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Reviewer 1:
Comment to ESPS 2015 00742046 In general, this is a well-documented article. Some comments are shown below. 1. Since the main goal of neoadjuvant chemotherapy is a shrinkage of relatively bulky-size tumor of breast cancer, the final extent of the disease is important, partly because of providing an adequate safe margin for tumor excision and partly because of avoidance of much more destructive surgery for the breast, which subsequently results in cosmetic problem and increased morbidity. Therefore, precise and accurate information is important. I suggest that authors might discuss the relationship between the image size and pathological size of the tumors. In addition, I highly recommend the following parameters might be better. One is the discrepancy between final pathological tumor size and diagnostic image tumor size. The other is a safe margin between the tumor and excisional cut end. 2. As shown by authors, biological markers might also act as confounding factors to influence the correlation between image tumor size and pathological tumor size. What is the authors' suggestion for these potential parameters. If the predictive rate should depend on many parameters, the value of any parameter might be limited. I personally preferred the image diagnostic value. 3. Finally, what is the authors' opinion for computed tomography-positron emission tomography? Since the authors tried to analyze the value of MRI, different modalities of MRI, and other imaging tools might be needed for the discussion.

Reviewer 1 - Thank you for these insightful comments.

We have added information on the actual size discrepancy seen between tumor size on MRI and surgical pathology, showing that discrepancies of 2 cm or more are less common in Her2+ and TN subtypes (see page 8 of attached manuscript).

In response to the question about the safe margin between the tumor and excisional cut, knowing if surgical margins are clear at the time of excision is a dilemma faced by every surgeon. We must clarify that the available data on MRI in the post-neoadjuvant chemotherapy shows correlations between tumor subtype, MRI phenotype, and pathologic tumor size. While these associations may be used in pre-operative decision making and counseling, whether or not they translate to fewer positive margins remains to be seen. This issue is complicated by the fact that an inaccurate MRI could result in fewer positive margins—for example, if an MRI overestimates disease and prompts a surgeon and patient to opt for mastectomy instead of breast conservation, that patient is likely to have negative margins. This has been seen in the adjuvant setting (Obdejin et al. Preoperative breast MRI can reduce the rate of tumor-positive resection margins and reoperations in patients undergoing breast conservation surgery. AJR 2013). For many surgeons, the real issue is predicting which MRI is a false negative, and when breast conservation can be achieved. The available data support the notion that false negatives are rare in Her2+, HR-, and triple negative patients, and if the MRI shows a small amount of disease, attempting breast conservation is likely safe. Outcomes including margin status and re-excision rates need to be addressed, but are beyond the scope of the current review.

Additionally, since the determination of a clear margin is done microscopically, we will need to depend on other available technology to give us real time information about whether or not the surgical margins are clear microscopically. A discussion about the technology available to determine margin status intra-operatively is not the current focus of this paper.

The interpretation of a post neoadjuvant chemotherapy MRI takes into consideration multiple factors, as suggested by the reviewer. All of the factors – MRI phenotype, chemotherapy regimen, and tumor subtype - must be taken into account. No one factor is necessarily more significant than another and as such, we make the recommendation for a tailored interpretation strategy. The reviewer suggests placing more weight on the diagnostic value of pre-operative imaging; the available data suggest that the amount of weight placed on this imaging may vary by tumor subtype and phenotype, as the accuracy of imaging is different in each of these groups.

In North American, PET-CT is used for systemic staging of breast cancer patients. It is not standard of care to use this modality to evaluate the breast itself. A sentence (with 7 references) has been added to the manuscript to describe MRI's superior accuracy in the neoadjuvant setting compared with mammography, ultrasound and physical examination (see page 4 of attached manuscript)

Reviewer 2:
The manuscript reviews the use of MRI following neo-adjuvant chemotherapy in advanced local breast cancer. Although well written, the manuscript would benefit from 1- The addition of Tables summarizing findings of the different research efforts (e.g., MRI-tumor phenotype; MRI-biomarker expression; MRI- residual tumor) 2- The MRI provided should be introduced in the context of the review i.e., highlighting the correlation / or not of MRI with clinical, pathological evidences 3- Additional references pertinent to the review should be considered (e.g, Tomida et al, 2014 Mol Clin Oncol. 2:783-788; Ooe et al, 2012. Breast Dis. 34:9-17.

Reviewer 2 – Thank you for these insightful comments.

While the suggestion of a table to summarize the findings of the various research efforts is well taken, a table was not created because we do not believe that the findings can be easily summarized into table form. The findings from these studies offer a framework by which to interpret an MRI in the setting of neoadjuvant chemotherapy, but by no means give an absolute method for interpreting every MRI. As we suggested in our paper, every MRI must be subjected to a tailored interpretation.

As suggested, references to the provided images have been inserted into the text of the manuscript (see pages 7 and 9 of attached manuscript).

Thank for bringing our attention to these two recently published papers. We agree the Tomida paper should be included as a reference in our discussion of responses to neoadjuvant chemotherapy differing by phenotypic appearances. This has been added (see page 6 of attached manuscript). As the study by Ooe et al does not focus on the assessment of outcome of neoadjuvant chemotherapy in different breast cancer subtypes, we believe it is outside the scope/focus of our manuscript.

Reviewer 3:
This review article is very nice and the reviewer could read it joyfully. However, it lacks two important articles in reference. Kim MJ et al. Acta Radiol 2014; Sep 16 pil: 0284185114548507 Parikh J et al. Radiology 2014; 272(2): 100-12. Please add them in the text and discuss again.

Reviewer 3 – Thank you for calling our attention to these 2 papers. Findings from the paper by Kim et al have been added to the manuscript (see pages 8 and 10 of attached manuscript).

While an interesting study, the paper by Parikh et al assesses overall tumor changes during neoadjuvant chemotherapy without distinguishing among the molecular subtypes. The focus of our manuscript is the impact of molecular subtype on MRI findings/interpretation, and therefore we believe the Parikh paper is outside the scope of our manuscript.

Reviewer 4:
How to evaluate the curative effect after breast cancer neoadjuvant chemotherapy ? The authors give us the methods. Deficiency in the relationship between the image size and pathological size of the tumors. And the lack of assessment standard, and other imaging tools might be needed for the discussion

Reviewer 4 – Thank you for these insightful comments
A sentence (with 7 references) has been added to the manuscript to describe MRI's superior accuracy in the neoadjuvant setting compared with mammography, ultrasound and physical examination (see page 4 of attached manuscript).

Reviewer 5:
This is well-designed review article. 1) Please provide the definition of subtype precisely, especially in HER2 positive subtype. 2) Following sentence,'Indiscriminate interpretations will prevent MRI from achieving its maximum potential in the pre-operative setting.' which was repeatedly used in the abstract and main-text should be revised.

Reviewer 5 – Thank you for these insightful comments

We are unclear on the request to define the Her2 positive subtype – standard of care is the assessment of Her2 as either positive or negative. We would be happy to re-address this question if we are misunderstanding. In addition to addressing the status of individual tumor receptors, the biomarkers can categorize tumors into different subtypes. Tumor subtypes include a luminal subtype (ER/PR positive Her2 negative), Her2 positive subtype, and basal subtype (ER/PR/Her2 negative). A sentence explaining this has been added (see page 7 of attached manuscript).

Thank you for pointing out this redundancy. The sentence has been removed from the Introduction and reworded in the Conclusion (see pages 5 and 11 of attached manuscript).