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

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INTRODUCTION

Breast cancer is the most commonly diagnosed cancer in women, and nearly all will receive some form of surgery as one treatment component. For early-stage breast cancer, several large randomized trials have demonstrated a comparable clinical outcome for mastectomy and breast conservation surgery (BCS) followed by radiation.^{1,2} The choice between BCS and mastectomy depends on numerous factors, including tumor size, location, histology, grade, the ratio of tumor size to breast volume, and the multi-focality or multi-centricity of the tumor.^{3,4}

For locally advanced breast cancer, neoadjuvant chemotherapy (NAC) is the standard of care used to downstage the tumor prior to surgery. Patients who received NAC first, followed by surgery, were found to have an equivalent prognosis compared to those receiving surgery first, followed by adjuvant chemotherapy. Patients with operable cancer may also choose to receive NAC to facilitate breast conservation surgery.^{5,6} Recommendations and guidelines based on the results of large series trials for such patients have been published.^{7–10} As more effective therapies have become available, the goal of NAC has changed from down-staging the tumor to achieving a pathological complete response (pCR). Emerging evidence suggests that induction of a pCR, or minimal residual tumor burden, is predictive of a favorable long-term survival.^{6,11,12} With newer chemotherapy regimens, even large, locally advanced tumors can be treated to achieve pCR or minimal residual disease.

The increasing ability to achieve a pCR with neoadjuvant therapy highlights the question of whether to recommend a less aggressive surgical procedure on the basis of NAC response. Depending on the extent of residual disease, a lumpectomy may be performed, provided a negative margin can be achieved.^{7–10} Based on the finding that BCS with radiation has an equivalent outcome compared to mastectomy, NAC patients presenting with locally advanced disease may be excellent candidates for the BCS. For patients who have achieved pCR, a lumpectomy confirming no residual cancer might be sufficient.

Research evidence has suggested that BCS after NAC results in acceptable low rates of locoregional or ipsilateral recurrence in appropriately selected patients, even in those with T3/

T4 or multi-focal/multi-centric cancers.^{13–15} Factors that predict early recurrence include residual pathologic tumor size > 2 cm, multifocal tumor, and lymphovascular invasion.¹⁶ Therefore, an accurate pre- and post-NAC disease staging is critical for selecting patients suitable for BCS without a high risk of local recurrence. MRI has been proven superior to physical examination, sonography, and mammography for the assessment of tumor response following NAC. As a result, MRI may serve as an optimal imaging modality to aid in the selection of suitable BCS candidates.^{17, 18}

In the clinical setting, the two most important factors in determining the surgical procedure are the surgeon's recommendation and the patient's personal preference.^{19, 20} This study is designed to evaluate how the presentation of the lesion on MRI and the response following neoadjuvant chemotherapy influence the type of surgery recommended by the surgeon. Three questions are addressed: 1) how does the MRI presentation of the pre-treatment lesion influence the initial pre-NAC surgical recommendation, 2) will a good NAC response, as evaluated by MRI, change the surgical recommendation after NAC, and 3) after NAC, what type of pathological findings allow surgeons to feel comfortable recommending breast conservation surgery (BCS) versus mastectomy? Understanding how MRI findings are incorporated into the decision-making process of surgeons will help establish appropriate guidelines for recommending BCS after NAC based on the MRI results.

MATERIALS AND METHODS

Patient Characteristics

In a period of 4 years (2003–2007), 76 patients with biopsy-proven breast cancer undergoing NAC were included in this study. The age range was 30–77 years old, with a mean age of 49. The cancer types included 70 invasive ductal carcinomas (IDC), 4 infiltrating lobular cancers (ILC), one mixed IDC/ILC, and one micro-papillary cancer. The tumor T staging according to the American Joint Committee on Cancer (AJCC) included T1 (N=7), T2 (N=43), T3 (N=21), and T4 (N=5). The pre-treatment tumor size (longest dimension) ranged from 0.7 to 21 cm, and mean $\pm$ standard deviation of 4.8 ± 3.2 cm. This study was approved by the Institutional Review Board and was HIPAA-compliant. All patients gave written informed consent to participate in the MRI response monitoring study, and gave a separate consent if they chose to receive the NAC protocol offered at our institute.

Treatment Protocol

Most patients received the research treatment protocol offered at our institute, starting with bi-weekly Adriamycin (Doxorubicin) and Cyclophosphamide (AC) with growth factor support as the first-line regimen. After the first two cycles, the oncologist evaluated the patient's response and tolerance, and decided whether the patient should continue to receive 2 additional cycles of AC, or be switched to the second-line taxane-based regimen. The taxane regimen consisted of Paclitaxel or Nab-paclitaxel (Abraxane®), combined with Carboplatin. HER-2-positive patients also received trastuzumab (Herceptin®) with taxane. Some HER-2-negative patients received bevacizumab (Avastin®) with taxane. Several early patients received the standard treatment protocol, including 4 cycles of AC every 3 weeks, followed by Paclitaxel without Carboplatin, Herceptin, or Avastin.

All patients had serial breast MRI exams: pre-treatment baseline MRI, at least 2 follow-up studies during the course of therapy, and a final MRI after completing the therapy protocol. Following NAC, a definitive surgery was performed. 44 patients received mastectomy and 32 patients received lumpectomy. Table 1 summarizes the clinical information and the imaging and pathological findings of all patients.

MRI Studies

The MRI study was performed using a 1.5 T MR scanner with a 4-channel phased-array bilateral breast coil (Philips Medical Systems, Cleveland, Ohio). The imaging protocol consisted of pre-contrast T1 weighted imaging and bilateral dynamic contrast-enhanced imaging using a 3D SPGR (RF-FAST) pulse sequence. Thirty-two axial images with 4 mm slice thickness were used. The scan time was 42 sec per acquisition. The sequence was repeated 16 times for dynamic acquisitions, four pre-contrast, and 12 post-contrast frames. The contrast agent (Omniscan®, 0.1 mmol/kg body weight) was manually injected at the beginning of the 5th acquisition, followed by 10 cc saline to flush in all contrast medium.

After the dynamic scan was completed, subtraction images were generated by subtracting the pre-contrast images acquired in Frame #3 from the contrast-enhanced images acquired in Frame #6. Lesion morphology was described according to ACR BI-RADS MRI lexicon as mass lesion or non-mass type lesion.²¹ In pre-NAC baseline MRI study, 54 patients presented as mass type lesions (including circumscribed solitary mass and multiple mass lesions), and 22 patients presented as non-mass type lesions that showed contrast enhancements on MRI without clearly defined tumor boundary.

Tumor Size Measurement on MRI

For each patient, all serial MRI studies (pre-treatment and all follow-up) were analyzed in one sitting to ensure consistent determination of the tumor boundary. The detailed tumor size measurement procedures and tumor response evaluation have been published previously.²² One radiologist (JHC), with three years of experience on breast MRI, performed the size measurement. The maximum intensity projections (MIPs) were generated from the subtraction images for size measurements (as shown in Figure 1). When the enhancement was low on MIP, the corresponding color-enhanced subtraction images were used. Two lines (the longest dimension and the longest perpendicular dimension) were drawn to obtain the 2-dimensional sizes based on the WHO criteria. The 2-dimensional measurements were particularly important to evaluate the change in size of non-mass lesions because the longest dimension may be subject to change, depending on the positioning of the breast in the MRI coil. However, since the RECIST criteria were the most commonly used, we also reported the longest dimension of the lesion before treatment, and so our patient cohort can be compared to others in the literature. For evaluating the size response, the 2-dimensional sizes were converted to a one-dimensional size (by calculating the square root of their product) to calculate the percent reduction after completing NAC. Of the 76 patients, 35 patients had clinical complete response (CCR), 38 had partial response (PR) with size reduction $\geq 30\%$, and 3 patients had stable disease (SD) with a size reduction $< 30\%$.

Pathological Examination

The surgical specimen was cut into 5mm slices, fixed in 10% neutral buffered formalin and processed for histological examination using hematoxylin and eosin (H&E) staining. Since patients with only residual DCIS (ductal carcinoma in-situ) were found to have a similar prognosis to patients without any residual malignancy;²³ it is widely accepted that residual DCIS after completing NAC is considered as pCR. However, residual DCIS still needs to be completely resected at surgery. Therefore, in this study it was reported as a separate category. Of all 76 patients, 21 patients achieved complete pathologic response without any residual malignancy, 7 patients had only residual DCIS, and 48 patients had residual invasive cancer.

Recommendation of Surgical Procedures Based on MRI Findings

In a retrospective review session, two experienced breast surgeons (JAB and DJH) reviewed the MRI of all patients, and made recommendations for surgical procedures based solely on

the MRI findings. They were accompanied by one radiologist and one breast MR imaging scientist who described the findings. The Maximum Intensity Projection (MIP) images and color-coded contrast-enhanced subtraction images of each patient were presented to the surgeons. First, the pre-NAC study was shown, and the surgeons were asked to make a recommendation of mastectomy or lumpectomy. If mastectomy was recommended, they were asked about the major reason(s) for their decision, including tumor size, extent, location, tumor multiplicity, tumor to breast volume ratio, and pathological tumor type.

Following the pre-NAC evaluation, all follow-up MRI studies were presented sequentially in order to establish the pattern of gradual response. Based on the extent of residual disease on the final MRI, the surgeons were asked to make a post-NAC recommendation of mastectomy or lumpectomy. According to the pre- and post-NAC recommendations, the patients were separated into three groups: $M \rightarrow M$ (mastectomy pre-NAC and post-NAC), $M \rightarrow L$ (mastectomy pre-NAC, and changed to lumpectomy post-NAC), $L \rightarrow L$ (lumpectomy pre-NAC and post-NAC). Please note that lumpectomy includes segmentectomy and quadrantectomy. The surgical recommendations were made by each surgeon independently and the results were analyzed separately. Only the consensus cases were used in the statistical analysis.

Lastly, the surgeons were given the pathology results and asked to retrospectively decide the most appropriate surgical procedure. For cases in which the most appropriate surgical procedure based on pathology was different from that based on MRI findings, the imaging and pathology findings were reviewed to determine the reason for the discrepancy.

Statistical Analysis

The tumor size, both pre-and post-NAC, and the percentage change in tumor size induced by NAC were compared among three groups: $M \rightarrow M$, $M \rightarrow L$, and $L \rightarrow L$. Two-tailed student t-test was used, and $P < 0.05$ was considered significant.

RESULTS

Surgical Recommendations before NAC

Table 2 summarizes the number of cases for each surgical procedure and also within each of the three groups ($M \rightarrow M$, $M \rightarrow L$, and $L \rightarrow L$). Before NAC, surgeon-1 recommended mastectomy in 52 patients and lumpectomy in 24 patients; surgeon-2 recommended mastectomy in 53 patients and lumpectomy in 23 patients. Consensus recommendations were mastectomy for 51 patients, lumpectomy for 22 patients, and discordant recommendations for 3 patients.

A large tumor size was the primary determining factor for recommending mastectomy. The mean tumor size in the mastectomy group was 5.3 ± 3.4 cm (longest dimension based on RECIST criteria) or 4.5 ± 2.6 cm (equivalent 1-dimension size based on WHO criteria). The tumor size in the lumpectomy group was 3.2 ± 1.6 cm (longest dimension based on RECIST criteria) or 2.6 ± 1.3 cm (equivalent 1-dimension size based on WHO criteria), which was significantly smaller with $P = 0.0001$. Other factors leading to a mastectomy recommendation included: cancer type (ILC, mixed, and inflammatory cancers) ($N=10$), multiple lesions ($N=9$), tumor location ($N=5$), small breast size ($N=5$), recurrent tumor ($N=3$), and diffuse lesion ($N=2$). These factors were mentioned by the surgeons, and not included in the statistical analysis of this study. Mastectomy recommendation for one patient may be due to multiple reasons.

Surgical Recommendations after NAC

After the NAC, results were available for only 74 of 76 patients. A surgical recommendation could not be made for 2 patients due to insufficient findings on MRI. As shown in Table 2, the

consensus recommendations were mastectomy for 21 patients and lumpectomy for 44 patients, with 9 discordant recommendations between the two surgeons. Of the 44 lumpectomy recommendations post-NAC, the pre-NAC recommendations were 22 mastectomy (M→L), and 22 lumpectomy (L→L).

The mean tumor size of consensus cases in each of the 3 different groups is listed in Table 3. In the M→M group, 21 mastectomy candidates who remained as mastectomy had a pre-treatment tumor size of 5.8 ± 3.2 cm (RECIST, 7.4 ± 4.5 cm), post-treatment tumor size of 1.5 ± 2.5 cm, with a NAC size reduction of $74 \pm 33\%$. All 4 patients with lobular cancer were in this group. In the M→L group, 22 mastectomy candidates were changed to lumpectomy after NAC. Compared to the M→M group, the M→L group had a smaller pre-treatment tumor size of 3.5 ± 1.7 cm (RECIST, 4.2 ± 2.1 cm) ($p = 0.01$), smaller post-treatment tumor size of 0.4 ± 0.6 cm, and a greater NAC size reduction of $87 \pm 22\%$. In the L→L group, 22 lumpectomy candidates remained as such after NAC. Their pre-treatment tumor size was 2.6 ± 1.3 cm (RECIST, 3.2 ± 1.6 cm), with post-treatment tumor size of 0.4 ± 0.6 cm and NAC size reduction of $84 \pm 26\%$.

Surgical Recommendations after Disclosure of Pathological Findings

When the final pathological result was disclosed, the surgeons were asked to determine the most appropriate surgical procedure based on the pathological finding for each patient. In the M→M group, in which the surgeons recommended post-NAC mastectomy, the recommendation was revised to lumpectomy by: surgeon-1 in 7 cases (3 without any malignancy, 3 with only DCIS, and 1 with minimal invasive disease); and surgeon-2 in 10 cases (5 without any malignancy, 3 with only DCIS, and 2 with minimal invasive disease). The results suggest that the surgeons agree that BCS could be performed in patients achieving complete response or with minimal residual disease (residual invasive foci < 3 mm, or confined cancer cell clusters). In the M→L group, both surgeons would change 2 patients from lumpectomy to mastectomy due to the large extent of residual multi-focal disease with scattered cell clusters. Figure 1 demonstrates four representative cases: M→M; M→M but changed to lumpectomy due to pCR; M→L; and L→L. MIP images from pre-, during, and post-NAC studies are shown.

Comparison of Surgeon's Recommendation with Patient's Choice

Table 4 summarizes the final surgical procedures performed in each of the three different consensus groups (M→M, M→L, and L→L), from the 65 patients. When comparing the patient's actual choice of surgical procedure to that recommended by the surgeon, only 57% (37/65) were consistent with the recommendation. In the M→M group, the majority of patients 71% (15/21) chose mastectomy. In 6 lumpectomy patients, 1 had a positive margin. In the L→L group, the majority of patients 64% (14/22) chose lumpectomy, and 2 had positive margins. Interestingly in the M→L group with surgeons' recommendations changing from mastectomy to lumpectomy, only 36% (8/22) chose lumpectomy, and 2 had positive margins. The majority of patients 64% (14/22) still chose the original recommendation of mastectomy, despite of their excellent response to the NAC. The results seem to suggest that when an excellent NAC response was found, surgeons were more willing to accept BCS; whereas patients were more reluctant. The margin status of all lumpectomy patients is also listed in Table 4. The rate was higher in the M→L group (2/8, 25%) compared to that in the M→M group (1/6, 17%) and in the L→L group (2/14, 14%), but not significantly different.

DISCUSSION

NAC is a well-established treatment strategy for management of breast cancer. In recent years, NAC has become more widely used in operable cancer to facilitate BCS.^{7–10} Evidence has

suggested better survival outcomes in patients achieving pCR (or minimum residual cancer burden near pCR) at the time of definitive surgery after the NAC.^{6,11,12,23} With the established prognostic role of pCR and the applicability to operable cancer, the use of NAC for breast cancer treatment is expected to increase further.

Many factors may influence the decision that determines the optimal surgical procedure.^{1–6, 10,24–32} It has been consistently reported that the objective factors for a physician's recommendation for mastectomy include large pre- and post-NAC tumor size, lobular histology, central location, multi-focality and small breast size. Several studies have investigated the factors that predict higher rates of recurrence on NAC patients receiving BCS.^{13,16,33,34} Chen et al. found that advanced nodal involvement at initial diagnosis, residual tumor > 2 cm, multifocal residual disease, and lymphovascular space invasion were predictive of recurrence.^{13,16} Beriwal et al. showed that advanced stage at initial presentation and positive margin after surgery were associated with increased recurrence risk.³³ Garimella et al. found that vascular invasion was the only factor significantly associated with overall recurrence.³⁴ Overall, the high recurrence was associated with advanced stage, multifocality or multicentricity, and aggressive pathology such as lymphovascular invasion. Nevertheless, acceptable low rates of locoregional or ipsilateral recurrence may be achieved in appropriately selected patients for BCS, even in patients with T3 or T4 disease.¹³ For patients achieving pCR after NAC, Peintinger et al. reported 96.5% 10-year disease-free survival rates.¹⁴ Oh et al. reported that patients with multi-focal or multi-centric cancer at the time of diagnosis have similar 5-year locoregional control, disease-free survival, and overall survival as those with unicentric disease.¹⁵ Therefore, to date, there are no established criteria or guidelines that would exclude patients from BCS. An accurate evaluation of tumor extent before and after NAC is crucial for surgical planning to achieve tumor free margin.

Many studies have demonstrated that dynamic contrast-enhanced MRI (DCE-MRI) provides optimal information for evaluation of post-NAC residual disease for guiding BCS.^{34–36} The residual tumor size measured by MRI has been shown to be highly correlated with pathologically-determined tumor size.^{22,37,38} The accuracy of MRI has been shown to be much higher compared to that of clinical examination and conventional imaging using mammography and ultrasound.^{17,18,37,39–41} Therefore, MRI may be an optimal imaging modality for evaluating pre- and post-NAC extent of disease, and used for selecting patients suitable for breast conservation surgery. In this study we conducted a systematic analysis to investigate how the pre- and post-NAC imaging findings shown on MRI affect a surgeon's recommendation for the definitive surgical procedure.

The surgeons involved in this study were specialists in breast surgical oncology. It is known that a surgeon's specialty is an important factor in the decision-making process and also in patient satisfaction.⁴² In our study, it was noted that the consensus rate for lumpectomy or mastectomy before NAC is very high, achieving 96% (73/76) with only 3 discordant cases. However, after NAC, the consensus rate is lowered to 88% (65/74). There were 9 discordant cases, including diffuse infiltrating lesions (N=4), a large mass before NAC (N=3), and multiple lesions (N=2). The extent of disease all decreased substantially after NAC in these 9 patients. These findings demonstrated the difficulty in making surgical decisions for patients with large, diffuse, or multiple lesions that showed a substantial response to NAC. Even for experienced breast surgeons who had worked together at one institute for many years, they had difficulty reaching a consensus.

In pre-treatment MRI, the tumor size and disease extent were the main factors determining mastectomy vs. lumpectomy. In the M→M group, the pre-treatment tumor size was 5.8 ± 3.2 cm. For patients in the M→L group, they had a smaller pre-treatment size of 3.5 ± 1.7 cm and a greater size reduction. The results suggested that in patients with extensive pre-treatment

disease, surgeons may still apply an aggressive approach and recommend mastectomy, despite the excellent response to NAC. In patients whose pre-treatment tumor was smaller, the surgeons were more likely to recommend lumpectomy post-NAC. The pre-treatment tumor size was 2.6 ± 1.3 cm in the L→L group, which was the smallest among all 3 groups. This result strongly suggested that the pre-treatment disease extent carried a heavy weight into surgeon's decision-making.

We further investigated the discrepancy cases, where the optimal surgical procedure determined based on pathological findings was different from the surgeons' recommendation based on MRI imaging findings after NAC. There were a total of 9 such cases that has consensus between the 2 surgeons. In the M→M group, the surgeons agreed that 7 patients who had final pathologic complete response or minimal residual disease should receive lumpectomy. In contrast, in the M→L group, 2 patients who were initially recommended for mastectomy and then changed to lumpectomy due to negative MRI imaging after NAC, should ultimately receive a mastectomy, since the pathologic findings show a large extent of residual tumor in a wide region. Therefore, from these results, one can conclude that if BCS can achieve a tumor free margin, this type of procedure is acceptable; but, if the extent of residual disease is too large, then a mastectomy should be performed. Thus, one key question is: before surgery, how accurate is MRI in showing the extent of pathologic residual disease in the breast?

Although many MRI studies have been published to investigate its accuracy in predicting the final pathological extent of disease, very few studies have investigated prediction of pCR or minimal residual disease. Therefore, the role of MRI to predict such minimal disease needs to be further investigated and validated. As the use of MRI for predicting NAC response matures, it may enable surgeons to recommend conservation surgery more frequently and with a greater confidence. A recent study by Chen et al.²² showed MRI could predict pCR with high accuracy in HER-2 positive breast cancer, but had a much higher false negative rate in HER-2 negative cancers. Our recent results also suggested that MRI is highly accurate in predicting the residual disease of mass lesions that have clearly defined boundaries. However, MRI cannot detect residual disease that presents as scattered cells/clusters within a large fibrotic region, which is more likely to occur in lobular cancer and in lesions that present as non-mass enhancements on MRI without clearly defined tumor boundaries. For these cases where MRI may have a high false negative rate, the recommendation of BCS will have to be made with greater caution. In this situation the mammographic findings may play an important role. If the distribution of microcalcifications suggests extensive involvement of diseases, or if multicentric diseases are present, a mastectomy may be a more appropriate procedure.

Finally, we compared the surgical procedure recommended by the surgeon during this review study and that chosen by the patient. Disagreement seemed to be the greatest in women with larger tumors that responded remarkably well to NAC, yielding pCR or minimal residual disease. While the majority of patients chose the surgeons' recommendation in both the M→M group and the L→L group, 15/21(71%) and 14/22 (64%), respectively; in the M→L group, only 8/22 (36%) agreed with the surgeons' post-NAC recommendation and chose lumpectomy. These results suggest that patients are more inclined to stay with the original pre-NAC mastectomy recommendation, regardless of their excellent NAC response shown by MRI. It has been shown that if a candidate who is suitable for BCS prefers mastectomy, the surgeon's recommendation of lumpectomy is overshadowed by the patient's fear of cancer.⁴³ On the other hand, some patients might prefer BCS as long as tumor-free margins could be achieved. For example, the surgeons recommended that the 4 patients with lobular cancer receive mastectomy both before and after NAC (in the M→M group), but all 4 patients chose lumpectomy. Three patients had tumor-free margins, but the other had positive margins and subsequently received mastectomy. The final pathology in the mastectomy specimen revealed scattered cancer cells and clusters within a 6.0 cm region.

In conclusion, the three questions for which this study was designed have been answered. 1) Yes, the presentation of the pre-treatment lesion on MRI indeed affects the initial surgical recommendation. The features associated with mastectomy include: large lesion size or extent of disease, multifocal disease, lobular histology, and central lesion location in small breasts. 2) Yes, a good NAC response on MRI will allow surgeons to feel comfortable in changing their surgical recommendation from mastectomy to BCS. However, for lesions that have a very large size or extent of disease before treatment, the surgeons might still apply a more aggressive approach and recommend mastectomy. 3) It appears that the main guideline to determine the most appropriate surgical procedure depends upon whether the tumor-free margins can be achieved at surgery. MRI can provide helpful information to aid in choosing the optimal surgery type for patients receiving NAC, but with the caveat that MRI may not detect scattered cells/clusters distributed in a large fibrotic region, which is more likely to occur in lobular cancer and non-mass lesions. When recommending BCS for these patients, other clinical information, such as the mammographic findings, will have to be incorporated into the decision-making process. As more studies validating the accuracy of MRI findings in patients receiving NAC become available, the information may help establish appropriate guidelines for recommending BCS after NAC based on the MRI results.

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Figure 1.

The pre-, during, and post-NAC MIP images (from top down) for 4 case examples. (a) $M \rightarrow M$ example: A 60 year-old patient with pre-treatment tumor size of 6.1 cm, decreasing to 3.2 cm after NAC. The pre- and post-NAC recommendation was mastectomy, and the final surgery was mastectomy. (b) $M \rightarrow M(L)$ example: A 50 year-old patient with 8.8 cm inflammatory breast cancer, completely regressed after NAC and pathologically proven as pCR. The pre- and post-NAC recommendation was mastectomy, but when results showed pCR, both surgeons agreed to change to lumpectomy. Final surgery was mastectomy. (c) $M \rightarrow L$ example: a 35 year-old patient with a pre-treatment tumor size of 8.4 cm, decreasing to 4 mm after NAC. The pre-NAC recommendation was mastectomy, which changed to lumpectomy post-NAC. Despite the good response, the final surgery was mastectomy. (d) $L \rightarrow L$ example: a 48 year-old with a pre-treatment tumor size of 2.9 cm, completely regressed after NAC and pathologically proven as pCR. The pre- and post-NAC recommendation was lumpectomy, and the final surgery was lumpectomy.

Table 1

Clinical, imaging, and pathological characteristics of 76 patients

Characteristics	Case Number (N)	Percentage (%)
Tumor types		
IDC	70	92 %
ILC	4	5 %
Mixed, Papillary	2	3 %
Tumor T staging		
T1	7	9 %
T2	43	57 %
T3	21	27 %
T4	5	7 %
MRI morphology		
Mass type	54	71 %
Non-mass type	22	29 %
Tumor response Evaluated by MR		
CCR (complete response)	35	46 %
PR (> 30% reduction)	38	50 %
SD (< 30% reduction)	3	4 %
Final surgery		
Mastectomy	44	58%
Lumpectomy	32	42%
Final pathology		
pCR (no residual malignancy)	21	28 %
Residual DCIS only	7	9 %
Residual invasive cancer	48	63 %

Table 2

Surgeons' recommendation of surgical procedure before and after NAC

	Pre-NAC (N=76)		Post-NAC (N=74) ^a			
	Mastectomy	Lumpectomy	M → M	M → L	L → L	
Surgeon-1	52	24	25	25	24	
Surgeon-2	53	23	24	28	22	
Consensus	51	22	21	22	22	

^aNo post-NAC recommendations were made for 2 patients, due to insufficient MRI findings.

M → M: mastectomy pre-NAC, and remain as mastectomy post-NAC

M → L: mastectomy pre-NAC, and change to lumpectomy post-NAC

L → L: lumpectomy pre-NAC, and remain as lumpectomy post-NAC

Table 3

Tumor size and percentage reduction in 3 different recommendation groups

Recommendation	Pre-NAC		Post-NAC	1-dimensional tumor size reduction %
	tumor size (cm) RECIST ^a	tumor size (cm) WHO ^b	tumor size (cm) WHO ^b	
Mastectomy → Mastectomy	7.4 ± 4.5	5.8 ± 3.2	1.5 ± 2.5	74 ± 33 %
Mastectomy → Lumpectomy	4.2 ± 2.1	3.5 ± 1.7	0.4 ± 0.6	87 ± 22 %
Lumpectomy → Lumpectomy	3.2 ± 1.6	2.6 ± 1.3	0.4 ± 0.6	84 ± 26 %

^a the longest dimension measured on the MIP (maximum intensity projection), based on the RECIST criteria.

^b the equivalent 1-dimensional size calculated from the longest dimension and the longest perpendicular dimension measured on the MIP (square root of their product), based on the WHO criteria.

Table 4

Surgeons' recommendation and patients' choice of surgical procedures

Surgeons' recommendation	Patients' choice		
	Mastectomy	Lumpectomy	Positive margin ^d
M → M (N=21)	15 (71%) ^a	6 (29%)	1/6
M → L (N=22)	14 (64%) ^b	8 (36%)	2/8
L → L (N=22)	8 (36%)	14 (64%) ^c	2/14
Total (N=65)	37 (57%)	28 (43%)	5/28

^a majority (71%) of patients in M → M group chose the surgeon's recommendation.

^b majority (64%) of patients in M → L group chose the pre-NAC recommendation, despite of their response.

^c majority (64%) of patients in L → L group chose the surgeon's recommendation.

^d the number of lumpectomy patients who had positive margin, higher in the M → L group, not significant.