

Effect of respiratory gating on reducing lung motion artifacts in PET imaging of lung cancer

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Positron emission tomography (PET) has shown an increase in both sensitivity and specificity over computed tomography (CT) in lung cancer. However, motion artifacts in the ^{18}F fluorodeoxyglucose (FDG) PET images caused by respiration persists to be an important factor in degrading PET image quality and quantification. Motion artifacts lead to two major effects: First, it affects the accuracy of quantitation, producing a reduction of the measured standard uptake value (SUV). Second, the apparent lesion volume is overestimated. Both impact upon the usage of PET images for radiation treatment planning. The first affects the visibility, or contrast, of the lesion. The second results in an increase in the planning target volume, and consequently a greater radiation dose to the normal tissues. One way to compensate for this effect is by applying a multiple-frame capture technique. The PET data are then acquired in synchronization with the respiratory motion. Reduction in smearing due to gating was investigated in both phantoms and patient studies. Phantom studies showed a dependence of the reduction in smearing on the lesion size, the motion amplitude, and the number of bins used for data acquisition. These studies also showed an improvement in the target-to-background ratio, and a more accurate measurement of the SUV. When applied to one patient, respiratory gating showed a 28% reduction in the total lesion volume, and a 56.5% increase in the SUV. This study was conducted as a proof of principle that a gating technique can effectively reduce motion artifacts in PET image acquisition. © 2002 American Association of Physicists in Medicine. [DOI: 10.1118/1.1448824]

Key words: positron emission tomography, gated-PET, respiration, standard uptake value (SUV), planning target volume (PTV), ^{18}F -Fluorodeoxy-glucose (FDG)

I. INTRODUCTION

Computed tomography (CT) is the most common imaging technique for providing anatomical information on the size and location of tumors in the body. However, for lung cancer, ^{18}F fluorodeoxyglucose positron emission tomography (FDG-PET) has been proved to have a higher sensitivity (89% compared to 57% in CT).¹ Because of the long (50 min) duration of the whole body PET scans, respiratory motion can be a major challenge for accurate localization and quantification of PET-FDG images. Respiration causes the lesion to be smeared and the image to be blurred. Smearing may reduce image quality, quantification of FDG uptake, target-to-background (T/B) (contrast), ability to define the correct lesion size and the standard uptake value [SUV (g/ml)]. The SUV is defined as the tissue concentration of FDG

in the structure encompassed by the ROI (KBq/m) divided by the activity injected per gram body weight (KBq/g).² The SUV is the most clinically utilized quantitative parameter of FDG accumulation. SUV is a frequently used parameter to stratify lesions as malignant or benign, to stage disease, and monitor their response to treatment.³⁻⁵ Studies showed that the SUV of FDG was significantly higher in recurrent tumors than in noncancerous lesions.⁶ A SUV cutoff threshold, combined with other parameters like the lesion site and shape, may indicate whether the lesion is benign or malignant.⁷ Reports showed a SUV cutoff threshold ranging from 2.5 g/ml⁶ to 5.0 g/ml.⁸ This variability in defining this threshold is due to the image reconstruction algorithm.⁹ Most of the tumor SUV data available in the literature are reported using the filtered back projection (FBP) algorithm.⁹ However, with an

iterative reconstruction segmented attenuation correction (IRSAC) algorithm, which showed an improvement in the image quality compared to the FBP one,¹⁰ higher SUV cutoff thresholds were reported.⁹

Motion produced image blurring degrades the quality and reduces the qualitative accuracy of PET, resulting in the misidentification of the lesions. Also, distortion of the lesion shape and volume can potentially compromise the efficacy of PET in radiotherapy planning. Motion artifacts can be reduced by gating PET images in correlation with respiration. In this study, data were acquired in multiple time bins synchronized with the respiratory cycle. In each bin, the lesion is at a different characteristic position within the breathing cycle. Respiratory gating techniques have been utilized in CT, MRI, and radiotherapy to reduce the effects of breathing motion.^{11,12} In radiotherapy, studies have shown that gating improves target localization and permits reduction of tumor margins with a consequent reduction in the volume of normal tissue irradiated. This may allow further dose escalation to the target volume, and more normal tissue sparing.^{11–13}

In this paper, we address the problems caused by respiratory motion, in FDG-PET images, based on a group of phantom studies. Respiration gated-PET technique was evaluated by the amount of reduction in the smearing effect as a function of gate width, lesion size, and motion amplitude. Smearing is quantified by the ratio of gated-to-nongated measurements performed on the lesion. The gating technique is then appraised on one patient. All results in this paper are reported based on the IRSAC image reconstruction algorithm, using the same reconstruction parameters used by Ramos *et al.*⁹

II. METHODS AND MATERIALS

(1) *PET scanner*: Data referenced in this paper were acquired using the GE advance PET camera (GE Medical Systems, Waukesha, WI), a whole body scanner with a transaxial field of view of 55 cm with 14.75 cm along the axial direction. The scanner contains retractable septa and can be used in two dimensions (2D) (septal extended) for high-resolution imaging or in three-dimensional (septal retracted) for higher sensitivity (1200 kcps/mCi/cc). The axial and the transaxial image resolutions are, respectively, 4.0 and 3.8 mm full width at half-maximum at the center of the gantry.¹⁴ All data presented in this study were acquired in 2D mode.

(2) *Gating system*: The Varian Real-Time Position Management (RPM) Respiratory Gating System (Varian Medical Systems, Palo Alto, CA) was designed for radiotherapy gating. It is designed to allow irradiation of moving lesions only during time intervals predefined by the user. The RPM system tracks the motion of passive reflective markers, 5 mm in diameter each, and 3 cm apart in the vertical direction. By simultaneous tracking of the two markers, the system maintains calibration of the vertical component of the motion. The markers are rigidly mounted on a lightweight plastic block, set on the patient's abdomen. The motion of the marker block is monitored by an infrared video camera, mounted on the end of the patient couch (Fig. 1), and interfaced to a PC with vendor-supplies software. An illuminator ring surround-

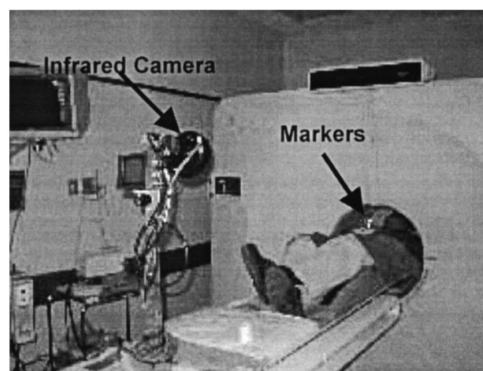


FIG. 1. Patient positioned in the Alpha Cradle for gated-PET scan. The marker block (the bright spot) is set on the patient's abdomen. The infrared video camera is also mounted to the PET table.

ing the camera floods the room with infrared light. The camera detects reflections from the marker. The detected signal is fed into the PC, and processed. A trace of the vertical marker motion (corresponding to the motion of the patient's chest) is shown on the PC monitor. Figure 2 shows an example of the motion trace provided by the RPM for a breathing phantom. The user sets a trigger at a specified amplitude or phase within the breathing wave form.

(3) *Data acquisition*: The output of the RPM system, in addition to the trace of the patient's chest motion, is a signal to a relay switch, which will be turned into the "ON" mode for 0.5 s, when the respiratory cycle crosses the lower threshold of the gate. The PET scanner is designed to operate with cardiac gating, using heart beats to trigger the gating cycle. We have built a trigger circuit to provide the same trigger signal used for cardiac gating, but synchronized with respiration instead. This trigger circuit has as input, the output of the RPM relay, and as output a -5 VDC, which is switched into a $+5$ VDC only while the relay is in the "ON" mode. This trigger signal is used to initiate the gating cycle of the PET scanner. This corresponds to the position of the pulse, in each breathing cycle in Fig. 2. The period of the respiratory motion is then divided into discrete bins, into which PET data are acquired. The number of time bins and the duration of each bin is set prior to the scan on the PET console.

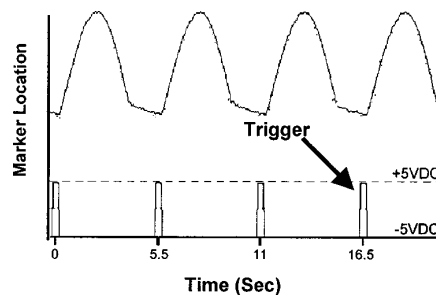


FIG. 2. Trace of a breathing phantom. Phase gating is illustrated, the pulses correspond to the trigger position within the breathing cycle. The left and right edges of the pulse are predefined by the user.

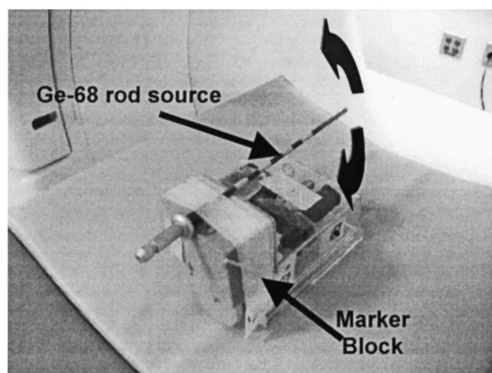


FIG. 3. The Ge-68 rod source, inside the PET gantry, mounted to the breathing phantom, with one end pivoted, while the other end is free to oscillate vertically. The motion direction is represented by the two arrows.

Consequently, multiple PET images are reconstructed, each corresponding to a time bin within the respiratory cycle. Since the time interval within each bin is smaller than the period of the breathing cycle, one would expect respiratory motion artifacts and image smearing to be reduced.

(4) *Phantoms*: Phantom measurements were performed using four cylindrical position-emitting sources of 4.7, 10, 15, and 26 mm in diameter, respectively, with an activity concentration of $1 \mu\text{Ci/cc}$, which is comparable to the average activity concentration observed within lung lesions. A breathing phantom, able to simulate human respiratory motion, was used to set each of the four radioactive phantoms in oscillatory motion. Each of the radiation sources was pivoted at one end, while the other end oscillated in the vertical plane, along the PET gantry axis (see Fig. 3). The maximum amplitude was approximately 5.2 cm in the vertical plane with a period of 5 s.

To investigate the smearing effects as a function of motion amplitude, transaxial PET images were reconstructed along the rod source from the pivot point to the end of maximum amplitude, for the Ge-68 rod source and for each cylinder. In all cases, a 3 min transmission scan (for attenuation correction purpose), a 3 min nongated emission scan, and a 10 min gated emission scan, with the trigger set at the beginning of the stationary states in the phantom oscillation.

(5) *Patient acquisition*: The gating technique was applied to one female patient with non-small-cell lung cancer. The patient was scanned using radiation therapy immobilization fixtures, an Alpha Cradle (Alpha Cradle Molds, Akron, OH) that was produced at the time of CT simulation, 40 min postinjection with $370\text{MBq } ^{18}\text{F-FDG}$. The patient first received a nongated PET scan according to our routine FDG scan procedure. This consisted of a five-bed position (14.5 cm/bed-position) scan from the bottom of the ear to the pelvis. The total scan time took 35 min (7 min/bed-position), which includes 4 min of emission and 3 min of transmission scans. The partial body data set was reconstructed to determine the location of the lesion. The couch was then moved so as to position the lesion at the center of the field of view. A gated PET scan was then acquired, using the RPM system

to track the motion of a gating block on the patient's chest. The total acquisition time was 16 min, consisting of a 10 min gated emission scan, a 3 min nongated emission scan for evaluation purpose, and a 3 min transmission scan.

The RPM system uses a training set taken just before the initiation of the PET scan to determine the duration and the regularity of the breathing cycle. Irregularities in the breathing cycle fall into categories. First, the bin one can fall out of phase (or amplitude in the amplitude threshold case). In this case, no trigger will be set by the RPM to signal reinitialization of the breathing cycle, and consequently PET data will not be acquired for that breath in the breathing cycle. The second category is when the period of the breathing cycle increases or decreases due to irregularity in the patient breathing cycle. With the breathing rate, PET data will be acquired just for a period of time corresponding to preset cycle time ($n \times \text{duration of the time bin}$) and bin one reinitialized upon detection of the trigger. When the breathing rate decreases, PET data will be acquired in the preset cycle time and wait until a new trigger is detected before the first bin is initialized. The consequence of binning PET data in this way is that bin one contains the most synchronous data, with progressive dephasing of the breath cycle occurring with increasing bin number.

III. ANALYSIS

The acquired PET data were reconstructed into 128×128 matrices using the IRSAC algorithm, with segmented attenuation correction, applying corrections for scatter and randoms using the manufacturer software.

The gated-PET images were evaluate relative to the nongated PET images, for the four phantoms. Since the cylindrical sources oscillate orthogonal to the axis of the gantry, each transaxial slice in the reconstructed image corresponds to a cross section subject to a different vibrational amplitude. The reduction in the smearing effect due to gating was evaluated through a parameter, the "area reduction factor" (ARF), which we defined as

$$\text{ARF} = \frac{[A_G]_{\text{ap}}}{[A_{\text{NG}}]_{\text{ap}}}, \quad (1)$$

where $[A_G]_{\text{ap}}$ and $[A_{\text{NG}}]_{\text{ap}}$ are the apparent object (lesion) areas in both the gated and nongated modes, respectively. The ARF was computed for each bin and then averaged over the number of bins.

To determine the areas, we used the procedure recommended by Erdi *et al.*¹⁵ The upper gray scale threshold was set to the maximum activity concentration value within the lesion, while the lower threshold was set to a level of 42% of the value of the upper one.¹⁵ The areas were then measured as the number of pixels with activity concentration greater than the value set to the lower threshold.

Different numbers of time bins were evaluated to help determine the optimal number that minimizes the motion within the corresponding interval, while maintaining an acceptable number of counts and noise level in the images. Applying this procedure to the four FDG phantoms allowed

us to evaluate the technique for different lesion sizes. Next, the effect of gating on recovering the SUV was evaluated by comparison between the measured SUV in the gated and the nongated PET images.

In the clinical study, the lesion images were evaluated to assess the reduction of the smearing effect in the patient, as compared to the nongated PET images. Comparison between the gated and nongated PET images for all the transaxial images through the patient's lesion was performed, and then the reduction in the apparent lesion volume due to gating was evaluated. The lesion volume was determined as the product of the slice thickness, (4.25 mm), with the sum of the lesion cross sections, determined by the thresholding method,¹⁵ in all transaxial slices including lesion. Finally, the effect of gating on the SUV was investigated.

IV. RESULTS

Figure 4 shows the effect of motion on the activity distribution, in two extreme transaxial slices. The first slice [4(a)] was considered near the pivot point, where the amplitude is negligible or smaller than the PET resolution. The second slice [4(b)] corresponds to a motion amplitude of approximately 4.7 cm. Results are reported from the 4.7 mm in diameter source study. For a stationary point source, an approximately Gaussian distribution of the activity concentration within the simulated lesion was observed, as expected [see Fig. 4(a)]. However, if the source is set in motion, the activity concentration under the Gaussian distribution will be redistributed over the motion range [see Fig. 4(b)]. The number of counts, thus the activity concentration, at each position is a function of the time spent at each position. The two peaks at the extremes of the distribution correspond then to the maxima and the minima of the oscillation. This motion-generated distribution of activity concentration gives rise to four major effects. First, the overall shape of the activity concentration distribution changes. Second, the source size is overestimated. Third, as the number of counts acquired during the same scan time is now spread over a larger region, a drop in the maximum activity concentration is observed, leading to a reduction in the T/B ratio. Finally, as a consequence of the previous two, there is a reduction in the SUV.

Four, five, and ten-bin-gated emission scans were performed, each for the same 10 min duration. In each case, n images were reconstructed for each of the 35 transaxial slices, where n is the number of bins. Each of the n images corresponds to a different position of the oscillating source within the motion range. Figure 5 shows an example of one nongated transaxial image (a), and the corresponding four images acquired in a four-bin acquisition mode. Each of the four images corresponds to one quarter of the oscillation period, triggered at the zero phase point by the RPM, for the same transaxial slice shown in Fig. 5(a). The amount of smearing within each time bin varies according to the amount of motion swept out within each time segment. The process of image summation among the images corresponding to the four time bins would result in the image shown in Fig. 5(a). The ARF was calculated only for the slices con-

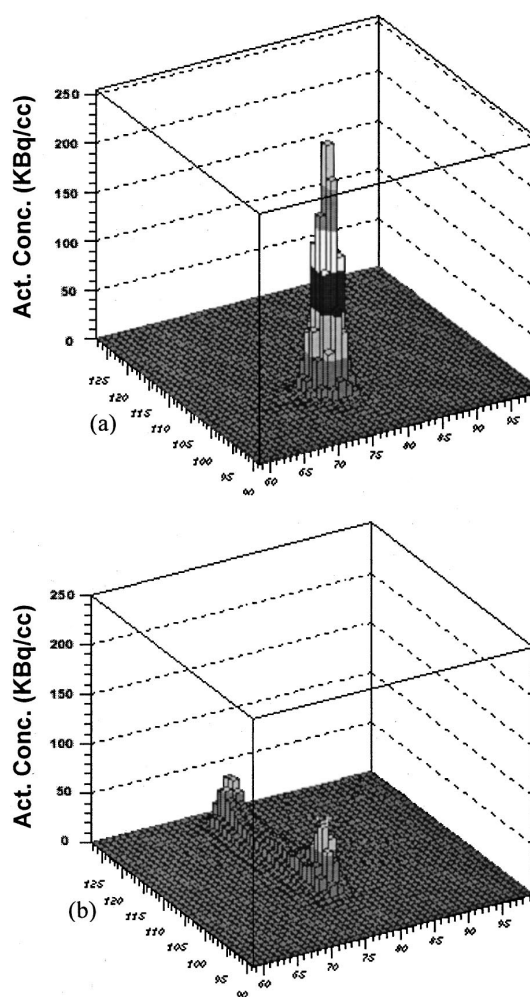


FIG. 4. (a) Apparent activity concentration for a stationary point source shows a Gaussian distribution, as expected. (b) The activity concentration of the same point source is stretched due to the motion. The two peaks correspond to the end points of the oscillating motion. The x and y axes refer to the pixel number within the transaxial image (128×128 matrix).

taining the source within the field of view (19 of 35 slices). The remaining 16 slices covered the support structure of the phantom, and they were excluded from the analysis. The reconstructed slices correspond to different vertical motion amplitudes along the oscillating source. Figure 6 shows the reduction in the smearing effect for the four-bin study as a function of the amplitude of vertical displacement of the phantom within the slice. Figure 6 also shows a dependence of the reduction in the smearing effect as a function of the motion amplitude, approaching an asymptote at large amplitudes. Results from the three studies (four-, five-, and ten-bin acquisition) showed an expected reduction in smearing with increasing number of bins.

For clinical application, the number of bins must compensate for irregularity in the human breathing cycle as well as provide an acceptable S/N ratio, maintain an acceptable scan

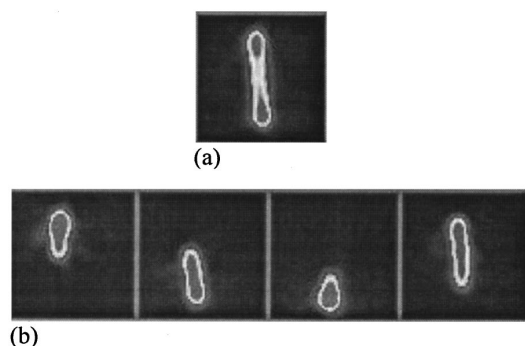


FIG. 5. (a) Apparent image of an oscillating point source. (b) Four images of the same oscillating point source corresponding to the four bins. The reduction in the smearing effect is a bin dependent.

time as compared to the nongated scan time (3 min per FOV), in order to minimize the additional motion due to patient discomfort. In this study, we measured for each slice the area of the simulated lesion in each time bin, and then calculated the standard deviation of this distribution in each slice. This measurement showed a reduction in the standard deviation from 9.84% for four bins, to 7.24% for ten bins.

The effect of gating on the lesion size was determined using the ratio of the gated image size averaged over all bins to the nongated one, calculated for each of the transaxial images included in the FOV. A plot of the ARF versus the slice number, thus motion amplitude, for the three different tubes showed a reduction in the smearing effect as a function of the lesion size.

A study of the maximum activity concentration (MAC) was performed using a ten-bin gating technique. Figure 7 shows the MAC, which corresponds to the SUV per unit lesion mass, per unit body mass, and per unit injected activity. The MAC was measured within the simulated lesions images for all 35 transaxial slices, for the static, oscillating (nongated), and oscillating (gated-first bin) phases. Figure 7 shows that motion reduces the MAC values compared to the stationary case, and that this reduction in the MAC is a function of the motion amplitude. However, gating allows recovery of the lost information.

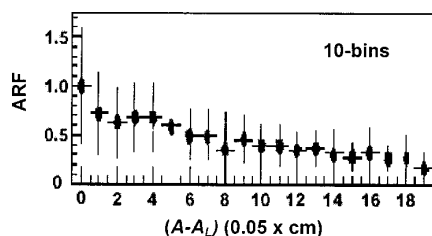


FIG. 6. ARF vs amplitude, for the Ge-68 rod source, for ten-bin gating. A_L is the actual lesion size. The reduction in the smearing effect shows a dependence on the number of bins. The data show an improvement in the reduction of the motion effect (decrease in the ARF values) as the motion amplitude increases, for a defined number of bins. The data also show an asymptotic behavior at large motion amplitudes. This is a result of the choice of the phantom and its motion.

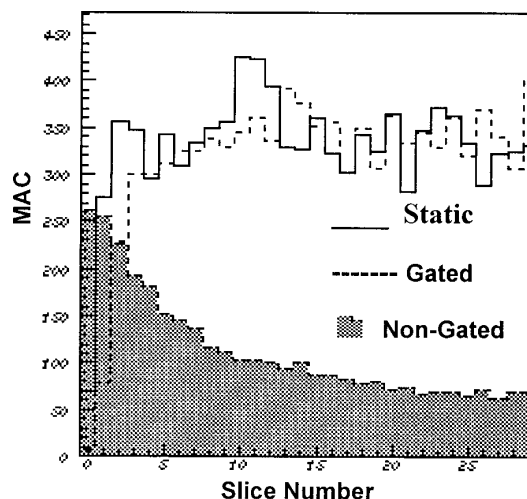


FIG. 7. MAC vs slice number (amplitude). Motion yields a reduction in the SUV in function of motion amplitude. However, gating (ten-bin) enables recovery of the SUV.

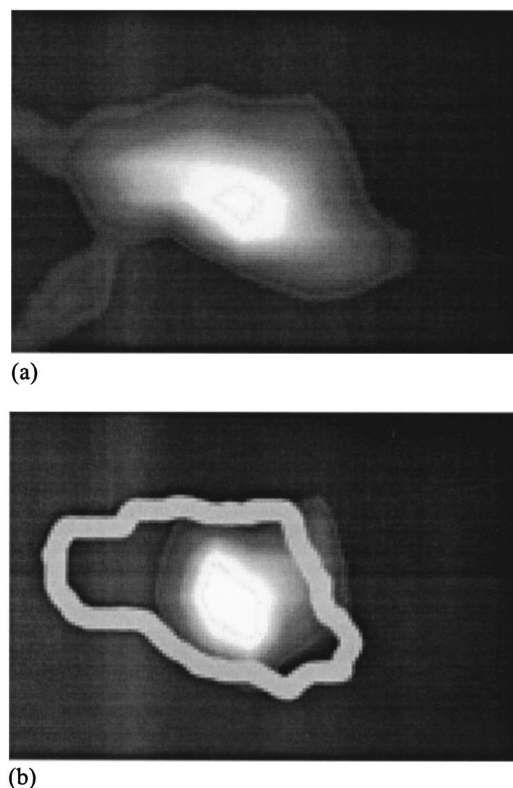


FIG. 8. Transaxial PET image through the patient's lesion. The lesion is shown in both the nongated mode (a) and gated mode (b). The contour refers to the nongated lesion size and position. This corresponds to the first slice in Fig. 7.

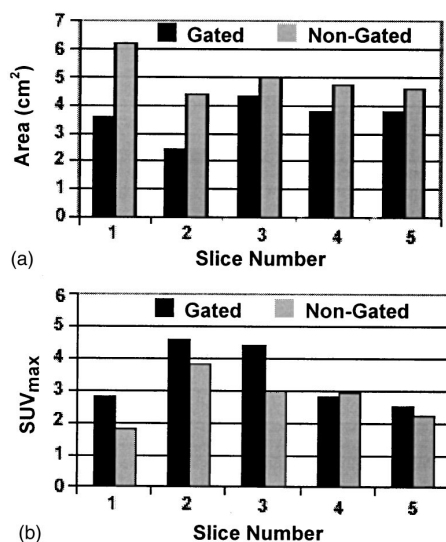


FIG. 9. Area (a) and SUV_{max} (b) for the transaxial slices through the patient's lesion, measured in the gated and nongated modes.

Finally, as a proof of principle, the ten-bin gating technique was applied to a 69-year-old nonsmall lung cancer patient. The FDG-PET scan showed an increased radiotracer uptake in the left hilar region, with a maximum and average SUV (from the nongated PET scan) of 2.945 and 2.011 g/ml, respectively. Comparison between the gated and the nongated PET images for this clinical study showed a reduction in the measured lesion volume of 28%. Figure 8 shows an example of the gating effect, for one transaxial slice through the patient's lesion for which the ARF is 58%. The gated study for this patient confirmed that the SUV increases due to the suppression of lesion motion. Figure 9 shows a comparison between the gated and nongated modes of the apparent lesion areas (a), and the maximum SUV (b), for the various transaxial slices through the patient's lesion. The maximum SUV, in the gated mode, has increased from 2.945 g/ml to a value of 4.609 g/ml, representing a 56.5% increase.

V. CONCLUSION

We have shown that respiratory gating can reduce the degrading effect of breathing motion on PET images. It allows a more complete recovery of the true counts within the lesion and a more accurate estimation of the lesion volume. Phantom studies showed a dependence of the reduction in the smearing effect as a function of the lesion size, motion amplitude, and bin size. This yielded an increase in the signal-to-noise ratio, as well as to a recovery of the SUV values. Application to a patient study demonstrated that the technique was successful in reducing the smearing effect, and correcting the SUV. This is very critical in terms of

lesion investigation, especially when the SUV is close to the threshold, which may affect clinical judgment.

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