Author's response to reviews

Title: Magnetic resonance imaging-radioguided occult lesion localization (ROLL) in breast cancer using Tc-99m macro-aggregated albumin and distilled water control

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Author's response to reviews: see over
Dear editorial board of BMC Medical Imaging:

Enclosed, please find the revised manuscript: “Magnetic resonance imaging-radioguided occult lesion localization in breast cancer using Tc-99m macroaggregated albumin and distilled water control”, by Fernanda Pereira et al., to be submitted as an original research article to the journal BMC Medical Imaging. All co-authors have seen the contents of the manuscript and support the data. We do not have any conflicts of interest to declare. We certify that this submission is not under review at any other publication.

In this manuscript, we report a technique used to perform magnetic resonance imaging-radioguided occult lesion localization, a procedure that was recently presented in the literature and that requires further study. We also describe our initial results obtained using this technique.

We believe that our manuscript could be of interest to the readers of BMC Medical Imaging because it describes a new technique useful for diagnosing breast cancers that can only be observed by magnetic resonance imaging (MRI), the use of which is increasing. To the best of our knowledge, there is only one study in the literature describing the use of radioactive substances in MRI-guided localization using a different technique than the one described here. Radio-guided localization allows a better surgical outcome compared to wire localization; however, it has been mainly used for mammography and ultrasonography, not for MRI.

Next, point-by-point response to the reviewers concerns:

First reviewer

1) The authors should refer how do they know that the lesion discovered by MRI was exactly excised. It is a pivotal surrogate to estimate the predictive capacity of the new method. - The rate of exactly excised lesions was evaluated by 6-month’s
postoperative MRI, as you can see in the revised manuscript.

2) By the way, it should be worthy to discriminate the parameters employed for the estimation, explaining a, b, c and d values used in the 2x2 table, because the statistical method is not well explained - Sorry, even after extensive research we did not find out exactly what the reviewer suggested for this table, mainly what are the parameters to be employed. Based on the data about 2x2 table in the literature, we decided to add the table 4. But we are ready to modify things that are found to be relevant.

3) In my opinion the casuistic is too small and it is very difficult to obtain conclusions with this size of sample of patients - We agree with the reviewer about the casuistic. However, the small casuistic can be justified, because it is a new method with an initial sample and good preliminary results.

4) Quality of written English: Not suitable for publication unless extensively edited – The manuscript English was edited by a native-English speaker with scientific expertise.

**Second reviewer**

1) First of all: how did the Authors evaluate the correct position of the tip of the needle respect to the target-lesion before injection of radioactive substance? In particular in the 8 lesions presenting as NMLE? - The needle is evident as a low-signal intensity structure with adjacent susceptibility artifact and the lesion as an enhancing high-signal structure in T1-weighted sequence. The distance between the tip of the needle and the edge of the lesion was measured and the optimal position for the tip of the needle is inside the lesion.

2) The second unclear point is the following: all 16 procedures were defined accurate
by the Authors' (see Abstract and Conclusions, first paragraph). They evaluated if there was a concordance between MRI findings and histologic results at surgical specimens. If we look at the Tables 1 and 2: a “mass with oval shape, smooth margins and type 2 curve” was considered concordant with an histologic diagnosis of 7 mm IDC grade 1 in Table 1 and with a 6 mm fibroadenoma with atypia in Table 2. The same MRI finding may be considered concordant with two very different histopathologic results (B5b and B3 lesion)? - The reviewer is correct. We should have explained this better: the concordance between MRI findings and histologic results on surgical specimens is important for benign and high-risk lesions. For malignant lesions the concordance is not necessary. For this malignant lesion with benign features the concordance shows that it is a false negative.

3) In the last paragraph of the Results there is confusion between number of lesions and number of patients and also confusion between tip of the wire and tip of the needle - It was corrected in the revised manuscript.

4) Also, a comment regarding the economic aspect of pre-operative localization with ROLL versus pre-operative wire localization could be useful to obtain a more complete discussion. - Thanks, we accepted your suggestion.

Sincerely yours,

Fernanda Pereira and Lea Fonseca on behalf of the authors