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Analysis of Factors that Influence the Accuracy of Magnetic Resonance Imaging for Predicting Response after Neoadjuvant Chemotherapy in Locally Advanced Breast Cancer
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Analysis of Factors that Influence the Accuracy of Magnetic Resonance Imaging for Predicting Response after Neoadjuvant Chemotherapy in Locally Advanced Breast Cancer

Neoadjuvant chemotherapy (NAC) has become an important treatment modality for patients diagnosed with locally advanced inoperable breast cancer, or patients with immediately operable cancer who will need some form of chemotherapy as part of treatments. Among all breast imaging modalities, MRI is proven as the most accurate to diagnose post-NAC residual tumor size. A correct evaluation of the extent of residual disease can provide very important information for planning of optimal surgeries and other subsequent treatment procedures. Furthermore, if a complete pathological response can be diagnosed with a high confidence, imaging may be used to select candidate patients who can be spared of surgery and only treated with prophylactic radiation alone.(1) NAC has become a popular treatment option for almost a decade now, and several large series studies to investigate factors influencing the accuracy of MRI were published very recently.(2-6) It was commonly reported that the accuracy of MRI is dependent on molecular biomarkers, cellular types, tumor grades, and tumor morphology patterns.

In this article, Ko and colleagues analyzed a single-site dataset of NAC patients enrolled between April 2007 and December 2010, with a total of 166 patients. The main findings were consistent with those reported in the literature, showing that the accuracy of MRI (defined as the difference

of residual tumor size measured in post-NAC MRI and in pathology) was significantly related to molecular subtype, nuclear grade, and tumor morphological pattern on MRI. Several sub-groups were defined in each category; and the significance is mainly driven by one sub-group. For molecular status, the mean tumor size difference was 8.0 mm in triple negative group, 10.1 mm in HER2-positive group, and 17.2 mm in ER-positive/HER2-negative group (significantly higher compared to the other two). For nuclear grade, the mean size difference was 28.5 mm for Grade-1 (significantly higher compared to the other two), 9.3 mm for Grade-2, and 11.8 mm for Grade-3. For MR morphological pattern, the mean tumor size difference is 7.2 mm for single mass, 9.1 mm for multiple mass, 22.0 mm for non-mass-like enhancement (significantly higher than the other three), and 4.7 mm for focal non-mass-like enhancement. For chemotherapy regimen, although not significant, the tumor size difference in HER2/Neu monoclonal antibody-based chemotherapy group (8.8 mm) is smaller than the size difference in the other regimen groups (12.8 to 16.9 mm). These results were highly consistent with another paper published very recently by Chen et al.,(2) also using a single-site NAC database to evaluate the impact of similar cellular, molecular, and morphological factors. In general, it is known that the accuracy of MRI is worse in tumors that are less likely to show a good response to chemotherapy (e.g. ER-positive/HER2-negative and low nuclear grade).

In terms of traditional diagnosis performance evaluating sensitivity, specificity and accuracy, there were 5 false negative diagnoses and 14 false positive diagnoses. The main reason for the false negative diagnosis is attributed to the very small residual tumor size, with a range of 3-9 mm and a mean of 6.6 mm. This result is a bit surprising- because several studies have reported that non-mass-like enhancement lesions that have tumors breaking up as scattered cells or cell

clusters is a major reason leading to a false negative diagnosis.(2, and references therein) In this series by Ko et al., 41 patients have relatively large tumors greater than 80 mm, but after NAC the mean size difference between MRI and pathology is only 7.6 mm. This highly accurate MRI diagnosis in relatively large tumors of > 8 cm is surprising; unfortunately this issue was not discussed. The measurement of residual tumor size in pathological examination will be greatly dependent on the effort of pathologists to meticulously examining the entire specimen thoroughly, especially in those cases that show minimal residual disease. It would help if the authors can explain or show more case examples to illustrate how they could achieve such a high accuracy in large tumors.

Among the 14 false positive cases, in fact 10 of them have residual DCIS; therefore MRI did correctly detect the residual disease and that was very important for surgical planning. In this article, the pathological complete response (pCR) was defined as no invasive cancer, which was mainly based on a study by Mazouni et al. showing residual DCIS does not adversely affect patient outcome.(7) However, a more recent study by von Minckwitz et al. analyzing a much larger NAC patient database (6,377 patients) report that when pCR is defined as no invasive and no in situ residuals in breast and nodes it can best discriminate between patients with favorable and unfavorable outcomes.(8) It was further recommended that patients with noninvasive DCIS should not be considered as having achieved pCR. If this new pCR definition was used, then there was only 4 false positive diagnoses in this series. Therefore, among their 166 patients, there were only 5 false negative and 4 false positive diagnoses, with an overall accuracy of 95%- this seemed to be too good to be true.

The impact of leaving residual cancer cells behind in the breast (without surgically removing them) on the prognosis of patients has yet to be determined. Until it is proven that leaving the minimum residual disease in the breast will not increase the risk of recurrence or metastasis, a rigorous evaluation of the limitation of MRI (or other breast imaging modalities) to detect any residual disease based on a thorough pathological examination result as the reference is needed for surgical planning, as well as for guiding personally tailored treatment strategies following NAC.

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References

1. Ring A, Webb A, Ashley S, et al. Is surgery necessary after complete clinical remission following neoadjuvant chemotherapy for early breast cancer? *J Clin Oncol.* 2003;21(24):4540-5.
2. Chen JH, Bahri S, Mehta RS, et al. Impact of factors affecting the residual tumor size diagnosed by MRI following neoadjuvant chemotherapy in comparison to pathology. *J Surg Oncol.* 2013 Oct 28. doi: 10.1002/jso.23470. [Epub ahead of print]
3. De Los Santos JF, Cantor A, Amos KD, et al. Magnetic resonance imaging as a predictor of pathologic response in patients treated with neoadjuvant systemic treatment for operable breast cancer. *Translational Breast Cancer Research Consortium trial 017. Cancer.* 2013 May 15;119(10):1776-1783.

4. Moon HG, Han W, Ahn SK, et al. Breast cancer molecular phenotype and the use of HER2-targeted agents influence the accuracy of breast MRI after neoadjuvant chemotherapy. *Ann Surg.* 2013 Jan;257(1):133-137.
5. Hayashi Y, Takei H, Nozu S, et al. Analysis of complete response by MRI following neoadjuvant chemotherapy predicts pathological tumor responses differently for molecular subtypes of breast cancer. *Oncol Lett.* 2013 Jan;5(1):83-89.
6. Cruz Ciria S, Jiménez Aragón F, García Mur C, Esteban Cuesta H, Gros Bañeres B. Magnetic resonance imaging in breast cancer treated with neoadjuvant chemotherapy: Radiologic-pathologic correlation of the response and disease-free survival depending on molecular subtype. *Radiologia.* 2013 Jan 4. pii: S0033-8338(12)00272-X. doi: 10.1016/j.rx.2012.10.004. [Epub ahead of print]
7. Mazouni C, Peintinger F, Wan-Kau S, et al. Residual ductal carcinoma in situ in patients with complete eradication of invasive breast cancer after neoadjuvant chemotherapy does not adversely affect patient outcome. *J Clin Oncol.* 2007 Jul 1;25(19):2650-2655.
8. von Minckwitz G, Untch M, Blohmer JU, et al. Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes. *J Clin Oncol.* 2012 May 20;30(15):1796-1804.