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Impact of respiratory motion on the detection of small pulmonary nodules in SPECT imaging

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Abstract

The objective of this investigation is to determine the impact of respiratory motion on the detection of small solitary pulmonary nodules (SPN) in single photon emission computed tomographic (SPECT) imaging. We have previously modeled the respiratory motion of SPN based on the change of location of anatomic structures within the lungs identified on breath-held CT images of volunteers acquired at two different stages of respiration. This information on respiratory motion within the lungs was combined with the end-expiration and time-averaged NCAT phantoms to allow the creation of source and attenuation maps for the normal background distribution of Tc-99m NeoTect. With the source and attenuation distribution thus defined, the SIMIND Monte Carlo program was used to produce SPECT projection data for the normal background and separately for each of 150 end-expiration and time-averaged simulated 1.0 cm tumors. Normal and tumor SPECT projection sets each containing one lesion were combined with a clinically realistic noise level and counts. These were reconstructed with RBI-EM using 1) no correction (NC), 2) attenuation correction (AC), 3) detector response correction (RC), and 4) attenuation correction, detector response correction, and scatter correction (AC_RC_SC). The post-reconstruction parameters of number of iterations and 3-D Gaussian filtering were optimized by human-observer studies. Comparison of lesion detection by human-observer LROC studies reveals that respiratory motion degrades tumor detection for all four reconstruction strategies, and that the magnitude of this effect is greatest for NC and RC, and least for AC_RC_SC. Additionally, the AC_RC_SC strategy results in the best detection of lesions.

I. Introduction

Respiratory motion is known to cause artifacts and decrease the tumor detectability in medical imaging [1,2]. In some imaging modalities it is possible to acquire a complete study of the chest during a single breath hold. In radionuclide emission imaging acquisition times may require 20 minutes or longer. In such circumstances where it is clearly impossible for breath holding, alternative strategies such as respiratory gating may result in improved tumor detection due to reduced motion blurring of the tumor [3]. However, collecting events only during a portion of the respiratory cycle when little motion has occurred results in acquisitions with a measurable decrease in total counts due to the omission of events from outside of the selected portion of the cycle. Thus acquisitions obtained only during that portion of the respiratory cycle associated with minimal motion have the disadvantage of an increase in noise.

We have previously investigated the movement of structures within the lungs during respiration and displayed these findings as motion vectors [4]. It was shown that these motion vectors vary in magnitude and direction regionally within the lung. In several regions of the lung, the extent of this movement is on the same order of magnitude as the spatial resolution intrinsic to emission imaging in which the total resolution of the system is equal to the square root of the sum of the squares of component resolutions. It thus becomes important to determine if the blur associated with respiratory motion significantly degrades the accuracy of lesion detection using Tc-99m depreotide (NeoTect), and whether this effect is uniform throughout the lung or dependent upon the region in which the lesion is located.

The most widely used digital phantom for defining source and attenuation maps for simulated emission imaging is the mathematical cardiac torso (MCAT) [5]. The original MCAT has been modified to include a dynamic component that includes respiratory motion and a beating heart [6]. However, this 4D dynamic MCAT phantom is limited in its ability to realistically model the true shape and variations of anatomic organs. Non-uniform rational B-splines (NURBS), which are commonly used in 3-D computer graphics, are capable of describing three-dimensional surfaces. A NURBS based MCAT has been developed by Segars [7] and has been in use as a newer generation of spline-based MCAT phantoms. This non-uniform rational B-spline MCAT, or NCAT, is designed to allow the “warping” of surfaces to correctly fit the shape of anatomic structures imaged by conventional MRI or CT imaging techniques. A dynamic NCAT can be created as the result of generating an entire set of individual NCAT phantoms, with each phantom being rendered at a specific time point within the cycle of interest [8].

The purpose of this study is to compare the detection of solitary pulmonary nodules (SPN) as a function of image reconstruction technique, lesion location, and presence or absence of respiratory motion using simulated images.

II. Methods

The respiratory cycle associated with normal tidal breathing lasts approximately five seconds and correlates to a volume change on the order of 500 ml. Inspiration occurs during the first two seconds and expiration takes place during the remaining three seconds. The equations used for describing this variation herein are

$$\begin{aligned} V(t) &= -250ml \cos\left(\frac{\pi t}{2}\right) + 250ml & \text{for } 0 \leq t \leq 2 \\ V(t) &= -250ml \cos\left(\frac{\pi(5-t)}{3}\right) + 250ml & \text{for } 2 \leq t \leq 5 \end{aligned} \quad \text{eq. 1}$$

where $V(t)$ is the volume in ml and t is the time in seconds.

Two NCAT phantoms were initially created corresponding to two different CT data sets obtained at two different states of respiration closely corresponding to normal tidal breathing. With the assumption that structures move between the two different states along the x, y, and z directions according to the change in volume given by the above equations, and with $\Delta t = 0.156$ seconds, a total of 32 NCAT phantoms were generated over one full respiratory cycle beginning with end-expiration (EE) through end-inspiration (EI) and ending again at end-expiration. Additionally, a respiration-averaged NCAT phantom was generated as well.

We have previously modeled the respiratory motion of SPN based on the two CT image data sets obtained at the two different states of respiration [4]. We base our current investigation on our observations regarding the motion of specific anatomic structures and identical points that were selected and marked on the CT images at the two different states of respiration. In order

to begin our study using simulated images it was necessary to first incorporate our findings regarding the complex motion of SPN into the NCAT phantoms. To do so, SPN were first modeled as spheres 1 cm in diameter centered at a number of locations throughout the lungs. A total of 150 points were selected as locations for the 1.0 cm lesions. The locations were equally divided between the right lung and left lung with seventy-five points in each. Of the 150 locations, fifty points were selected from the upper third of the lung (lung apices), fifty from the middle third, and fifty from the lower third (lung bases). Using the NCAT generating software, and similarly based on the volume curves described in equation 1, one hundred fifty sets of separate NCAT phantoms, each consisting of only a 1.0 cm diameter sphere, were generated over the full respiratory cycle (32 frames each) as well as the respiration averaged NCAT sphere.

The radiopharmaceutical selected for investigating the impact of motion in single photon emission computed tomographic (SPECT) imaging for SPN is Tc-99m labeled depreotide (NeoTect). Tc-99m NeoTect is a low molecular weight radiolabeled polypeptide capable of binding to the somatostatin receptor which is often expressed on the cell surface membrane of both small cell and non-small cell lung carcinomas [9]. Tc-99m NeoTect has been approved by the Food and Drug Administration for use in the evaluation of SPN. The relative concentrations and distribution of Tc-99m NeoTect within the various tissues and organs contained within the NCAT phantom were obtained from pharmacokinetic data supplied by the manufacturer. Source and attenuation maps for Tc-99m NeoTect were created for the respiration-averaged NCAT phantom (frame av) and the first frame (frame 1) of the 32 NCAT phantoms generated which corresponds to end-expiration of the respiratory cycle.

Projection data were generated using the SIMIND Monte Carlo program [10] for these two NCAT phantoms (frame av and frame 1). The projection data output from SIMIND was subsequently binned and summed for both the photopeak window (primary plus scattered photons) and for the scatter window (primary plus scattered photons) using a program written in Interactive Data Language (IDL). Six clinical NeoTect acquisitions were analyzed and the counts in various anatomic areas determined and then averaged. Poisson noise was then added to the projection data, and based on the averaged counts, the projection data was then scaled to the total number of counts that would correspond to an actual clinical acquisition. For the purposes of this study, the same total counts were assigned to the respiration-averaged NCAT phantom (frame av) and to the NCAT phantom corresponding to end-expiration (frame 1).

Preliminary human-observer localization receiver operating characteristics (LROC) studies [15] using frame 1 were conducted to determine the level of lesion contrast prior to the optimization of the reconstruction parameters. An optimal level of lesion contrast is based on generating images in which the lesion is neither so faint that it is rarely seen nor so bright that it is almost always identified. This corresponds to areas under the LROC curve that range on the order between 0.6 and 0.9. The two different reconstruction strategies used in determining the optimal lesion contrast were rescaled block-iterative (RBI) reconstruction with attenuation correction and RBI with detector response correction. In each strategy, a single combination of the number of iterations and σ of the three-dimensional (3-D) post Gaussian filter was used. For the RBI with attenuation correction strategy, the reconstruction parameter of two iterations with σ of 1.0 was used. For the RBI with detector response correction, the reconstruction parameter of six iterations with σ of 1.0 was used. The human-observer LROC results from the contrast determination studies were also used in defining the radius of correct localization for subsequent work.

Four different RBI reconstruction strategies were selected for our analysis: 1) RBI with no correction (NC), 2) RBI with attenuation correction (AC), 3) RBI with detector response correction (RC), and 4) RBI with attenuation correction, detector response correction and

scatter correction (AC_RC_SC). Because of improved performance at high noise levels, the attenuation map generated by the block-iterative transmission AB (BITAB) algorithm was used for the RBI reconstruction [11]. To obtain this attenuation map, transmission projection data was first generated from the original source distribution using the analytic projector. The projection data was then binned, rescaled and noise added. With the above projection data as input, the actual attenuation map was generated using the BITAB reconstruction algorithm [12]. The Gaussian diffusion method for detector response correction was chosen because of the feasibility and enhanced performance of this approach in single activity detection tasks [13]. The two-energy window (TEW) method was selected for scatter correction [14]. To obtain the scatter correction estimate, the output data from the SIMIND scatter window was first binned, rescaled and noise added. The correction methods described above served as input to the 3-D RBI reconstruction algorithm.

The reconstruction parameters of number of iterations and post-reconstruction 3-D Gaussian filter was subsequently optimized by human-observer LROC studies for each of the four different reconstruction strategies of NC, AC, RC, and AC_RC_SC.

Human-observer LROC studies were then conducted for both the stationary tumors (frame 1) and for the tumors blurred out by simulated respiration (frame av). Five observers read two sets of images for each of the four reconstruction strategies both for frame 1 and frame av for a total of sixteen sets. Each set first consisted of 48 training images in which feedback was provided regarding the absence or presence of a lesion and its correct localization when present. This was then followed by 102 study images.

III. Results and Discussion

The results of our preliminary LROC study to set lesion contrast are displayed in table 1. Initially, two contrasts were evaluated at 11.5 and 14 times that of the scaled background using images corresponding to the stationary tumors (frame 1). However, in tumor-present cases, the lesion was seen rather easily in almost all instances. Two additional contrasts were then selected for evaluation at 6.5 and 9 times that of the scaled background using the two reconstruction strategies of RBI with AC and RBI with RC. It was observed that at these two lower contrasts, observer performance was satisfactory, and areas under the LROC curve varied between 0.60 and 0.95.

The LROC results from the contrast determination studies were analyzed to determine the radius of correct localization. As shown in figure 1, the number of correct localizations is plotted as a function of the radius in pixels from the center of the actual lesion. Lesion contrasts of 6.5, 9, and 11.5 times that of the scaled background and the reconstruction strategies of RBI with AC and RBI with RC were used in this analysis. The radius of correct localization was determined to be 8.5 pixels.

The results of the optimization of the RBI reconstruction parameters were determined using the two lower levels of contrast and images corresponding to the stationary tumors (frame 1). The two reconstruction parameters that were optimized were the number of iterations and the σ of the 3-D post Gaussian filter, where 2.35 times σ equals the full width-half maximum (FWHM) of the 3-D post Gaussian filter. The optimization results of the human-observer LROC studies for each of the four different reconstruction strategies of NC, AC, RC, and AC_RC_SC are shown in table 2. For each of the four reconstruction strategies, the optimal value of σ was 1.0. For the NC and AC strategies, the optimal number of iterations was two. For the RC and AC_RC_SC strategies, the optimal number of iterations was four. The maximum areas under the LROC curve varied between 0.80 and 0.90.

Sample images from the final human-observer LROC studies are shown in figure 2. The upper two images correspond to a stationary tumor (frame 1) for the with noise case (left) and without noise case (right). The lower two images correspond to the same tumor blurred out by simulated respiration (frame av) for the with noise case (left) and without noise case (right). The lesion can be identified without much difficulty except in the case of simulated respiration with noise.

The human-observer LROC results indicating the impact of simulated respiratory motion on detection are shown in table 3. The results presented are based on pooled data of five observers each reading two sets of 102 images. The results indicate that simulated respiratory motion adversely affects tumor detection in all four of the reconstruction strategies and that the magnitude of this effect is dependent on the particular reconstruction strategy that was evaluated.

The results summarized in table 3 were subjected to statistical examination using the two-way analysis of variance (ANOVA) with Scheffe's multi-comparison test. Statistical significance at the $P < 0.05$ level was found between the stationary tumors (frame 1) and for the tumors blurred out by simulated respiration (frame av) for RBI with NC and for RBI with RC. In the ideal case of stationary tumors (frame 1), statistical significance at the $P < 0.05$ level was found for both RBI with NC and RBI with AC as compared to RBI with RC and RBI with AC_RC_SC. Similarly, for the tumors blurred out by simulated respiration (frame av), statistical significance at the $P < 0.05$ level was found for both RBI with NC and RBI with AC as compared to RBI with RC and RBI with AC_RC_SC. Additionally, for the tumors blurred out by simulated respiration (frame av), statistical significance at the $P < 0.05$ level was found between RBI with RC as compared to RBI with AC_RC_SC.

Three different contrast levels were used in the final human-observer LROC studies to determine the impact of motion on detection. The lesion contrasts were 6.5, 7.5, and 9 times that of the scaled background. Therefore when added to the background, the actual contrast ratios were 7.5:1, 8.5:1, and 10:1. The human-observer LROC results indicating the impact of contrast on detection for the tumors blurred out by simulated respiration (frame av) are shown in table 4.

The results shown in table 4 indicate that RBI with RC significantly improves detection while RBI with AC_RC_SC provides the best results particularly at lower levels of contrast.

The human-observer LROC results indicating the impact of lesion location on detection for the tumors blurred out by simulated respiration (frame av) are shown in table 5.

The results shown in table 5 indicate that detection of tumors in the upper third of the lung is difficult although there is relatively little motion in the apex. The variation of the areas under the LROC curve for each of the four reconstruction strategies demonstrates the influence of regional differences within the lung on lesion detection. Additionally, RBI with AC_RC_SC provides the best detection for all tumor locations. Although the data are not shown, the exact same trends were found in the ideal case of stationary tumors (frame 1).

IV. Conclusions

Simulated respiratory motion adversely affects tumor detection in all four of the reconstruction strategies that were part of this investigation. The magnitude of this effect is greatest for NC and RC, and least for AC_RC_SC. The combination of AC_RC_SC has been shown to do the most in reducing the impact of respiratory motion on the detection accuracy of SPN. At low levels of tumor contrast, RBI with AC_RC_SC results in the best detection, while RBI with RC also confers a significant improvement. There are regional differences in tumor detection both for the tumors blurred out by simulated respiration (frame av) and for the stationary tumors

at end-expiration (frame 1). The upper third of the lung is the region where detection of SPN was shown to be the worst, even though lesions in the apex are associated with little respiratory motion. The results presented in this investigation will be used in our further work that is designed to evaluate several different approaches aimed in reducing the impact of respiratory motion on the detection of solitary pulmonary nodules with radionuclide SPECT tumor imaging with NeoTect.

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Fig. 1.

Number of Correct Localizations for 32 Lesions plotted as a function of the Radius in Pixels from Center of Actual Lesion. The top two curves correspond to a contrast of 11.5 for RBI with AC and RBI with RC. The middle two curves correspond to a contrast of 9 for RBI with AC and RBI with RC. The lower two curves correspond to a contrast of 6.5 for RBI with AC and RBI with RC. All six curves reach an inflection point at 8.5 pixels.

Fig. 2.

Sample Images from Final Human-observer LROC Studies. The upper two images correspond to a stationary tumor (frame 1) for the with noise case (left) and without noise case (right). The lower two images correspond to the same tumor blurred out by simulated respiration (frame av) for the with noise case (left) and without noise case (right). The arrow indicates the location of the tumor. The lesion can be identified without much difficulty except in the case of simulated respiration with noise.

Table 1

LROC Results of Lesion Contrast. Two observers participated in a preliminary LROC study and viewed sets of images of different contrasts. Four different contrasts were selected for two different study sets (RBI with AC and RBI with RC). The results indicate that at contrasts of 6.5 and 9 times that of the scaled background, observer performance was satisfactory.

	Area Under LROC Curve			
	AC Contrast 6.5	AC Contrast 9	RC Contrast 6.5	RC Contrast 9
Observer 1	0.62	0.81	0.57	0.88
Observer 2	0.60	0.83	0.69	0.95

Table 2

LROC Results for Reconstruction Parameter Optimization. The area under the LROC curve ranged from 0.80 for RBI with AC to 0.90 for RBI with AC_RC_SC. The optimal value of σ was 1.0 for each reconstruction strategy. The optimal number of iterations was two for RBI with NC and for RBI with AC. The optimal number of iterations was four for RBI with RC and for RBI with AC_RC_SC.

Maximum Area Under LROC Curve			
NC	AC	RC	AC_RC_SC
0.83	0.80	0.89	0.90
$\sigma = 1.0$	$\sigma = 1.0$	$\sigma = 1.0$	$\sigma = 1.0$
2 Iterations	2 Iterations	4 Iterations	4 Iterations

Table 3

LROC Results Indicating Impact of Motion on Detection. The areas under the LROC curve indicate that simulated respiratory motion adversely affects tumor detection in all four of the reconstruction strategies and that the magnitude of this effect is dependent on the particular strategy.

NC	Area Under LROC Curve		
	AC	RC	AC_RC_SC
Frame 1	0.60 ± 0.03	0.61 ± 0.08	0.75 ± 0.02
Frame av	0.47 ± 0.04	0.50 ± 0.07	0.62 ± 0.02
			0.80 ± 0.04
			0.74 ± 0.06

Table 4

LROC Results Indicating Impact of Contrast on Detection for Frame av. The areas under the LROC curve indicate that RBI with RC significantly improves detection. However, at lower contrast levels RBI with AC_RC_SC provides the best results.

	NC	Area Under LROC Curve		
		AC	RC	AC_RC_SC
Contrast 6.5	0.32 ± 0.01	0.30 ± 0.09	0.48 ± 0.05	0.62 ± 0.06
Contrast 7.5	0.45 ± 0.05	0.57 ± 0.07	0.59 ± 0.04	0.81 ± 0.06
Contrast 9	0.64 ± 0.06	0.64 ± 0.07	0.79 ± 0.03	0.79 ± 0.06

Table 5

LROC Results Indicating Impact of Lesion Location on Detection for Frame av. The areas under the LROC curve indicate that detection of tumors in the apex where little motion occurs is difficult. The influence of anatomic location of lesions on detection is evident for each reconstruction strategy. For all tumor locations, RBI with AC_RC_SC provides the best results.

	NC	Area Under LROC Curve		
		AC	RC	AC_RC_SC
Upper third	0.41 ± 0.06	0.40 ± 0.08	0.50 ± 0.03	0.64 ± 0.07
Middle third	0.57 ± 0.05	0.50 ± 0.11	0.77 ± 0.06	0.85 ± 0.07
Lower third	0.43 ± 0.10	0.61 ± 0.04	0.60 ± 0.08	0.75 ± 0.07