
Factors Influencing the Uptake of ^{99m}Tc -Sestamibi in Breast Tissue on Molecular Breast Imaging

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The purpose of this study was to evaluate the impact of changes to a patient's prandial status, metabolic status (rest vs. exercise), and peripheral blood flow (via caffeine or warming) on the uptake of ^{99m}Tc -sestamibi in breast tissue. **Methods:** A total of 154 subjects participated in 1 of 4 study groups that evaluated the effects of 4 types of intervention on the uptake of ^{99m}Tc -sestamibi in breast tissue (effect of fasting, light exercise, caffeine, and peripheral warming). Molecular breast imaging was performed before and after each intervention. Count density was assessed in counts/cm²/MBq from the mediolateral oblique view in all studies. **Results:** Uptake of ^{99m}Tc -sestamibi in breast tissue increased by approximately 25% from 6.6 counts/cm²/MBq in the fed state to 8.3 counts/cm²/MBq with fasting. Peripheral warming also resulted in an approximately 20% increase in count density from 9.1 to 10.9 counts/cm²/MBq. Conversely, exercise caused a 35% drop in count density relative to the resting state. Uptake did not seem to be influenced by caffeine and did not correlate with a patient's height, weight, or breast thickness. There was only a weak correlation between breast activity and body surface area. **Conclusion:** The combined effects of fasting and warming resulted in an approximately 50% increased uptake of ^{99m}Tc -sestamibi in breast tissue relative to that observed in a reference group to whom no preparatory instructions had been given. Optimal patient preparation before administration of ^{99m}Tc -sestamibi should permit a corresponding reduction in either acquisition time or required dose of ^{99m}Tc -sestamibi.

Key Words: ^{99m}Tc -sestamibi; breast; fasting; exercise

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Nuclear medicine breast imaging techniques, including both single-photon and positron emission technologies, have been evaluated for several diagnostic indications because of their ability to detect mammographically occult disease (1–5). We have reported on the use of molecular breast imaging (MBI), performed with ^{99m}Tc -sestamibi and

a dual-head cadmium zinc telluride γ camera, for screening of women with mammographically dense breasts (6,7). In the most recent trial (7), supplemental screening with MBI in women with dense breasts improved the breast cancer detection rate from 3.2 per 1,000 with mammography alone to 12 per 1,000 with the combination of MBI and mammography ($P < 0.001$).

A key consideration in the acceptance of MBI for screening use is the need to reduce the associated radiation dose of this procedure. Early studies with nuclear breast imaging technologies, including scintimammography (8) and breast-specific γ imaging (I), used administered activities of ^{99m}Tc -sestamibi in the range of 925–1,110 MBq (25–30 mCi), which result in effective doses to the body of 6.8–8.1 mSv (9) and were considered too high for screening (10). By comparison, the effective dose from digital mammography is 0.5 mSv and that from current mammography combined with digital breast tomosynthesis is 1.2 mSv—a factor of approximately 7 times less (10,11). Our laboratory has implemented several technical improvements to MBI to allow reduced doses of ^{99m}Tc -sestamibi to be used, including use of a registered high-sensitivity collimator and widened energy acceptance window. These changes allow MBI to be performed using administered activities of ^{99m}Tc -sestamibi of approximately 300 MBq (8 mCi) (12–14), with no degradation in image quality or sensitivity of the technique for the detection of breast cancer (7).

Further, we have previously shown that ^{99m}Tc -sestamibi has a propensity to adhere to the surface of many commonly used syringes, resulting in a substantial percentage of the activity (~20%) remaining in the syringe after administration (15). In our practice, selection of the appropriate type of syringe has resulted in reduction in both the magnitude and the variability of residual ^{99m}Tc -sestamibi activity. With less residual activity and residual measurements that are more reproducible, a further reduction in the necessary dispensed activity of ^{99m}Tc -sestamibi can be achieved, resulting in administered activities of approximately 240 MBq (6.5 mCi), with an effective dose of 1.7 mSv.

Efforts to further reduce administered activities for MBI below this level have been confounded by wide interpatient and inpatient variation in the measured uptake

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of ^{99m}Tc -sestamibi in breast tissue (16). The reason for this variation in breast uptake has not been previously studied, and a better understanding of the behavior of ^{99m}Tc -sestamibi in the body may allow more optimal patient preparation and enable further dose reduction through improved uptake of ^{99m}Tc -sestamibi in breast tissue.

On injection, ^{99m}Tc -sestamibi is rapidly cleared from the bloodstream, with a half-life of 2–4 min (17). The primary organ of uptake is the liver, with approximately 20% of the administered dose accumulating in that organ when the subject is at rest (17). The proportion of uptake in breast tissue is low and significantly less than that in the myocardium, which itself accumulates only 1% of the administered dose (17). Hence, the availability for uptake in breast tissue is highly dependent on the status of blood flow to the liver, kidneys, muscle tissue, and other organs at the time of injection of the ^{99m}Tc -sestamibi. To date, there has been little or no information available on the effect of normal physiologic variations in blood flow, caused by diet, exercise, or environmental factors, on the uptake of ^{99m}Tc -sestamibi in breast tissue. Although complete standardization of a patient's physiologic status may not be feasible in a clinical setting, parameters such as prandial status can easily be controlled, as can physical activity and body temperature. Because the breast tissue takes up only a small amount of the ^{99m}Tc -sestamibi, it is likely to be sensitive to changes in a patient's physiologic status and be a barometer for how these changes may influence the biodistribution of ^{99m}Tc -sestamibi in other organs such as the parathyroid glands. This study was designed to evaluate the effects of 4 parameters that can easily be controlled in the clinical environment: fasting, exercise, caffeine, and body temperature.

Submaximal exercise is known to significantly reduce hepatic blood flow (18). An upright posture (compared with supine) is also thought to reduce hepatic blood flow (19). Conversely, after a meal, splanchnic arterial resistance decreases and hepatic blood flow increases (18). Therefore, alterations to hepatic blood flow from either exercise or fasting may have a significant effect on the availability of ^{99m}Tc -sestamibi for uptake by breast tissue.

Caffeine is known to have no effect on either hepatic or superior mesenteric blood flow (20). However, caffeine does dilate peripheral blood vessels, decreasing peripheral vascular resistance (21), and hence may cause an increase in blood flow to the breast tissue relative to that to the liver, resulting in greater accumulation of ^{99m}Tc -sestamibi in breast tissue. Dilation of the peripheral blood vessels can also be achieved through warming of the body (22). Patients waiting for breast examinations are normally required to change into light gowns and may have to wait 10–20 min before imaging, often becoming slightly chilled in the process, with a consequential reduction in peripheral blood flow. Keeping a patient warm over this period through means of a towel, robe, or heating blanket may maintain or increase peripheral blood flow.

The purpose of this study was therefore to evaluate the impact of changes to a patient's prandial status, metabolic

status (rest vs. exercise), and peripheral blood flow (via caffeine or warming) on the uptake of ^{99m}Tc -sestamibi in breast tissue.

MATERIALS AND METHODS

Overview of Study Design

This study was performed under an institutional review board-approved, Health Insurance Portability and Accountability Act-compliant research protocol, and written informed consent was obtained from all participants. Each participant was enrolled into 1 of 4 study groups that evaluated the effects of an intervention on the uptake of ^{99m}Tc -sestamibi in breast tissue: group 1—effect of fasting; group 2—effect of light exercise; group 3—effect of caffeine; and group 4—effect of peripheral warming. We used a paired study design in which MBI was performed on 2 occasions in all subjects, before and after the intervention.

All subjects were required to be nondiabetic and older than 40 y, have no current breast concerns, and have undergone mammography within the last 15 mo, with a negative result. Breast density from their last mammogram was recorded using the American College of Radiology Breast Imaging Reporting and Data System (23) and was classified as fatty replaced, scattered fibroglandular densities, heterogeneously dense, or extremely dense. All subjects were required to fast overnight before beginning study imaging. The subjects' height and weight were recorded at the time of entry into the study and used to calculate body surface area and body mass index. Subjects participating in the exercise group were required to have a body mass index of less than 25.

Study Size Estimation

On the basis of an analysis of background activity in the mediolateral oblique (MLO) views of 40 previous MBI examinations performed in our practice, we expected that the average count density in the breast would be approximately 7.7 ± 3.0 counts/cm²/MBq (mean \pm SD). We hypothesized that in groups 1 and 2, the interventions would result in a 30% change in the relative uptake of ^{99m}Tc -sestamibi in breast tissue and that the SD of the count density after intervention would be comparable to that of the initial measurement. Because each patient acted as her own control, a paired *t* test powered to 90% confidence with 25 subjects in each group would be able to demonstrate a 30% change in breast uptake with an α of at least 0.05.

For groups 3 and 4, we hypothesized that the interventions would result in a smaller change (20%) in the relative uptake of ^{99m}Tc -sestamibi in breast tissue and again that the SD of the count density after intervention would be comparable to that of the initial measurement. For these groups, a paired *t* test powered to 90% confidence indicated that 52 subjects would be required in each group to demonstrate a 20% change in breast uptake.

MBI

The MBI system comprises 2 compact cadmium zinc telluride detectors with 1.6×1.6 mm pixels (LumaGem; Gamma Medica) and is equipped with high-sensitivity registered collimators (14). An energy acceptance window of 110–154 keV was used (12,13).

Because ^{99m}Tc -sestamibi is known to adhere to plastic walls of syringes (15), the dispensed dose was increased by 10% to allow for residual dose adhering to the syringe. Hence, for all studies a dispensed dose of approximately 220 MBq (6.0 mCi) of ^{99m}Tc -sestamibi was used with the goal of an administered dose of

200 MBq (5.4 mCi). All doses were administered by intravenous injection, and residual syringe activity was measured after injection. The times of injection, imaging, and measurement of dose activity were recorded for all studies to permit accurate correction for decay of the ^{99m}Tc and computation of exact administered activities. For all MBI examinations, imaging commenced within 2–5 min of injection.

For the first MBI examination in each participant, performed before intervention, a single view was acquired in the MLO projection of the left breast. The compressed thickness of the breast in this MLO projection was recorded, such that the same breast thickness could be used for subsequent left breast MLO projections. After the appropriate intervention, a second injection of approximately 220 MBq (6.0 mCi) was administered and cranio-caudal and MLO views of both breasts were acquired. All views were acquired for 10 min per view with light compression applied to limit breast motion.

Background Correction

Because the 2 MBI examinations performed on each participant were done within the same study visit, a background correction was applied to the count density measured on the postintervention MBI examination to account for activity in the breast remaining from the first injection. For groups 1 (fasting) and 3 (caffeine), an additional MBI image was acquired immediately before the second injection of ^{99m}Tc -sestamibi and used to individually correct each subject's postintervention MBI for background activity from the first injection. For groups 2 (light exercise) and 4 (peripheral warming), it was not possible to obtain this background correction image without interfering with the planned intervention, and a different scheme was used to correct for background activity as described below in "Count Density Analysis."

Study Interventions

Group 1—Effect of Fasting. In 25 subjects, MBI was first performed after an overnight or 6-h fast. They then consumed 237 mL (8 fluid ounces) of Ensure (350 kilocalories). At 30 min after consumption of the meal, all subjects underwent a repeated MBI (left MLO view only) for calculation of residual activity in the breast from the first injection. The subjects then received the second injection of ^{99m}Tc -sestamibi, and a complete MBI examination comprising bilateral cranio-caudal and MLO views was performed.

Group 2—Effect of Light Exercise. In 25 subjects, MBI was first performed after an overnight or 6-h fast. They were then taken to the nuclear cardiology laboratory, where they performed moderate exercise for 6–10 min at a heart rate of 70%–80% of maximum predicted for age. Exercise was performed on a treadmill using a modified Bruce protocol (24). Once the subjects had achieved 70%–80% of maximum predicted heart rate for age, they received a second injection of ^{99m}Tc -sestamibi and continued to exercise for an additional 2 min. After exercise, the subjects were allowed to cool down and rest for 10 min and then returned to the breast imaging laboratory for the second MBI examination.

Group 3—Effect of Caffeine. In 52 subjects, MBI was first performed after an overnight or 6-h fast. They then consumed 200 mg of caffeine in tablet form. This dose of caffeine is considered to be at the upper range of the caffeine content in 237 mL (8 fluid ounces) of brewed coffee (25). Forty-five minutes after consumption of the caffeine tablet, all subjects underwent a repeated MBI (left MLO view only) for calculation of residual activity in the breast from the first injection. The subjects then received the

second injection of ^{99m}Tc -sestamibi, and a complete MBI examination was performed.

Group 4—Effect of Peripheral Warming. A total of 52 subjects participated in this group. After an overnight or 6-h fast, they were asked to change into the standard light dressing gown used in our breast imaging area, and a skin temperature sensor was taped to the forearm. The subjects were then asked to sit quietly for 15 min in the waiting room (ambient room temperature, 21°C [70°F]). Skin temperature (forearm) was recorded immediately before the first injection of ^{99m}Tc -sestamibi, and MBI was performed 2–3 min later. After completion of the first MBI examination, all subjects were then given a heated blanket. After 30 min, skin temperature was again recorded immediately before injection of the second dose of ^{99m}Tc -sestamibi. The second MBI examination was then performed.

Count Density Analysis

Quantitative measurements of ^{99m}Tc -sestamibi uptake were performed to determine the relative change in uptake between the MBI scans performed before and after the various interventions. For all patient studies, region-of-interest (ROI) analysis was performed using a Xeleris workstation (GE Healthcare). ROIs were drawn to encompass most of the breast tissue on the initial MLO images (upper and lower detectors). The geometric mean of the average counts per pixel from the upper- and lower-detector images was calculated and normalized to a standard administered dose to obtain a count density in units of counts/cm²/MBq.

For subjects in groups 1 and 3, the ROIs were then copied and applied to the same regions of the breast as seen in the second and third set of MLO images (second set acquired immediately before second injection of ^{99m}Tc -sestamibi), and the count density was determined. Figure 1 shows an example of ROI placement on the MLO images of a subject in group 1.

For subjects in groups 2 and 4, no background MBI was performed immediately before the intervention. Hence, in the 77 subjects who participated in groups 1 and 3, we determined the relationship between the change in breast activity and time between the first and second MBI acquisitions by linear regression analysis (with correction for decay of the ^{99m}Tc). Breast background activity from the first injection was then computed using this relationship and used to correct for background activity from the first injection for subjects in these groups.

For all 4 groups, changes in normalized count density (counts/cm²/MBq) were then computed to determine whether each intervention had an effect.

Reference Study Group

To determine whether the interventions had altered the average uptake previously observed in breast tissue, we retrospectively reviewed and analyzed the breast activity in a group of 60 subjects who had participated in a previous clinical trial at our institution. For all 60 subjects, the times of injection, imaging, and measurement of dose activity had been recorded, allowing for accurate correction for decay of the ^{99m}Tc and computation of exact administered activities. The left MLO images were processed in a manner identical to that described above, and normalized count density (counts/cm²/MBq) was then computed for this group.

Statistical Analysis

For comparison within each group, a paired *t* test was used to test the null hypothesis that the intervention did not alter breast

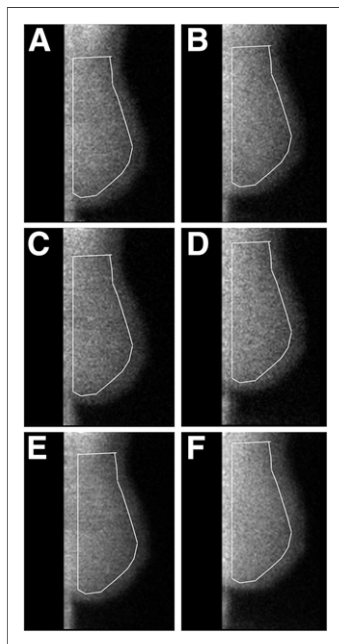


FIGURE 1. Upper and lower left MLO images from subject in group 1 after initial injection (A and B) of ^{99m}Tc -sestamibi and immediately before (C and D) and after (E and F) second injection of ^{99m}Tc -sestamibi. Identical ROI was copied onto all images for measurement of count density.

activity. For comparison of results obtained in all fasting subjects against subjects under different conditions, an unpaired *t* test was used to test the null hypothesis. Data are presented as mean \pm SD. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

For all injections of ^{99m}Tc -sestamibi (2 performed per participant), the average dispensed dose was 226 ± 12 MBq (6.12 ± 0.33 mCi). The average residual syringe activity was $8.4\% \pm 3.6\%$, and the average administered dose was 203 ± 13 MBq (5.48 ± 0.36 mCi). For the 25 subjects from group 1 and the 52 subjects from group 3, the average interval between the 2 injections of ^{99m}Tc -sestamibi was 60 ± 3 min, with a range of 52–74 min. After correction for decay of the ^{99m}Tc , the average washout of ^{99m}Tc -sestamibi over that time was 6% (ratio of counts, 0.94 ± 0.07). However, there was considerable variability in the washout factor, and no correlation was found between washout and time interval, indicating that other imaging and patient factors had an impact on the results (Fig. 2). Hence, a fixed value of 6% washout was used for all studies in groups 2 and 4.

Analysis of the preintervention images from all 154 subjects (i.e., all subjects fasting) showed no correlation between patient height, weight, breast thickness, or body mass index and count density in the breast. A weak correlation between body surface area and breast activity was observed (Fig. 3). Average count density in the breast was 8.96 ± 2.51 counts/cm²/MBq, with a range of 6.0–12.4 counts/cm²/MBq (10th–90th percentiles). Breast activity showed a small dependence on the radiologist's assigned breast density category (Fig. 4), and subjects with heterogeneously or extremely dense breast tissue had a small but significant increase in count density relative to those with fatty replaced breast tissue (*P* < 0.05). Table 1 presents the

results from the 4 groups, showing the mean, SD, median, and 10th–90th percentile ranges before and after each intervention. The results observed in the reference group are also shown for comparison.

Figure 5 shows the average counts in breast tissue before and after administration of a meal in group 1. Although there was good intrasubject agreement between the 2 studies, there was large intrasubject variation in breast activity, with a count density range of 5.61–12.80 counts/cm²/MBq (10th–90th percentiles). After the subjects had eaten, the mean breast activity showed a significant decline from 8.33 to 6.59 counts/cm²/MBq (*P* < 0.001). Figure 6A shows the percentage change in breast activity between fasting and fed states. On average, the ratio of breast activity in the fasting state to breast activity in the fed state was 1.29 ± 0.16 .

Table 1 shows that light exercise resulted in a significant decrease in breast activity, from a mean of 10.14 to 6.63 counts/cm²/MBq (*P* < 0.001). There was a poor correlation between breast activity before and after exercise. This may be due to the variability in the amount of functioning muscle tissue and level of exertion achieved in each subject. Caffeine appeared to have little effect on breast activity, with no significant difference observed in uptake in breast tissue before and after ingestion of 200 mg of caffeine (*P* = 0.38).

Maintaining good peripheral blood flow through warming of the subject up to the time of ^{99m}Tc -sestamibi injection appeared to affect its uptake in breast tissue. With a warming blanket, the breast activity showed a significant increase from a mean of 9.13 to 10.86 counts/cm²/MBq. Figure 6B shows the percentage change in breast activity between the normal unwarmed state and the warmed state. On average, the ratio of breast activity in the warmed state relative to normal conditions was 1.22 ± 0.18 . Measurement of forearm skin temperature showed a significant

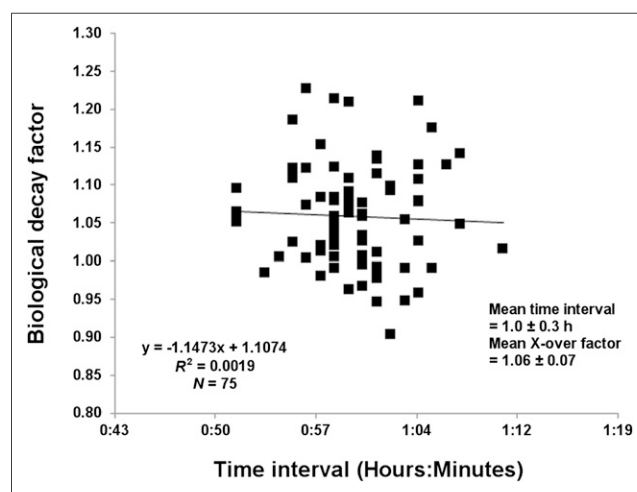


FIGURE 2. Relationship between measured biologic washout factor of ^{99m}Tc -sestamibi and interval between imaging of subjects in groups 1 and 3.

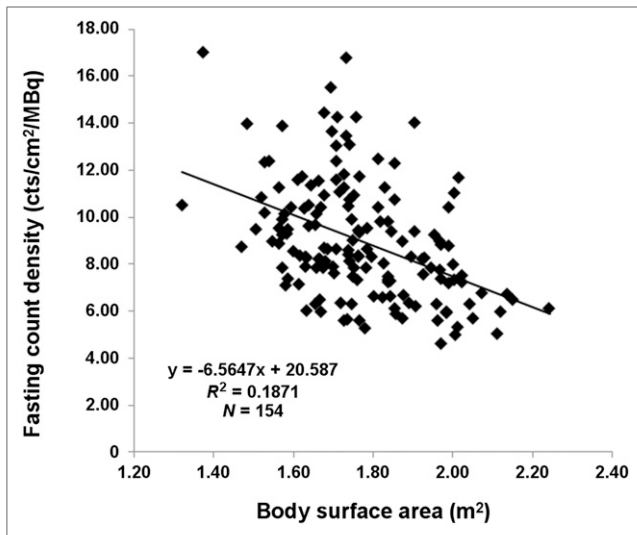


FIGURE 3. Relationship between count density in all participating subjects, assessed in fasting state, and body surface area.

increase from $30.2^{\circ}\text{C} \pm 1.2^{\circ}\text{C}$ to $31.8^{\circ}\text{C} \pm 1.1^{\circ}\text{C}$ ($86.3^{\circ}\text{F} \pm 3.3^{\circ}\text{F}$ to $89.3^{\circ}\text{F} \pm 3.1^{\circ}\text{F}$). However, the relative change in skin temperature showed no correlation with the absolute or relative changes in breast activity.

Figure 7 summarizes the effects of the 4 interventions relative to the fed group. Only the group that fasted and exercised failed to show a significant increase in breast activity relative to the fed group.

DISCUSSION

The results from this study indicate that with relatively minor modifications to patient preparation, it is possible to significantly increase the uptake of $^{99\text{m}}\text{Tc}$ -sestamibi in breast tissue. In this study, the combined effects of fasting (Fig. 6A)

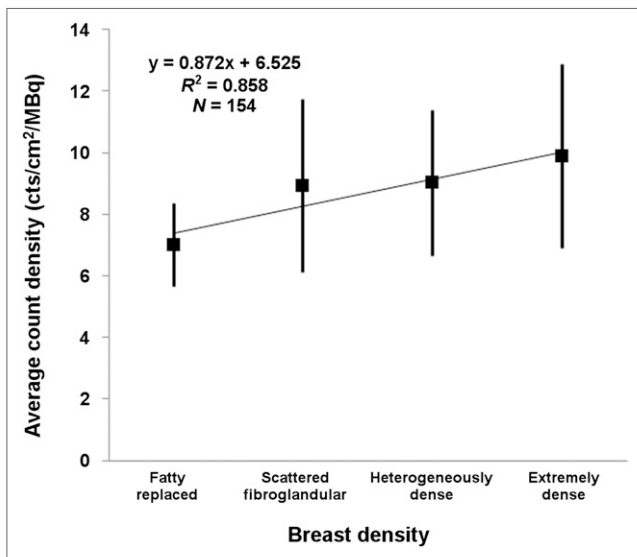


FIGURE 4. Relationship between count density, assessed in fasting state in all participating subjects, and breast density assessed from most recent mammogram.

and warming (Fig. 6B) resulted in a more than 50% increase in the breast activity relative to the fed group from group 1.

The effects of fasting on breast uptake of $^{99\text{m}}\text{Tc}$ -sestamibi were not unexpected, given the known effects of food on prandial and hepatic blood flow (18). Decreased hepatic blood flow resulted in a 25%–30% increase in breast activity. This is a significant gain in breast uptake that can be readily achieved in clinical practice. It was not anticipated that maintaining the patient in a warmed environment would result in a significant increase in breast uptake (Fig. 6B). In many clinical practices, subjects are required to change into light dressing gowns and wait 15–20 min before being brought into the procedure room. Even at room temperature, this wait time may be long enough for subjects to become slightly chilled, with a consequent reduction in peripheral blood flow. Figure 6B shows that keeping subjects warm has the beneficial effects of increased breast activity and patient comfort. The degree of peripheral warming achieved in this study was difficult to quantitate because measurement of changes in forearm skin temperature before and after warming did not correlate with changes in breast activity. This finding may be more a reflection of the location of the skin temperature probe. However, placement of the probe directly on the breast tissue would have been too near the heating pad and would have provided a spuriously elevated measurement of skin temperature.

Although exercise is known to reduce hepatic blood flow and significantly lower $^{99\text{m}}\text{Tc}$ -sestamibi uptake in the liver (17), it was not expected that $^{99\text{m}}\text{Tc}$ -sestamibi uptake in functioning muscle tissue would increase to such a degree that any advantage of reduced hepatic blood flow would be negated. Table 1 shows that exercise resulted in a significant reduction in $^{99\text{m}}\text{Tc}$ -sestamibi uptake in breast tissue. Subjects

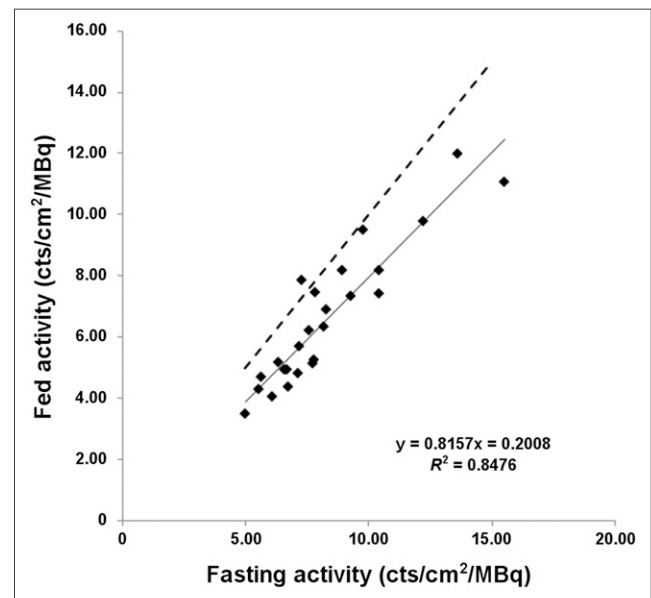


FIGURE 5. Correlation between count density in breast from subjects in group 1 in fasting and fed states. Dotted line = line of identity.

TABLE 1
Summary of Breast Activity in the 4 Groups and Reference Group

Group	State	n	Breast activity (counts/cm ² /MBq)					P
			Mean	SD	Median	Percentile		
						10th	90th	
1	Fasting	25	8.33	2.54	7.76	5.61	12.80	0.014
	Fed		6.59	2.25	6.22	4.18	10.29	
2	Fasting/rest	25	10.14	2.79	10.73	6.15	14.07	<0.001
	Fasting/exercise		6.63	1.58	6.40	4.48	8.99	
3	Fasting	52	8.54	2.36	8.30	5.62	12.15	0.38
	Fasting/caffeine		8.13	2.31	8.16	5.19	10.89	
4	Fasting/cold	52	9.13	2.34	8.63	6.36	12.17	<0.001
	Fasting/warm		10.86	2.71	10.46	7.49	15.56	
All fasting studies		154	8.96	2.51	8.57	5.95	12.36	<0.001
Reference group		60	7.08	1.92	6.81	4.92	9.88	

Reference group vs. fed group, $P = 0.49$.

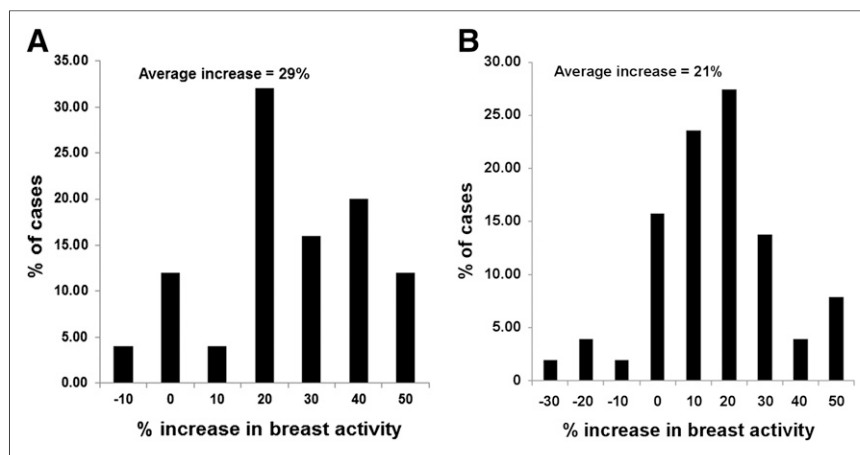
in this study exercised to 80% of maximum predicted heart rate. At this exercise level, ^{99m}Tc-sestamibi in the blood appears to be diverted from both liver and soft tissue to functioning muscle. Although we have not evaluated the effects of milder exercise regimes, it is likely that any increase in blood flow to muscle tissue will adversely affect uptake in breast tissue. Hence, it appears that for optimal breast uptake of ^{99m}Tc-sestamibi, the patients should be at rest at the time of injection to minimize uptake in muscle tissue.

Caffeine in high doses is known to make subjects restless and anxious. It is also known to dilate peripheral blood vessels, decreasing peripheral vascular resistance (21). How these changes influence the uptake of ^{99m}Tc-sestamibi in breast tissue has never been determined, but given that caffeine is a widely consumed drug, it is important to ascertain its potential effects. Table 1 and Figure 7 indicate that caffeine appears to have no significant impact on uptake of ^{99m}Tc-sestamibi in breast tissue. This is a fortuitous finding, as use of caffeine is widespread and a requirement to abstain from caffeinated drinks may be more problematic to many patients than the requirement to abstain from food.

The reference group represented subjects who were not provided with any guidelines on fasting, exercise, caffeine, or warming before their MBI study. Table 1 shows that there was no significant difference in breast activity between subjects who were fed in group 1 and subjects who were in the reference group. Hence, the breast activity observed in the fed group can be considered representative of that which would be observed in routine clinical use. The increase in breast activity with fasting and warming over that observed in the fed group should enable MBI studies to be performed with either a lower dose or a shorter acquisition time. Previously reported studies (7) have used a dose of approximately 240 MBq (~6.5 mCi). With appropriate patient preparation, the increase in breast uptake of ^{99m}Tc-sestamibi should allow the administered dose to be further reduced to approximately 156 MBq (~4.2 mCi) with no reduction in measured count density in the breast.

It was hoped that with better patient preparation, we would observe more consistent and reproducible uptake of ^{99m}Tc-sestamibi in breast tissue. However, in all groups of this study, the range of uptake of ^{99m}Tc-sestamibi in breast

FIGURE 6. (A) Average percentage increase in breast count density between fasting and fed states for subjects in group 1. (B) Average percentage increase in breast count density between subjects before and after peripheral warming (group 3).



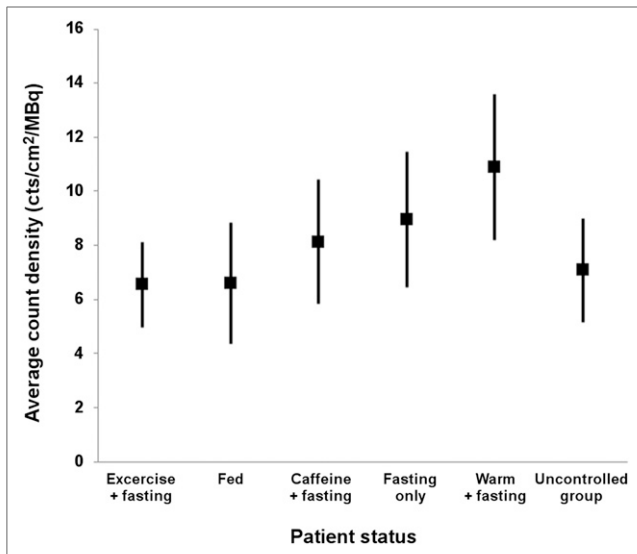


FIGURE 7. Summary of count density in breast for subjects in each of the 4 study groups and those in reference group.

tissue (10th–90th percentiles) varied by at least a factor of 2 (Table 1). No strong correlation could be found between patient height, weight, breast thickness, and breast activity. Furthermore, in all studies, there was only a moderate correlation between breast activity before and after intervention. These findings suggest that other confounding factors not controlled for in this study dictate the uptake of ^{99m}Tc-sestamibi in breast tissue. Given the small percentage of ^{99m}Tc-sestamibi that is deposited in the breast, it is possible that other physiologic variables that were not monitored, such as blood pressure, heart rate, and hydration, may also affect the amount of ^{99m}Tc-sestamibi deposited in the breast. Given the inability to accurately determine the amount of ^{99m}Tc-sestamibi that will be taken up in the breast, it appears that the optimal way to ensure adequate image quality in clinical studies is to require that acquisition times be based on count density rather than a fixed time period.

Reduction of the average administered activity of ^{99m}Tc-sestamibi from approximately 240 MBq to approximately 156 MBq reduces the effective dose from approximately 1.8 to 1.1 mSv. The Food and Drug Administration (FDA) Mammography Quality Standards Act program requires that the average glandular dose delivered during a single craniocaudal view of an FDA-accepted phantom simulating a standard breast not exceed 3.0 mGy per exposure. This is equivalent to an effective dose of 1.4 mSv for a standard 2-view mammogram of both breasts (26). Hence, the effective dose from approximately 156 MBq of ^{99m}Tc-sestamibi is now below the FDA Mammography Quality Standards Act requirements for mammography and is comparable to the effective dose from a combined digital mammography and breast tomosynthesis examination (10,11). Further reduction in the required dose of ^{99m}Tc-sestamibi below approximately 156 MBq will likely need to await future improvements to the cadmium zinc telluride detector technology.

The findings in this study have implications beyond breast imaging. ^{99m}Tc-sestamibi is also an accepted and well-proven radiopharmaceutical for a variety of oncologic and nononcologic imaging applications, including brain, thyroid cancer, and thyroid and parathyroid adenoma. Optimal patient preparation should permit a reduction in the administered dose of ^{99m}Tc-sestamibi for these applications with no loss in image quality.

CONCLUSION

In this study, we showed that the uptake of ^{99m}Tc-sestamibi in breast tissue is influenced by the patient's prandial state, by exercise, and by changes in peripheral blood flow. Increased uptake was observed in the fasting condition and when the subject was kept warm. Conversely, decreased uptake was observed during moderate exercise. Uptake did not seem to be influenced by moderate caffeine intake.

Breast activity was observed to vary by more than a factor of 2 between subjects and did not appear to be correlated with a patient's height, weight, or breast thickness. There was only a weak correlation between breast activity and body surface area. The combined effects of fasting and warming resulted in approximately 50% increased uptake of ^{99m}Tc-sestamibi in breast tissue relative to that observed in the same subjects in a fed and unwarmed state. Optimal patient preparation before administration of ^{99m}Tc-sestamibi should permit a corresponding reduction in either acquisition time or required dose of ^{99m}Tc-sestamibi.

DISCLOSURE

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