Reproducibility of lymphoscintigraphy before and after excisional biopsy of primary breast lesions: A study using superficial peri-areolar injection of the radiotracer

M. Asadi\textsuperscript{a}, H. Shobeiri\textsuperscript{a}, M. Aliakbarian\textsuperscript{a}, A. Jangjoo\textsuperscript{a}, V.R. Dabbagh Kakhki\textsuperscript{b}, R. Sadeghi\textsuperscript{b,\textasteriskcentered}, M. Keshtgar\textsuperscript{c}

\textsuperscript{a} Surgical Oncology Research Center, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
\textsuperscript{b} Nuclear Medicine Research Center, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
\textsuperscript{c} Royal Free Hospital and University College London, London, United Kingdom

\section*{A R T I C L E   I N F O}

\textbf{Article history:}
Received 18 June 2012
Accepted 26 July 2012

\textbf{Keywords:}
Breast cancer
Excisional biopsy
Lymphoscintigraphy
Intradermal injection
Peri-areolar injection
Lymphatic drainage change

\section*{A B S T R A C T}

\textbf{Objective:} A major controversial issue in the sentinel node biopsy of the breast is the applicability of sentinel node mapping in patients with the history of previous excisional biopsy of the breast lesions. In the current study, we evaluated the reproducibility of lymphoscintigraphy before and after excisional biopsy of the primary breast lesions using superficial peri-areolar injection of the radiotracer.

\textbf{Material and methods:} Eighteen patients scheduled for excisional biopsy of breast lesions were included in the study. The patients received intra-dermal injection of the radiotracer in the peri-areolar area of the index quadrant 1 to 2 h before surgery. Imaging was performed the day after surgery. Immediately after completion of the first imaging, the patients received another injection of the radiotracer with the same technique, dose, and location. Other sets of lymphoscintigraphy images were taken immediately and 4 h post second injection. The two sets of lymphoscintigraphy images were compared.

\textbf{Results:} In 2 patients, sentinel node could not be identified in either set of images. In the remaining 16 patients, one sentinel node was detected in both lymphoscintigraphy image sets. The sentinel nodes of the second image sets were all in the same location of the first sets with at least 5 times higher count.

\textbf{Conclusions:} Excisional biopsy of the primary breast lesions does not seem to change the superficial lymphatic drainage pattern from the areola of the breast and sentinel node mapping can be performed after this procedure using superficial periareolar technique.

© 2012 Elsevier España, S.L. and SEMNIM. All rights reserved.

\section*{Reproducibilidad de la linfogammagrafía antes y después de la biopsia excisional de las lesiones primarias de mama: estudio utilizando la inyección periareolar superficial del radiotrazador}

\section*{R E S U M E N}

\textbf{Objetivo:} Una cuestión de gran controversia en la biopsia del ganglio centinela de la mama es la aplicabilidad del estudio del ganglio centinela en pacientes con historia previa de biopsia excisional de las lesiones de la mama. En el presente estudio, evaluamos la reproducibilidad de la linfogammagrafía antes y después de la biopsia excisional de las lesiones primarias de mama utilizando la inyección periareolar superficial del radiotrazador.

\textbf{Material y métodos:} Se incluyó en el estudio a 18 pacientes programadas para biopsia excisional de lesiones de mama. A las pacientes se les administró una inyección intradérmica del radiotrazador en el área periareolar del cuadrante con tumor, con 1 o 2 h antes de la cirugía. La imagen se obtuvo el día posterior a la operación. Inmediatamente tras la primera imagen, a las pacientes se les administró otra inyección del radiotrazador con la misma técnica, dosis y localización. Se realizaron inmediatamente otras series de imágenes de linfogammagrafía, y a las 4 h después de la segunda inyección. Se compararon las 2 series de imágenes de linfogammagrafía.

\textbf{Resultados:} En 2 pacientes no se pudo identificar el ganglio centinela en ninguna de las series de imágenes. En las 16 pacientes restantes se detectó un ganglio centinela en ambas series de imágenes de linfogammagrafía. Los ganglios centinela de las segundas series de imágenes se detectaron en la misma localización que las primeras series de imágenes, con un contaje al menos 5 veces superior.

\textbf{Conclusiones:} La biopsia excisional de las lesiones primarias de mama no parece modificar el patrón del drenaje linfático superficial desde la areola de la mama, pudiendo realizarse el estudio del ganglio centinela tras esta intervención, utilizando la técnica periareolar superficial.

© 2012 Elsevier España, S.L. y SEMNIM. Todos los derechos reservados.

* Corresponding author.
E-mail addresses: sadeghi@mums.ac.ir, raminsadeghi1355@yahoo.com (R. Sadeghi).

2253-6089/ – see front matter © 2012 Elsevier España, S.L. and SEMNIM. All rights reserved.
Introduction

Sentinel node biopsy is considered as the standard of care in staging of early breast cancer.\textsuperscript{1} This method has considerably decreased the morbidity of breast cancer treatment, since patients with pathologically negative sentinel nodes can be spared unnecessary axillary lymph node dissection.\textsuperscript{2,3}

Despite widespread acceptance, many aspects of sentinel node mapping in breast cancer patients are still under debate.\textsuperscript{4,5} A major controversial issue is the applicability of sentinel node mapping in patients with the history of previous excisional biopsy of the breast lesions. Although many researchers do not consider excisional biopsy as a contra-indication for sentinel node biopsy,\textsuperscript{6} the bulk of evidence has come from the studies comparing detection and false negative rates in patients with and without history of excisional biopsy.\textsuperscript{7,8} These studies have indirectly evaluated the effect of excisional biopsy on the accuracy of sentinel node mapping and the possible change of lymphatic drainage pattern after excisional biopsy of the primary breast lesion is still debatable.\textsuperscript{9,10}

In the current study, we evaluated the reproducibility of sentinel node imaging (or lymphoscintigraphy) before and after excisional biopsy of the primary breast lesions using superficial peri-areolar injection of the radiotracer.

Material and methods

Eighteen patients who were scheduled for excisional biopsy of breast lesions with the suspicion of malignancy were included into the study. None of the patients underwent any axillary or breast surgery procedure. No patient had previous history of radiotherapy or chemotherapy.

The study was approved by the local ethical committee of our institution, and all the patients gave their written informed consent before inclusion into the study.

One to two hours before surgery patients were sent to the nuclear medicine department for lymphoscintigraphy. The procedure has been explained elsewhere.\textsuperscript{11,12} In brief, the patients received intra-dermal injection of 37 MBq in 0.2 mL $^{99m}$Tc-Antimony sulfide colloid in the peri-areolar area of the index quadrant. In case of malignant pathological result of the excisional biopsy, the patients would be referred to the nuclear medicine department for imaging and second injection of the radiotracer. Imaging was performed the day after surgery using a dual head variable angle gamma camera (ECAM Siemens) equipped with low-energy high resolution collimators in anterior and lateral projections (128 x 128 matrix, 5 min/projection). Immediately after completion of the first lymphoscintigraphy imaging, the patients received another injection of $^{99m}$Tc-Antimony sulfide colloid (of the same batch of radioactive material as the first injection) with the same technique, dose, and location. Other sets of lymphoscintigraphy imaging were taken immediately (dynamic imaging 10 s/frame for 20 min), and 4 h post second injection with the exact same protocol as the first images. Patients with malignant tumor of the breast underwent definite surgery for breast cancer the same day of the second radiotracer injection alongside sentinel node detection. In case of positive frozen section of the sentinel node, axillary dissection would be performed.

The two sets of lymphoscintigraphy images were evaluated by two expert nuclear medicine specialists. The location and number of sentinel nodes and semi-quantitative evaluation (using ROIs over the sentinel nodes) of the sentinel node counts were used for comparison between the pre and post excision images. Concordance between two images was defined as increase in the sentinel node counts of the first image set after second injection. Discordance was defined as any new sentinel node visualized after second injection or no increase in the sentinel node count.

Results

The characteristics of the patients are presented in Table 1. Biopsy results of all patients were invasive carcinoma. In two patients (number 2 and 4), sentinel node could not be identified in either set of images. In the remaining 16 patients, one sentinel node was detected in both lymphoscintigraphy image sets. The sentinel nodes of the second image sets were all in the same location of the first sets with at least 5 times higher count. Fig. 1 shows images of patient 7 of our study.

Discussion

Despite widespread acceptance of sentinel node biopsy in the management of breast cancer patients, many technical aspects of this procedure is under debate.\textsuperscript{10} One of the controversial issues is the impact of excisional biopsy of the breast lesions on the accuracy of sentinel node biopsy. Many studies reported comparable results in patients with and without history of excisional biopsy and others reported quite the opposite.\textsuperscript{6,7} A recent meta-analysis showed that surgical biopsy of the primary breast lesions does not affect the detection rate. However, false negative rate seems to be slightly (clinically insignificant) higher in patients with the history of excisional biopsy.\textsuperscript{5}

However, none of the above-mentioned studies directly evaluated the possible change of lymphatic drainage after excisional biopsy. To our knowledge only one study reported the reproducibility of lymphoscintigraphy imaging before and after excisional biopsy of the primary breast lesions. In this study, Estourgie et al. reported axillary drainage reproducibility of only 32%. Eleven out of 25 patients showed altered axillary lymph node drainage (in 7 no axillary nodes was detected on the post-excisional biopsy images) and 10 out of 13 patients with internal mammary drainage before excisional biopsy showed altered drainage into this basin after excision.\textsuperscript{9} The results of our study were in complete contrast to Estourgie et al. as we found 100% reproducibility in the lymphoscintigraphies before and after excisional biopsy of the breast lesions. This difference can be explained by different injection technique we used in our study. We used intradermal injection of the radiotracer in the peri-areolar region which has more efficient and faster migration in the lymphatic system compared to the intra-tumoral method as Estourgie et al. used in their studies.\textsuperscript{13,14} Sluggish movement of the radiotracer in the lymphatic system (due to edema and inflammation post excisional biopsy) has been shown to decrease sentinel node detection rate using deep injections of the radiotracer,\textsuperscript{15} which is what occurred in 7 patients of Estourgie et al. study with pre and post excisional biopsy lymphoscintigraphy axillary discrepancy. On the other hand, excisional biopsy does not have any considerable effect on the axillary sentinel node detection rate using intra-dermal injection of the radiotracer\textsuperscript{6,17} and this can explain the high detection rate post-excision in our study. Another aspects of our study were also different from Estourgie et al. such as particle size (which is smaller by $^{99m}$Tc-Antimony sulfide colloid compared to $^{99m}$Tc-Nanocolloid), and the time interval between the first and second imaging (which was much longer in the Estourgie et al. study). These differences can also contribute to the disparity between the results of our study and Estourgie et al. study. It is also worth mentioning that internal mammary nodes are not usually visualized by intra-dermal injection of the radiotracer\textsuperscript{11} and we could not evaluate the change in drainage pattern in this location as Estourgie et al. did.
In our study we did not merely compare detection rates on pre and post excisional biopsy images. We performed post-excision lymphoscintigraphy the morning after surgery and used these images as a template for exact localization of post-excision sentinel nodes (Fig. 1). Dynamic imaging immediately after second (post-excisional biopsy) injection also helped to reveal the lymphatic drainage pathways (Fig. 1c). All patients with detected sentinel nodes in the axilla on the first set of images had at least 5 times increase in the radioactivity count of the sentinel nodes on the second lymphoscintigraphy images. No other hot area in the axilla was detected on the second lymphoscintigraphy images. This shows that the same sentinel nodes received the radiotracer of the second (post-excision) injection and no change in the lymphatic drainage occurred.

Vasques et al. reported another study with some resemblance to ours in 2011. They evaluated the impact of previous peri-areolar incision in the upper outer quadrant of the breast on the localization of the sentinel lymph nodes in dogs. For this purpose they evaluated the concordance of peri-areolar pre-excision radiotracer injection and peri-incisional post excision blue dye injection methods.10

![Fig. 1](image)

**Fig. 1.** Pre (a) and post (b) excision lymphoscintigraphy images of patient 7. Sentinel lymph node counts were increased 10 and 7 folds on the anterior and lateral projections respectively using ROIs (not shown in the image). No other hot spot in the axilla was apparent on the post excision images. Bottom image (c) is the dynamic anterior view after the second injection. Note the lymphatic pathway which is draining into the same lymph node which was present since the pre-excision injection (arrow). The scale of the images is increased to better visualize the lymphatic pathway.

### Table 1

Characteristics of the included patients.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age (year)</th>
<th>Tumor size (mm)</th>
<th>Tumor location</th>
<th>Biopsy results</th>
<th>Number of sentinel node on the first set images</th>
<th>Number of sentinel nodes on the second set of images</th>
<th>Ratio of sentinel node count on the second set of images to the first set of images (ANT view)</th>
<th>Ratio of sentinel node count on the second set of images to the first set of images (LAT view)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39</td>
<td>22</td>
<td>UOQ</td>
<td>IDC</td>
<td>1</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>2</td>
<td>56</td>
<td>30</td>
<td>C</td>
<td>ISC</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>15</td>
<td>LOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>10.01</td>
<td>12.90</td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>22</td>
<td>UOQ</td>
<td>IDC</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>22</td>
<td>LOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>7.46</td>
<td>7.26</td>
</tr>
<tr>
<td>6</td>
<td>45</td>
<td>32</td>
<td>UOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>5.34</td>
<td>4.87</td>
</tr>
<tr>
<td>7</td>
<td>37</td>
<td>21</td>
<td>UOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>10.32</td>
<td>7.35</td>
</tr>
<tr>
<td>8</td>
<td>45</td>
<td>33</td>
<td>UIQ</td>
<td>ILC</td>
<td>1</td>
<td>1</td>
<td>10.03</td>
<td>11.46</td>
</tr>
<tr>
<td>9</td>
<td>44</td>
<td>40</td>
<td>C</td>
<td>ILC</td>
<td>1</td>
<td>1</td>
<td>6.56</td>
<td>6.32</td>
</tr>
<tr>
<td>10</td>
<td>28</td>
<td>25</td>
<td>UOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>8.81</td>
<td>7.13</td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>30</td>
<td>UOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>10.92</td>
<td>12.41</td>
</tr>
<tr>
<td>12</td>
<td>84</td>
<td>45</td>
<td>UOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>10.24</td>
<td>9.09</td>
</tr>
<tr>
<td>13</td>
<td>36</td>
<td>30</td>
<td>LOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>14.86</td>
<td>17.26</td>
</tr>
<tr>
<td>14</td>
<td>76</td>
<td>33</td>
<td>UOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>5.43</td>
<td>6.54</td>
</tr>
<tr>
<td>15</td>
<td>54</td>
<td>32</td>
<td>UOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>5.92</td>
<td>4.93</td>
</tr>
<tr>
<td>16</td>
<td>58</td>
<td>39</td>
<td>UOQ</td>
<td>ILC</td>
<td>1</td>
<td>1</td>
<td>8.28</td>
<td>8.12</td>
</tr>
<tr>
<td>17</td>
<td>69</td>
<td>38</td>
<td>UOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>8.48</td>
<td>6.72</td>
</tr>
<tr>
<td>18</td>
<td>76</td>
<td>29</td>
<td>UOQ</td>
<td>IDC</td>
<td>1</td>
<td>1</td>
<td>16.72</td>
<td>11.80</td>
</tr>
</tbody>
</table>

C: Central; IDC: Invasive ductal carcinoma; ILC: Invasive lobular carcinoma; ISC: In situ carcinoma; LOQ: Lower outer quadrant; UIQ: Upper inner quadrant; UOQ: Upper outer quadrant.
Their study supports the results of ours since they had 82% agreement between the two injections which is fairly high. Besides being an animal study, Vasques et al. experiment differs from ours; the location of second injection was peri-incisional (upper border of the incision line) and they used blue dye for the post-excision injection.

Conclusion

Excisional biopsy of the primary breast lesions does not seem to change the superficial lymphatic drainage pattern from the areola of the breast and sentinel node mapping can be performed after this procedure using superficial periareolar technique.

Financial support

This study was supported by a grant from vice chancellery of research of Mashhad University of Medical Sciences, and is the result of a thesis under the approval number of 88682 which was performed in the Nuclear Medicine and Surgical Oncology Research Centers. The financial sources did not have any participation in the study design, data collection, analysis or interpretation of these in the writing of the manuscript or in the decision to submit it for publication.

Conflict of interest

The authors declare no conflict of interest.

References