Utility and Reproducibility of Semiquantitative Analysis of Sestamibi Breast Images

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Technetium-99m-sestamibi scintimammography has been shown to be a useful diagnostic test in the detection of breast cancer. The purpose of this study was two-fold to: (a) evaluate semiquantitative indices of tracer uptake in lesions and determine if they are helpful in distinguishing benign from malignant breast lesions; and (b) test the reproducibility of these measures of sestamibi uptake in breast images.
Methods: Prone lateral planar imaging was performed on 27 patients after intravenous injection of 20–30 mCi ^{99m}Tc-sestamibi. Data were analyzed by creating three regions of interest (ROIs) over designated areas: lesion, normal breast and right chest wall. Lesion-to-normal (L:N) and lesion-to-chest wall (L:CW) ratios were calculated for each patient. Reproducibility was assessed by having two independent observers draw ROIs (interobserver) and one observer draw two independent sets of ROIs (intraobserver).
Results: L:N and L:CW ratios were significantly different for malignant versus benign lesions ($p < 0.001$ for both ratios). Intraobserver and interobserver reproducibility showed good correlation with $r = 0.98$ (L:CW ratio).
Conclusion: Semiquantitative analysis of sestamibi breast imaging results in reproducible uptake ratios that may be helpful in objectively interpreting imaging results.

Key Words: breast imaging; breast cancer; technetium-99m-sestamibi; semiquantitative ratios; regions of interest

J Nucl Med Technol 1997; 25:106–109

Technetium-99m-sestamibi scintimammography has been shown to be a useful diagnostic test in the detection of breast cancer. There are several indications in which sestamibi breast imaging may be helpful in clinical settings. Sestamibi scintimammography may provide characterization of suspicious masses as seen on mammography (*1,2*). In addition, it may help in cancer detection in women with dense or postsurgical breasts (*3,4*). With the use of planar and SPECT imaging, sestamibi may be useful in the detection of axillary nodal metastases (*5,6*). Serial studies of prone lateral sestamibi breast images may have a role in monitoring a patient's response to neo-adjuvant chemotherapy (*7,8*).

Sestamibi scintimammography has been largely qualitative to date. Semiquantitative analysis may provide physicians with additional information in the following areas: (a) classification of lesions as benign or malignant (*9*); (b) characterization of malignant lesions (*10–12*); and (c) measuring a lesion's response to neo-adjuvant chemotherapy (*7,8*). Previous studies using sestamibi have analyzed data and generated target-to-background count ratios or activity ratios using tumor-to-normal breast, tumor-to-positive axillary nodes, normal breast-to-lung and axillary nodes-to-lung (*5,10,13*). Piccolo et al. (*14*) have studied semiquantitative analysis of ^{99m}Tc-MDP uptake in breast lesions, using the normal breast to define the background region and generating time-activity curves. In this study, we have quantitated images with standard ROIs using two indices: the lesion-to-normal breast ratio and lesion-to-right chest wall ratio. We investigated semiquantitative tracer uptake ratios as an objective way to help distinguish benign from malignant lesions. We have also evaluated the reproducibility of these ratios on sestamibi breast images.

MATERIALS AND METHODS

Imaging

A total of 27 patients (26 women, 1 man; age range 32–82 yr; mean age 55.5 yr) were included in this study. Patients presented with 25 malignant lesions and eight benign lesions. A subset of 22 patients had pathological follow-up of their lesions with 13 surgical biopsies, eight core biopsies and one fine-needle aspiration. In this subset group, lesion size (in cm) was available for 16 patients with 14 malignant lesions and three benign lesions.

Prone lateral imaging was performed as described by Diggles et al. (*15*). Twenty to 30 mCi (740–1110 MBq) of ^{99m}Tc-sestamibi were administered intravenously in the arm contralateral to the side of the lesion, or in a foot vein if disease was suspected in both breasts. All injections were followed with a 20- to 30-cc saline flush. Images were acquired with a single-head GE 400 AC or XCT large field-of-view camera. Image acquisition began 5–10 min postinjection. An acrylic tabletop overlay with bilateral breast cut-outs was used to

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FIGURE 1. ROI placement on prone sestamibi scintimammogram.

obtain prone lateral views. The following static images were acquired for 10 min per view: (*1*) bilateral prone laterals, imaging the lesion side first due to potential tracer washout, (*2*) anterior supine, with arms above the head to view the axilla, and (*3*) posterior obliques, if necessary, to provide better separation for lesions close to the chest wall. Nipple marker images for 1 min per view were acquired on both prone laterals. Any surgical scars were also marked at this time. Using a high-resolution collimator, images were acquired in a 256 × 256 matrix with an area covering 400 mm in diameter. The photopeak was centered over 140 keV with a 13% symmetric energy window.

Image Analysis

Three ROIs were created on the prone lateral images: (a) the region encompassing the lesion pixel with maximum counts (hottest portion of lesion); (b) the normal breast tissue on the contralateral side; and (c) the right chest wall. The right chest wall was chosen due to potential interference from cardiac uptake on the left. The ROI box size in pixels (0.6 mm/pixel) was standardized for each area as follows: (a) lesion: 6 × 6-pixel region containing the maximum pixel; (b) normal breast tissue: 10 × 10-pixel region; and (c) right chest wall: 6 × 15-pixel region. Some patients, especially younger patients with dense breasts, tended to have more diffuse uptake in the normal contralateral breast. Therefore, it was important to define a region in the normal breast with relatively homogeneous, normal-appearing tissue. If a patient had a prior mastectomy, the normal breast region was drawn on the same breast as the lesion region, again ensuring the most homogeneous area was chosen for the normal breast region. ROI placement of the right chest-wall region was midway between the axilla and the liver in the cranial-caudal direction on the edge of the chest wall, as seen as the boundary between low-level uptake in superficial tissue and more intense uptake in the chest wall musculature (Fig. 1). Exceptions were made if there were obvious chest wall abnormalities. Two ratios were then calculated using the average counts for each region: lesion-to-normal breast (L:N) and lesion-to-right chest wall (L:CW).

Intraobserver and interobserver reproducibility were assessed in this study. Intraobserver reproducibility was tested by having one observer drawing two independent sets of ROIs. These regions were drawn at two separate sessions, with patient order varied. Interobserver reproducibility was tested by having two observers creating one set of ROIs each, with observers blinded to each other's results.

RESULTS

In the evaluation of semiquantitative indices, there was a significant difference for benign versus malignant lesions for both the lesion-to-normal breast (L:N) and lesion-to-right chest wall (L:CW) ratios, $p < 0.001$ for both ratios (Fig. 2).

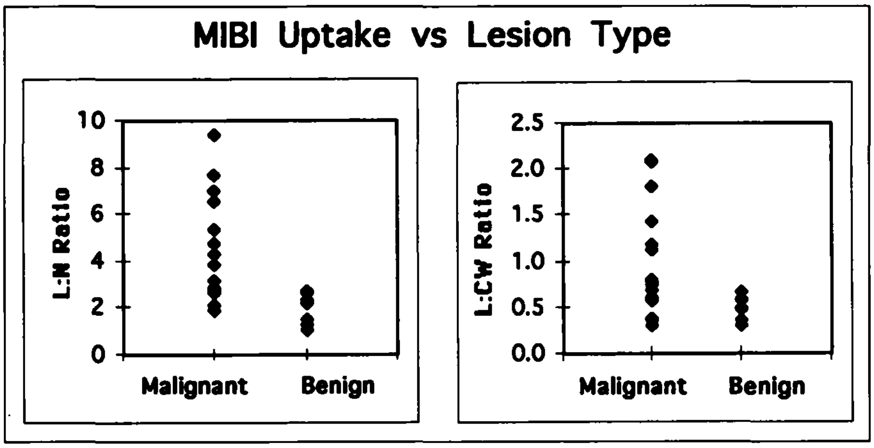

FIGURE 2. Semiquantitative results for L:N and L:CW ratios showing separation between malignant and benign lesions.

TABLE 1
Sestamibi Uptake Ratio Results

	L:CW		L:N	
	Malignant	**Benign**	**Malignant**	**Benign**
Mean	0.94	0.5	4.2	1.9
s.d.	0.59	0.13	2.3	0.7
Range	0.30–2.10	0.30–0.67	1.9–9.4	1.0–2.7

L:CW = lesion-to-chest wall; L:N = lesion-to-normal.

TABLE 2
Reproducibility Results

	Intraobserver		Interobserver	
	ROI Set 1 versus Set 2		Observer 1 versus 2	
	L:N	L:CW	L:N	L:CW
Correl	0.98	0.98	0.94	0.98
Slope	1.0	0.97	0.84	1.15
Intercept	0.1	0.05	0.32	−0.07
s.e.e./Mean	11%	12%	18%	13%

L:N: lesion-to-normal; L:CW = lesion-to-chest wall.

There was a separation between malignant and benign lesions, with some overlap occurring between small, low-grade malignancies and benign lesions (Table 1). Both uptake ratios correlated with the size of the lesion (Fig. 3). The average lesion size (greatest diameter) was 3.5 cm with a maximum of 7.0 cm and a minimum of 0.3 cm.

Table 2 summarizes intraobserver and interobserver reproducibility results. Intraobserver and interobserver variability are plotted for L:N and L:CW ratios in Figure 4. Both indices showed excellent reproducibility with inter- and intraobserver correlation coefficients of 0.94 or better. The L:CW ratio was less variable than the L:N ratio for both intraobserver and interobserver reproducibility. The difference between the two ratios is thought to be due to diffuse uptake, which is at times visualized in the normal contralateral breast, this may result in variability in the L:N ratio.

DISCUSSION

Quantification of ^{99m}Tc-sestamibi scintimammography is simple to perform and reproducible results can be obtained. Semiquantitative measures of tracer uptake reflect lesion characteristics and, therefore, help distinguish benign from malignant lesions and correlate with lesion size. Our results suggest the uptake ratios are dependent on the size of the lesion, which is expected for simple indices of planar images. Our results also suggest that the L:CW ratio may be slightly better than the L:N ratio in reproducibility and the separation of benign and malignant lesions. This result is likely due to the variability of low-level uptake seen in the normal breast. The level of uptake may be dependent on where a woman is in her menstrual cycle and we have not accounted for this variable (*16,17*). Our findings suggest that uptake in the chest wall viewed in the prone dependent position may have less variability. Possible exceptions may exist under certain clinical conditions. For example, we have experience with patients on a chemotherapeutic regimen containing a marrow-stimulating drug (i.e., GCSF) and we saw increased tracer uptake in these patients' sternums and/or ribs. In this class of patients, the L:N ratio may be preferable.

Besides helping to distinguish benign from malignant lesions, there are several potential applications of semiquantitative analysis of sestamibi breast images. We have used this analysis by measuring the response of breast cancer to neo-adjuvant chemotherapy using serial studies (*7*). We have also investigated sestamibi uptake ratios correlation with pathologic features of malignant lesions (*11,12*).

CONCLUSION

Semiquantitative analysis of ^{99m}Tc-sestamibi breast images results in reproducible uptake ratios, which may be helpful in objectively interpreting imaging results. These indices may also provide additional information in evaluating a lesion's response to neo-adjuvant chemotherapy.

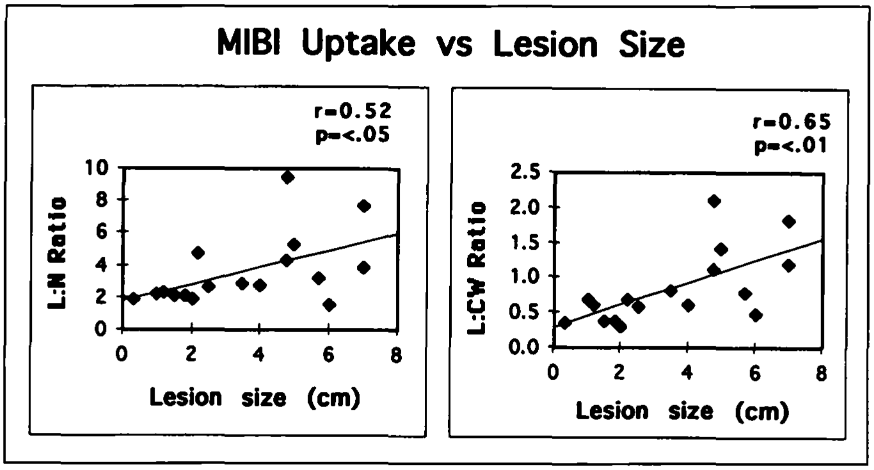

FIGURE 3. Scatter plot of sestamibi uptake ratios (L:N on left; L:CW on right) versus size of lesion.

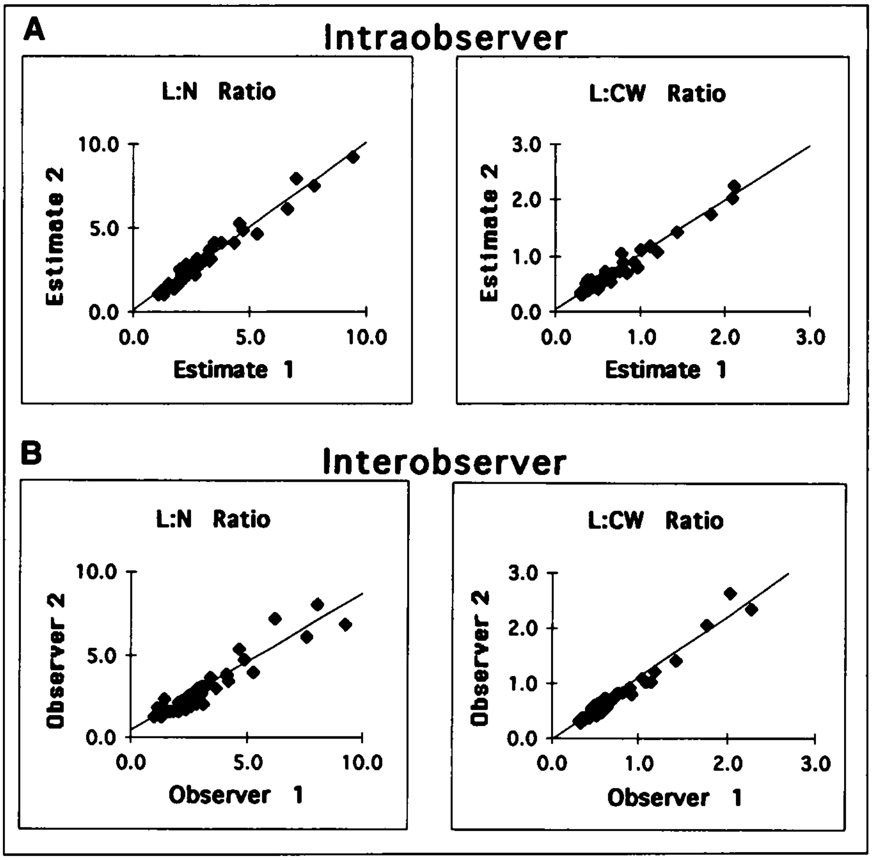

FIGURE 4. Reproducibility results of L:N and L:CW uptake ratios showing good correlation for both (A) intraobserver and (B) interobserver.

ACKNOWLEDGMENTS

We thank the members of the University of Washington Breast Specialty Clinic for their support of this project. This work was supported in part by American Cancer Society grant number IRG-184C and NIH grant number CA72064.

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