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Improved Detection of Small Pulmonary Nodules Through Simultaneous MR/PET Imaging

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MR/PET; Lung nodule; Motion correction

INTRODUCTION

The development of the MR/PET imaging platform provides, for the first time, a true synergistic imaging platform whereby information from each of the component modalities can be used to improve their individual image quality. Examples would be the use of high-resolution MR imaging scans to improve the quality of the PET images¹ or the use of PET images to reject undersampling artifacts from highly undersampled dynamic MR imaging scans.² The installed base of MR/PET systems is currently relatively small. However, the complementary nature of the information provided by the two modalities together with the synergisms implicit in collecting simultaneous information have allowed this platform to become the preferred choice for the diagnosis of conditions, such as dementia, neurofibromatosis, and epilepsy. For oncologic imaging, there are several applications whereby the MR/PET technology is poised to make significant improvements because of its improved workflow and capabilities. One of the oncologic applications that might benefit greatly from the capabilities of a simultaneous MR/PET acquisition is lung cancer. Lung cancer is the leading cause of cancer-related death in the Western world. Early detection of lung cancer is challenging, as the symptoms are often very similar to those of other common respiratory ailments. Multidetector computed tomography (MDCT) is routinely used for evaluation of disease in the lung and can be routinely performed without intravenous contrast administration and with a low radiation dose.³ Although MDCT has high sensitivity for nodule detection, it has limited specificity in discriminating malignant from benign nodules even in setting of primary malignancy.⁴ Assessment of metabolic activity within lung nodules with fludeoxyglucose F18 (18F-FDG) PET is often improved when compared with computed tomography (CT) for discriminating benign from malignant nodules,^{5,6} making PET/CT the preferred modality to assess whole-body metastatic burden in many primary malignancies.

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However, there are concerns with respect to the accuracy of PET/CT in the detection and characterization of subcentimeter pulmonary. Specifically, nodules of less than 1 cm in diameter have a high (40%) false-negative rate.^{7,8} The high false-negative rate of FDG PET for small lesions seems to be related to respiratory and cardiac motion and the sequential nature for the acquisition of the PET and CT images when using a conventional PET/CT scanner.^{9,10} Studies have demonstrated mild improvements of standardized uptake value (SUV) quantification in PET/CT of pulmonary nodules when respiratory motion correction, via external monitoring devices, is used.^{11,12} Thus, motion-corrected PET reconstruction can potentially improve detection and characterization of pulmonary nodules.¹³

Hybrid PET/MR systems allow for simultaneous acquisition of PET and MR imaging. It has been shown that PET acquisition performed simultaneously with free-breathing radial T1-weighted MR acquisition has similar accuracy as PET/CT for FDG-avid lesions and lesions larger than 5 mm in size.¹⁴ However, despite simultaneous acquisition of PET and MR, hybrid PET/MR has had low sensitivity for small pulmonary nodules that did not show FDG avidity. Thus, similar to PET/CT, conventional (without motion correction) simultaneous PET/MR remains limited for detection and characterization of small pulmonary nodules because of its inability to confidently detect FDG uptake in small lesions, which is likely related to motion blur and respiratory motion.

LUNG MOTION CORRECTION IN MAGNETIC RESONANCE/PET: PREVIOUS LIMITATIONS

Abdominal motion is still an outstanding concern for PET image reconstruction, particularly in the abdomen where rigid body approximations do not apply. Most of the motion correction algorithms previously used for PET image reconstruction rely on the use of retrospective corrections whereby the data are grouped according to the time of acquisition relative to the phase of the respiratory cycle (or any other motion of interest) as assessed by an additional motion tracking device (usually a respiratory belt/cushion). In this setting, different segments from the list-mode data set, corresponding to different data acquisition times, will often be grouped together, regardless of whether the respiratory motion is periodic and/or the physiologic process stationary. As a result, the performance of such algorithms is highly variable as it depends strongly on the reproducibility of the respiratory motion throughout the examination. Unfortunately, studies have demonstrated that breathing motion varies considerably for healthy human controls and much more so for those individuals whereby lesion is present.¹⁵ Consequently, respiratory motion correction via external tracking devices has limited effectiveness¹³ and continues to be an area of active research in PET image reconstruction.^{16–28} As a result, there is no standard for dealing with this challenge and the available methods are not often part of the clinical workflow for PET/CT and MR/PET examinations.

Retrospective Motion Correction for Magnetic Resonance/PET Data

Motion correction algorithms for MR/PET data were introduced shortly after the first system prototypes were delivered.^{21,29,30} In the setting of MR/ PET, the use of a simultaneous acquisition mode, whereby both MR and PET data are acquired at the same time, allows

tracking the respiratory motion using MR signals (images or raw data). Use of the MR-based tracking information can be done prospectively and retrospectively. Retrospective approaches^{21,31–34} are, conceptually, very similar to those previously used for PET/CT, whereby the data are, again, retrospectively reordered. Therefore, these algorithms are easy to implement but have limited effectiveness because they still suffer from some of the limitations stated earlier.

Prospective Motion Correction for Magnetic Resonance/PET Data

Prospective motion correction algorithms^{26,27} rely on continuous information about the abdomen's deformation for the generation of motion fields that can then be used to dynamically distort the system matrix so that all the list-mode data can be intrinsically coregistered to a single-motion state or gate. As such, they do not require the respiratory motion to be periodic and can also be used during dynamic studies by simply binning the list-mode data for physiologically appropriate time windows. This approach is conceptually different from the methodology presented elsewhere in this volume. A brief description of its fundamental elements is, therefore, presented later.

In order to obtain a single-motion free PET reconstruction using this approach, the conventional straight-line model is extended by a motion component in which respiratory motion information is integrated within the PET system matrix. To achieve this, the expectation maximization algorithm

$$f^{k+1} = f^k \frac{1}{X^T 1} X^T \frac{g}{X f^k} \quad (1)$$

is modified to

$$f^{k+1} = f^k \frac{1}{(XM)^T 1} (XM)^T \frac{g}{(XM) f^k} \quad (2)$$

where X represents the classic system matrix, M is the motion operator, f represents the desired image, and g contains the acquired emission data (ignoring attenuation and scatter correction for simplicity).

Fig. 1 illustrates the basic elements of a prospective elastic body motion correction approach. In this approach, list mode PET data are assigned system matrices according to the object's deformation at the time of their acquisition, as identified from MR-based signals (images or raw data). When motion is present, this is equivalent to elastic warping of the lines of response, thereby mapping the object to its original (reference) configuration. When the motion is periodic, this approach is functionally equivalent to a retrospective motion correction. However, when breathing is irregular, it still allows for correction of the PET counts as long as the configuration state of the abdomen can be readily identified from the MR imaging signal. Strategies for how to accomplish this last goal in a continuous fashion during a concurrent MR/PET examination are described later.

METHODS

All data were collected on a MR/PET scanner (Siemens Healthcare, GmbH, Germany). The system consists of a whole-body 3-T scanner, which is fitted with an MR imaging-compatible PET subsystem. The PET subsystem relies on an array of lutetium orthosilicate crystals coupled to avalanche photodiode scintillation detectors. The MR and PET subsystems are both electrically and mechanically independent, which allows for the acquisition of simultaneous data for both modalities. The MR subsystem has multichannel reception and is equipped with a whole-body gradient set capable of 45 mT/m (150 mT/m/s slew rate). The PET subsystem has 488 individual detectors (56 detector blocks, 8 detectors per block), which enable a nominal spatial resolution for the PET system of $4 \times 4 \times 4$ mm in fully 3-dimensional mode.

Patients were recruited under an Institutional Review Board-approved protocol. All patients fasted for 4 hours before being administered a single intravenous injection of ^{18}F -FDG. After resting in a quiet room, the patients underwent a standard-of-care, clinically prescribed, PET/CT examination and were then transported to the MR/PET facility to undergo a simultaneous MR/ PET scan (on average 1.5 hours after the PET/CT examination).

Simultaneous MR/PET data were acquired using a 3-dimensional, radial T1-weighted sequence and list-mode data. The radial sequence sampled a set of parallel disks in the X-Y plane using golden angle increments for the radial views and standard phase encoding steps along the Z axis. This sequence, being self-navigated, provides the ability to order acquired views according to their position in the respiratory cycle. Images were then reconstructed using a compressed sensing algorithm to obtain an effective spatial and temporal resolution of $2 \times 2 \times 4$ mm³ and 3 seconds, respectively. Each one of the acquired lines in k-space was time indexed in the PET list-mode data so that the temporal correspondence between acquired lines and lines of response could be accurately established. On reconstruction of the views ordered according to their phase on the respiratory cycle, a transformation matrix providing a nonelastic transformation (motion vectors) from each respiratory-ordered motion state to a reference state was calculated. These motion vectors then provide the prescription for distorting the lines of response as illustrated on Fig. 1.

RESULTS

The effects of stable respiratory motion on the performance of retrospective reordering are presented in Fig. 2 where the MR-derived respiratory ordered signals are presented for 2 different subjects with vastly different respiratory cycles. As shown in Fig. 2, for the subject with the more regular respiratory cycle (top panel), the PET counts can be more uniformly distributed across 5 respiratory gates. As a result, motion correction leads to a measurable improvement in image quality. For the subject with the less regular respiratory cycle (bottom panel), the irregularity in the respiratory cycle leads to a large number of PET counts being mis-assigned; as a result, motion correction leads to nonsignificant improvements in image quality. These images illustrate the importance of conceptual advantage of prospective

respiratory motion correction schemes as well as the inherent disadvantages of retrospective motion correction approaches.

As mentioned earlier, lung nodule detection could be considerably improved by the use of the combined MR/PET platform. This point is illustrated in Fig. 3 whereby PET images from a subject with suspected malignancy in the lung are presented. The subject's respiratory motion leads to significant blurring of the signal from the small lesion and as a result the assessed SUV could not warrant an aggressive course of action (left panel). On motion correction (center panel), the blurring is significantly reduced leading to both improved lesion localization as well as improved quantitative assessment of the tracer uptake (67% signal increase, rightmost panel).

Fig. 4 presents another example of improved small lesion detection using MR/PET-based motion correction. As in the previous case, the motion information was harnessed by retrospective reordering of the MR imaging data using the signal from the k-space center to synthesize 5 motion states. This time, despite the small lesion size, a sizable (>40%) improvement in SUV can be observed after the blurring in the images is ameliorated through the use of the motion correction algorithm.

DISCUSSION

The development of the PET/CT platform in the late 1990s clearly illustrated the clinical throughput and diagnostic advantages of combining image modalities that have inherently complementary information.³⁵ The developmental motivation for the PET/CT platform, though simple in concept, led to the widespread adoption of the PET/CT technology over conventional PET-only scans. Over the years, however, the sequential nature of the PET and CT acquisitions, and the need to keep the CT acquisition short, have not allowed for a true synergistic interaction between PET/CT's component modalities in which the combined platform allows the generation of better images than those that could be individually acquired with each modality on its own.

MR/PET is the first hybrid-imaging platform whereby the images that could be generated for each of its component modalities could, in principle, be of improved quality when the salient features for the individual imaging modalities are combined in a synergistic fashion. In MR/PET this is due by and large to the simultaneous nature of the acquisition, which allows collecting information about the imaged volume with intrinsic temporal and spatial colocalization. Such colocalization allows exploiting the differences in the acquisition physics and geometry to improve image quality. One of the most readily immediate advantages of MR/PET derives from MR's speed of acquisition and customizable acquisition strategies. Specifically, by rapidly acquiring images in complete synchrony with the detection of PET events information about the geometric configuration of the imaged volume could be used in near real time to compensate for the deleterious effects of abdominal motion. The aforementioned examples illustrated that the gains to be had from such capabilities can be harnessed without an inherent burden to the overall data acquisition time.

Self-navigated imaging sequences such as the one used in the aforementioned examples represent an ideal vehicle for the integration of motion correction capabilities in a combine MR/PET scan. There are, however, other options to gather motion information from the MR imaging signal that could potentially lead to more comprehensive and robust means to assess the geometric changes in the imaged volume.³⁶ Although such methods are still in early development, initial results indicate that they have intrinsic advantages for the assessment irregular and nonstationary motion. Overall, the technical developments and experimental results shown to date indicate that PET motion correction is likely to be one of the most robust and salient features of the MR/PET platform. Initial clinical experience (as illustrated earlier) indicates that there are considerable benefits to be gained from such methodology with very minimal (if at all) disruption to patient workflow. At the time of this writing, commercial prototypes for approaches similar to the one presented here have been in active evaluation by equipment manufacturers, which suggests that such methodology will quickly become part of the standard workflow for MR/PET examinations of the abdomen.

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KEY POINTS

- Assessment of small lung nodules is challenging because of the significant blur due to respiratory (and often nonperiodic motion).
- Tracking respiratory motion during PET/computed tomography and MR/PET imaging using external devices is limited because of the small dynamic range of the devices and the inherent assumption that the respiratory motion is periodic throughout the examination.
- Prospective respiratory motion tracking and correction does not require the motion to be periodic and, as a result, leads to improved quantitative assessment of standard uptake values for small pulmonary nodules.

Fig. 1.

Prospective nonrigid body motion correction scheme. Motion at different phases of the respiratory cycle is incorporated via a modified system matrix with lines of response warped to account for the object's motion. The warping is specific to each motion state and does not require the object's displacement to be periodic.

Fig. 2.

Retrospective motion correction of nonrigid motion in MR/PET. Left: gate assignment trace. Center: uncorrected image. Right: reconstructed image based on a reordering of the PET list-mode data mode using the amplitude of the k-space center during a radial acquisition. Nonperiodic respiration compromises the effectiveness of the correction for the subject on the bottom row.

Fig. 3.

Prospective elastic motion correction in MR/PET. Left: uncorrected image. Center: reconstructed image based on a dynamic motion model derived from a volumetric radial data set with at time resolution of 1 second. Right: plot of signal along the vertical line in the leftmost image demonstrating increased signal (67%) for the lung lesion as a result of motion correction.

Fig. 4.

Another example of prospective elastic motion correction in the lung. Left: uncorrected image. Center: reconstructed image based on a dynamic motion model derived from a volumetric radial data set with a time resolution of 1 second. Right: plot of signal along the vertical line in the leftmost image demonstrating increased signal (40%) for the lung lesion as a result of motion correction.