Original Article

Evaluation of the Lymph Flow to the Sentinel Lymph Node (SLN) in Breast Cancer Using CT Imaging

Edson Boasquevisque;[1] Renata Reis Pinto; [2] Augusto Cavalcante Filho;[3] Gustavo Boasquevisque;[1] Jorge Wagner E Silva;[4] Eduardo C Millen[3]

1 Radiology Department, National Cancer Institute, INCA, Ministry of Health, Brazil

2 Universidade Federal de São Paulo

4 Radiology and Pathology Department, Santa Casa de Misericordia de Barra Mansa

3 Laboratory and Pathology/ FCM-UERJ

This work was developed at Radiology and Pathology Department, Santa Casa de Misericórdia de Barra Mansa

Abstract

Background: Axillary nodal status remains the best survival predictor for patients with early–stage breast cancer. Accurate identification of sentinel lymph node (SLN) is the first step for biopsy. **Purpose:** To evaluate the lymph flow to SLN with Computerized Tomography using small volume of low molecular iodinated contrast medium. **Material and Methods:** Thin section and 3D CT images of the breast and axilla were acquired from 20 patients with early stage breast cancer. Images were acquired before subcutaneous injection of a small volume of water soluble iodinated contrast medium in the periareolar region and 1-7 minutes latter. Location of SLN and CT density were assessed at CT lymphography and the positive group was compared with negative one. **Results:** In all patients, CT lymphography allowed localization of SLN and its afferent lymphatic vessel, as well as measuring the contrast medium uptake and washout from SLN. The negative group presented grater and faster contrast medium uptake and washout compared to the positive one. **Conclusion:** CT lymphography provides good anatomical localization of SLN and may be useful for its lymph flow analysis, allowing a better distinction of positive from negative metastatic nodes.

Keywords: Breast neoplasms. Sentinel lymph node biopsy. Lymphography.

Introduction

The lymphatic vasculature has precollector vessels coalescing into lymphatic ducts, which drain into lymph nodes.[1]

Lymph drainage of the skin overlying the breast is continuous with that of the underlying mammary gland proper, draining into the same axillary lymph nodes.[2] The sentinel lymph node is defined as the first lymph node draining this body area, and due to this metastatic cells from the tumor may pass through it. Therefore, the sentinel lymph node is taken to represent the negative or positive status of the entire lymphatic drainage basin.[3] Axillary dissection may be prevented when a negative result is found.[4-5]

Axillary node status is one of the most important prognostic indicators in breast cancer and it is of particular value in the choice of adjuvant therapy.[6-7] The dissection of

Correspondence
JE Boasquevisque, MD, PhD
Rua Carvalho Azevedo 36/303
224 71220, Rio de Janeiro, Brazil
Phone: 55 21 25876416
Fax: 55 21 25876416
E-mail: Boasquevisque@gmail.com

the axillary node chain is an important staging procedure in the surgical treatment of breast cancer, although its morbidity is rather high and should be avoided.[8]

Many investigators, using different techniques to identify SLN,[9-19] used vital dye and some of them also used radioactive colloid.[18-20] Combinations of these procedures offer better results than each one isolated.[5,10,21] The lymph flow in breast cancer may be impaired by metastatic cell bulk.[2,3,14]

Colloidal particle uptake in the SLN may be reduced by impairments of the phagocytosis capacity of macrophages.[22-23] Thus, lymph node uptake is dependent on at least two main factors,[11] including lymph flow and cell function. The contrast peak point of SLN which was reached at the first minute after subcutaneous injection of contrast medium was reported by Minato and coworkers.[13] Lymph flow may be evaluated using water soluble contrast medium,[12-13,24] whose molecular weight is close to vital blue dye.

The aim of this study was to analyze how lymph flow behaves to positive and negative SLN in breast cancer.

Patients and Methods

Twenty patients with breast cancer (clinical stage T1-T2, N0) without any previous manipulation had SLN investigated with Computerized Lymphotomography (CT-L) and vital blue dye subcutaneous injection.[11,13] CT was done on the day before surgery in order to identify SLN and to mark the skin over the lymph node site.Vital blue dye (5% concentration) was injected into the same site used to inject contrast medium during operation procedure.[10-11]

CT study protocol was performed before and after contrast medium subcutaneous injection into four points of the periareolar area (Figure 1).[13] Two milliliters of non ionic iodine contrast medium was used (water soluble contrast solution of iodine with molecular weight of 777.09 Daltons, 370mg I/ml and 780 mOsm/kg – Iopamiron - 370).[14] Imaging with 2mm thick contiguous acquisition, including the breast and axilla, before and after injection, at one, three and seven minutes of procedure was done by a helical CT scanner (Somaton Sprit +, Siemens, Erlangen, Germany). The CT scan worked at 120kV and 80mA, with a FOV of 26cm and 512 x 512 matrix.

All patients had SLN identified by both techniques,

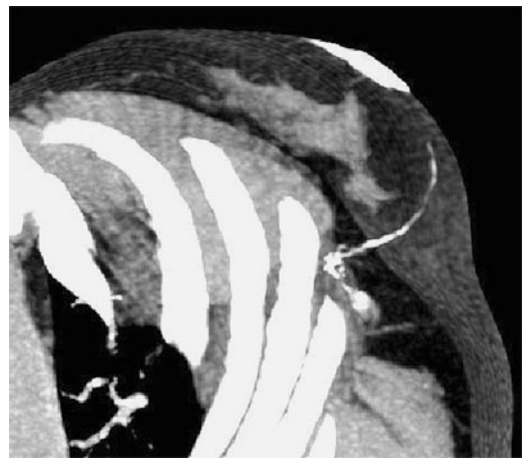

Figure 1 - CT lymphography in a negative SLN (3 min image); SLN - small arrow, breast nip afeter contrast medium injection - curved arrow

and the positive cases underwent resection of SNL and four additional LN around it.

CT images were analyzed on a workstation connected to the CT unit and SLN identified and its density measured in HU (d). For assessment of the contrast medium uptake by SLN, a region of interest (ROI) was drawn on the consecutive CT images for all SLN opacified on post contrast CT images. The ROI size had to be large enough to encompass at least 60% of the total SLN area.

To evaluate the washout of the contrast medium from SLN, the slope of the regression curve was calculated from the descending phase of CT density curve (Figure 2).

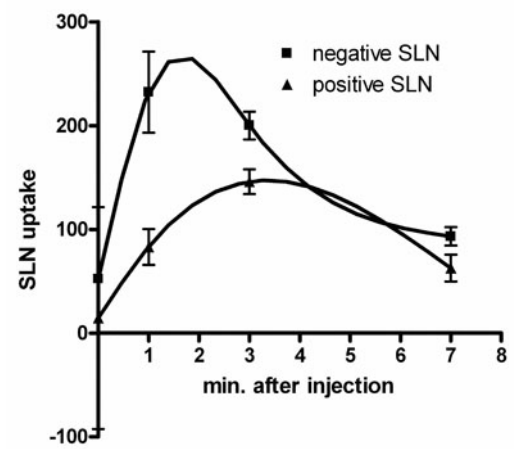

Figure 2 - Curve of dynamic process of lymph flow in the sentinel lymph node

Pathologic analysis of serial sectioned SLN was performed with hematoxylin-eosin staining.

The results of the negative and positive groups were compared using the unpaired Student t test, with $p \leq 0.05$.

Results

All positive patients had only the first echelon of axillaries lymph nodes compromised and LN measurements were 0.63±0.1cm for the small diameter and 1.0±.0.2cm for the great one (range of 0.5cm x 1.0cm to 0.8cm x1.1cm). In sixteen patients without metastasis to SLN, lymph node enhancement after contrast medium injection was greater and faster (first minute peak) than that shown by the positive group (third minute peak) ($p<0.05$). The descending phase of the curve (washout) was also different in both groups ($p<0.05$). The negative group curve had a steeper slope (A= -26.34 d/min) than the positive one (B = -20.85 d/min). The peak time was three times longer in the positive group and the washout of contrast medium was 26.3% greater in the negative nodes $p<0,05$ (Figure 2).

Discussion

Sentinel lymph node biopsy in T1-T2, N0 breast cancer is usually recommended by the American Society of Clinical Oncology.[25] Vital blue dye is the most widely used marker for this purpose.[11,26]

All patients of both groups had SLN identified by vital blue dye and CT-lymphography. The peak time of the uptake curve of negative lymph nodes was in the same range as indicated in the literature.[13] However; the time to peak in the positive group was three times longer than that observed for the negative one, and the curve amplitude was also lower than that of the negative group. As the molecular weight of the contrast medium used and the vital blue dye are very similar, the different uptake by the two groups may reflect the pathophysiological status of SLN. The reduced uptake and slow lymph flow is more likely to be due to compromised nodes in breast cancer.[13,27] The reduced uptake of the contrast medium seen in positive SLN may be due to its occupation by malignant cells which disrupt the node structure and block the lymph flow.[13,27-28] Micrometastasis to the SLN may be present in 9% to 39% of breast cancer patients,[29-31] but the differentiation between cases involving macro- and micrometastasis have to be investigated separately in order to determine the behavior of the lymph flow to lymph nodes. The increased metastasis to secondary lymph nodes in these cases has been reported by some investigators.[28,32] The negative group of SLN in our study had a greater and faster uptake of the contrast medium and a higher washout compared to the positive one. It is important to point out that no one else has analyzed the contrast medium washout of SLN, which may be more important than the first curve phase,[12-13,24] although amplitude and slope of the descending phase to the distal nodes (second echelon) have been reported.[13,24] Our data from SLN may be used along with image analysis to help identify the appropriate surgical procedure, and further ongoing investigations by us are being done to validate the accuracy of this model.

Acknowledgement

This research was partially supported by Rio de Janeiro Foundation for Scientific Research (Faperj, www.faperj.br).

We are grateful to Professor Carlos Alberto Mandarim-de-Lacerda from Rio de Janeiro State Uuniversity Medical School for his help in revision of manuscript.

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