Reviewer’s report

Title: PRE-OPERATIVE AND INTRA-OPERATIVE DETECTION OF AXILLARY LYMPH NODE METASTASES IN 108 PATIENTS WITH INVASIVE LOBULAR BREAST CANCER UNDERGOING MASTECTOMY

Version: 1 Date: 25 Aug 2017

Reviewer: Albert Chao

Reviewer’s report:

The authors submit a revision of a previously submitted manuscript evaluating the utility of axillary ultrasound (AUS), ultrasound-guided fine-needle aspiration biopsy (US-FNAB), and intra-operative imprint cytology (IIC) in predicting patients with invasive lobular carcinoma (ILC) who will require axillary lymph node dissection (ALND), in the hope of being able to perform ALND at the same time as the index operation, rather than at a separate operation. The authors find that use of AUS, US-FNAB, and/or IIC allowed surgeons to perform ALND during the mastectomy procedure in 20/46 (43%) patients with lymph node metastasis. The authors conclude that "pre operative AUS, US-FNAB, and/or IIC are/is beneficial in patients with ILC planned for mastectomy in order to decrease the number of two stage axillary procedures."

The authors should be commended on their analysis of their institutional experience.

I would offer the following prior to consideration for publication:

- The overall rate of identifying ILC patients who would require ALND was 43% in this study. This seems relatively low. However, the authors' approach could potentially be justified with further analysis. First, it would be helpful if the authors' could compare their finding with the rate of identifying patients who require ALND using other commonly used approaches as a control (e.g., intraoperative SLN frozen section only). Ideally, the most meaningful comparison is if the authors had a separate cohort at their institution who were not part of their algorithm to compare to, or alternatively by comparing it with figures in the literature. Second, if possible, it might be helpful if the authors could provide a cost-analysis, as identifying 43% of patients who require ALND must be considered in the context of what it would cost to perform AUS/US-FNAB/IIC in 100% of patients, versus the cost savings associated with avoiding a second operation in 43% of patients.

- It would be helpful to clarify the flow chart figure. First, including percentages as well as "n" would be helpful. Second, it would be helpful to separately present the outcomes of patients who did not undergo IIC, and those who did undergo IIC but had a negative result, rather than combining them.
- The authors' approach had varying sensitivities and specificities depending on factors such as tumor stage. It would be helpful if the authors discuss whether they feel their approach, based on their results, should be used in all cases, or just select cases.

- It would be helpful for the authors to state the false-positive and false-negative rates of their approach.

- It would be helpful if the authors elaborated on what factors led surgeons to elect to perform IIC in some patients but not others. Furthermore, it would be helpful for the authors to discuss whether this may potentially act as a confounding factor (selection bias)?

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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