Imaging moving heart structures with PET

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DEGRADATION OF CARDIAC PET IMAGES BY MOTION

Cardiac, respiratory, and also patient body motions can create serious limitations to high-resolution PET, resulting in a loss of spatial resolution, in particular for coronary artery imaging. Respiratory motion can cause the heart to move more than 1 cm in natural tidal breathing, as shown in Figure 1 on low-dose cine-CT imaging during free breathing and superposition of the maximum and minimum intensity projections of the cine-CT images over one respiratory cycle.¹ In fact, if we consider the heart as a large tissue mass above the diaphragm, we could consider findings with regards to the magnitude of ‘tumor’ motion extensively reported in radiation treatment literature, as well as technologies deployed in radiation therapy to cope with respiratory motion. The seminal paper by Seppenwoolde et al² using fluoroscopy to measure respiratory motion clearly demonstrated that most of the respiratory motion is in the craniocaudal direction, which was later shown as well in PET.³ More recently, average respiratory motion during PET acquisition was found to be about 8 mm in 11 patients,⁴ with the results being patient specific. By comparison, the mean myocardial motion during a cardiac cycle has been reported to be 12–13 mm,⁵ and average motion amplitudes of the coronary arteries have been reported to be 8–26 mm, depending on the artery

and landmark location, with the most pronounced motion in the right coronary artery (RCA).⁶ PET imaging resolution can be at best 6–8 mm⁷ in a clinical imaging setting, although reported NEMA image resolution can reach 4 mm for stationary objects.⁸ New high-resolution reconstruction techniques, which take advantage of resolution recovery compensation, have been developed by PET instrumentation vendors⁹ and have been applied to cardiac PET.¹⁰ These new techniques could allow PET to reach a static resolution of 2 mm,⁹ thus heart motion, rather than the physical resolution of the PET scanner, will likely be the most important factor when determining the overall effective imaging resolution for beating hearts imaged with PET.

RESPIRATORY-GATED PET

Respiratory-gated PET techniques were first proposed in oncological studies. It has been demonstrated that more accurate definitions of the lesion volumes with respiratory gating can improve the quantification of specific activity of ¹⁸F-FDG.¹¹ Respiratory gating can be accomplished with external devices such as an elastic belt with pressure sensor monitor,¹² or by an optical method with a camera that follows chest wall displacement.¹³ These methods have been applied in research settings to PET-guided radiotherapy.¹⁴ However, potential patient motion due to the extended acquisition time needed to maintain appropriate count statistics (at least 10 extra minutes need to be added to a >20 minute standard clinical whole body PET) severely limits the application of respiratory gating. Extension of respiratory gating to cardiac imaging, with stress imaging and short-lived isotopes such as ⁸²Rb, and the need for simultaneous cardiac and respiratory gating (so called dual gating) may prove to be even more challenging than in oncological applications. The use of respiratory-gating devices may complicate cardiac imaging protocols and may significantly increase patient discomfort. To alleviate this problem, simultaneous acquisition of

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Figure 1. An axial image on the left and a coronal CT image on the right demonstrating the magnitude of heart motion induced by respiratory motion during normal patient breathing. The images are obtained from superposition of the maximum and minimum intensity projection images of the low dose cine thoracic CT images obtained without contrast for oncological purposes.¹ The radiation dose for the low dose cine CT was about two times radiation dose of a regular helical CT.

both respiratory and cardiac gating signals using bio-impedance techniques and signals obtained from standard ECG electrodes during cardiac PET⁴ and techniques based on accelerometers¹⁵ have been recently proposed. These techniques have the potential to simplify the challenging logistics of dual gating for cardiac imaging.

Simplified, self-gated, and data-driven techniques have also been proposed, which derive respiratory-gating signals retrospectively from the raw list-mode PET data, rather than using an external device. This software approach tracks the respiratory motion of the myocardium directly from the PET data using image processing algorithms—for example, tracking the centroid of the myocardial activity without external measurements of patient's respiration. This method has shown to be comparable to techniques based on external monitoring and has been applied to cardiac imaging with some success.¹⁶ However, such software techniques depend on the tracer uptake in the organs of interest, and thus may not be readily applicable to coronary PET imaging, where very little activity is detected in the myocardium.

When dual gating is employed in cardiac PET imaging, it presents some image quality challenges since the count statistics in individual gates are much lower than in the original ungated or static images. Even if a limited number of gates are utilized for cardiac and respiratory binning, the noise in a frame containing counts from only a portion of the cardiac and respiratory

cycle is significantly larger than that in the image from the entire cycle. Nevertheless, dual respiratory/cardiac gating has been shown to allow better resolution of the myocardial walls as compared with ungated acquisition.⁴ Generally speaking, the trade-off between image noise and gating has to be carefully considered,¹⁷ and due to practical difficulties, respiratory motion of the heart during the cardiac cycle is typically neglected in the cardiac PET practice.

CORONARY PET IMAGING

Increasing cardiac PET resolution may be of particular importance when studying coronary artery uptake, where accurate superposition with high-resolution CTA angiography and localization of small plaque lesions are critical.^{18,19} In coronary plaque imaging, PET activity originating from very small moving volumes of non-calcified plaques (perhaps as small as a few cubic mm) needs to be quantified with respect to standard uptake value and target-to-background ratio. These measurements will be severely affected by motion of the arteries, effectively reducing both quantified values. In the case of coronary ¹⁸F-FDG imaging, an additional complication is presented by myocardial activity, which may overlap with plaque activity due to arterial/myocardial motion.²⁰ Heart motion could be one reason why ¹⁸F-FDG studies investigating coronary plaques have not been strongly conclusive.¹⁸ To partially mitigate blurring due to cardiac motion during

coronary imaging, a recent ^{18}F -NaF coronary imaging study utilized only one cardiac phase with 1/4th of the counts compared to the full PET acquisition.¹⁹ This approach, however, results in reduced count statistics with higher image noise. It would not be practical to further reduce the available counts by eliminating even more of the collected PET data to eliminate respiratory motion. Due to these practical difficulties, none of the coronary plaque PET studies published to date have utilized respiratory gating.

In this issue of *Journal of Nuclear Cardiology*, Kokki et al²¹ investigate the relation between spirometric lung volume or pressure belt signal, and the motion of coronary vessels by MR imaging in 9 healthy volunteers. Measurements with MR were slightly compromised due to a variation in repeat breath-holds. They compare the results to the established method based on the pressure transducer respiration (belt) and spirometry (measurement of the lung volume changes). Spirometry, which correlated better with MR-derived motion of the vessels than the belt measurements, was further applied to ^{18}F -FDG cardiac PET study to determine a quantitative relation between volume change and motion of the center of myocardium activity (CMA) in 9 other patients. The linear equation between volume change and CMA motion reported a maximum error of 2.5 mm for the estimated CMA motion. They conclude that spirometric volume change linearly estimates the motion of myocardium in PET with good accuracy and can be used for respiratory gating. This is certainly a novel study shedding some new light on the respiratory motion of the coronary arteries and can have implications for PET imaging. Managing respiratory motion is an important step when imaging coronary arteries, although cardiac motion, especially for the RCA, may have a larger magnitude.⁶ The derived relationship of an external breathing signal (spirometry) with PET myocardial motion does have implications for myocardial perfusion respiratory corrected studies—rather than for coronary PET imaging. It may be of particular importance for new tracers, which may fulfill the potential of high-resolution PET imaging.²² Nevertheless, the study has major limitations that reduce the potential of application of the described technique to routine motion tracking of coronary arteries on PET.

The authors study cardiac MR imaging at three breath-holds (inspiration, mid-expiration, and expiration) to estimate the respiratory motion of the left main coronary artery and the coronary sinus (two relatively large coronary vessels) over a respiratory cycle; respiratory PET gated imaging is used to estimate the motion of the myocardium. The respiratory motion as measured by MR in this study is different than quiet tidal breathing during PET acquisition. The use of breath-hold positions

during MR imaging likely results in more respiratory motion than if the data were taken during normal tidal breathing. Additionally, the Bland Altman plots (Figure 9 in the article) show that the 95% limits for estimating the respiratory motion of the arteries range from 5 to 7 mm, as measured by MR imaging, even if the estimated mean error (as computed by the authors) is reported to be lower. This error is reported for two specific points in the arteries, and it is not clear if the derived linear equations could be applied if coronary lesions were positioned in other parts of the arteries, especially in the RCA. In the PET part of the study, the authors include cine 4D-CT for phase-matched attenuation correction, but they do not analyze the heart motion obtained from this acquisition (as shown in Figure 1 in this editorial). In PET analysis, the motion of the CMA on PET, as measured by authors, can be different from the motion of the arteries (especially RCA), as they acknowledge. Therefore, the correlation of spirometry with PET motion is not directly applicable to coronary artery motion. The exact patient breathing pattern during the PET study can also be unstable throughout the scan. Therefore, it is not likely that the derived equations could be used directly for motion tracking (and ultimately motion correction) of the heart but could potentially be used for the estimation of the optimal number of respiratory gates.

BEYOND GATING: CARDIAC, RESPIRATORY, AND PATIENT MOTION CORRECTION FOR PET

While cardiac gating or dual gating allows for image resolution recovery in individual frames, it does so at the expense of count statistics, since only a portion of the counts is used in each gating frame. Individual frames, therefore, have low signal-to-noise ratios due to reduced counts. For example, a dual-gated study with 4 respiratory gates and 8 cardiac gates would have only 1/32 of the counts in the ungated PET image. Elastic image registration methods could be applied to increase the signal-to-noise ratio, as has been shown in phantom images²³ and more recently in cardiac images.²⁴ This technique has been applied to oncological imaging.²⁵ In nuclear cardiology imaging, cyclical heart motion may present equal or bigger problems than respiratory motion. Both of these motions may need to be corrected if high-resolution imaging is required for coronary plaque imaging, or when attempting to distinguish between transmural and non-transmural perfusion defects. If the myocardium is well defined in the gated images, heart motion could be computed directly from them. We have previously proposed techniques for cardiac “motion-frozen” correction of cardiac motion, aimed at increasing imaging resolution in cardiac SPECT and PET,^{5,26} based on the application of

nonlinear warping methods after determining motion vectors from the gated left ventricular segmentation. Ultimately, a motion-incorporated reconstruction method for gated PET studies could be applied by utilizing the motion vector directly during the image reconstruction.²⁷ The benefits of such an approach over the post-processing method will need to be evaluated.

Apart from cardiac and respiratory motion, which have been studied in detail in the recent PET literature, voluntary patient motion during acquisition can further affect the quality of the images. Therefore, appropriate correction and detection of such motion may also be very important, if high resolution is required.²⁸ Patient motion of up to 5 mm has been reported by Woo et al in 10 minute ¹⁸F-Flurpiridaz studies.²⁸ Presumably, higher patient motion amplitudes would occur in longer studies, such as coronary imaging with 30-minute-long acquisitions.¹⁹ As a general rule, all of the correction techniques for cardiac, respiratory, and patient motion depend directly on the detection of moving structures in potentially noisy individual gates of PET images, and their effectiveness can be reduced if PET images do not offer suitable landmarks.

THE PROMISE OF PET/MR

One potential solution for PET motion correction is the use of a simultaneous PET/MR system, where the PET and MR imaging data are acquired at the same time. The motion of the heart structures could be accurately captured via MR, and the position of the annihilation photons detected by PET at a particular time could be associated with the information obtained from MR. Therefore, blurring due to cardiac motion could potentially be removed entirely, allowing for the physical limits of PET resolution to be reached—even for the imaging of moving organs such as heart. Preliminary techniques for PET/MR-based motion correction have been proposed. PET/MR results show that tagged MR-based motion correction yielded significant improvements in defect/myocardium contrast recovery and lesion detectability.^{29,30} Furthermore, respiratory motion can be detected using 1D navigator MRI data acquired perpendicular to the diaphragm, eliminating the need for external respiratory gating.³¹ This would allow for the detection of the diaphragm position for respiratory gating. Image registration techniques can then be used to align the respiratory gates. Potentially, (ECG and navigator free) self-gated MR imaging could be used to resolve both cardiac and respiratory motion of the coronaries at the same time³² and then be applied to PET imaging during image reconstruction, with motion information incorporated directly in the reconstruction without the need for

image registration. Although PET/MR techniques may allow for improvement of PET resolution of cardiac structures, PET/CT is likely to remain the preferred modality for this application, due to the ability of CT angiography to depict coronary plaques.

CONCLUSION

Cardiac, respiratory, and voluntary patient motion can degrade PET image quality and limit the effective image resolution that can be achieved by this modality. The recovery of spatial resolution lost due to heart motion may be especially important for coronary artery imaging. Various new techniques are being proposed to address this issue. They include respiratory gating, since respiration is one (but not the only) source of gating. Thus far, respiratory gating has not been widely adopted in cardiac PET imaging, due to complex logistics and post-processing requirements. Advanced software registration may need to be used for motion freezing of the data obtained with respiratory and cardiac gating, to reduce image noise. Potentially, PET/MR cardiac imaging may allow for more accurate motion correction due to simultaneous detection of local heart motion.

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