Effect of Patient Age, Breast Density, and Topical Anesthetic Cream on Perceived Pain with Sentinel Lymph Node Scintigraphy

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Although an extremely useful technique for sentinel lymph node (SLN) identification in breast cancer, injections of ^{99m}Tc-sulfur colloid can be quite painful. The purpose of this study was to determine whether there is a correlation between perceived pain of injection and age, breast density, or timing of topical anesthetic cream administration. **Methods:** A retrospective review was conducted of women with breast cancer who received injections for sentinel lymphoscintigraphy from 2008 to 2010. After receiving 4 unilateral, intradermal, periareolar injections, women ranked their pain using a comparative scale (0 = no pain; 10 = unbearable pain). There were 3 categories based on length of time that topical anesthetic cream (2.5% lidocaine and 2.5% prilocaine) was applied before injection (1 h prior, 20 min prior, or no cream). In addition, other demographic information and breast density on mammography were analyzed for correlation with the comparative pain scale. **Results:** Among the 82 women (mean age, 58 y; range, 32–87 y), a wide spectrum on the comparative pain scale was recorded (mean, 4.0; SD, 2.6), with 35% attesting to significant pain, rated 5 or greater. The demographic information and breast density per the Breast Imaging Reporting and Data System were retrospectively reviewed (density: fatty, 14.6%; scattered fibroglandular, 36.6%; heterogeneous, 39.0%; extremely dense, 9.8%). Using bivariate linear regression, no correlation between the comparative pain scale and age (R^2 = 0.0029, P = 0.63) or breast density (R^2 = 0.00049, P = 0.84) was identified. Most patients had topical anesthetic cream applied 20 min before injection (n = 47, or 57.3%) with 24 (29.3%) having topical anesthetic cream applied 1 h beforehand. Eleven women (13.4%) had no topical anesthetic cream applied because of patient preference or concern about allergy. Again, no correlation was found between comparative pain scale and time of application or use of topical anesthetic cream (Kruskal–Wallis: χ^2_2 = 1.0, P = 0.61). **Conclusion:** A wide range of pain is experienced with sentinel lymphoscintigraphy injections. In this study, the severity of perceived pain did not correlate with age or breast density. There was no correlation between the use or timing of anesthetic cream and perceived pain from injection. The use of topical anesthetic cream may need to be reexamined, and other means of pain control should be further investigated.

Key Words: breast; lymphoscintigraphy; perceived pain; sentinel node

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Staging and recurrence risk of disease in patients with breast carcinoma is determined by the extent of disease found in the regional lymph node basin (*1,2*). Identification of the sentinel lymph node (SLN), or first node draining the primary tumor site, is essential in the effective management of breast carcinoma patients. Nuclear medicine plays a significant role in assisting in the surgical staging of breast carcinoma patients by mapping the drainage flow of the tumor and identifying the sentinel node within the axilla (*3–5*). In patients with breast carcinoma, the lymphatic channel draining a primary tumor could ultimately carry malignant cells from the tumor site into the sentinel node. The danger is that these cells could eventually proliferate into nodal metastasis. By identifying the SLN, surgeons are often able to avoid classic lymph node dissections, reducing complications in patients with breast carcinoma by decreasing scarring, numbness, lymphedema, and pain typically caused by more extensive surgical exploration and dissection of lymph nodes.

Although the benefits of SLN scintigraphy have been well established, the injections needed for mapping can be uncomfortable, frequently being cited as the most difficult part of the surgical experience for the patient (*6*). It is important for patient care that pain control be examined, identified, and corrected, if needed, to improve the experience for patients undergoing this extremely beneficial procedure. The purpose of this study was to help identify the potential benefit, if any, of topical anesthetic cream, breast density, and age on perceived pain during injections for nuclear medicine sentinel node lymphoscintigraphy.

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MATERIALS AND METHODS

After obtaining institutional review board approval for this Health Insurance Portability and Accountability Act–compliant study, a retrospective collection of data and review of patients diagnosed with breast carcinoma undergoing SLN scintigraphy from 2008 through 2010 was performed. Our standard SLN injection technique was used on all patients in this study. Using sterile technique, 4 intradermal, periareolar injections of ^{99m}Tc-labeled filtered sulfur colloid were performed by the nuclear medicine physician. Each injection contained 3.7–14.8 MBq (0.1–0.4 mCi) of activity within a total volume of less than 0.1 mL per injection. The injections were administered in the quadrant of the tumor, 1 cm from the areolar margin, with a 25-gauge needle, generating an intradermal wheal (Fig. 1). The induced pain was evaluated immediately after the injections, with the patient scoring pain using a linear comparative pain scale with values ranging from 0 to 10 (0 = no pain; 10 = unbearable pain). For this study, patients without allergies to lidocaine were given topical anesthetic cream (2.5% lidocaine and 2.5% prilocaine) by the nuclear medicine technologist either 20 or 60 min before the SLN injections. The topical anesthetic cream was applied to the skin corresponding to the quadrant of the tumor and covered with an adhesive patch to prevent the cream from being wiped off accidentally.

In addition to patient age, breast density was also determined for correlation with the comparative pain scale, using the Breast Imaging Reporting and Data System (BIRADS) in correspondence with the patient's most recent mammogram before SLN (BIRADS 1 = fatty breast tissue; 2 = scattered fibroglandular tissue; 3 = heterogeneous tissue; 4 = dense breast tissue). Statistical analysis was performed using JMP 9.0 statistical software with linear regression analysis and Kruskal–Wallis χ^2 tests as appropriate. A P value of less than 0.05 was considered significant.

RESULTS

Eighty-two women with a diagnosis of breast carcinoma underwent SLN from 2008 to 2010 and were included in this study. The mean age was 58 y, with a range from 32 to 87 y. All breast densities were well represented, with most patients (75.6%) who underwent SLN having BIRADS 2 or 3 breast density (Fig. 2). A wide spectrum on the comparative pain scale was recorded (mean, 4.0; SD, 2.6), with 35% of patients attesting to significant pain, rated 5 or greater.

Breast Density and Age

A wide variation on the comparative pain scale was obtained for the SLN procedure (range, 0–10; mean, 3.9; SD, 2.6). No correlation was found between patient age at the time of SLN and comparative pain scale (R^2 = 0.0029, P = 0.63) (Fig. 3). A fatty breast density was found in 14.6% of patients, a scattered fibroglandular density in 36.6%, a heterogeneous density in 39.0%, and extremely dense breasts in 9.8%. No correlation was found between BIRADS breast density and comparative pain scale (R^2 = 0.00049, P = 0.84) (Fig. 3).

Exposure Time to Topical Anesthetic Cream

Forty-seven patients (57.3%) had a topical anesthetic cream exposure time of 20 min, whereas 24 patients (29.3%) had a topical anesthetic cream exposure time of 60 min. The difference between the 2 groups' exposure times was due to an attempt to facilitate the availability of SLN patients for transfer to the operative suite for early-morning surgery. Eleven patients (13.4%) did not receive topical anesthetic cream because of possible allergies. Again, no correlation was found between comparative pain scale and use of topical anesthetic cream or exposure time to the cream (Kruskal–Wallis: χ^2_2 = 1.0, P = 0.61) (Fig. 4).

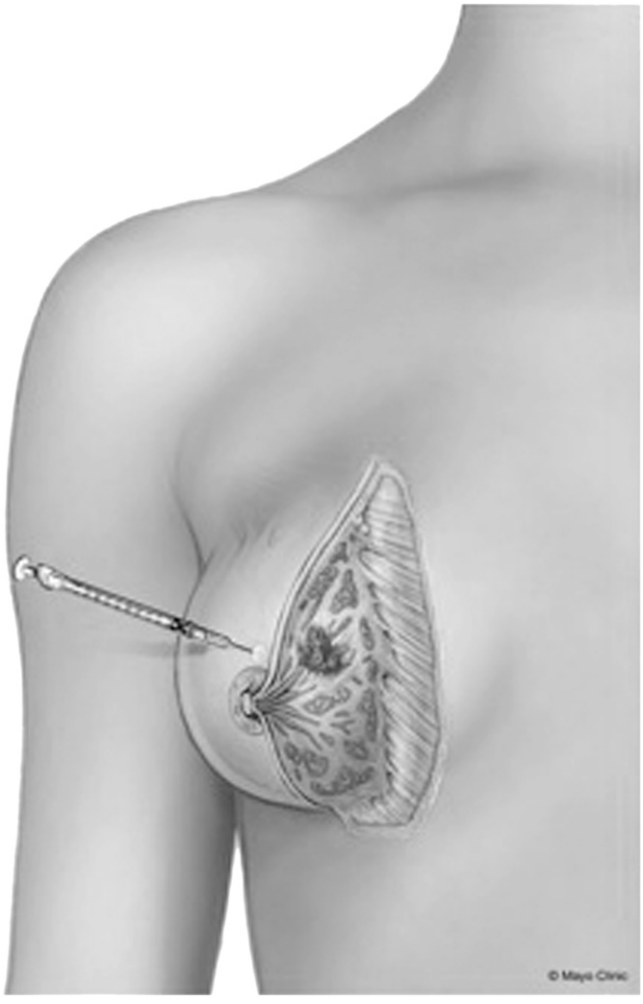

FIGURE 1. Depiction of our standard SLN injection practice. Four intradermal, periareolar injections of ^{99m}Tc-labeled filtered sulfur colloid are placed in quadrant of tumor before imaging. Injections are placed near one another. (Reprinted with permission of the Mayo Foundation for Medical Education and Research, all rights reserved.)

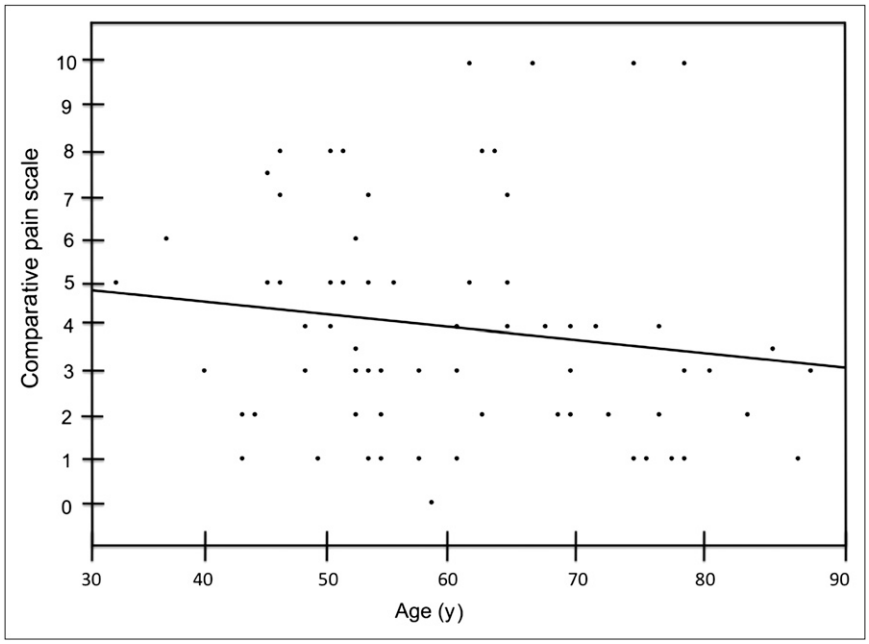

FIGURE 2. Despite wide range of ages for patients undergoing SLN, no correlation between patient age and comparative pain scale was found ($R^2 = 0.0029$, $P = 0.63$).

DISCUSSION

At our institution, our breast surgeons rely on SLN scintigraphy for intraoperative localization of the SLN draining the affected breast. In addition to helping limit the extent of the axillary nodal dissection, SLN scintigraphy can also help detect alternative drainage pathways besides the axilla, such as via the internal mammary chain (*3,7,8*). Although multiple techniques have been described for injections of the radiotracer for SLN scintigraphy, in discussions with our surgeons we have opted for intradermal injections of ^{99m}Tc-labeled filtered sulfur colloid within the quadrant of the tumor. We have found this option gives reliable and relatively rapid results that facilitate the patient's transfer to the operating room.

Despite the proven utility of SLN scintigraphy, this procedure remains uncomfortable for our patients and frequently is cited as one of the most painful portions of the entire treatment process. In an effort to reduce the discomfort of this procedure, topical anesthetic cream has been advocated and is a routine part of our practice (*9*). Despite the addition of topical anesthetic cream, patients have reported significant discomfort from the

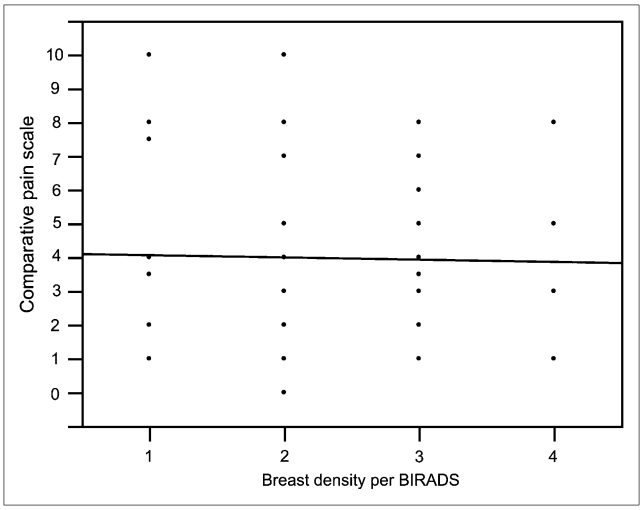

FIGURE 3. Comparative pain scale plotted vs. BIRADS breast density demonstrates no correlation ($R^2 = 0.00049$, $P = 0.84$). 1 = fatty density; 2 = scattered fibroglandular tissue; 3 = heterogeneous tissue; 4 = dense breast tissue.

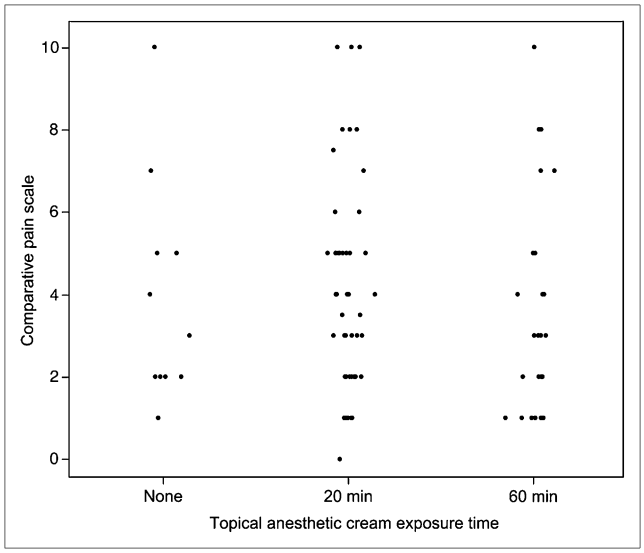

FIGURE 4. Topical anesthetic cream exposure time of 20 or 60 min did not correlate with comparative pain scale. In addition, use or disuse of topical anesthetic cream did not correlate with statistically significant difference in comparative pain scale (Kruskal–Wallis: $\chi^2_2 = 1.0$, $P = 0.61$).

intradermal injections. This study was performed to formally evaluate the timing of the topical anesthetic cream as well as to attempt to identify patients who may be at higher risk for discomfort because of age or breast density. Initially, the topical anesthetic cream was applied 20 min before the intradermal injections. When significant pain was still noted for many patients, our protocol was changed to allow for a topical anesthetic cream exposure time of 60 min. No statistically significant difference could be found between the 2 groups. In addition, in those patients who had a relative contraindication to topical anesthetic cream and did not receive it, significant pain was noted on the comparative pain scale but the pain was not statistically different from either group that received topical anesthetic cream. In addition, age and breast density did not correlate with perceived pain on the comparative pain scale.

Mixing 1% lidocaine into the SLN injections was considered to reduce pain; however, because ^{99m}Tc-sulfur colloid is a heat- and acid-catalyzed radiopharmaceutical, it was unclear if the addition of lidocaine to the radiopharmaceutical would degrade the particles, reducing the integrity of the procedure. This possibility was not evaluated in the study.

Although we find the results of this study frustrating, we do not find them surprising. We postulate that the topical anesthetic cream works primarily on the nociceptive C-fibers. Although this means may minimize the discomfort associated with the skin puncture, the stretch nociceptive mechanism mediated by larger A-δ myelinated fibers may be unaffected or only partially blunted by the topical anesthetic cream (*10*). This pain mechanism would also be unaffected by varying patient age and breast density, accounting for our lack of correlation with the comparative pain scale.

This study was limited by its retrospective design, without a true control or matched groups. In addition, even though a linear comparative pain scale has been well validated for pain assessment, it is still a subjective measurement. The possibility remains that an individual patient may benefit from topical anesthetic cream, despite our group data suggesting the absence of demonstrated pain control.

The interpretation of pain is subjective and extremely sensitive to numerous factors that can alter the perception. Patients undergoing breast lymphoscintigraphy are often in a delicate emotional state before, during, and after the procedure due to the new diagnosis, anticipation, unclear prognosis, or other factors. The goal of this study was to determine, to the best of our ability, with a retrospective data collection, the correlation between pain that women are feeling and patient age, breast density, or the use of topical anesthetic. A masked, more controlled study may allow these factors to be evaluated for effects on pain perception.

CONCLUSION

Our data suggest that the use of topical anesthetic cream alone is not likely to be sufficient for pain control in patients undergoing SLN scintigraphy with intradermal injections of ^{99m}Tc-sulfur colloid for breast carcinoma. Neither patient age nor breast density was a risk factor that predisposes certain patients to an increased pain response. Because of the limitations of this study, continued efforts to explore other techniques to reduce pain associated with SLN scintigraphy are needed, as well as further investigation into pain control of SLN scintigraphy for melanoma patients.

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REFERENCES

1. Chagpar AB, Kehdy F, Scoggins CR, et al. Effect of lymphoscintigraphy drainage patterns on sentinel lymph node biopsy in patients with breast cancer. *Am J Surg.* 2005;190:557–562.
2. Ehrenström Reiz GM, Reiz SL. EMLA: a eutectic mixture of local anaesthetics for topical anaesthesia. *Acta Anaesthesiol Scand.* 1982;26:596–598.
3. Goyal A, Mansel RE. Recent advances in sentinel lymph node biopsy for breast cancer. *Curr Opin Oncol.* 2008;20:621–626.
4. Heuts EM, van der Ent FWC, von Meyenfeldt MF, Voogd AC. Internal mammary lymph drainage and sentinel node biopsy in breast cancer: a study on 1008 patients. *Eur J Surg Oncol.* 2009;35:252–257.
5. Kesmodel SB, Canter RJ, Terhune KP, et al. Use of radiotracer for sentinel lymph node mapping in breast cancer optimizes staging independent of site of administration. *Clin Nucl Med.* 2006;31:527–533.
6. Ogasawara Y, Yoshitomi S, Sato S, Doihara H. Clinical significance of preoperative lymphoscintigraphy for sentinel lymph node biopsy in breast cancer. *J Surg Res.* 2008;148:191–196.
7. Shen P, Glass EC, DiFronzo LA, Giuliano AE. Dermal versus intraparenchymal lymphoscintigraphy of the breast. *Ann Surg Oncol.* 2001;8:241–248.
8. Mansel RE, Goyal A, Newcombe RG, Group AT. Internal mammary node drainage and its role in sentinel lymph node biopsy: the initial ALMANAC experience. *Clin Breast Cancer* 2004;5:279–284.
9. Ozmen V, Cabioglu N. Sentinel lymph node biopsy for breast cancer: current controversies. *Breast J.* 2006;12(suppl):S134–S142.
10. Fetzer S, Holmes S. Relieving the pain of sentinel lymph node biopsy tracer injection. *Clin J Oncol Nurs.* 2008;12:668–670.