Intra-Operative Digital Specimen Radiography of Sentinel Lymph Nodes as an Alternative to Frozen Section Diagnosis

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Abstract

Introduction

Frozen section analysis is the established modality to diagnose breast cancer metastasis to sentinel lymph node(s) (SLN). Studies using ultrasound imaging of axillary lymph nodes to predict metastasis opens the possibility of alternative diagnostic modalities to frozen section.

Objectives

To use intra-operative digital specimen radiography of SLN to predict breast cancer metastasis to the SLN.

Methods

After Institutional Review Board (IRB) approval, the Biopics, pkXray 100, digital specimen radiography system was used to intra-operatively image the SLN of thirty consecutive women. This was performed prior to delivery of the SLN to the pathology suite. The digital specimen radiography interpretation was then compared to final histopathology. For each SLN imaged, the following three data points were defined and recorded: size (long axis in cm.), shape (short axis to long axis ratio), and texture (cortical thickness to diameter ratio). A histological blinded one, two or three point score was then assigned to each of the three parameters with the calculation of an overall mean and standard deviation. A total image score of three to nine points was assigned to each SLN evaluated. The Mann-Whitney U Test was used to calculate statistical significance.

Results

Thirty consecutive clinically node negative patient’s SLN specimens were imaged. All women had a biopsy proven pre-operative diagnosis of breast cancer. This cohort of thirty patients yielded 35 retrieved SLN. 4/35 (11.4%) SLN contained axillary metastatic disease on H&E pathologic evaluation and an additional two nodes (5.7%) were IHC positive for micrometastasis. Of the 35 SLNs sent to pathology, four nodes (11.4%) contained metastatic disease on H&E pathologic evaluation and an additional two nodes (5.7%) were IHC positive for micrometastasis. Frozen section evaluation identified only three of the four H&E positive SLNs (sensitivity 75%, specificity 100%).

Conclusions

• Specimen radiography is non-inferior in assessing breast cancer metastasis to the axilla and allows for detection of morphological changes in axillary lymph nodes.
• Lymph node shape and texture are more specific morphologic manifestations of axillary lymph node response to breast cancer metastasis.
• The radiographic changes seen in SLNs can be used to predict axillary metastatic disease. The nine point scoring system is based on a mean and standard deviation and is a simple, accurate and reproducible method to make predictions of axillary status.

References


Background

Advancements in technology have produced portable digital imaging machines which can be located in the operating room and provide high quality images of resected breast specimen. Specimen radiography is currently used to assess adequacy of the resection in breast surgery. Radiographic evaluation of lymph nodes for metastatic disease relies on the premise that metastatic breast cancer alters lymph node morphology: histological axillary lymph nodes studies from breast cancer patients show both depletion and inversion of the T-cell to B-cell ratio which changes a lymph node shape from reniform to spherical. Depilation of lymphoid follicles in the cortex and hypocellularity of the paracortex was associated with a 32% and 47% incidence of lymph node invasion by breast cancer respectively.

This premise is already being used to predict breast cancer metastasis to axillary lymph nodes using ultrasound technology. Ultrasound lymph node morphology, specifically size, shape and consistency, have been found to have wide range of sensitivity of 36-95% and specificity of 46-100% in predicting metastatic axillary lymph node disease in various studies.

Methods

After Institutional Review Board (IRB) approval, the Biopics, pkXray 100 digital specimen radiography system was used to intra-operatively image specimens from axillary SLN biopsy procedures. All SLNs were subsequently underwent immediate pathological evaluation by frozen section, H&E and immunohistochemistry (IHC) to detect metastasis. The nine point scoring systemic is based on a mean and standard deviation which was  used to devise a score system. The American College of Surgeons Oncology Group Z0011, the current standard of care for management of a positive SLN is a Level I and II axillary lymph node dissection (ALND) in all patients, with inspection of level III.

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• The current standard of care for management of a positive SLN is a Level I and II axillary lymph node dissection (ALND) in all patients, with inspection of level III.
• The American College of Surgeons Oncology Group Z0011, phase 3 trial showed unchanged survival with SLN biopsy alone vs. ALND in patients with metastatic breast cancer burden.
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Conclusions:

• Thirty-five SLNs were imaged from axillary SLN biopsy procedures performed on clinically node negative patients. The patients had an mean age of 71 with a biopsy proven pre-operative diagnosis of invasive ductal carcinoma in 76.2%, invasive lobular carcinoma in 19.5% and invasive colloid carcinoma in 4.8%. The mean tumor size was 2.5 cm. 61.9% of patients were treated with partial and 38.1% total mastectomy. Of the 35 SLNs sent to pathology, four nodes (11.4%) contained metastatic disease on H&E pathologic evaluation and an additional two nodes (5.7%) were IHC positive for micrometastasis. Frozen section evaluation identified only three of the four H&E positive SLNs (sensitivity 75%, specificity 100%).

When compared using final H&E pathology, positive SLNs were statistically different (p = 0.05) than histologically negative SLNs, based on radiographic parameters of size, shape and texture. All three radiographic parameters (size, shape and texture) became statistically significant when SLNs were compared using H&E and IHC diagnosed micrometastasis (p = 0.03, 0.05, 0.63).

Lastly a histological blinded assignment of total points of each of the three combined imaging parameters was calculated for each SLN. An image score of ≥ 7 had a 100% sensitivity for predicting SLN metastasis vs. < 7% sensitivity by frozen section evaluation, when compared to only permanent H&E histopathology. When IHC micrometastasis were added to the overall analysis, the sensitivity of the SLN image score remained at 100%, while specificity dropped to 50% for frozen section interpretation.

References: