On-board SPECT for localizing functional targets: A simulation study

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(Received 29 September 2008; revised 23 February 2009; accepted for publication 16 March 2009; published 16 April 2009)

Single photon emission computed tomography (SPECT) was investigated for imaging on-board radiation therapy machines in order to localize functional and molecular targets. A computer-simulated female NCAT phantom was positioned supine on a flat-top treatment couch. Twenty tumor locations were defined in the upper torso. The eight lung tumors were subject to the effects of respiratory motion. Tumor diameters of 10.8, 14.4, and 21.6 mm were simulated for tumor-to-background ratios of 3:1 and 6:1 that are characteristic of the radiotracer ^{99m}Tc-sestamibi. Projection images representing scan times of 4, 8, and 20 min were simulated for an anterior, half-circular trajectory. Images were reconstructed with attenuation correction by ordered-subsets expectation maximization (OSEM) using six subsets and five iterations. Contrast-to-noise ratios (CNRs) were calculated from ensembles of 25 images. Cross correlation with a noise-free tumor template was used to select the most suspicious tumor location within a 14.4-mm-radius search volume surrounding each tumor, with only that one tumor in each search volume. Localization accuracy was assessed by calculating average distances between measured and true tumor locations. Localization accuracy and CNRs were strongly affected by tumor location relative to the detector trajectory. For example, CNR values near the chest wall were greater by a factor of 3.5 than for tumors near the spine and posterior ribs, a much greater effect than the factor of 1.6 difference in CNR between 6:1 and 3:1 tumor uptakes. Typically, tumors of 6:1 uptake were localized as accurately with 4 min of scan time as tumors of 3:1 uptake that had been imaged for 20 min. Using 4 min scans, 14.4 and 21.6 mm anterior tumors of 6:1 uptake were localized within 2 mm. These results suggest that SPECT, on-board radiation therapy machines, may be a viable modality for localizing certain functional and molecular targets using relatively short scan times. © 2009 American Association of Physicists in Medicine. [DOI: [10.1118/1.3113902](https://doi.org/10.1118/1.3113902)]

Key words: SPECT, on-board imaging, target localization

I. INTRODUCTION

Functional imaging modalities such as positron emission tomography (PET) and single photon emission computed tomography (SPECT) rely on radiotracers to identify physiological processes—such as angiogenesis, apoptosis, hormone receptor status, hypoxia, and proliferation—that have important implications in cancer management.¹ In the context of radiation therapy, such functional information can be used to define biological target volumes and, when combined with the dose sculpting capabilities of intensity modulated radiation therapy (IMRT), may provide enhanced therapeutic success.² To date, SPECT and PET have been utilized for diagnosis, staging, and treatment planning. We propose that functional imaging may also have an important role in the treatment room for the delivery of radiation therapy. Currently, treatment-room imaging is composed mainly of x-ray transmission imaging and ultrasound imaging, which are predominantly anatomical imaging modalities.³ Imaging with these modalities immediately prior to delivery has improved patient alignment and reduced normal tissue damage for some sites,³ but there are limitations. Notably, anatomical differences between tumor and surrounding tissue may not be substantial enough to directly visualize tumor. Consequently, localization is often performed instead with indirect

markers such as bony anatomy, that may not necessarily indicate tumor position.^{4–6} This limitation may be particularly important when high gradients are used to sculpt dose around biological targets that cannot be visualized using current treatment-room imaging modalities. Further, ultimately radiation therapy may be directed to temporally varying functional targets, such as hypoxia, which at treatment time may be in a location different from their location during planning CT or planning functional imaging.⁷

One possible method for directly localizing biological targets is to image with SPECT inside radiation therapy treatment rooms. SPECT has been used for a wide array of tumor imaging applications,^{8,9} and ongoing research is expanding the already broad array of radiotracers.^{10–15} While spatial resolution is somewhat limited compared with many anatomical imaging modalities, contrast between tumor and background can be substantially greater, and this stronger tumor signal may improve treatment-room tumor localization.

Though SPECT has been studied extensively for diagnostic tasks, SPECT has not been developed for the treatment-room environment where new challenges await. Notably, SPECT scans typically last 20 min or more, and this amount of time is too long in terms of patient motion and machine throughput. Shorter imaging times are needed, which implies

FIG. 1. (A) Coronal view of radiotracer distribution in phantom; (B) uptake pattern for different tumor sizes in transaxial slice.

greater image noise. Additionally, treatment-room couches are wider and supporting rails are typically deeper than diagnostic SPECT couches. As such, treatment couches may challenge detector-to-patient proximity and increase attenuation, which in turn degrade image quality with poorer spatial resolution and increased noise. While these constraints will negatively impact image quality, it is important to consider that the task for on-board SPECT would be different than with most diagnostic SPECT scans. Because target size and approximate location are known, it may be possible to accurately localize functional targets. Furthermore, SPECT detector trajectories can be optimized for imaging the treatment region, a factor which may enhance SPECT images in the region of interest (ROI) as compared to diagnostic scans which typically have to survey a larger volume.

II. METHODS AND MATERIALS

II.A. Phantom

A female anthropomorphic phantom was generated with NCAT software.^{16,17} The phantom was placed supine on a flat-surface treatment couch. Twenty tumor locations were arranged periodically on a square grid with centroid-to-centroid spacing of approximately 6 cm. Tumors were centered on voxels in an axial slice superior to the heart. For each tumor location, three tumor diameters—10.8, 14.4, and 21.6 mm with true volumes of 0.980, 2.10, and 6.49 cm³—were simulated in separate phantoms as shown in Fig. 1. The 8 deepest tumors were located in the lungs where they were subject to respiratory motion, while the remaining 12 tumors were stationary in soft tissues or bone. Activity distribution was modeled for the radiotracer ^{99m}Tc-sestamibi that has been used to image a number of tumors, including breast cancer and its metastases.^{18–20} Activity concentrations were 5.0 μ Ci/ml in the gall bladder and myocardium, 2.5 μ Ci/ml in the liver, kidneys, and spleen, and 0.25 μ Ci/ml in other healthy tissues. Left- and right-sided tumor activity concentrations were 1.75 and 1.5 μ Ci/ml, re-

FIG. 2. Attenuation map of phantom and treatment couch with dimensions.

spectively, as these uptake values relative to normal tissues—3:1 and 6:1—have been noted clinically.¹⁹

We used NCAT software to generate a CT-like image of linear attenuation coefficients for 140 keV photons in the following tissues: 0.149–0.157 cm⁻¹ in soft tissues and 0.163–0.220 cm⁻¹ in bone. The attenuation phantom had the exact geometry of the activity phantom. The couch was assigned a linear coefficient of 0.250 cm⁻¹, which corresponds to a predominately carbon-based material with physical density of 1.8 g/cm³.²¹ A map of attenuation coefficients and dimensions for a slice containing tumor are shown in Fig. 2.

The effects of respiration were considered by averaging 16 phases of a respiratory cycle where the diaphragm moved 20.0 mm and the chest expanded by 12.0 mm. Normal structures experienced varying degrees of 2D motion in the anteroposterior (AP) and superoinferior (SI) dimensions. Identical motion vectors were applied to laterally symmetric left- and right-sided lung tumors to minimize differences other than activity concentration. Lung tumor motion was characterized by one of four maximum centroid-to-centroid displacements according to tumor location: anteromedial (7.20 mm SI, 7.20 mm AP), anterolateral (10.8 mm SI, 10.8 mm AP), posteromedial (7.20 mm SI, 3.60 mm AP), posterolateral (10.8 mm SI, 3.60 mm AP). Tumors outside the lungs were stationary. Activity and attenuation phantoms were implemented on a 384 × 384 × 384 grid of 0.18-cm-wide voxels. Attenuation phantoms, one for each tumor size, were also placed on a coarser grid with 0.36-cm-wide voxels and were used to correct for nonuniform attenuation during reconstruction.

II.B. Projection data simulation and image reconstruction

SPECT imaging was simulated with an analytical, ray-driven software using the code SPECT-MAP which has been utilized and tested in this and many previous studies, e.g., Refs. 22–26. Projection images were modeled for a gamma camera with 46 × 23 cm² active surface area and parallel-hole, low-energy, high-resolution collimation. Simulated collimator holes were 2.7 cm long by 0.14 cm in diameter.

FIG. 3. Line source profiles for measured and simulated data that show the effects of distance-dependent collimator resolution. Measurements were made with a Trionix Triad SPECT scanner.

Distance-dependent spatial resolution was determined by fitting an analytical form to measured projection data. This spatial resolution modeling was implemented by tracing a cone of 121 rays from multiple subdivisions of each detector bin. The resolution modeling was validated by comparing measured line spread functions to those calculated using 121-ray cones, as shown in Fig. 3. Intrinsic resolution was modeled with a 2D, 0.34-cm-FWHM Gaussian kernel. Also modeled were the efficiencies of the collimator, scintillator, and branching ratio of ^{99m}Tc . SPECT-MAP calculations of efficiency and attenuation were checked against hand calculations. Scatter was not considered.

Projection images were simulated for step-and-shoot mode every 3° over a half-circular trajectory by rotating the detector from right lateral over the chest to left lateral as shown in Fig. 4. Bins in projection images were 0.36 cm wide. Finite bin width was modeled by tracing four cones from each bin, i.e., one cone from the center of the four quadrants; thus in total $4 \times 121 = 484$ rays were traced from

FIG. 4. Detector trajectory spanning 180° anteriorly is displayed with overlapping gray bars. Axis of rotation is marked with an asterisk. Common volume—voxels projected onto the detector at every view—is inside the dashed line.

each detector bin. The detector-to-image-plane radius of rotation was 26.5 cm with the axis of rotation centered near the phantom spine. Using this detector and trajectory, there was no truncation of the transaxial slices containing tumors, as demonstrated in Fig. 4 by the dashed line that encloses the common volume, i.e., the region that is projected onto the detector surface at every angle. These simulated noise-free 2D projection images were degraded with varying levels of Poisson noise corresponding to scan times of 4, 8, and 20 min. Ensembles of 25 independent noisy projection images were generated for each combination of scan time and tumor size.

Image ensembles were reconstructed via ordered-subsets expectation maximization (OSEM) (Ref. 27) using six subsets and five iterations, which are in the range of typically used values.²⁸ Attenuation correction was achieved by modeling photon detection probabilities within OSEM. In the reconstructed images, the intensities of deep background regions were similar to those in the phantom, thus validating attenuation correction. Our reconstructions did not model distance-dependent spatial resolution, as is typical of most clinical SPECT imaging. Image voxels were 0.36 cm wide, a factor of 2 coarser than voxels of grids on which phantoms were placed for simulating projections. During reconstruction, four rays were traced from every projection bin through the reconstruction grid in order to average over the finite detector bin width. Rays were oriented perpendicular to the image plane and spaced equally from one another in the transaxial dimension of a bin. Additional rays were not traced along the axial (superior-inferior) dimension because of the exact axial alignment between projection bins and image voxels at every detector view. Noisy reconstructed images were smoothed with 3D Gaussian kernels of 8, 14, and 20 mm FWHMs.

II.C. Image analysis

Contrast-to-noise ratios (CNRs) and localization metrics were calculated from noisy image ensembles. For CNR calculations, 3D ROIs were drawn around the tumor. Approximately 7.2 mm away from these ROI boundaries, shell-like ROIs were defined in the background. ROIs were approximately spherical for stationary tumors. For lung tumors, ROIs were irregularly shaped so as to account for the asymmetric blurring effects of respiratory motion. Both tumor and background ROIs were the size of tumor volumes and encompassed 21, 45, and 139 voxels for respective tumor diameters of 10.8, 14.4, and 21.6 mm.

Contrast was defined as

$$C_i = \frac{\bar{T}_i - \bar{B}_i}{\bar{B}_i}, \quad (1)$$

where $\bar{T}_i$ and $\bar{B}_i$ are mean tumor and background ROI intensities in image i . Mean contrast,

$$\hat{C} = \frac{\sum_{i=1}^N C_i}{N}, \quad (2)$$

was calculated from the $N=25$ noisy reconstructed images. This definition of contrast allows for negative values when the background is hotter than the tumor in order to avoid upward bias of mean contrast values when background noise dominates the tumor signal. Noise was calculated as the standard deviation of contrast:

$$\sigma_{\hat{C}} = \sqrt{\frac{\sum_{i=1}^N (C_i - \hat{C})^2}{N-1}}. \quad (3)$$

Ensemble average contrast-to-noise ratio was

$$\text{CNR} = \frac{\hat{C}}{\sigma_{\hat{C}}}. \quad (4)$$

Localization accuracy and precision were assessed by calculating the mean and standard deviation of distances between true and measured tumor centroids over ensembles of noisy reconstructed images. Tumor locations in noisy images were selected via a forced choice task using nonprewhitening filters.²⁹⁻³¹ This approach is relevant to radiation therapy delivery because disease is known to exist; yet the exact position varies with each time the patient is positioned on the treatment table.

Since the approximate tumor location is known from treatment-planning images, the search can be limited to a relatively small volume. In this study, 3D search volumes—14.4-mm-radius spherical ROIs—were defined around each tumor. The size of each search volume was intended to encompass the uncertainties in tumor location that are typical for radiation therapy. Each search volume contained 257 voxels that were subdivided three times in each dimension. The location in the ROI that had the highest cross correlation (XC) with a noise-free tumor template was selected as the measured tumor centroid:

$$\text{XC}_i = \frac{\text{template}_j \cdot \text{image}_i}{\sqrt{(\text{template}_j \cdot \text{template}_j)(\text{image}_i \cdot \text{image}_i)}}, \quad (5)$$

$$r_{m,i} = \arg \max_{j \in \Omega} (\text{XC}_{i,j}), \quad (6)$$

where template_j represents the template centered at voxel j within ROI Ω of ensemble image i . The denominator in the above cross-correlation equation normalizes the response such that it does not depend on voxel intensities. As such cross-correlation values were suppressed for hot background structures (e.g., heart) that would have otherwise elicited greater responses than the nearby tumor. Tumor templates were generated by convolving true tumor geometries with a 14.4-mm-Gaussian kernel that approximates typical spatial resolutions in these images. For lung tumors, the true tumor geometry included asymmetric blurring from respiratory motion. Tumor templates were constructed on cubic grids of 0.12-cm-wide voxels with grid widths of 27, 33, and 39 voxels for tumor diameters of 10.8, 14.4, and 21.6 mm, respectively.

FIG. 5. Sample reconstructed images, smoothed with 14-mm-FWHM Gaussian, for each combination of tumor size and scan time.

Mean localization error $\overline{dr}$ was defined as the offset distance dr between true $r_t = (x_t, y_t, z_t)$ and measured tumor centroids $r_{m,i} = (x_{m,i}, y_{m,i}, z_{m,i})$ averaged over the ensemble of $N=25$ noisy reconstructed images:

$$dr = \sqrt{(x_m - x_t)^2 + (y_m - y_t)^2 + (z_m - z_t)^2}, \quad (7)$$

$$\overline{dr} = \frac{1}{N} \sum_{i=1}^N dr_i. \quad (8)$$

Standard deviation in localization error was computed as

$$\sigma_{dr} = \sqrt{\frac{\sum_{i=1}^N (dr_i - \overline{dr})^2}{N-1}}. \quad (9)$$

III. RESULTS

III.A. Reconstructed images

Reconstructed images for each combination of tumor diameter and scan time are presented in Fig. 5. These images are noisy realizations, not ensemble averages, and have been smoothed with a 3D, 14-mm-FWHM Gaussian kernel. Grids are superimposed on images such that each square element is centered on a tumor.

Qualitative trends are apparent in these images. As scan time increases, noise decreases, thereby improving the tumor visibility. For instance, with the 4 min scans, image noise resembles the expected signal for 10.8 and 14.4 mm diameter tumors in some locations, especially in the lungs and near posterior of the phantom. When scan time is increased to 8 and then 20 min, there are fewer and fewer hot spots off center of the grid, which suggests that the apparent activity is the true tumor signal. Tumor-to-background uptake ratios have a substantial effect on tumor visibility, as those on the patient right side with 6:1 uptake ratios are more noticeable than left-sided tumors with 3:1 uptake ratios. Also note the impact of tumor location relative to the detector trajectory: Tumors near the chest wall, which are on average closer to the detector, are strikingly more apparent than lung tumors and stationary tumors near the spine. The detector trajectory also affects apparent tumor shape. Anterior tumors are ap-

FIG. 6. CNRs calculated from ensembles of noisy reconstructed images and presented as a function of location for each combination of scan time and tumor diameter.

proximately circular, while other visible tumors are elliptical with varying degrees of eccentricity. Greater eccentricity occurs when the detector-to-tumor distance is substantially different over the detector trajectory.

III.B. Contrast-to-noise ratio

CNRs were calculated from ensembles of noisy reconstructed images using Eqs. (1)–(4). CNR values are displayed in Fig. 6 as a function of anatomy for the investigated scan times and tumor diameters. Many of the visual trends noted in the reconstructed images from Fig. 5 are expressed quantitatively in Fig. 6 as ensemble CNRs. CNRs increase approximately by the square root of imaging time. Right-sided tumors with 6:1 radiotracer uptake ratios have higher CNRs than their laterally symmetric counterparts of 3:1 uptake by an average factor of 1.6. CNRs of anterior tumors are typically 3.5 times greater than their posterior counterparts. These trends are shown in Fig. 7, thus demonstrating the

FIG. 7. Differences in CNR due to radiotracer uptake and anatomical location. Circles represent differences in CNR between anterior tumors and their posterior counterparts. Diamonds indicate the CNRs of laterally symmetric tumors that differ by radiotracer uptake.

relative impact of radiotracer uptake versus the detector trajectory on CNR.

III.C. Localization

Localization metrics—the mean localization error $\overline{dr}$ and ensemble standard deviation σ_{dr} —were calculated using Eqs. (5)–(9) and are reported in Fig. 8. Mean errors are represented by white and black boxes that respectively correspond to tumors of 6:1 and 3:1 radiotracer uptakes. Error bars indicate standard deviations. The different tumor sizes are separated by rows. Columns differentiate tumor locations. Note the diagram above each column in Fig. 8 that specifies anatomical locations. Within each column there are six data points—three white and three black boxes—that correspond to scan times of 4, 8, and 20 min for each uptake ratio. When viewing Fig. 8 from left to right, tumor locations vary from anterior to lateral to posterior. A bold dashed line separates stationary and lung tumors. The relative order of lung tumors is the same as that of stationary tumors.

In all but the regions of poorest SPECT image quality, tumors of 6:1 uptake are typically localized as accurately with 4 min of scan time as tumors of 3:1 uptake that are imaged for 20 min. This trend is demonstrated in Fig. 8 by observing the relative height of boxes, specifically the first white and the third black boxes within a column. For locations at which noise and blur are severe, localization is determined primarily by random chance for both 3:1 and 6:1 uptake ratios. In these cases, localization accuracy is similar and poor for the two uptake ratios. This effect is illustrated by the 10.8 mm tumors in the lungs.

Tumor location has a major impact on localization accuracy. In Fig. 8, there is a general trend where localization errors worsen when tumor location changes from anterior to lateral to posterior. As with CNRs, tumor location relative to the detector trajectory can have a larger effect on localization error than radiotracer uptake ratio. These effects are shown in Fig. 8 when making comparisons among stationary tumors near the chest wall of different uptake ratios, and then with

FIG. 8. Ensemble localization errors for different combinations of tumor size, location, radiotracer uptake, and imaging time. Mean errors are displayed as black and white boxes for respective uptake ratios of 3:1 and 6:1. Error bars indicate standard deviations. Tumor sizes are separated by rows and tumor locations by columns. Within each column, there are six data points that correspond with scan times of 4, 8, and 20 min for laterally symmetric tumors of different uptake ratios.

counterparts near the spine and posterior ribs. Though localization is generally poor for posterior tumors, certain results are encouraging. When using relatively short 4 min scans, anterior tumors with diameters of 14.4 and 21.6 mm and 6:1 uptake ratios had mean localization errors less than 2 mm.

III.D. Localization accuracy as a function of contrast-to-noise ratio

Mean localization errors are plotted as a function of CNRs in Fig. 9. There is a noticeable trend. When CNRs are

FIG. 9. Mean localization errors plotted as a function of CNRs. Tumors of 3:1 and 6:1 uptakes are differentiated by square and diamond markers. Markers that are crossed signify lung tumors, while solid markers represent stationary tumors.

close to zero, localization errors are around 11 mm, which is the expected error when randomly selecting radial locations from a 14.4-mm-radius search volume. In this regime, noise dominates and SPECT provides very little information. As CNRs increase to around 5, localization errors improve rapidly because SPECT is providing more information. Improvements in localization are more modest as CNRs continue to increase. In this region, there is comparatively less to gain from enhancing the already pronounced tumor signal.

There are other more subtle effects in Fig. 9. In the CNR range of 3–5, localization is typically better for tumors of 6:1 than 3:1 uptake. Localization error is generally better for stationary tumor of the same uptake ratio than lung tumors with similar CNRs. Two stationary tumors of 3:1 uptake with relatively high CNRs are noticeably skewed above the other data points. The unexpected degradation in localization error is attributable to proximity to the heart where radiotracer concentrations are much higher and suppress tumor signal inferiorly. These results show potential challenges for localizing targets near a hot background.

IV. DISCUSSION

In this simulation study, on-board SPECT was investigated for localizing functional and molecular targets. Several parameters were considered: Scan time and tumor location, diameter, and uptake ratio. Among these, one of the most influential factors was radiotracer uptake in tumor relative to

background: As indicated by CNRs, localization metrics, and visual inspection. Tumors of 6:1 uptake were strikingly more noticeable than their laterally symmetric counterparts of 3:1 uptake. These visual observations were supported by quantitative values—CNRs and localization accuracy. CNRs were on average 1.6 times greater for the tumors of 6:1 radiotracer specificity. The observed ratio of 1.6 is less than the true phantom contrast ratio of 2.5. In the absence of spatial resolution modeling, blurring from limited spatial resolution has a relatively greater impact on contrast recovery of 6:1 tumors compared with those of 3:1 uptake. This result is consistent with the findings of Ref. 32 where scatter, a type of blurring, more substantially reduced the recovered contrast of hotter lesions.

Typically, tumors of 6:1 uptake were localized as accurately using 4 min scans as 3:1 tumors that had been imaged for 20 min. This difference in time has important implications, especially in the context of radiation therapy delivery where short scans are important in minimizing patient motion and ensuring machine throughput. Thus, radiotracer specificity will be an important criterion when selecting or developing potential radiotracers for on-board SPECT imaging. Conversely, diagnostic or treatment-planning SPECT images could be used to estimate tumor characteristics—radiotracer uptake and size—that affect localization in a predictable way in order to gauge whether individual patients would benefit from on-board SPECT. Further, diagnostic or treatment-planning SPECT images could provide radiotracer-concentration templates for estimating localization. Such templates may be particularly useful for localizing tumors with inhomogeneous radiotracer uptake that is comparable in width to, or wider than, the on-board SPECT spatial resolution.

This study utilized a 180° orbit in order to avoid viewing the patient through the couch. Radiation therapy couches are thicker and wider than typical diagnostic imaging couches, such that SPECT data acquired through the couch would be substantially attenuated, and the SPECT detector would be displaced away from the patient, thereby degrading spatial resolution. Averaging over all angles of the 180° orbit, tumors near the chest wall are on average closer to the detector, which implies better spatial resolution, and they are less attenuated by tissue. Because of attenuation, image noise was greater near the spine than the chest wall. Quantum noise is not reversible even with attenuation correction. As is typical for most clinical SPECT imaging, the reconstructions did not model spatial resolution. Consequently, poorer spatial resolution and poorer contrast are expected for the posterior tumors. Modeling spatial resolution would increase image reconstruction time—an important consideration for on-board SPECT. That noted, spatial resolution modeling is worth evaluating in a future study, since it has potential to improve localization.³³ Because localization is better in regions proximal to the detector trajectory and since tumor location is known approximately, on-board SPECT trajectories could be optimized for imaging specific tumor sites.

CNR and localization error are related, but one metric may not necessarily be a good predictor of the other. In this

study, noisy reconstructed images were smoothed using Gaussian kernels with FWHMs of 8, 14, and 20 mm. CNRs and localization errors were calculated for noisy images and for images with each degree of smoothing. CNRs improved with smoothing. In contrast, localization errors improved at certain anatomical locations but worsened for others. On average localization errors were comparable across different degrees of smoothing. These results demonstrate that localization errors cannot be estimated directly from CNRs. Encouragingly, these results also suggest that localization accuracy is somewhat robust to smoothing. It follows that they may be robust to iteration number when using iterative reconstruction since smoothness is highly correlated with iteration number. Smoothing did, however, impact localization for certain tumors, and these effects need to be studied further.

CT provides anatomical information that would be valuable for correcting nonuniform attenuation in on-board SPECT images. Attenuation coefficients could be estimated from on-board cone beam CT or from registered CT images.

We do not anticipate that on-board SPECT imaging would be used for every fraction in a highly fractionated treatment because of associated imaging time and patient dose. On-board SPECT is better suited for treatments with a limited number of fractions such as stereotactic body radiation therapy (SBRT). SBRT is used to treat a variety of tumors, including breast oligometastasis.^{34,35} For SBRT, imaging time is less of an issue because additional time is allotted for patient positioning as compared with most highly fractionated treatments. Concerning patient dose, a typical 25 mCi injection of ^{99m}Tc-sestamibi³⁶ results in an effective dose of 7.9 mSv,³⁷ which is about 1/3 the effective dose of an on-board CBCT chest scan.³⁸ Cost is also an issue that would have to be evaluated along with any improvements in morbidity and/or mortality through clinical studies.

Localization values may change depending on the coarseness of image voxels or the size of the search volume. In this study, centroids were estimated on a voxelized grid, limited by the half width of a subvoxel. Localization would likely worsen by using a larger search volume with more locations where random noise fluctuations could mimic tumor, particularly for barely visible tumors.

Our simulation study makes absolute estimates regarding localization. Localization values will change—likely for the worse as additional factors such as scatter (estimated to account for 20%–40% of the detected counts in scanner data³⁹), tumor diffuseness, and tumor inhomogeneities are considered. Localization accuracy, however, will likely change for the better as trajectories are focused on the target region, as scatter correction is implemented, and as estimation methods are developed specifically for tumor inhomogeneities. This current study contributes as a significant first step, by incorporating a significant degree of realism (e.g., spatial resolution and attenuation), clearly defining that level of realism, and then returning absolute numbers for localization accuracy and precision. Such absolute estimates are necessary in order to access whether on-board SPECT is even

possibly feasible, and these estimates form a baseline which will help in quantifying and understanding the effects of future developments.

V. CONCLUSION

SPECT imaging was investigated for localizing functional and molecular targets immediately prior to radiation therapy. CNRs and localization errors were analyzed as a function of scan time and tumor size, location, and radiotracer uptake using computer simulations. Localization errors were less than 2 mm for certain tumors using relatively short 4 min scans. These encouraging results warrant further investigation of on-board SPECT for localizing functional and molecular targets.

ACKNOWLEDGMENTS

This project was supported in part by NIH Grant No. T32EB007185 from the National Institute of Biomedical Imaging and Bioengineering and by the Department of Defense Breast Cancer Research Program Predoctoral Fellowship (Grant No. BC073559). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Biomedical Imaging and Bioengineering, the National Institutes of Health, or the Department of Defense. The authors would like to thank the reviewers for helpful comments which have improved the paper.

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