Impact of MRI-Evaluated Neoadjuvant Chemotherapy Response on Change of Surgical Recommendation in Breast Cancer

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Purpose:

The traditional role of neoadjuvant chemotherapy (NAC) has been to downstage breast cancer, render inoperable tumor operable, and facilitate breast conservation surgery for operable tumors. As more effective therapies have become available, and evidence has shown that a better prognosis is anticipated when a patient achieves pCR (pathological complete response), the role of neoadjuvant chemotherapy has gone beyond down-staging with a more far-reaching purpose of reaching pCR. Consequently, many locally advanced tumors have been treated to achieve minimal disease or pCR. One question arising with this trend is which definitive surgical procedure to use following a response to NAC. Pre-treatment advanced disease may require mastectomy, but subsequent minimal residual disease or pCR after treatment may qualify the patient for conservation surgery, or even a minimum excision. In a clinical setting, the recommendation of the surgeon is important. In this study, we investigated how the NAC response, as determined by MRI, affects the surgeon's recommendation for the definitive surgery. Using the pre-treatment disease extent shown on MRI before NAC, we first analyzed the determinant factors used for recommendation of mastectomy vs. lumpectomy, and then analyzed whether the NAC response changed the surgical recommendation. Lastly, we also evaluated whether the recommendation would have changed, had the surgeon known the final pathological findings following NAC.

Methods:

Seventy-six breast cancer patients (30-77 years old, median 49) undergoing NAC were analyzed. Every patient received a pre-treatment MRI scan, then 3-4 follow-up (F/U) scans during the course of NAC. The treatment protocol consisted of 2-4 cycles of bi-weekly AC (doxorubicin and cyclophosphamide) with growth factor support, followed by Taxane regimen (TCa ± H), including paclitaxel or Nab-paclitaxel (Abraxane) and Carboplatin, with Trastuzumab (Herceptin) for Her-2 positive patients. Some Her-2 negative patients also received Bevacizumab (Avastin) in the Taxane regimen. Two experienced breast surgeons reviewed all cases. The contrast enhanced images and the Maximum Intensity Projection (MIP) were generated for all MRI studies done for each patient. First, the pre-treatment disease extent, including slice-by-slice enhancement maps and the MIP, was presented to surgeons and an initial surgical recommendation was made. Then the response of the tumor to NAC was determined by sequentially showing all follow-up MRI findings. The surgeons evaluated the overall response and extent of residual disease, and made a post-treatment surgical recommendation based on these MRI findings. Finally, the pathological results were disclosed and the surgeons were asked to decide whether they would change their post-NAC surgical recommendation had they known the pathology. This part of the analysis was designed to investigate how confident the surgeons were in trusting MRI-evaluated responses to make appropriate surgical recommendations.

Results:

Before NAC, consensus recommendations were mastectomy for 49 patients and lumpectomy for 23 patients, while discordant recommendations existed between two surgeons for 4 patients. The large disease extent was the main determinant factor for mastectomy. The mean tumor size was 4.4 ± 2.7 cm in the mastectomy group and 2.6 ± 1.3 cm in the lumpectomy group ($p = 0.0001$). Other mentioned factors also include lobular cancer type (N=11), multiple lesions (N=9), small breast (N=5), tumor location (N=5), recurrent tumor (N=3), and diffuse lesion (N=2). After NAC, consensus recommendations were mastectomy for 22 patients and lumpectomy for 46 patients, with discordant recommendations between two surgeons involving 6 patients. No recommendations were made for 2 patients due to insufficient findings by MRI. Based on consensus recommendation, 22 mastectomy candidates remained as mastectomy, with pre-treatment tumor size 5.6 ± 3.2 cm with NAC size reduction of 70% ± 36%. The recommendations of twenty mastectomy candidates were changed to lumpectomy. They had a smaller pre-treatment size of 3.6 ± 1.9 cm ($p=0.02$) and a greater NAC size reduction of 88% ± 22% ($p=0.03$). The tumor size and NAC induced shrinkage in these 3 groups are summarized in Table 1. When the final pathological result was disclosed, the finding of pCR or minimal residual disease resulted in the surgeons changing their recommendation from mastectomy to lumpectomy. Among those 22 patients with consensus post-NAC mastectomy recommendation, both surgeons agreed to change to lumpectomy for 5 patients, and had discordant opinion for 2 patients. Yet, when comparing the patient's actual choice of surgical procedure to that recommended by the surgeon, only 56% were consistent with the recommendation. 67% patients in M->M group chose mastectomy; 60% in M->L still chose mastectomy despite of their excellent response; and 64% in L->L group chose lumpectomy.

Table 1: Tumor size and % reduction in 3 groups

	Pre-NAC* (cm)	Post-NAC (cm)	reduction
M -> M	5.6 ± 3.2	1.6 ± 2.5	70±36 %
M -> L	3.6 ± 1.9	0.3 ± 0.6	88±22 %
L -> L	2.6 ± 1.3	0.4 ± 0.6	84±26 %

*** pre-NAC size significantly different in 3 groups**

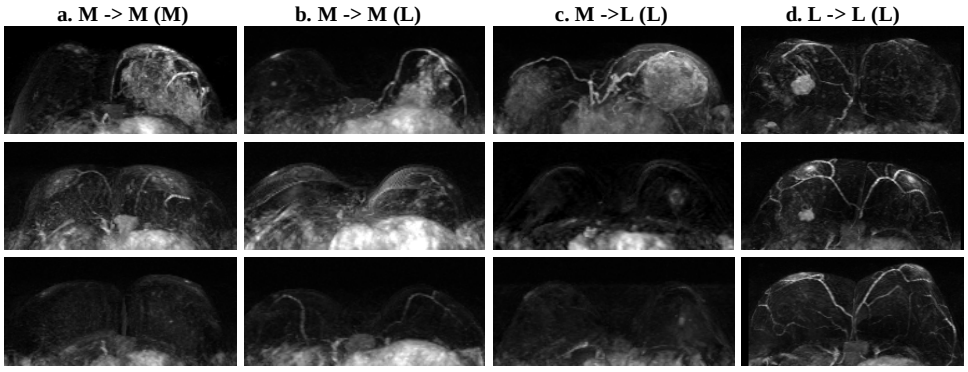

Fig.1: Four cases showing pre-, during, post-NAC MIP from top down. a: an inflammatory cancer for M. b: pre- and post-NAC recommendation for M, but the pCR would change recommendation to L. c: pre-NAC M but post-NAC changed to L. D: pre- & post-NAC for L.

Discussion:

The results indicate that in patients with more extensive pre-treatment disease, surgeons may still apply an aggressive approach and recommend mastectomy, despite an excellent response to NAC. The reason may be due to not well-tested and validated imaging findings. However, this study finds that surgeons would change their surgical recommendation to a less aggressive conservation surgery with the confirmation of pCR or minimal residual disease. As the use of MRI for NAC response prediction matures, such imaging studies are expected to enable breast surgeons to recommend conservation surgery more frequently and with greater confidence. Nevertheless, many patients still consider their own personal preferences and choose a surgery that is not consistent with the surgeon's recommendation. This is especially true in the mastectomy to lumpectomy good response group, where only 40% of patients chose their surgeon's recommendation for lumpectomy, regardless of their excellent NAC response. As the value of MRI becomes more established and the prognosis data becomes available, patients may be more willing to accept less aggressive surgery. For patients with advanced disease receiving NAC, the question of whether the definitive surgery should be based on pre-treatment or post-treatment staging, or both, needs to be further investigated. We hope to address this question as we continue to follow all of our enrolled patients, evaluating their prognosis for a disease-free outcome.

Acknowledgement: This work was supported in part by NIH/NCI CA90437 and California BCRP # 9WB-0020.