Emission data are blurred due to cardiac and/or respiratory motion. Although spatial resolution is 4 mm for standard clinical whole-body PET scanners, the effective resolution can be as low as 1 cm due to motion. Additionally, the deformation of attenuation medium causes image artifacts. Previously, gating is used to “freeze” the motion, but leads to significantly increased noise level. Simultaneous PET-MR modality offers a new way to perform PET motion correction. MR can be used to measure 3D motion fields, which can then be incorporated into the iterative PET reconstruction to obtain motion corrected PET images. In this report, we present MR imaging techniques to acquire dynamic images, a non-rigid image registration algorithm to extract motion fields from acquired MR images, and a PET reconstruction algorithm with motion correction. We also present results from both phantom and *in-vivo* animal PET-MR studies. We demonstrate that MR-based PET motion correction using simultaneous PET-MR improves image quality and lesion detectability compared to gating and to no motion correction.

I. Introduction

PET imaging, especially cardiac imaging, is limited by the degradation due to patient motion. The intrinsic spatial resolution of modern whole-body (WB) PET scanners is in the range of 4–5 mm for stationary objects [1–4]. However, this resolution may not be achieved because of motion. During free breathing, the heart moves in the range of 4.9–9 mm due to heartbeat and respiration [5, 6]. As the heart moves, its shape and density also changes. The heart motion is one of the most important causes of image degradation in cardiac PET imaging. The diaphragm and the liver move in the range of 7–28 mm and 5–17 mm, respectively, during respiration [5]. This motion makes lesions in the dome of the liver easy to miss [7, 8]. Even a lesion is detected in the liver, the SUV is well below the true value [9].

Attempts to develop practical and effective methodology to remove the effects of cardiac/respiratory motion were many (e.g., [5, 10–19]). Cardiac and/or respiratory gating strategies that “freeze” motion are popular in static PET, but have not been effective or successful in dynamic PET imaging of rapid dynamic functions, such as myocardial blood flow (MBF), due to the substantial noise associated with rejecting a large number of detected events in a short dynamic frame. Furthermore, it is important to highlight that it is not “just” the emission data that is corrupted by motion; there are often large reconstruction errors due to

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the deformation of the attenuating medium. In order to make proper use of emission data, one must know the corresponding attenuation at all times. Due to radiation exposure concerns, this data cannot be obtained routinely by conventional PET-CT. The full extent of the problem is seldom acknowledged, but experience has shown that even with PET-CT, it is difficult to obtain a valid attenuation correction in the face of subject movement, and the impact of the compounded effect of motion and attenuation is profound as it can yield false positive ischemic areas (see Fig. 1) as well as false negative ones. Moreover, even when not apparently recognized, these factors have a significant role in reducing the accuracy of PET quantification.

One elegant solution to the motion problem in PET is to use simultaneous PET-MR. The MR-measured motion fields will be used directly in the PET reconstruction, allowing non-rigid motion blurring to be completely removed without loss of signal-to-noise ratio (SNR). Thus it is possible to use MR-derived motion fields, to correct PET for non-rigid motion without additional radiation dose to the patient, while simultaneously providing useful clinical information about wall motion (cine MR). Beyond motion correction, MR will allow us to incorporate the motion fields of internal organs within the framework of PET reconstruction and enable the use of a “time-dependent” attenuation map that is deformed by the motion fields and is consistent with the PET emission distribution, in contrast to a single static attenuation map. This, if successful, will eliminate the breathing artifacts associated with inconsistencies in the position of the patient organs in emission and attenuation data that may occur when the attenuation map is acquired over a different time frame than the emission data as is the case, for example, with end-inspiration or end-expiration CT versus PET. This complete correction, not just freezing, of respiratory motion will have profound impact on image quality and will improve the quantitative abilities of cardiac PET imaging. In contrast, gating cardiac and respiratory motion in dynamic PET is extremely challenging to achieve given the high levels of noise associated with each short dynamic cardiac frame.

II. MR-based motion measurement

Heart motion measurement is the most challenging compared to other organs. Motion of the heart has three different components: motion caused by the pumping action of the four chambers (cardiac motion), motion caused by respiration, and voluntary or involuntary patient movement. The latter component is usually managed by means of patient cooperation or by means of sedation or anesthesia in pediatric. The relationship between the motion of the heart and the superior-inferior (SI) motion of the diaphragm is approximately linear although highly subject specific, with an element of hysteresis [20] (See Fig. 2).

MR tagging can be used to measure cardiac motion. In MR tagging, a special sequence of Radio Frequency (RF) pulses is applied causing a series of parallel strips, known as tags, on the muscle tissue. Next, a series of MR images is obtained in which the tags are visible. The deformation of the tags is used to estimate cardiac motion.

Respiratory phase can be monitored using a 1D navigator to acquire data along a column in the SI direction through the diaphragm. Diaphragm position along the SI direction is quantified and used to determine the respiratory phase. The navigator uses simultaneous application of RF power and a shaped gradient waveform. Only one line of data passing through the origin of k-space is acquired for 1D navigator. The excitation, 1D MR readout and reconstruction can be completed in less than 20 ms.

We present below a detailed procedure to measure both cardiac and respiratory motion fields using MR. Five bins are defined within the moving range of the diaphragm. However, because of the hysteretic behavior, we actually have 8 respiratory phases. Also, eight cardiac phases are defined corresponding to eight time frames within the cardiac cycle. Fig. 3 shows

a matrix of 64 combinations (squares) of cardiac and respiratory phases. One of the 64 squares is chosen as the reference square. The purpose of motion correction is to find the motion fields between any of the rest 63 squares to the reference square so that all the acquired PET data can be reconstructed within the reference phase. PET data will be acquired simultaneously with MR tagging data. Fig. 4 shows the MR acquisition procedure, which can be applied to both breath-holding and free-breathing. Before the sequence starts, a look-up table is first generated for each square in Fig. 3 to keep track of the acquired slices and phase-encoding lines. When an R-wave ECG trigger presents, a 1D navigator is first applied. The resulting diaphragm position is used to determine the respiratory phase (interpolation can be used to obtain more accurate respiratory phase information throughout the entire cardiac cycle). Next, a SPATial Modulation of Magnetization (SPAMM) tagging [21] is applied. This is followed by 8 gradient echo (GRE) acquisitions. The cardiac phase for each of the GRE acquisitions is determined by the duration between the ECG trigger and the GRE acquisition time. Knowing both the cardiac and the respiratory phases, the sequence can determine the slice and phase encoding lines to be acquired using the information from the lookup table. After all 8 GRE acquisitions, the sequence will wait for the next ECG trigger. It will be ideal to acquire all the slices and phase encoding lines for each square in Fig. 3. However, this is impractical because it requires a long imaging time. One solution is to keep acquiring data until all the cardiac phases in only one respiratory phase are fully sampled [the red column in Fig. 3]. Some squares may be under-sampled, but they can be reconstructed using compressed sensing technique to take advantage of the prior information provided by the images reconstructed from other fully sampled squares [22, 23]. When a square is severely under-sampled that its MR image volume cannot be reconstructed, its motion fields will be interpolated using the motion fields from the neighboring squares. Three orthogonal 1D tagged data will be acquired in successive studies. The entire full k-space tagging acquisition takes about 12 minutes using our method (4 minutes for each tagging direction). Using partial k-space acquisition [24, 25] and GRAPPA [26], the total acquisition time can be reduced to <5 minutes. During the acquisition, the ECG signal and navigator are recorded and will be used to assign a cardiac and a respiratory phase for each PET event.

To analyze the SPAMM tagged images, the HARmonic Phase (HARP) method, which was developed by Osman and colleagues [27, 28], can be used. HARP is based on the observation that the spatially periodic magnetization profile imposed on the image by SPAMM is evident in the raw (k-space) data as spectral peaks, separated by the complement of the distance of the tags (tag resolution). By band-pass filtering one of these “harmonic” peaks, and reconstructing the single peak into a low-resolution image by a complex inverse Fourier transform, the resulting image re-parameterizes the tagged image into a more useable form. The new image has the resolution of the tags (i.e. lower than the original image), and can be recast as a new low-resolution magnitude image, and a phase image. By choosing a single spectral peak, the tags are eliminated from the magnitude image, but the phase is now a parameterization of the tag locations by phase angle. Thus, each point in the tissue obtains a locally unique phase angle, which can be more easily tracked over the displacement evolution of the subject tissue. The parameterization by phase is still degenerate at 2π intervals in phase, but if the increment of displacement is less than the tag line spacing from image to image, the phase dynamic range for displacement in a single tag is not exceeded, and the tags can be easily and robustly tracked. Given the HARP processed images, the motion of points in an image plane must be tracked. Displacement between any pair of SPAMM encoded and HARP processed images can be evaluated for any point using Newton’s method [29].

Instead of the HARP method, B-spline nonrigid image registration, which is based on one of the two similarity measures - the sum of squared difference (SSD) or mutual information

(MI) [30, 31], can be used. The motion fields are estimated by minimizing the following cost function:

$$\Phi = M(\mathbf{f}_T, T\mathbf{f}_S) + \beta R(T), \quad \text{Eq. 1}$$

where $\mathbf{f}_T$ and $\mathbf{f}_S$ are the target and source image, respectively, T is the motion (image warp) operator, M is the similarity measure, $R(T)$ is a regularizer, and β a regularization parameter. Because motion estimation is an ill-posed inverse problem, regularization is used to achieve stable and realistic solution. Requiring the estimated motion to be invertible, i.e., the determinant of Jacobian of motion must be positive, has been shown to regularize the motion estimation problem. A simple regularizer that penalizes the difference of the adjacent B-spline coefficients [30] can be used. The regularization parameter, β , can be increased until all Jacobian determinant values at all voxels are positive. This regularizer can be applied to both B-spline SSD and MI based motion estimation algorithms. Cubic B-spline interpolation can be used for images and estimated motion fields. For motion fields, B-spline knots (coefficients) can be located with a spacing of 4 pixels in each x , y , z direction. Local minima problem can be avoided using a bi-level multi-resolution scheme. Motion fields were estimated between adjacent phases and B-spline interpolation was used for the composition of motion fields to estimate motions between different phases other than adjacent phases.

In addition to the above MR methods, we also want to point out that respiratory motion fields can also be determined using PET data. It has been demonstrated in the past that PET data alone can be used to estimate respiratory motion fields [6, 14, 16, 32–37]. The PET data for each respiratory phase are first reconstructed separately. The same image registration method shown in Eq. 1 can then be used to calculate the respiratory motion fields.

Some of the MR techniques and motion estimation algorithms described above can be applied to other organs including lungs, liver, and kidney. For example, the radial FLASH (Fast Low Angle SHot Magnetic Resonance Imaging) can be used to obtain a series of image volumes that include nodules and boundary of the lungs. The motion fields of lungs can then be obtained from the MR cine images using image registration [38–40].

III. Motion correction in PET reconstruction

The estimated MR measured motion fields can be integrated into the system modeling for PET reconstruction. A number of methods have been proposed to correct for rigid motion in PET that operate on reconstructed images [41, 42], however these registration type techniques are not easily extendable to non-rigid motion correction and are not formulated in a general optimization framework that respects the Poisson nature of PET data. Several authors have proposed instead to incorporate a motion model in the reconstruction procedure [43] (rigid), [18] (rigid and non-rigid), which has the advantage of being statistically correct. To our knowledge, Qiao et al. [18] are one of the few groups who showed that this framework can account for non-rigid motion in a simplified simulation study. In this section, we extend the work of Qiao et al. [18] and Qi and Huesman [43], to describe a reconstruction algorithm specifically tailored to list-mode PET data containing motion signals (e.g., from MR navigators) along with detected coincidences. In this approach, all counts are reconstructed into one reference frame in order to maximize SNR, while correcting for motion, in order to minimize motion blurring. This method can be easily extended to motion-corrected, frame-by-frame dynamic reconstruction.

We first put the motion information in the system model, and formulate the following system matrix:

$$\tilde{a}_{ni}(t) = P^{attn}(t) P^{norm} D(t) \quad \text{Eq. 2}$$

where $\tilde{a}_{ni}(t)$ is system matrix that includes motion field $D(t)$ and motion-dependent attenuation correction $P^{attn}(t)$, P^{norm} is the normalization. The attenuation map, $P^{attn}(t)$, is

obviously motion-dependent, and is modeled by $A_k = \exp \left\{ - \int_{LOR_k} \mu(l, t) dl \right\}$, where the line integral is computed using the deformed attenuation map (transformed by the measured motion fields) at time t . Note that this is an important departure from the traditional attenuation correction approach that assumes a static attenuation map. Indeed, modeling motion in the attenuation map in addition to the emission map will reduce artifacts (e.g., mushroom) due to mismatches between emission and attenuation data that are particularly severe at boundaries between lungs and soft tissues. Given above system matrix, when we compute a forward projection, we will first apply the motion fields to the motion-free reference image, and then calculate the rest of the forward projection. In the case of computing back project, we will back project the sinogram to image space, then apply the transpose of motion field matrix to the resulting image. One can prove that the operator of applying transpose of motion fields is approximately equal to applying the inverse of motion fields.

After we have the system modeling, we assume our measured PET data follows a homogeneous Poisson process and have the following log-likelihood function:

$$L = \sum_{n=1}^N \log \left[\sum_{i=1}^M \tilde{a}_{ni}(t_n) \rho_i + S c_n(t_n) + R_n(t_n) \right] - \sum_{i=1}^M \rho_i \tilde{s}_i, \quad \text{Eq. 3}$$

where $\{\rho_i\}_{i=1..M}$ is the motion-free image to be measured in the reference frame, $\tilde{s}_i$ is the sensitivity calculated using $\tilde{a}_{ni}(t)$, and $S c_n(t_n)$ and $R_n(t_n)$ are the average scatter and random counts in LOR n and time t_n respectively. Standard approaches to compute $S c_n$ and R_n are the single scatter simulation [44] for scatters, and delayed [45] or single-based approaches for randoms. Note that the scatter and randoms coincidences are time dependent only if the motion between frames is so large that different scatter and random sinograms must be used to correct different frames. In practice however, since motion does not change dramatically the scatter and randoms distributions, we assume at first order that $S c_n$ and R_n are equal to their time-average. In the future, motion-dependent scatter correction could be investigated for some application that motion is large in targeted area.

The above log-likelihood function of a moving subject can be integrated into a unified maximum a posteriori (MAP; or penalized maximum likelihood) framework for static image reconstruction. With an image prior, our penalized log-likelihood function is:

$$\hat{f} = \underset{\rho \geq 0}{\operatorname{argmax}} \left(L + \mu D(\rho, X^{MRI}) \right), \quad \text{Eq. 4}$$

where μ is the hyper parameter to control the trade-off between data fidelity and penalty, the function $L(\cdot)$ is the Poisson log-likelihood, and $D(\cdot)$ is the prior function. The prior can be the MR-based anatomical information (X^{MRI}) or a simple quadratic smoothing function. The reconstruction could be performed using a preconditioned conjugate gradient (PCG) as previously reported in [46, 47].

IV. Phantom and animal studies

Cardiac phantom study for MR-based motion correction using PET-MR has been previously reported [48]. A cardiac phantom, which mimics cardiac motion [See Fig. 5(A)], was constructed. Two different sizes of balloons were suspended in a hot background gel. The space between the two balloons was filled with “hot” gel to mimic a myocardium. The concentration ratio between the myocardium and the background was 3. Three “cold” gels were placed within the myocardium to mimic cardiac defects (Defect 1: transmural; Defects 2 and 3: non-transmural). The inner balloon was connected to a ventilator.

This deformable phantom was scanned in the simultaneous PET-MR brain scanner installed at Massachusetts General Hospital (MGH). The scanner consists of a PET system inserted into the bore of a standard Siemens 3T TIM Trio MR system. Each of the 32 PET detector modules has six $12 \times 12 \times 2.5 \times 2.5 \times 20 \text{ mm}^3$ LSO crystal array and one 3×3 avalanche photodiode (APD) array. The PET insert has a 19.25-cm transaxial and 32-cm axial field of view (FOV). The measured PET spatial resolution is about 2.1 mm full width at half maximum (FWHM) at the center of FOV.

Both ^{18}F PET list-mode and tagged MR data were collected. A GRE sequence ($\text{TE} = 2.41 \text{ ms}$, $\text{TR} = 100 \text{ ms}$, flip angle = 25° , tagging distance = 8 mm) as described in [49] was used. Tagged MR images were acquired separately for three orthogonal tagging directions and then combined together for motion estimation. Non-tagged MR data were also acquired for comparison [Fig. 5(B)]. Full and half k-space data were acquired separately, which lasted for 4 and 2.5 minutes, respectively (16 cardiac phase acquisitions, one tagging direction). A simplified model of motion, which uses B-spline based image registration with SSD similarity measure [21, 50], was computed and incorporated it into the PET system matrix of OSEM along with the motion-dependent attenuation map [16]. Fig. 5(C) shows the reconstructed PET images for uncorrected, gated, and motion-corrected (both full and half k-space acquisitions) studies. Next the improvement in lesion detection SNR with the MR motion corrections was assessed using Channelized Hotelling Observer (CHO) with 15 sets of PET-MR acquisition (50 million detected events for each noise realization) [21, 50, 51]. Fig. 6 shows that both gating and MR motion correction improve the contrast of lesions ($\text{contrast} = 1 - \text{defect}/\text{myocardium}$), but only MR motion correction can do so without increasing background noise (small σ for the motion corrected) or acquisition time. Our CHO studies confirm that the quantitative improvement in SNR, with MR motion correction methods as compared to the gating method. This study also shows that half k-space acquisition yields almost the same results as full k-space acquisition. For defect 1 and 2, which had large motion, we found that the lesion detection CHO SNR is improved by 181% and 209%, respectively, as compared to the uncorrected method. For defect 3, which had small motion, the improvement of CHO SNR is 92%. The greater the motion, the greater the improvement is in lesion detection SNR.

Previous simultaneous PET-MR *in-vivo* animal studies used rabbits and non-human primates [52]. Six beads were implanted in the liver and the diaphragm of two anesthetized, intubated rabbits to mimic hot lesions under an approved protocol by the Subcommittee on Research animal Care (SRAC), which serves as the Institutional Animal Care and Use Committee (IACUC) for MGH. Each rabbit was injected with ^{18}F FDG and scanned for more than one hour on the simultaneous brain PET-MR scanner at MGH. A similar MR sequence ($\text{TE} = 2.4 \text{ ms}$, $\text{TR} = 164 \text{ ms}$, flip angle = 25° , tagging distance = 8 mm) as described in the phantom study above was used. A total of 32 phases of tagged MR data were acquired. Motion fields [See Fig. 7(E)] were estimated from the tagged MR images using B-spline non-rigid image registration and then incorporated into a PET list-mode ordered subset expectation maximization (OSEM) reconstruction. The same motion fields were also used to

deform a reference attenuation map to all other time frames. Fig. 7(A–C) shows that MR-based motion correction method improves contrast and removes the blurring associated with breathing without increasing noise (as is the case with gating). The MR motion corrected method yields contrast comparable to that obtained by gating with six times longer acquisition [See Fig. 7(D)].

An anesthetized monkey was injected with about 7 mCi ^{18}F FDG and scanned for 32 minutes on the simultaneous brain PET-MR scanner at MGH. The Siemens respiratory bellows was used to generate gating signals. The same MR sequence and PET reconstruction method described in the rabbit study above were used. Fig. 8 shows that the MR-based motion correction method yielded PET images with higher contrast and same noise level compared to the uncorrected approach. The motion corrected images have almost the same contrast but with much lower variance as compared to the gated images. Fig. 8 also shows that MR-based motion correction approach with only six-minute acquisition achieved similar image quality compared to the gated approach with 30-minute acquisition.

V. Future outlook

MR-based PET motion correction using simultaneous PET-MR has been demonstrated to improve image quality and lesion detectability compared to gating and to no motion correction. Previous studies show that the MR imaging time for heart or liver motion measurement lasts about a few minutes. This implies that a typical PET scan can be made simultaneously as a MR motion measurement. However, additional MR scans, which are targeted to specific clinical applications, are usually needed. Therefore, it is still demanding to further reduce the MR imaging time for motion measurement.

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Figure 1.

Compounded effect of motion and attenuation: The arrows show an apparent myocardial perfusion defect due to different motion patterns between sequential PET and CT, which, associated to substantial differences in attenuation between lungs and soft tissue, yields the severe apparent anterolateral “defect”. No stenosis was seen on subsequent catheterization nor repeated imaging.

Figure 2.
The relationship between heart and diaphragm motion.

Figure 3.
A matrix of combinations of cardiac and respiratory phases.

Figure 4.
The MR sequence that is used to measure the cardiac motion and monitor the respiratory phase.

Figure 5. (A) Deformable cardiac phantom. (B) Coronal MR slice without and with tagging. (C) Coronal PET slices for Uncorrected, Gated, MR motion corrected with full k-space, and MR motion corrected with half k-space. Noise σ was computed over 15 noise realizations.

Figure 6. Contrast (1–defect/myocardium) and CHO SNR for each of the three defects placed in the cardiac phantom.

Figure 7. (A,B,C) PET images of a rabbit reconstructed from a 5-min scan using Uncorrected, Gated, and MR motion corrected methods. (D) PET image reconstructed from a 30-min scan using Gated method. (E) Tagged MR image with the estimated motion fields.

Figure 8.

(A,B,C) PET images of a free-breathing monkey reconstructed from a 6-min scan using Uncorrected, Gated, and MR motion corrected methods. (D) PET image reconstructed from a 30-min scan using Gated method.