

Peer Review File

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Reviewer Comments

In times of Covid-19 pandemic your manuscript is relevant for the management of patients with early stage breast cancer. However, some data may be confusing for readers. In order to facilitate a better understanding of the manuscript, I would suggest to clarify some aspects, listed below by line number:

Comment 1- - 80-81. The aim of the study is clear but the hypothesis is missing. Why superparamagnetic iron oxide could be an alternative tracer in SLNB?

Reply1- Agree we have added the hypothesis into line 81-2

Changes in Text-

We hypothesize that Magtrace® localisation is as effective as blue dye in the identification of the sentinel node.

Comment 2- “41% of patients had a mastectomy and sentinel node”. Previously, in the same paragraph you explained patient selection in absolute numbers. Maybe, both data (in absolute terms and percentage) would help to a better knowledge.

Reply We have added absolute numbers as well as percentages to line 113.

Changes in text

41 patients (41%) had a mastectomy and sentinel node with 3 (3%) having a skin sparing mastectomy and immediate reconstruction

Comment 3- Could you detail the conservative surgery technique used in the 54% of patients? You state that other 4% underwent conservative surgery, this data looks confusing.

Reply- We have amended to include the type of conservative technique in line 116-118

Changes in text-

Of the remainder, 5 patients (5%) had a central segmentectomy and 54 patients (54%) had breast conserving surgery with 13 Level 2 therapeutic mammoplasty and 41 level 1 wide local excisions

Comment 4 Are these 6 patients with DCIS and mastectomy included in the 41% of patients you previously reported? Please explain this data.

Reply

These 6 patients are included in the previous mastectomy numbers as part of the 41 patients total for mastectomy. We have amended line 119 to clarify.

Changes in text-Of the 41 mastectomies performed 6 were for DCIS and 35 for invasive disease

Comment 5- 119-120. When you present the results according to histological subtype, please specify which subgroup of patients are you referring; patients with conservative surgery, mastectomy or both. Probably a flow diagram could help to better understanding.

Reply

I have included a flow chart to better represent this instead of a table

Comment 6 -135. "25 % were node positive". It is unclear were these results come from

Reply We have clarified this as 25% of all SLN

Changes in text

On average, 2.2 nodes were sampled at time of sentinel node biopsy and 25% of all SNBs were node positive (25 patients).

Comment 7- 137-138. You mentioned that basal phenotype was associated with 25% of those positive on sentinel node. Is this association statistically significant? And with histological subtype? These characteristics have not previously been referred in the text.

Reply The histological subtypes are demonstrated in the flow chart and I have addressed the basal phenotype statistic. P value is not significant due to small sample size of positive slns.

Changes in text 138-142 A basal phenotype, ie Grade 3 Infiltrating Ductal carcinoma which was triple negative, was associated with 25% of those positive on sentinel node. Given the incidence of Triple negative breast cancers as 15% of all breast cancers (5) this would correlate with our findings of TNBCs as a more

Comment 8 There were no reported adverse reaction to the combined tracers". Further on, in discussion (line 164-166) you write that you find skin staining as an issue, but "this isn't an endpoint during the study". Please clarify this information aggressive tumour subtype (See Table 2).

Reply I have changed this to significant unexpected adverse reactions as staining from blue dye and tracer would be expected. We did not routinely record the skin staining so have no data on incidence.

Comment 9 - 160. Magseed® was used in 22% of cases and in 41% of breast conserving surgery (you reported 40% before). What happened to the 11 patients in which the Sienna® radiotracer was used? Is there any difference in the ability to detect sentinel node between both tracers or between breast conserving surgery or mastectomy?

Reply

Apologies yes it was 40% I have changed this in line 166.

We have addressed the Sienna patient is line 161-2 and that the blue dye failed to localize in 4 out of 5 patients having a mastectomy. This correlates with the data on the larger tumour size in the positive node group, Line126, 132-3

Changes in text

We used a Magseed[®] in 22% of cases and in 40% of breast conserving surgery.

Of the 11 patients where Sienna was used as a tracer they all demonstrated nodes positive for blue dye and tracer. Given the small sample size of this cohort a p value of significance is not possible.

Comment 10- Table 1: Abbreviations should appear at the foot of the table.

Reply This table has been replaced with a flow chart as suggested.

Comment 11 - Graph 1. These results seem confusing. You must specify which variable the Y-axis refers to. As before, abbreviations should appear at the foot of the table for a better understanding.

Reply

I have added axis to explain the variables and a title at the bottom of the images.

Comment 12- You conclude that the use of SMIO is a safe and reliable technique to detect sentinel node. Apparently, the combined technique increases the capacity to detect sentinel node but it is not clear if this benefit is present in all patients. You don't mention it in the discussion.

Reply

I believe we have addressed the 3% improvement in localization with the SMIO technique in the discussion Line 155-56

Comment 13 On the other hand, references must be cited following the order of the text and at least one reference is cited wrongly.

Reply

I have adjusted the references into a more fluent order.