Published in final edited form as:

Phys Med Biol. 2016 August 7; 61(15): 5547–5568. doi:10.1088/0031-9155/61/15/5547.

Transmission imaging for integrated PET-MR systems

Spencer L. Bowen¹, Niccolò Fuin¹, Michael A. Levine¹, and Ciprian Catana¹

Spencer L. Bowen: slbowen@nmr.mgh.harvard.edu

¹Athinoula A. Martinos Center for Biomedical Imaging Bldg. 149, Rm. 2301, 13th St.,
Charlestown, MA 02129. USA

Abstract

Attenuation correction for PET-MR systems continues to be a challenging problem, particularly for body regions outside the head. The simultaneous acquisition of transmission scan based μ -maps and MR images on integrated PET-MR systems may significantly increase the performance of and offer validation for new MR-based μ -map algorithms. For the Biograph mMR (Siemens Healthcare), however, use of conventional transmission schemes is not practical as the patient table and relatively small diameter scanner bore significantly restrict radioactive source motion and limit source placement. We propose a method for emission-free coincidence transmission imaging on the Biograph mMR. The intended application is not for routine subject imaging, but rather to improve and validate MR-based μ -map algorithms; particularly for patient implant and scanner hardware attenuation correction. In this study we optimized source geometry and assessed the method's performance with Monte Carlo simulations and phantom scans. We utilized a Bayesian reconstruction algorithm, which directly generates μ -map estimates from multiple bed positions, combined with a robust scatter correction method. For simulations with a pelvis phantom a single torus produced peak noise equivalent count rates (34.8 kcps) dramatically larger than a full axial length ring (11.32 kcps) and conventional rotating source configurations. Bias in reconstructed μ -maps for head and pelvis simulations was 4% for soft tissue and 11% for bone ROIs. An implementation of the single torus source was filled with ¹⁸F-fluorodeoxyglucose and the proposed method quantified for several test cases alone or in comparison with CT-derived μ -maps. A volume average of 0.095 cm⁻¹ was recorded for an experimental uniform cylinder phantom scan, while a bias of <2% was measured for the cortical bone equivalent insert of the multi-compartment phantom. Single torus μ -maps of a hip implant phantom showed significantly less artifacts and improved dynamic range, and differed greatly for highly attenuating materials in the case of the patient table, compared to CT results. Use of a fixed torus geometry, in combination with translation of the patient table to perform complete tomographic sampling, generated highly quantitative measured μ -maps and is expected to produce images with significantly higher SNR than competing fixed geometries at matched total acquisition time.

Keywords

positron emission tomography-magnetic resonance (PET-MR); attenuation correction;
transmission imaging; pelvis imaging; scatter correction

1. Introduction

Hybrid PET-MR may offer dramatic improvements in patient management compared to PET-CT in several clinical domains. For oncological imaging, PET-MR may aid in the local staging, restaging, and therapy response monitoring of head and neck (Queiroz et al. 2014), breast (Pace et al. 2014), pelvis (Wetter et al. 2013), and pediatric (Schäfer et al. 2014) cancers. Possible advantages in cardiology include improved workup of coronary and carotid artery disease, assessment of myocardial viability, and separation of nonischemic from ischemic cardiomyopathy (Rischpler et al. 2013). In neurology, PET-MR could aid in the diagnosis and prediction of dementia, assess salvageable tissue in ischemic stroke, and probe the biology of brain activation (Catana et al. 2012). In all of these applications quantitative PET metrics are expected to play an important role.

Potentially the greatest challenge in producing quantitative PET data sets on hybrid PET-MR systems is accurate estimation of photon attenuation. Gamma ray attenuation is primarily due to tissue electron density, while MR contrast is dictated by proton density and relaxation times, such that the widely used scaling of CT Hounsfield intensities to linear attenuation coefficients (LACs) at 511 keV used on PET-CT (Kinahan et al. 2003) systems is not directly possible with MR data. Several μ -map methodologies have been developed (Bezrukov et al. 2013), including the following: the conversion of MR images alone (i.e. without emission or transmission information) with segmentation schemes and/or *a priori* knowledge (Hofmann et al. 2011), using transmission (TX) imaging with external sources (Mollet et al. 2014, Panin et al. 2013), and the combination of MR data and emission measurements (Mehranian and Zaidi 2015). Approaches that use MR images alone without utilizing CT training sets include methods that produce segmented μ -maps (Catana et al. 2010) based on ultra-short echo time (UTE) sequences or, recently, continuous valued pseudo-CT μ -maps via a robust classifier and a combination of pulse sequences (Su et al. 2015). Algorithms that utilize CT training data; however, may have improved performance for modeling bone attenuation and include methods to continuously map UTE intensities to bone LACs (Ladefoged et al. 2015) or that register CT atlases to create patient specific μ -maps (Paulus et al. 2015, Izquierdo-Garcia et al. 2014, Torrado-Carvajal et al. 2016).

Attenuation correction (AC) strategies for hybrid PET-MR systems that utilize MR information alone have several notable limitations. Methods that compute μ -maps from registered MR and CT training sets acquired on standalone systems, such as patch or atlas based algorithms, may suffer from intra-subject registration errors (Hofmann et al. 2011). Limitations in registration accuracy may be particularly high in regions that frequently undergo deformable motion, such as organs in the abdomen or pelvis (Akbarzadeh et al. 2013). Furthermore, building such training data sets is logistically challenging for several reasons, including: the requirement to schedule scans on separate systems which may reduce subject enrollment, and the limited use of existing paired MR and CT patient scans due to the frequent lack of specialized MR pulse sequence data (e.g. ultrashort echo time). Additionally, errors in computing CT measured μ -maps are propagated into the final MR-based estimates, including: artifacts due to metal implants (Goerres et al. 2003) and truncation of the patients arms (Kinahan et al. 2003).

We propose that the simultaneous acquisition of TX scan derived μ -maps and MR images on hybrid PET-MR systems may significantly improve the validation and development of: (1) new MR-based μ -map algorithms and, (2) template approaches for coil and implant AC. Such an approach allows for intrinsically high registration accuracy between MR and μ -map volumes, production of gold-standard LACs across all tissue and material types, and dramatically lower effective dose delivered to the subject compared to CT exams (Wu et al. 2004). In the case of hardware μ -map generation the proposed TX scheme would eliminate the thorough validation frequently required in CT based approaches (Paulus et al. 2013). Conventional TX imaging, utilizing rotating sources, is challenging to implement on fully integrated clinical hybrid PET-MR systems as the patient table and relatively small diameter scanner bore significantly restrict radioactive source motion and limit tomographic sampling. Furthermore, in the case of the Biograph mMR (Siemens Healthcare) simultaneous singles and coincidence acquisitions is not possible, precluding the use of singles TX approaches (Bailey 1998).

The purpose of this work was to implement a coincidence TX strategy on the Siemens Biograph mMR capable of producing high accuracy, high SNR, and continuous valued μ -maps without activity in the subject (emission-free). We note that several TX approaches largely for time-of-flight (TOF) PET, for application on PET-MR systems, have been previously developed (Mollet et al. 2014, Panin et al. 2013, Watson 2014). However, the emphasis of these methods was to produce μ -maps with minimal impact on emission image quality during simultaneous TX and emission imaging, while we aimed to fully optimize TX image quality alone. Furthermore, the Biograph mMR does not have TOF capabilities, such that direct translation of many of these prior strategies for the purpose of enhanced TX performance is not possible. We emphasize that the proposed application of our TX scheme is not for routine subject imaging, but rather to improve and validate MR-based μ -map algorithms and template approaches. For this reason the inability to perform combined transmission-emission imaging is not a limiting factor of our method. In this study we optimized a fixed TX source geometry for image SNR and assessed the proposed TX scheme on accurate anthropomorphic phantoms with Monte Carlo simulations, and quantified an implementation of the TX approach for several test cases.

2. Materials and methods

2.1. Overview

We utilized Monte Carlo simulations to guide and assess the optimal choice of source geometry, and evaluated this implementation experimentally on a number of test objects. In section 2.2 we describe the Monte Carlo simulation model, and in section 2.3 how the model was used to determine what fixed source geometry, from several configurations, produced the maximum image SNR surrogate during subject scanning. In sections 2.4 and 2.5 we detail the reconstruction and scatter correction algorithms, respectively, that were specifically developed to deal with the limited tomographic sampling of several of the TX source geometries. The Monte Carlo simulation was utilized in section 2.6 to estimate reconstructed μ -map bias and noise for the ideal TX configuration during human imaging. Section 2.7 describes how the optimal source configuration was implemented on the

Biograph mMR, and how the proposed TX scheme performance was measured alone or in comparison to CT-derived μ -maps for tissue equivalent, patient implant, and scanner hardware test cases.

2.2. Biograph mMR simulation

The Biograph mMR is composed of a 3-T MRI and PET camera with 64 lutetium oxyorthosilicate (LSO) crystals (8×8 array) per a block, 56 blocks per a ring, and 8 detector rings (transverse field of view (FOV)=59.4 cm, axial FOV=25.8 cm) (Delso et al. 2010). The system was modeled in SimSET (Harrison et al. 1993) and included gaps between blocks and crystals, a model of the patient table, tungsten end-shields, and an approximation of the acquisition electronics for count losses and delayed coincidences. Along with simulations for trues+scatters separate simulations of singles events alone were run to estimate randoms sinograms and detector dead-time (Macdonald et al. 2008). To simulate noisy sinogram realizations initial raw high count prompts were scaled by the acquisition time, used as the mean to generate Poisson count statistics, and then exposed to dead-time losses on a count-by-count basis for each sinogram bin. The simulation model was validated with a decay experiment using a cylinder phantom uniformly filled with ^{18}F (see Supplementary Material section 1).

2.3. Monte Carlo transmission source geometry count rate optimization

Coincidence-based TX imaging typically produces reconstructed μ -maps with significantly lower SNR than singles-based approaches. We explored several fixed source geometries in order to optimize an SNR surrogate: noise equivalent count rates (NECR) (Dahlbom et al. 2005). NECR are proportional to SNR^2 for reconstructed images and are calculated entirely from raw coincidence count rates. We examined axially centered single torus, double torus, and ring source configurations. All stationary sources were assumed to be flush with the scanner bore cover (bore diameter=60 cm) with tube diameter or shell thickness set to 1.6 mm (excluding wall thickness) for the torus or ring geometries, respectively. Figure 1 shows the transverse and axial geometries of the stationary TX sources studied. We note that the tube diameter is close to the maximum that can fit within the pinch points between the patient table and scanner bore, allowing for use of a continuous source volume and unobstructed patient table motion. We additionally simulated rotating cylindrical point and line configurations. For consistency the radial offsets, tube diameters, and axial positions of the rotating sources matched the stationary geometries, with the axial extent of the point and line configurations set to 1.6 mm and matching the ring source, respectively. Although such moving source schemes would be challenging to implement on the Biograph mMR in practice, these geometries represent traditional TX geometries and are expected to have the least susceptibility to scattered photons. All sources were assumed filled with ^{68}Ge , although the results can be readily translated to other radionuclides (e.g. ^{18}F).

Emissions were restricted to the external TX sources (emission contamination free), while the digital attenuation phantoms were generated from the Zubal phantom with arms down (Zubal et al. 1994). Figure 2 shows the different attenuation phantoms studied. For the pelvis table position we modified the Zubal phantom such that the arms were folded above the head. Surface coils (e.g. head and spine) were not modeled. Coincidences were masked

based on thresholded forward-projections of the sources (“triple-point method” or “source windowing”) and attenuation phantoms and used to calculate NECR. NECR were calculated assuming variance reduced randoms and for events with lines-of-response (LORs) passing through the phantom and sources only as follows:

$$\text{NECR} = \frac{T^2}{T+S+R} \quad (1)$$

where T , S , and R are trues, scatter, and, randoms global count rates, respectively. We additionally computed the scatter fraction (SF) for the measurements, defined as $\text{SF} = S/(T+S)$.

As several of the source geometries (e.g. point, single torus, and double torus) require multiple overlapping table positions for full tomographic sampling of the emission FOV (see section 2.4) we also compared patient noise equivalent counts (PNEC) (Fukukita et al. 2010), defined as follows:

$$\text{PNEC} = \frac{\sum_{i=1}^U \text{NECR}_i \Delta t / U}{L} \quad (2)$$

where U are the total number of sub-table positions, t is the total acquisition time over all sub-tables, and L is the length of the axial FOV covered by the sub-tables. We use PNEC estimates as a surrogate for image quality comparisons in the case when total acquisition time is fixed for the different source geometries.

2.4. Reconstruction implementation

Several of the assessed TX source geometries have limited tomographic sampling, and as such, μ -maps reconstructed from these data sets would have significant artifacts if not compensated for. In order to acquire full projection sets satisfying 3D image sufficiency conditions for a single table emission FOV (Orlov 1975) we acquired multiple overlapping TX table positions. For convenience we refer to these individual overlapping TX positions as sub-tables and the full set as a multi-table acquisition. A fully 3D reconstruction algorithm was developed directly incorporating the multi-table acquisitions to produce a single μ -map estimate. TX sinogram measurements at a given sub-table position and sinogram bin i are given as:

$$(y_t)_i \sim \text{Poisson}((C_t \mathbf{b})_i \exp(-\mathbf{P} \mathbf{A}_t \boldsymbol{\mu})_i + (n_t)_i) \quad (3)$$

where $\mathbf{y}_t \in \mathbb{R}^{M \times 1}$ is the measured 3D TX sinogram data at sub-table position t , $\mathbf{b} \in \mathbb{R}^{M \times 1}$ is the blank sinogram (no attenuating medium in the FOV), $\mathbf{C}_t \in \mathbb{R}^{M \times M}$ is the diagonal matrix

used to match scan dependent parameters of $\mathbf{b}$ (e.g. acquisition time, radionuclide decay, detector dead-time) to those of $\mathbf{y}_b$. $\mathbf{P} \in \mathbb{R}^{M \times N}$ is the system matrix, $\mathbf{A}_t \in \mathbb{R}^{N \times Q}$ is the sub-table position image-space rigid transformation matrix, $\boldsymbol{\mu} \in \mathbb{R}^{Q \times 1}$ is the μ -map image, and $\mathbf{n}_t \in \mathbb{R}^{M \times 1}$ is the expectation of the sum of the scattered and randoms counts. For this application $\mathbf{A}_t$ accounts for the axial table motion only. The axial-extent of $\boldsymbol{\mu}$ was set to encompass the axial FOV covering all TX sub-table positions, such that the total number of voxels (Q) in the μ -map is much greater than in a single table emission FOV (N).

To estimate the μ -map image $\hat{\boldsymbol{\mu}}$ from acquisitions at all sub-table positions we minimize the log posterior density function:

$$\hat{\boldsymbol{\mu}}(\mathbf{y}) = \underset{\boldsymbol{\mu} \geq 0}{\operatorname{argmin}} [-L(\mathbf{y}|\boldsymbol{\mu}) + \beta R(\boldsymbol{\mu})] \quad (4)$$

$$L(\mathbf{y}|\boldsymbol{\mu}) = \sum_{i=1}^{MU} y_i \log(\bar{y}_i) - \bar{y}_i \quad (5)$$

where $L(\mathbf{y}|\boldsymbol{\mu})$ is the log-likelihood ignoring the constant terms, β is the hyperparameter, $R(\boldsymbol{\mu})$ is the roughness penalty function, and $\mathbf{y} = [\mathbf{y}'_1, \mathbf{y}'_2, \dots, \mathbf{y}'_U]'$ and $\bar{\mathbf{y}}$ both $\in \mathbb{R}^{MU \times 1}$ are the measured and expected TX sinogram data, respectively, incorporating data from all U sub-table positions. The complete forward model utilizing all acquisitions is defined as:

$$\bar{y}_i = (b_c)_i \exp(-(\mathbf{I}_t \otimes \mathbf{P})\mathbf{u}_c)_i + n_i \quad (6)$$

where $\mathbf{b}_c = [(C_1\mathbf{b})', (C_2\mathbf{b})', \dots, (C_U\mathbf{b})']'$ is the combined blank sinograms, $\boldsymbol{\mu}_c = [(A_1\boldsymbol{\mu})', (A_2\boldsymbol{\mu})', \dots, (A_U\boldsymbol{\mu})']'$ the shifted μ -map images, $\mathbf{n} = [\mathbf{n}'_1, \mathbf{n}'_2, \dots, \mathbf{n}'_U]'$ the collection of background projections, $\otimes$ is the Kronecker product, and $\mathbf{I}_t \in \mathbb{R}^{U \times U}$ the identity matrix.

The roughness penalty function ($R(\boldsymbol{\mu})$) is defined as:

$$R(\boldsymbol{\mu}) = \sum_{j=1}^Q \sum_{k \in \mathcal{N}_j} \kappa_{jk} V(\mu_j - \mu_k) \quad (7)$$

where $\mathcal{N}_j$ is the 26-voxel 3D neighborhood around voxel j , κ_{jk} is the inverse Euclidean distance between voxels j and k , and $V(\mu_j - \mu_k)$ is the Huber function. The Huber function is given by:

$$V(\mu_j - \mu_k) = \begin{cases} (\mu_j - \mu_k)^2 / 2\delta & \text{if } |\mu_j - \mu_k| \leq \delta \\ |\mu_j - \mu_k| - \delta/2 & \text{otherwise} \end{cases} \quad (8)$$

where δ was set to $1.0 \times 10^{-3} \text{ cm}^{-1}$ throughout.

Optimization of (4) was performed with an ordered subset version of the separable paraboloidal surrogates (SPS) algorithm developed by Erdogan *et al* (1999). A precomputed system matrix ($\mathbf{P}$) that exploits geometrical symmetries and incorporates an analytical representation of the system point spread function between crystal pairs was utilized (Qi et al. 1998) and the complete reconstruction algorithm was implemented in C++.

Reconstructed image sampling was $4.2 \times 4.2 \times 2.0 \text{ mm}$ on a grid of $172 \times 172 \times 129$ voxels, with voxel sizes largely limited by memory constraints of the precomputed system matrix.

2.5. Scatter Correction

Scatter sinogram estimates ($\hat{\mathbf{s}}_t$) were generated for each sub-table position independently for a multi-table acquisition. Scatter distribution sinograms were calculated using a fully 3D implementation of the single scatter simulation (SSS) method (Watson et al. 2004), assuming a known source distribution. The reconstructed μ -map estimate, without scatter subtraction, at a given sub-table ($\mathbf{A}\hat{\boldsymbol{\mu}}$) and blank source distribution were blurred to the scanner resolution using an anisotropic filter (Bowen et al. 2013) and used as input to the SSS algorithm. Scaling of the raw SSS scatter estimates was performed by tail fitting on the blank subtracted TX sinogram ($\mathbf{d}_t$):

$$\mathbf{d}_t = \mathbf{N} \mathbf{s}_t = \mathbf{N} (\mathbf{y}_t - \mathbf{C}_t \mathbf{b} - \bar{\mathbf{r}}_t) \quad (9)$$

where $\mathbf{s}_t$ is the noisy scatter sinogram at sub-table t , respectively, $\mathbf{N} \in \mathbb{R}^{M \times M}$ is the diagonal normalization matrix, and $\bar{\mathbf{r}}_t$ is the variance reduced randoms estimate generated using the manufacturer's software. The equality in (9) only holds true for sinogram bins with lines of response not intersecting the subject or hardware or where $\mathbf{b} = 0$. Tail regions were estimated from attenuation correction factors (ACFs) calculated from the scatter corrupted μ -map, defined as $\exp(\mathbf{P} \mathbf{A} \hat{\boldsymbol{\mu}})$, using a fixed threshold of 1.05. To compute the tail factors linear least squares fitting was performed between the raw SSS scatter distributions and the difference sinogram ($\mathbf{d}_t$) in the masked tail regions. Due to the relatively low SNR of the difference sinogram and sparse axial nature of the TX sinograms, particularly for the torus geometry, scale factors were computed for each sinogram segment as opposed to each 2D projection as is done typically (Watson et al. 2004). Further noise reduction was performed by filtering the segment scale factors via a moving average filter, applied over the positive and negative ring difference segments independently. Scatter was additionally reduced by imposing the “triple-point” method on the TX projections ($\mathbf{y}_t$) which involved masking sinograms to only include LORs passing through the source distribution. The whole scatter correction process can be iterated to refine the scatter estimate.

2.6. Monte Carlo reconstruction performance assessment

To quantify the performance of the multi-table μ -map estimation method we modeled TX acquisitions using the single torus source geometry (figure 1(b)) and Zubal phantom (figure 2). Each head and pelvis scan consisted of a total of five patient sub-table positions with an offset of 65 mm per a step, and total acquisition time of 8 minutes. The middle sub-table (i.e. number 3 of 5) matched the emission table position. A total of 10 Poisson noisy realizations with sinogram span=1 were generated for each table offset as in 2.2. For μ -map reconstructions with (4) we utilized 21 subsets with $\beta = 3.0 \times 10^9$ and assumed randoms, estimated from singles, and attenuation due to the patient table were known. Scatter was estimated iteratively as in section 2.5. The starting image was a uniformly filled cylinder occupying the complete FOV with LAC set to water in all cases.

The metrics used for quantifying μ -map reconstructions included the normalized absolute difference (NAD), coefficient of variation (CoV), and the normalized mean difference (NMD), computed over regions of interest (ROI), as follows:

$$\text{NAD}(\hat{\mu}, \mu) = \frac{\frac{1}{R} \sum_{r=1}^R \sum_{k \in \text{ROI}} |\hat{\mu}_{r,k} - \mu_k|}{\sum_{k \in \text{ROI}} \mu_k} \quad (10)$$

$$\text{CoV}(\hat{\mu}) = \frac{1}{|\text{ROI}|} \sum_{k \in \text{ROI}} \left[\frac{\sum_{r=1}^R (\hat{\mu}_{r,k} - \bar{\hat{\mu}}_k)^2}{(R-1) \bar{\hat{\mu}}_k^2} \right]^{1/2} \quad (11)$$

$$\text{NMD}(\hat{\mu}, \mu) = \frac{1}{R} \sum_{r=1}^R \left(\frac{\sum_{k \in \text{ROI}} \hat{\mu}_{r,k}}{\sum_{k \in \text{ROI}} \mu_k} - 1 \right) \quad (12)$$

where R is the number of Poisson noisy realizations generated, μ is the gold-standard μ -map generated from noiseless TX reconstructions, $|\text{ROI}|$ is the number of voxels in the support of the ROI, and $\bar{\hat{\mu}}$ is the voxel-wise average volume estimated from the R realizations of $\hat{\mu}$ (Kazantsev et al. 2012). Additionally, we calculated relative change (RC) for each voxel k using the equation $\text{RC}_k = 100(\bar{\hat{\mu}} - \mu_k) / \mu_k$.

2.7. Experimental study

An implementation of the simulated single torus TX source geometry was fabricated with a fillable polytetrafluoroethylene (PTFE) tube (ID=1.6 mm, OD=3.2 mm). Lure lock adaptors were fitted on the tube ends to allow for an uninterrupted torus and the tube was affixed

directly to the Biograph mMR bore cover at the axial center FOV as in Figure 1(b). The patient table had no visible mechanical interference with the TX source over its full range of travel. Figure 3 shows the implementation of the torus TX source. Reconstructions of μ -map images and scatter estimation was performed as in section 2.6, with the difference that span=11 sinograms were used. Additionally, to estimate the TX source distribution for use in scatter estimation and the triple-point method, the blank acquisitions were reconstructed with ordered subsets expectation maximization (OSEM) and thresholded to exclude background noise. The hardware μ -map for the patient table was generated from CT scans via the manufacturer and was included *a priori*. The approach included scanning with CT using an extended Hounsfield number (HU) scale (i.e. extending the HU dynamic range by a factor of 10), converting the HUs to LACs at 511 keV using a conventional patient bilinear transform, and clipping the maximum voxel value to 0.12 cm^{-1} .

To assess the performance of the experimental setup three separate phantoms were utilized: (1) a uniform water filled right cylinder phantom (OD=21 cm) positioned off-center, (2) a flangeless Esser PET phantom (Data Spectrum) (OD=22 cm) containing a water background with Teflon (cortical bone equivalent) and air cylindrical rods (D=25 mm), and (3) a metallic hip implant secured in a water background. Figure 4 shows the phantoms used for performance analysis. All phantoms were placed on a minimally attenuating pad on the patient table and scanned with the fabricated TX source. In each instance the source was filled with 1.0 mCi of ^{18}F -fluorodeoxyglucose (FDG) at the start of imaging and five sub-table positions were acquired, consistent with the Monte Carlo simulations in section 2.6. The offset between sub-table positions was set to 65 mm for the cylindrical and Esser phantoms, and 15 mm for the hip implant in order to maximize femoral head SNR. Total acquisition time was 15 minutes for the cylindrical and Esser phantoms and 25 minutes for the hip implant. Phantom μ -map reconstructions were quantified for relative and absolute uniformity with profile and ROI analyses.

We compared the proposed TX scheme with CT-derived μ -maps in two cases. The hip implant was scanned on a Discovery STE PET-CT scanner (GE Healthcare) (tube current=570 mA, tube voltage=140 kVp), converted to LACs using the bilinear transform, and registered via an affine transform to the torus TX images. Additionally, to assess the single torus TX approach for MR coil and hardware μ -map generation we reconstructed the hip implant phantom scan with no hardware priors, and compared the patient table LACs with those of the manufacturer CT derived μ -maps.

3. Results

3.1. Monte Carlo transmission source geometry count rate optimization

Figure 5 compares NECR curves for several TX source geometries scanning the head and pelvis phantoms. We used maximum singles per block for the abscissa to normalize the data for the very different total activity ranges of the studied TX sources. The results are summarized in Table 1, and represent the performance from a single sub-table position. In all cases, excluding the ring source geometry, peak NECR was measured at the maximum block singles rate before pileup mispositioning errors become significant (see Supplementary Material section 2). For both the pelvis and head phantoms the two torus

geometry, followed closely by the single torus, produced the highest peak NECR for the fixed source configurations. Notably, both torus geometries had more than three times the peak NECR of the ring source. In comparison to conventional rotating source geometries the single torus exceeded the peak NECR of the line source by >24 kcps for the pelvis phantom.

The PNEC results listed in Table 1 enable a performance comparison that accounts for the multi-table acquisition necessary for some source geometries. We assumed a total acquisition time (t) of 8 minutes. For the axial length (L) we assumed a value 51.8 cm (five sub-tables with 65 mm steps) for the point, single torus, and double torus and 25.8 cm (one sub-table) for the line and ring sources. The order of peak PNEC values for the different source geometries was consistent with peak NECR estimates. Notably, both the single and double torus configurations were more than 1.7 times the peak PNEC of the ring source. For performance and practical reasons the single torus was determined to be the optimal configuration, and all following sections utilize only this geometry.

3.2. Monte Carlo reconstruction performance assessment

Figure 6 demonstrates the influence of limited tomographic sampling on reconstructed μ -maps, inherent in using the single torus source geometry. Images were reconstructed from noiseless TX measurements. If only a single sub-table position is utilized the missing projection data results in μ -maps where cone shaped regions at both ends of the axial FOV maintain their initial values (0.096 cm^{-1}) and hence possess no information about the scanned object. Regions approaching the borders of the cones axially from the axial center of the FOV suffer increasing cone-beam artifacts due a decrease in tomographic sampling. Acquiring multiple sub-table positions produces μ -maps with no visible artifacts.

Table 2 details the bias and noise performance of the single torus TX approach for the head and pelvis anthropomorphic phantom simulations. A source activity of 1.2 mCi of ^{68}Ge was assumed, which is equal to 95% of the activity at peak NECR for the head scan (see Table 1). Results were compiled for μ -maps reconstructed with 50 iterations. Minimal bias and noise values were measured for images reconstructed after two scatter iterations, particularly for soft tissue ROIs, although the improvement in NMD compared to reconstructions after one scatter iteration was <4% in all cases. Cortical bone NMD was measured at 11% in all cases. We note that reductions in NAD were less than NMD as a function of scatter iteration number, suggesting that non-uniformities at the voxel level for a given ROI remained after scatter correction. We measured excellent agreement between the estimated and ground truth scatter sinograms (see Supplementary Material section 3).

Figure 7 shows μ -map reconstructions of a single noisy realization computed after two scatter iterations, and RC images calculated for all 10 Poisson noisy realizations. Cortical bone in both the skull, for the head phantom, and pelvis and long bones, for the pelvis phantom, were clearly visible. No significant artifacts due to the limited tomographic sampling of the torus source at a single TX sub-table position were observed, particularly in sagittal or coronal images. RC images demonstrated that for both phantoms the largest bias was at interfaces between soft tissue and either air or cortical bone. Specifically, bone LACs were typically underestimated while neighboring marrow or soft tissue was overestimated. Background uniformity was shown to be excellent.

3.3. Experimental study

Figure 8 shows reconstructed μ -maps of the uniform cylinder phantom. No obvious artifacts were visible and excellent uniformity in both the transverse and axial direction were observed. Figure 9 shows the quantitative analysis of the μ -map reconstructions. Consistent with Monte Carlo simulations, the optimal number of scatter corrections iterations was two, with a volume average of $\mu=0.095\text{ cm}^{-1}$ measured. Bias with respect to the volume mean was estimated for each transverse image by drawing an 18 cm circular ROI centered transversely on the phantom (Figure 9 (b)). The circular ROI was further divided into a grid of square 2.1 cm wide ROIs, to assess uniformity on a more granular level. For the full 18 cm ROI mean absolute bias was <4% over the complete FOV, while maximum or minimum absolute bias for an individual 2.1 cm wide ROI was <17%. We note that the the mean axial uniformity reported here is well within the 10% required to qualify for American College of Radiology Imaging Network (ACRIN) studies (Scheuermann et al. 2009).

Figure 10 shows reconstructed μ -maps of the Esser PET phantom. Both the Teflon and air rods were clearly visualized. For quantification 12.5 mm diameter circular ROIs were drawn centered on the Teflon and air rods, while a total of five 20.9 mm diameter circular ROIs were placed on the water background covering the transverse FOV. In both cases ROIs covered six consecutive axial slices, roughly spanning the lengths of each rod. Table 3 shows the results of the ROI analysis performed on reconstructed images generated after two scatter iterations. Bias between the reconstructed and expected LAC of the Teflon rod was <2% and negligible attenuation was measured in the air rod.

Figure 11 compares the proposed TX scheme with CT derived μ -maps of a hip implant phantom. The CT μ -map showed appreciable artifacts due to beam hardening and photon starvation, as well as saturated LAC values due to use of the standard HU scale (Coolens and Childs 2003) (i.e. from -1024 HU to 3071 HU). These artifacts were visible both within the hip implant and in the neighboring water background. Torus TX images; however, demonstrated no visible artifacts, resolved structures in the femoral head not visible on CT, and produced implant LACs with a dramatically larger dynamic range than on CT.

Figure 12 shows μ -maps and LAC histograms of the Biograph mMR patient table generated from the manufacturer's CT-based method and using the proposed TX scheme. Torus TX images were generated without and with the same 0.12 cm^{-1} LAC clipping as applied in the manufacturer's approach (see section 2.7). All structural details visible in the CT-derived image were seen in the torus TX results, and LAC values were largely similar. A notable exception; however, was the copper cable bundle running the length of the patient table, which was measured to be much greater (0.18 vs. 0.12 cm^{-1}) in the torus TX μ -map without clipping (Figure 12(b)) compared to that of the manufacturer. Histogram analysis (Figure 12(d)) performed over the full μ -map demonstrated that clipping had a much larger influence on LACs for the torus TX approach compared with the manufacturer's method, with 817 and 9 voxels measured at the upper 0.12 cm^{-1} limit bins, respectively. Furthermore, almost the entirety of the clipped voxels in both instances were located in the cable bundle.

4. Discussion

The proposed fixed torus TX strategy produced μ -maps with comparable accuracy to conventional external source methods and recent TOF schemes. For example, a gold-standard method employing a rotating ^{68}Ge point source for a 2D PET camera measured 0.095 cm^{-1} for a water cylinder (Ranger et al. 1989), which is equal to the value measured in the uniform phantom cylinder study presented here. Methods that utilize a fixed ring or shell of activity have been recently proposed for estimating attenuation images with activity in the subject on TOF PET systems. Use of TOF information significantly improves the consistency of attenuation images estimated in these approaches (Panin et al. 2013, Mollet et al. 2014), and as such, a direct comparison with the proposed fixed torus strategy is not straightforward. However, assuming that the scatter fraction for the different methods is comparable, our fixed torus approach produced similar soft tissue accuracy to a TOF method utilizing a robust scatter correction algorithm and a rotating line source (Panin et al. 2013).

We determined that the torus geometry offered the optimal trade-off between NECR performance and ease of implementation for a fixed source configuration. For a multi-table acquisition the single torus would greatly exceed the ring source peak PNEC at equal total acquisition time. This would translate into significantly higher reconstructed μ -map SNR for the single torus compared to the ring at matched image resolution. We note that as the difference in peak PNEC between the multi-table acquisition source geometries and the ring is inversely related to the axial FOV length (L), use of a reduced L would allow for further reconstructed μ -map SNR improvements for the single torus. The choice of five sub-tables and steps of 65 mm was chosen to minimize limited tomographic sampling artifacts over the complete emission FOV. A reduced number of sub-tables and/or steps could be utilized if the object of interest is smaller than the axial FOV (e.g. for patient implants or coil hardware). We note that although in this analysis L was matched for the multi-table geometries the increased tomographic sampling of the double torus geometry may allow for the use of a smaller axial FOV length compared to the single torus, thereby possibly improving reconstructed μ -map SNR at matched total acquisition time. A rigorous analysis of reconstructed image performance as a function of sub-table numbers and steps is beyond the scope of this work; however, the slight SNR advantage of the double torus is expected to be negligible at matched multi-table acquisition parameters. Furthermore, as the fixed torus is currently manually placed, use of a single source leads to reduced radiation exposure and installation effort during positioning compared to two toruses; factors that are important in the relatively tight confines of the scanner bore.

We note that the combination of the fixed torus geometry and movement of the patient table to acquire complete tomographic sampling is analogous to previous implementations which utilize an axially centered rotating ^{137}Cs source for singles TX measurements. Additionally, early TX AC approaches for 2D PET scanners utilized a fixed ring of activity (Bailey 1998); however, to our knowledge this is the first report using a torus TX source in combination with patient table motion for 3D PET μ -map generation. The proposed scatter correction scheme, where tails of the blank subtracted TX sinogram were fitted for the purpose of scaling the raw SSS estimate, is another unique aspect of this study. Previously, researchers assumed a-priori the composition of LACs and scaled based on μ -map histograms

(Vandervoort and Sossi 2008) or utilized dual energy methods (Mollet et al. 2014), to name a few. Tail fitting is a commonly used method in emission scatter estimation, but this is the first instance to our knowledge where it has been applied to TX imaging.

The radiation dose delivered to a subject during a torus source TX study is expected to be much lower than during a CT and/or PET emission exam. Based on dose studies from conventional PET TX schemes (Wu et al. 2004)(Table 3), if we assume a single torus source filled with 1.0 mCi of Ge^{68} and a total acquisition time of 10 minutes we would expect an effective dose of $\sim 4 \mu\text{Sv}$. For perspective, in a typical PET exam, where a subject is injected with 10 mCi FDG, the effective dose is 7 mSv (Brix et al. 2005), for a low-dose CT specifically for attenuation 1.2 mSv (Montes et al. 2013), while a standard chest x-ray delivers 20 μSv (Fazel et al. 2009). Thus, the proposed TX scheme delivers greater than two orders of magnitude lower effective dose than even a low-dose CT scan.

Monte Carlo simulations using anthropomorphic phantoms demonstrated that the proposed measured TX scheme can produce quantitative μ -maps during subject scanning. For both soft tissue and cortical bone ROIs bias (NMD) did not exceed 11% for an 8 minute acquisition (Table 2). We measured the greatest negative bias in cortical bone ROIs, including the skull, pelvis, and long bones. This may be attributed to the increase in bias (reduced spatial resolution) for MAP reconstructions at relatively low count statistics (Qi and Leahy 2000). We utilized a β that was a compromise between noise and bias for the eight minute Poisson realizations; however, optimally β should be adjusted based on the quantification needs of the application. Limited accuracy of the model based scatter estimation and scaling approach likely did not contribute to increased cortical bone bias, as soft tissue bias after two scatter iterations was 4% in all cases. The increased bias for relatively small bony structures may have also been caused by the partial volume effect, as many of the cortical bone walls were as small as a single voxel.

There were several limitations in our study. We did not estimate the influence of the measured μ -map performance on emission reconstruction quantification. As the main application of the proposed approach is to improve and validate MR-based attenuation algorithms, which often rely on voxel-by-voxel comparisons with training attenuation map data, we focused on μ -map quantification. Bias in tracer uptake estimates from reconstructed emission images is often less than a given percent error in LACs for a given ROI (Mollet et al. 2014), but further studies are needed to calculate the performance of the proposed measured attenuation approach on emission reconstruction performance. Additionally, the torus TX method was optimized for emission contamination free imaging on a non-TOF system. The choice of the fixed torus source geometry, with the majority of singles flux on a limited number of detectors and the relatively high total activity explored were all chosen to maximize TX reconstructed image SNR, and as such would be expected to have limited performance if utilized post-injection. A similar methodology as used in this study; however, could be applied to develop the optimal source geometry for combined TX and emission scanning on TOF systems. This may be particularly applicable to the recently released TOF capable GE SIGNA PET-MR (Levin et al. 2016), which also has a relatively small diameter bore and tight space confines. We only examined source geometries capable of fully tomographic acquisitions. Use of a stationary point source in combination with segmented

MR images was utilized to estimate segmented μ -maps for a PET-MRI scanner (Kawaguchi et al. 2014). In all cases use of source schemes that produce sinograms with significant lack of tomographic sampling would be expected to produce artifacts if unconstrained reconstructions (i.e. without the use of MRI priors) are utilized. As the purpose of our TX method is to estimate attenuation to improve MRI-based AC schemes, we chose to exclude the study of such limited coverage source geometries.

The proposed TX strategy may have several applications for improving and developing new PET-MR AC schemes. For instance, simultaneously acquired TX scan μ -maps and MR images of implants (e.g. hip prosthetics) alone or in subjects could be utilized to produce and assess a template approach to derive attenuation maps for a range of implant types. Particularly for regions of the body that frequently undergo deformable motion, utilizing MR and single torus TX scans as training data for MR-based atlas or patch AC approaches may limit the error due to inter-modality registration mismatches. In the case of non-human primate imaging of the brain, where current human MR-based attenuation correction schemes may be inadequate, TX measured μ -maps could be acquired intermittently and used for subsequent exams simply by registering MR images. Finally, for dynamic imaging exams, where the subject initially has no activity present, with the automation of source placement and removal the single torus TX scheme could be used directly to construct a measured μ -map. In several of these applications registering standalone MR and coincidence TX images from legacy PET scanners might provide the same information; however, the increasing lack of such PET systems and the logistical challenges of performing standalone scans limits this approach.

Potentially the most promising applications for the single torus TX scheme are areas where CT-based μ -map estimation has known limitations. These include the estimation of patient implant, and scanner coil or hardware attenuation images. CT-based μ -maps in such cases show severe streaking artifacts and/or LAC bias, which ultimately leads to reduced quantification in the PET uptake estimates (Abdoli et al. 2012). Even with advanced CT metal artifact reduction methods, including use of an extended HU scale, inaccuracies can remain, particularly for very dense and attenuating materials (e.g. in a hip prosthetic) (Abdoli et al. 2012). Our experimental results (Figures 11 and 12) demonstrated that use of the torus TX method for implant or hardware attenuation estimation dramatically improved quantification compared with CT μ -maps. For the patient table analysis, LACs measured in the copper cable bundle were considerably greater with our approach compared with that of the manufacturer, with more subtle variations between the μ -maps noted (Figure 12). Currently Siemens utilizes a template approach to generate hardware μ -maps, such that the patient table in our institution's scanner is not the same as that used for the template. Thus, the observed LAC differences may have been attributed largely to structural variations between the two tables and marginally to the 0.12 cm^{-1} clipping (Figure 12(d)). Such geometrical variations for the cable bundle would be particularly influential on reconstructed LACs due to copper's relatively high stopping power at 511 keV in combination with the partial volume effect. Thus, the torus TX scheme could be used to produce scanner coil or hardware μ -maps directly on a given PET-MR system without the need for, and frequent limitations often associated with, separate CT-based estimates.

For applications focused on μ -map generation of in-vivo tissues, the benefit of the proposed TX method compared to CT will depend both on logistical reasons (i.e. access to MR and CT systems) and on the magnitude of registration error that may result from separate standalone MR and CT scans. Regarding image quality between the two approaches, PET uptake estimates corrected by CT measured μ -maps largely agree with coincidence TX corrected results for most tissue types; however, Nakamoto *et al* (2002) determined that especially for radiodense tissues (e.g. osseous lesions) CT μ -maps led to significantly higher activity concentrations than coincidence TX. Thus, although the proposed torus approach may underestimate attenuation for small bony structures (see Table 2), CT μ -maps may tend to overestimate attenuation in dense tissues. Of course CT has significantly higher SNR than coincidence TX images, so the performance benefits of the proposed scheme for a particular application must be weighed accordingly.

5. Conclusions

Using Monte Carlo simulations and phantom scans we have developed an optimized TX scheme for emission-free imaging on a combined PET-MR scanner. Use of a single torus source geometry, in combination with a multi-table acquisition, offered the optimal tradeoff between NECR performance and ease of implementation. The single torus configuration is expected to produce reconstructed images with significantly higher SNR than competing fixed geometries for matched total acquisition time. Anthropomorphic simulation results demonstrated the ability of the measured TX scheme to produce highly quantitative measured μ -maps, particularly for pelvis imaging. An implementation of the single torus approach for the Siemens Biograph mMR produced minimal bias in LACs over a range of materials for phantom scans, and this configuration can be directly utilized for subject imaging. Comparisons with CT-derived μ -maps demonstrated that the proposed method may especially aid in improving attenuation correction of patient implants and scanner hardware; areas where CT has known limitations. Future research will compare the proposed TX scheme to CT for the development of patch or atlas based MR attenuation correction algorithms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank Grae Arabasz, Shirely Hsu, Regan Butterfield, and Kevin Chen for technical assistance, Charles Watson for providing technical details for the Siemens Biograph mMR, useful discussions and manuscript preparation, and David Faul for Siemens Biograph mMR technical details. Funding was provided in part by the National Institutes of Health (grant nos. NIH-NIBIB R01 EB014894-01A1, 1S10RR023401-01A2, 1S10RR019307, and 1S10RR023043).

References

Abdoli M, Dierckx RAJO, Zaidi H. Metal artifact reduction strategies for improved attenuation correction in hybrid PET/CT imaging. *Med Phys*. 2012; 39(6):3343–3360. [PubMed: 22755716]

- Akbarzadeh A, Gutierrez D, Baskin A, Ay MR, Ahmadian A, Riahi Alam N, Lvblad KO, Zaidi H. Evaluation of whole-body MR to CT deformable image registration. *J Appl Clin Med Phys*. 2013; 14(4):4163. [PubMed: 23835382]
- Bailey DL. Transmission scanning in emission tomography. *Eur J Nucl Med*. 1998; 25(7):774–787. [PubMed: 9662601]
- Bezrukov I, Mantlik F, Schmidt H, Schlkopf B, Pichler BJ. MR-Based PET attenuation correction for PET/MR imaging. *Semin Nucl Med*. 2013; 43(1):45–59. [PubMed: 23178088]
- Bowen SL, Byars LG, Michel CJ, Chonde DB, Catana C. Influence of the partial volume correction method on 18f-fluorodeoxyglucose brain kinetic modelling from dynamic PET images reconstructed with resolution model based OSEM. *Phys Med Biol*. 2013; 58(20):7081–106. [PubMed: 24052021]
- Brix G, Lechel U, Glatting G, Ziegler SI, Munzing W, Muller SP, Beyer T. Radiation Exposure of Patients Undergoing Whole-Body Dual-Modality 18F-FDG PET/CT Examinations. *J Nucl Med*. 2005; 46(4):608–613. [PubMed: 15809483]
- Catana C, Drzezga A, Heiss WD, Rosen BR. PET/MRI for neurologic applications. *J Nucl Med*. 2012; 53(12):1916–1925. [PubMed: 23143086]
- Catana C, van der Kouwe A, Benner T, Michel CJ, Hamm M, Fenchel M, Fischl B, Rosen B, Schmand M, Sorensen AG. Toward implementing an MRI-Based PET Attenuation-Correction method for neurologic studies on the MR-PET brain prototype. *J Nucl Med*. 2010; 51(9):1431–1438. [PubMed: 20810759]
- Coolens C, Childs PJ. Calibration of CT hounsfield units for radiotherapy treatment planning of patients with metallic hip prostheses: the use of the extended CT-scale. *Phys Med Biol*. 2003; 48(11):1591–1603. [PubMed: 12817940]
- Dahlbom M, Schiepers C, Czernin J. Comparison of noise equivalent count rates and image noise. *IEEE T Nucl Sci*. 2005; 52(5):1386–1390.
- Delso G, Martinez-Miller A, Bundschuh RA, Ladebeck R, Candidus Y, Faul D, Ziegler SI. Evaluation of the attenuation properties of MR equipment for its use in a whole-body PET/MR scanner. *Phys Med Biol*. 2010; 55(15):4361–4374. [PubMed: 20647598]
- Erdogan H, Fessler JA. Ordered subsets algorithms for transmission tomography. *Phys Med Biol*. 1999; 44(11):2835–2851. [PubMed: 10588288]
- Fazel R, Krumholz HM, Wang Y, Ross JS, Chen J, Ting HH, Shah ND, Nasir K, Einstein AJ, Nallamothu BK. Exposure to Low-Dose Ionizing Radiation from Medical Imaging Procedures. *N Engl J Med*. 2009; 361(9):849–857. [PubMed: 19710483]
- Fukukita H, Senda M, Terauchi T, Suzuki K, Daisaki H, Matsumoto K, Ikari Y, Hayashi M. Japanese guideline for the oncology FDG-PET/CT data acquisition protocol: synopsis of Version 1.0. *Ann Nucl Med*. 2010; 24(4):325–334. [PubMed: 20401547]
- Goerres GW, Ziegler SI, Burger C, Berthold T, Von Schulthess GK, Buck A. Artifacts at PET and PET/CT caused by metallic hip prosthetic material. *Radiology*. 2003; 226(2):577–584. [PubMed: 12563158]
- Harrison RL, Vannoy SD, Haynor DR, Gillispie SB, Kaplan MS, Lewellen TK. Preliminary experience with the photon history generator module of a public-domain simulation system for emission tomography. *IEEE Nucl Sci Symp Conf Rec*. 1993:1154–1158.
- Hofmann M, Bezrukov I, Mantlik F, Aschoff P, Steinke F, Beyer T, Pichler BJ, Schlkopf B. MRI-based attenuation correction for whole-body PET/MRI: quantitative evaluation of segmentation- and atlas-based methods. *J Nucl Med*. 2011; 52(9):1392–1399. [PubMed: 21828115]
- Izquierdo-Garcia D, Hansen AE, Frster S, Benoit D, Schachoff S, Frst S, Chen KT, Chonde DB, Catana C. An SPM8-based approach for attenuation correction combining segmentation and nonrigid template formation: application to simultaneous PET/MR brain imaging. *J Nucl Med*. 2014; 55(11):1825–1830. [PubMed: 25278515]
- Kawaguchi H, Hirano Y, Yoshida E, Kershaw J, Shiraishi T, Suga M, Ikoma Y, Obata T, Ito H, Yamaya T. A proposal for PET/MRI attenuation correction with mu-values measured using a fixed-position radiation source and MRI segmentation. *Nucl Instrum Meth A*. 2014; 734:156–161.

- Kazantsev D, Arridge SR, Pedemonte S, Bousse A, Erlandsson K, Hutton BF, Ourselin S. An anatomically driven anisotropic diffusion filtering method for 3D SPECT reconstruction. *Phys Med Biol*. 2012; 57(12):3793–3810. [PubMed: 22617131]
- Kinahan PE, Hasegawa BH, Beyer T. X-ray-based attenuation correction for positron emission tomography/computed tomography scanners. *Semin Nucl Med*. 2003; 33(3):166–179. [PubMed: 12931319]
- Ladefoged CN, Benoit D, Law I, Holm S, Kjr A, Hjgaard L, Hansen AE, Andersen FL. Region specific optimization of continuous linear attenuation coefficients based on UTE (RESOLUTE): application to PET/MR brain imaging. *Phys Med Biol*. 2015; 60(20):8047–8065. [PubMed: 26422177]
- Levin CS, Maramraju SH, Khalighi MM, Deller TW, Delso G, Jansen F. Design Features and Mutual Compatibility Studies of the Time-of-Flight PET Capable GE SIGNA PET/MR System. *IEEE T Med Imaging*. 2016 In press.
- Macdonald LR, Schmitz RE, Alessio AM, Wollenweber SD, Stearns CW, Ganin A, Harrison RL, Lewellen TK, Kinahan PE. Measured count-rate performance of the Discovery STE PET/CT scanner in 2D, 3D and partial collimation acquisition modes. *Phys Med Biol*. 2008; 53(14):3723–3738. [PubMed: 18574308]
- Mehranian A, Zaidi H. Joint Estimation of Activity and Attenuation in Whole-Body TOF PET/MRI Using Constrained Gaussian Mixture Models. *IEEE T Med Imaging*. 2015; 34(9):1808–1821.
- Mollet P, Keereman V, Bini J, Izquierdo-Garcia D, Fayad ZA, Vandenberghe S. Improvement of attenuation correction in time-of-flight PET/MR imaging with a positron-emitting source. *J Nucl Med*. 2014; 55(2):329–336. [PubMed: 24434291]
- Montes C, Tamayo P, Hernandez J, Gomez-Camintero F, Garca S, Martn C, Rosero A. Estimation of the total effective dose from low-dose CT scans and radiopharmaceutical administrations delivered to patients undergoing SPECT/CT explorations. *Ann Nucl Med*. 2013; 27(7):610–617. [PubMed: 23568252]
- Nakamoto Y, Osman M, Cohade C, Marshall LT, Links JM, Kohlmyer S, Wahl RL. PET/CT: comparison of quantitative tracer uptake between germanium and CT transmission attenuation-corrected images. *J Nucl Med*. 2002; 43(9):1137–1143. [PubMed: 12215550]
- Orlov SS. Theory of 3-dimensional reconstruction.1. conditions for a full set of projections. *Kristallografiya*. 1975; 20(3):511–515.
- Pace L, Nicolai E, Luongo A, Aiello M, Catalano OA, Soricelli A, Salvatore M. Comparison of whole-body PET/CT and PET/MRI in breast cancer patients: lesion detection and quantitation of 18f-deoxyglucose uptake in lesions and in normal organ tissues. *Eur J Radiol*. 2014; 83(2):289–296. [PubMed: 24331845]
- Panin VY, Aykac M, Casey ME. Simultaneous reconstruction of emission activity and attenuation coefficient distribution from TOF data, acquired with external transmission source. *Phys Med Biol*. 2013; 58(11):3649–3669. [PubMed: 23648397]
- Paulus DH, Quick HH, Geppert C, Fenchel M, Zhan Y, Hermosillo G, Faul D, Boada F, Friedman KP, Koesters T. Whole-Body PET/MR Imaging: Quantitative Evaluation of a Novel Model-Based MR Attenuation Correction Method Including Bone. *J Nucl Med*. 2015; 56(7):1061–1066. [PubMed: 26025957]
- Paulus DH, Tellmann L, Quick HH. Towards improved hardware component attenuation correction in PET/MR hybrid imaging. *Phys Med Biol*. 2013; 58(22):8021–8040. [PubMed: 24168832]
- Qi J, Leahy RM. Resolution and noise properties of MAP reconstruction for fully 3-D PET. *IEEE T Med Imaging*. 2000; 19(5):493–506.
- Qi J, Leahy RM, Cherry S, Chatziioannou A, Farquhar TH. High-resolution 3d bayesian image reconstruction using the microPET small-animal scanner. *Phys Med Biol*. 1998; 43(4):1001. [PubMed: 9572523]
- Queiroz MA, Hillner M, Kuhn F, Huber G, Meerwein C, Kollias S, von Schulthess G, Veit-Haibach P. Use of diffusion-weighted imaging (DWI) in PET/MRI for head and neck cancer evaluation. *Eur J Nucl Med Mol I*. 2014; 41(12):2212–2221.
- Ranger NT, Thompson CJ, Evans AC. The application of a masked orbiting transmission source for attenuation correction in PET. *J Nucl Med*. 1989; 30(6):1056–1068. [PubMed: 2786947]

- Rischpler C, Nekolla SG, Dregely I, Schwaiger M. Hybrid PET/MR imaging of the heart: potential, initial experiences, and future prospects. *J Nucl Med*. 2013; 54(3):402–415. [PubMed: 23404088]
- Schäfer JF, Gatidis S, Schmidt H, Gckel B, Bezrukov I, Pfannenberger CA, Reimold M, Ebinger M, Fuchs J, Claussen CD, Schwenzer NF. Simultaneous whole-body PET/MR imaging in comparison to PET/CT in pediatric oncology: initial results. *Radiology*. 2014; 273(1):220–231. [PubMed: 24877983]
- Scheuermann JS, Saffer JR, Karp JS, Levering AM, Siegel BA. Qualification of PET scanners for use in multicenter cancer clinical trials: the American College of Radiology Imaging Network experience. *J Nucl Med*. 2009; 50(7):1187–1193. [PubMed: 19525463]
- Su KH, Hu L, Stehning C, Helle M, Qian P, Thompson CL, Pereira GC, Jordan DW, Herrmann KA, Traughber M, Muzic RF, Traughber BJ. Generation of brain pseudo-CTs using an undersampled, single-acquisition UTE-mDixon pulse sequence and unsupervised clustering. *Med Phys*. 2015; 42(8):4974–4986. [PubMed: 26233223]
- Torrado-Carvajal A, Herraiz JL, Alcain E, Montemayor AS, Garcia-Caamaque L, Hernandez-Tamames JA, Rozenholc Y, Malpica N. Fast Patch-Based Pseudo-CT Synthesis from T1-Weighted MR Images for PET/MR Attenuation Correction in Brain Studies. *J Nucl Med*. 2016; 57(1):136–143. [PubMed: 26493204]
- Vandervoort E, Sossi V. An analytical scatter correction for singles-mode transmission data in PET. *IEEE T Med Imaging*. 2008; 27(3):402–412.
- Watson CC. Supplemental transmission method for improved PET attenuation correction on an integrated MR/PET Nucl. Instrum Meth A. 2014; 734, Part B:191–195.
- Watson, CC.; Casey, ME.; Michel, C.; Bendriem, B. Advances in scatter correction for 3d PET/CT. In: Seibert, JA., editor. *IEEE Nucl Sci Symp Conf Rec*. 2004. p. 3008-3012.
- Wetter A, Lipponer C, Nensa F, Beiderwellen K, Olbricht T, Rbhen H, Bockisch A, Schlosser T, Heusner TA, Lauenstein TC. Simultaneous 18f choline positron emission tomography/magnetic resonance imaging of the prostate: initial results. *Invest Radiol*. 2013; 48(5):256–262. [PubMed: 23462678]
- Wu TH, Huang YH, Lee JJS, Wang SY, Wang SC, Su CT, Chen LK, Chu TC. Radiation exposure during transmission measurements: comparison between CT- and germanium-based techniques with a current PET scanner. *Eur J Nucl Med Mol I*. 2004; 31(1):38–43.
- Zubal IG, Harrell CR, Smith EO, Rattner Z, Gindi G, Hoffer PB. Computerized three-dimensional segmented human anatomy. *Med Phys*. 1994; 21(2):299–302. [PubMed: 8177164]

Figure 1. Schematic of tested TX source geometries. (a) Transverse distribution for all fixed source configurations (magenta shading) showing anthropomorphic attenuation phantom, and maximum intensity projection axial (sagittal) views of (b) torus, (c) 2-torus, and (d) ring geometries.

Figure 2. Anthropomorphic attenuation phantom used in Monte Carlo simulations. (a) Coronal view of full Zubal phantom with yellow and red boxes denoting the head and pelvis table stations, respectively. Representative (b) transverse head, (c) sagittal head, (d) transverse pelvis, and (e) sagittal pelvis slices.

Figure 3. Implementation of the single torus TX source geometry for the Siemens Biograph mMR. (a) Fillable continuous torus source and (b) maximum intensity projection of source reconstruction and patient table template μ -map.

Figure 4. Phantoms used to assess the implementation of the single torus TX scheme on the Siemens Biograph mMR. (a) 21 cm OD uniform fillable cylinder phantom, (b) flangeless Esser PET phantom, and (c) hip implant secured in water background.

Figure 5. Comparison of NECRs for several TX source geometries. (a) Head and (b) pelvis phantom results. The vertical gray line denotes the maximum singles count rate before mispositioning errors due to count pileup become significant (see Supplementary Material section 2).

Figure 6.

Impact of single torus source geometry limited tomographic sampling on μ -map estimates. Coronal images near the center of the transverse FOV from acquisitions of (a) one and (b) five sub-table positions. (c) Back-projection of a blank acquisition at the same coronal slice for a single sub-table position, demonstrating the effective sampled region of the FOV.

Figure 7.

Typical μ -map and RC images from the Monte Carlo simulation of the single fixed torus TX exam after two scatter iterations. (Top row) Reference high count, (middle row) 8 minute TX scans, and (bottom row) RC images compiled from all 10 Poisson noisy realization for the (a) head and (b) pelvis phantoms.

Figure 8.

Transverse and coronal μ -map reconstructions after two scatter iterations of the uniform cylinder phantom acquired on the Biograph mMR. (top) Full and (bottom) reduced linear grayscale window. The transverse image is the average computed over the full reconstructed volume and shows the ROI used for profile analysis (yellow box), while the coronal image represents a single slice.

Figure 9.

Quantification of the experimental torus TX scheme for a uniform water cylinder phantom scan on the Biograph mMR. (a) Transverse profile with the constant dashed line at $\mu=0.096$ cm⁻¹ for data without (uncorrected) and with several iterations of scatter correction and (b) bias with respect to the volume mean for each reconstructed transverse plane after two scatter iterations, with dashed line at zero.

Figure 10.

Transverse and sagittal μ -map reconstructions of the Esser PET phantom after two scatter iterations acquired on the Biograph mMR. The transverse image is the average computed over six slices, while the sagittal image represents a single slice.

Figure 11. Comparison of CT (CTAC) and experimental torus (TXAC) μ -map estimates of a hip implant phantom. (a) CT μ -map, (b) torus μ -map, and (c) profile comparison, with the vertical yellow box in (b) denoting the profile location.

Figure 12.

Comparison of manufacturer provided CT and experimental torus μ -map estimates of the Biograph mMR patient table. (a) CT (CTAC) and torus TX (TXAC) (b) full range (full) and (c) clipped maximum LAC (clipped) transverse μ -map images. (d) Histogram of LACs for the three methods computed over the complete μ -map volumes, with the gray vertical line marking the 0.12 cm^{-1} clipping limit.

Table 1
Count rate performance comparison of several TX source geometries for the head and pelvis phantoms.

Phantom	Geometry	Peak NECR (kcps)	Activity @ Peak (mCi)	Singles @ Peak (kcps)	Scatter Fraction (%)	Peak PNEC (kcounts/cm)
head	point	3.86	0.08	115.00	8.9	35.81
	line	8.24	0.20	115.00	14.8	153.39
	torus	33.66	1.27	115.00	12.9	311.94
	2-torus	36.93	2.27	115.00	13.5	342.18
	ring	11.08	1.42	68.30	19.5	193.64
pelvis	point	4.55	0.08	115.00	11.2	42.18
	line	10.31	0.21	115.00	20.2	191.73
	torus	34.82	1.28	115.00	16.2	322.70
	2-torus	42.54	2.32	115.00	17.1	394.24
	ring	11.32	1.32	62.90	25.6	194.79

Table 2
Influence of the number of scatter iterations on estimated μ -map percent (%) bias and noise.

Phantom	ROI	Scatter Iteration							
		Uncorrected				1			
		NMD	CoV	NAD		NMD	CoV	NAD	
head	skull	-17.6	12.9	18.8	-10.2	11.7	13.2	-10.9	11.9
	spine	-17.2	13.5	19.9	-7.0	11.9	13.9	-8.3	12.3
	gray matter	-8.0	14.1	13.6	1.1	11.5	10.4	0.0	12.0
	hippocampi	-10.6	13.1	13.9	1.8	9.5	9.2	-0.2	10.6
pelvis	fat	-10.7	15.3	15.1	-0.9	12.1	11.4	-1.6	12.0
	skeletal muscle	-9.2	8.8	11.9	1.7	6.7	7.4	0.5	6.6
	cortical+marrow	-21.1	8.2	25.0	-8.5	6.4	20.0	-10.5	6.5
	prostate	-10.4	6.0	12.4	7.5	6.3	9.4	3.7	4.8
									7.7

Table 3

Mean ROI analysis of the proposed TX method for the Esser PET phantom.

Material	Expected LAC (cm^{-1})	Measured LAC (cm^{-1})
Teflon	0.182	0.185
Air	0.000	0.002
Water	0.096	0.104