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Case Report

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Breast-Conserving Surgery after Neoadjuvant Chemotherapy Using a Three-Dimensional-Printed Surgical Guide Based on Supine Magnetic Resonance Imaging: A Case Report

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ABSTRACT

Tumor localization in patients receiving neoadjuvant chemotherapy (NACT) is challenging because substantial therapeutic remission of the original tumor after NACT is often noted. Currently, there is no guidance device that allows for an accurate estimation of the resection range in breast-conserving surgery after NACT. To increase the accuracy of tumor resection, we used a 3-dimensional-printed breast surgical guide based on magnetic resonance imaging (MRI) in the supine position for a breast cancer patient who underwent breast-conserving surgery after NACT. Using this device, the breast tumor with apparent therapeutic changes after NACT on imaging was successfully removed with clear resection margins by identifying the original tumor site in the affected breast. Irrespective of whether the residual tumor area after NACT is well defined, it is possible to confirm and target the tumor area on pre-NACT MRI using this device.

Keywords: Mastectomy, segmental; Neoadjuvant therapy; Printing, three-dimensional

INTRODUCTION

As an important component of modern breast cancer care, neoadjuvant chemotherapy (NACT) has been increasingly used in patients with locally advanced and early-stage breast cancer [1,2]. In addition to providing information on the therapeutic response to NACT regimens, tumor burden can be reduced after NACT, which allows patients who initially require mastectomy to become candidates for breast-conserving surgery [3]. The goal of breast-conserving surgery is to completely remove the breast tumor with clear resection margins and simultaneously maintain the natural breast shape. This requires accurate preoperative tumor localization; however, accurate localization of the tumor extent in

Conflict of Interest

BeomSeok Ko and Namkug Kim hold a patent for the 3D-printed breast surgical guide and are the founding members of Anymedi, Inc. Zhen-Yu Wu received consulting fees from Anymedi, Inc.

Author Contributions

Conceptualization: Wu ZY, Kim N, Ko B; Data curation: Wu ZY, Kim GB, Choi S, Lee S, Ko B; Formal analysis: Wu ZY, Lee S, Ko B; Funding acquisition: Ko B; Investigation: Wu ZY, Ko B; Methodology: Wu ZY, Kim GB, Choi S, Lee S, Kim N, Ko B; Project administration: Ko B; Resources: Kim GB, Choi S, Lee S, Kim N, Ko B; Software: Kim GB, Choi S, Lee S, Kim N, Ko B; Supervision: Ko B; Validation: Kim N, Ko B; Visualization: Wu ZY, Kim GB, Choi S, Lee S, Kim N, Ko B; Writing - original draft: Wu ZY; Writing - review & editing: Kim N, Ko B.

patients receiving NACT is challenging because there is often irregular shrinkage, scattering, or even complete remission of the initial tumor after NACT [4]. Currently, there is no guidance device that allows for the accurate estimation of the resection range in breast-conserving surgery after NACT. Here, we report the application of a supine magnetic resonance imaging (MRI)-based 3-dimensional (3D)-printed breast surgical guide (BSG) for precise breast-conserving surgery in a patient who received NACT.

CASE REPORT

This study was approved by the Institutional Review Board of Asan Medical Center, Seoul, Korea (No. 2019-1225). Informed consent was obtained from the patient. A 42-year-old woman who was diagnosed at her local hospital with invasive breast cancer at the 10 o'clock position of her right breast by core needle biopsy was referred to our department in October 2019. Physical examination revealed a well-defined palpable mass in the upper outer quadrant of the right breast. Ultrasonography of the right breast showed an irregular mass containing microcalcification in the 10 o'clock position, 4 cm from the nipple, and measuring 2.9 × 1.7 cm, which was consistent with the biopsy-confirmed malignancy (**Figure 1A**).

Core biopsy of the right-sided irregular mass showed invasive ductal carcinoma, nuclear grade (NG) 3/3, histologic grade (HG) 3/3, estrogen receptor (ER) (positive, 4/8), progesterone receptor (PR) (negative, 0/8), human epidermal growth factor receptor 2 (HER2) (negative, 1+), and Ki67 20%–30%. There was no evidence of distant metastasis on the whole-body computed tomography.

The patient's TNM stage was cT2N0M0. Following discussion with the patient, the patient agreed with the plan for NACT with 4 cycles of a doxorubicin-based regimen followed by 4 cycles of a taxane regimen. Pre-NACT enhanced breast MRI revealed an irregular heterogeneous enhancing mass in the 10 o'clock position, 5 cm from the nipple, and measuring 2.5 × 2.3 cm in the right breast, which was consistent with the biopsy-confirmed malignancy. Additionally, MRI revealed a segmental non-mass-like suspicious lesion in the right breast, 3.0 cm from the nipple, and with an extent diameter of 4.5 cm (**Figure 1B**).

The patient received 4 cycles of NACT with doxorubicin at 60 mg/m^2 (intravenous) and cyclophosphamide at 600 mg/m^2 (intravenous) plus docetaxel at 75 mg/m^2 (intravenous). After the fourth cycle, ultrasonography of the right breast showed that the known malignant mass

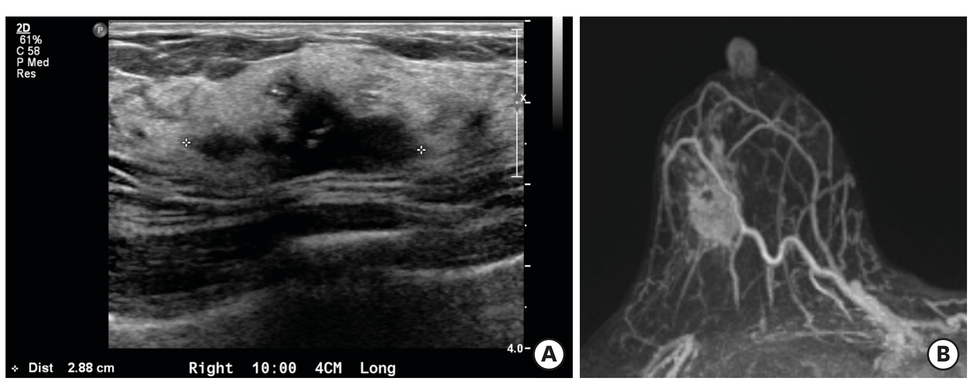

Figure 1. Pre-treatment imaging evaluation. (A) Ultrasonography. (B) Magnetic resonance imaging.

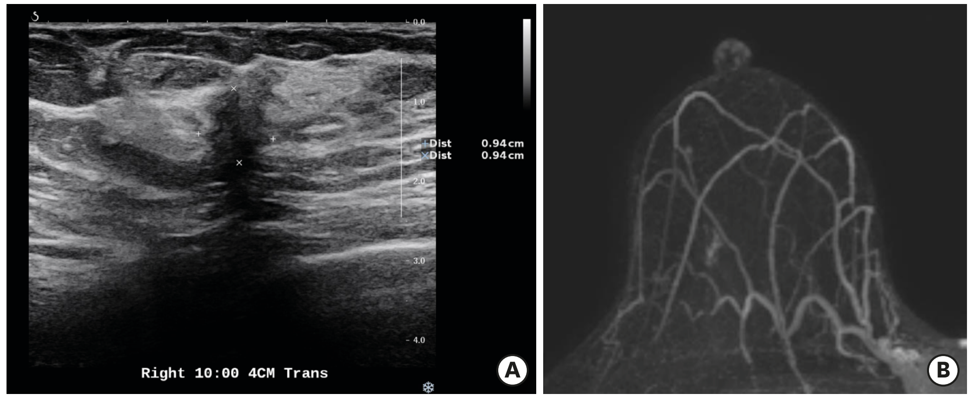

Figure 2. Post-treatment imaging evaluation. (A) Ultrasonography. (B) Magnetic resonance imaging.

had decreased in size (measuring 0.9 × 0.9 cm) (**Figure 2A**). Post-NACT MRI also showed substantial partial remission of the known malignant tumor and a suspicious non-mass-like lesion with a decrease in overall size, measuring 1.3 × 0.5 cm, in the right breast (**Figure 2B**).

We proposed breast-conserving surgery using a prone/supine MRI-based 3D-printed BSG to excise the biopsy-confirmed cancer. Breast imaging was performed using a 3.0 T MRI system (Ingenia; Philips Healthcare, Best, The Netherlands) with a dedicated bilateral 4-element breast coil. An additional supine MRI was performed to replicate the patient's position during the surgical procedure. The patient provided written informed consent and agreed to undergo supine imaging in addition to the standard baseline MRI protocol. Data obtained from the prone/supine MRI scans were analyzed. The tumor and normal breast tissues were separated using the image segmentation program Mimics Medical v17 (Materialise Inc., Leuven, Belgium). We designed a BSG to target the original tumor region by combining pre-NACT MRI of the tumor with post-NACT MRI of the breast (**Figure 3A and B**). The following specifications were used for modeling the BSG to accurately show the tumor resection boundary: 1) the BSG was made to fit precisely to the breast skin surface; 2) a hole was provided to accommodate the nipple and, in order to prevent rotation of the BSG, guidelines indicating the contralateral nipple and the suprasternal notch were included; 3) the BSG was manufactured with a groove for marking the original tumor area on the breast surface with a distance of 0.5 cm from the tumor boundary to ensure safe margins (**Figure 3C**).

Surgery was performed in June, 2020. The 3D-printed BSG was sterilized preoperatively. The surgical resection line was drawn on the breast skin surface along the groove, designed to match the tumor shape (**Figure 3D**). Intraoperative ultrasound examination was performed to localize the residual tumor (**Figure 4**). Right-side lumpectomy and sentinel lymph node biopsy were performed through a single axillary incision. Intraoperative frozen biopsy of the resection margins yielded negative results. A sentinel lymph node frozen biopsy showed a negative result for malignancy (0/3). The operation took 65 min to complete.

The final histopathological diagnosis of the specimen was residual invasive ductal carcinoma: NG 3/3, HG 3/3, ypT2 (3.7 cm) N0 (0/3) M0, stage IIA, ER (+, 4/8), PR (−, 0/8), HER2 (2+, SISH+), and Ki67 < 10%. All resection margins were free of tumor cells. The patient underwent adjuvant radiotherapy, hormonal therapy with tamoxifen combined with gonadotropin-releasing hormone analogs, and HER2-targeted therapy with trastuzumab. At the last follow-up before writing this report, the patient was in a stable condition.

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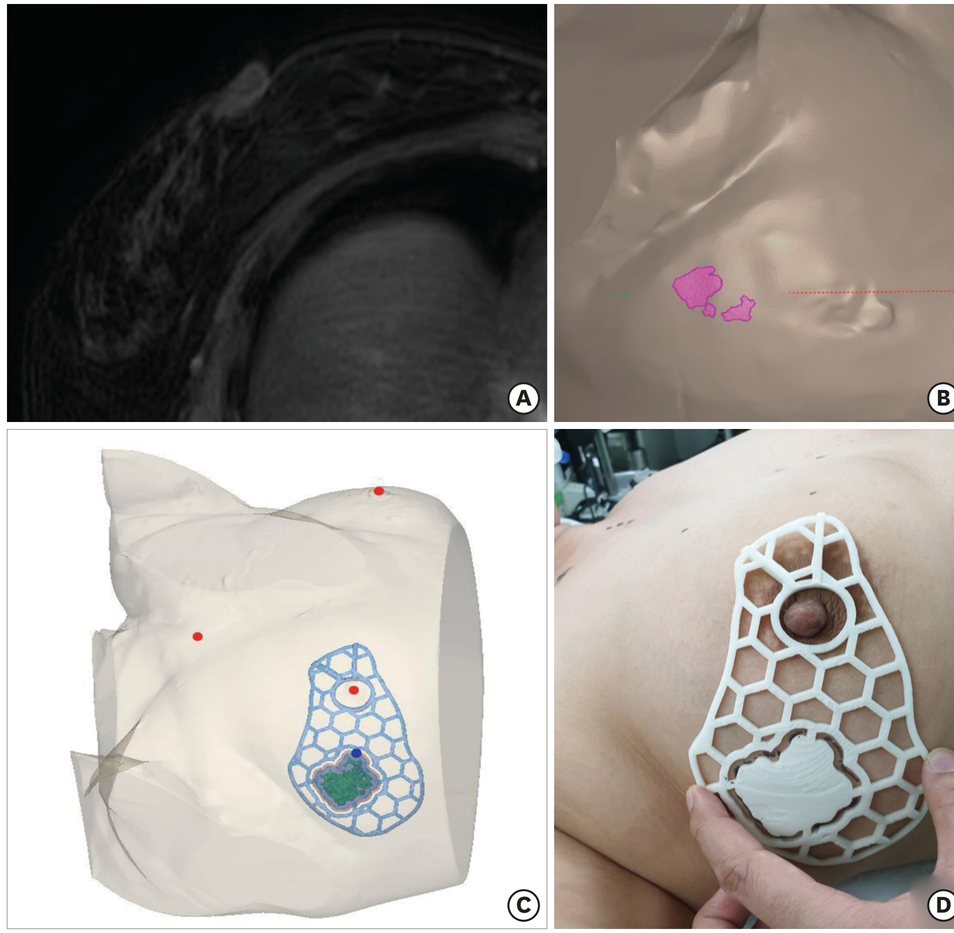

Figure 3. Post-treatment supine magnetic resonance imaging data regarding the breast and tumor (A, B). The breast surgical guide was manufactured with a groove for marking the original tumor area on the breast surface with a distance of 0.5 cm from the tumor boundary to ensure safe margins (C). The surgical resection line was drawn on the breast skin surface along the groove designed to match the original tumor area that had been reduced by treatment (D).

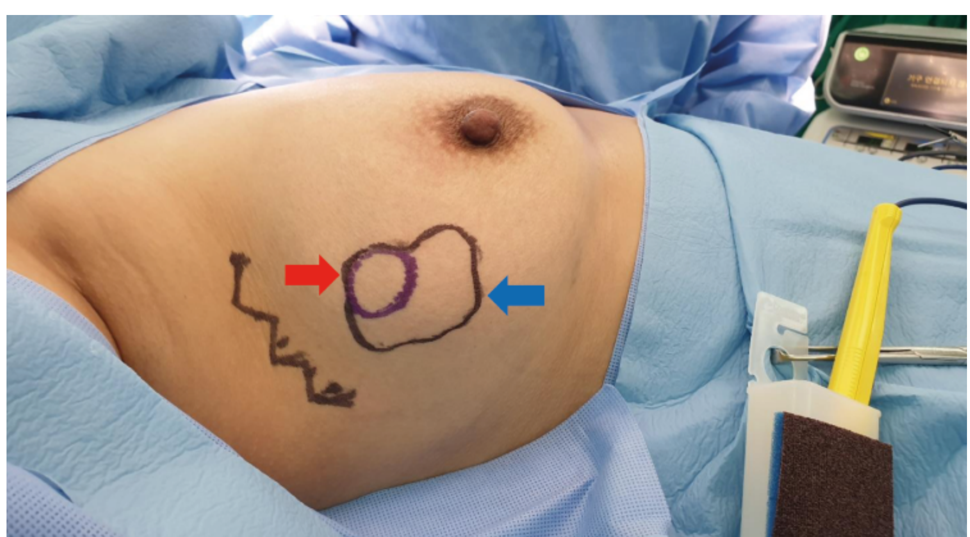

Figure 4. Intraoperative ultrasound examination was performed to localize the residual tumor (red arrow). The blue arrow indicates the area presumed to be the original tumor bed.

DISCUSSION

We used a 3D-printed BSG based on MRI information in the prone/supine position for a patient with breast cancer who underwent breast-conserving surgery after NACT. Using this device, the breast tumor with apparent therapeutic changes after NACT on imaging was successfully removed with clear resection margins by identifying the original tumor site in the affected breast.

In a meta-analysis involving 10 randomized controlled trials of NACT, more frequent local recurrence was associated with NACT compared with adjuvant chemotherapy (15-year risk of 21% for NACT vs. 16% for adjuvant chemotherapy) after breast conservation therapy [5]. This result highlights the importance of an accurate tumor localization strategy for patients undergoing breast-conserving surgery after NACT [5]. Breast cancer patients receiving NACT often experience irregular shrinkage, scattering, or even complete remission of the initial tumor. For these patients, precise localization of the original tumor bed before NACT is important to guide surgical resection. However, conventional localization methods such as hook wire-guided, clip marker insertion, or radioactive seeding techniques cannot accurately identify the original tumor bed after substantial remission following NACT [6-8]. Moreover, conventional localization methods have several inherent shortcomings, such as the need for additional intervention, increased patient discomfort and logistic challenges, and/or radiation exposure [6-9].

The development of new tumor localization techniques that can accurately identify the original tumor bed and better discriminate the tumor extent and normal breast tissues can substantially improve the precision of breast-conserving surgery, as well as local control. Previous studies have reported that MRI is more sensitive than mammography or ultrasonography for predicting breast tumor extent after NACT [10]. However, conventional localization methods are generally performed under the guidance of ultrasonography or mammography and are rarely compatible with MRI-guided localization in current clinical practice [6-8].

The 3D printing is a versatile technology with increasing applications in various medical fields [11]. In a previous pilot study at our institution, we used a prone MRI-based 3D-printed BSG for breast-conserving surgery in patients receiving NACT [12]. The BSG was customized using pre- and post-treatment MRI data obtained in the prone position, and we were able to preliminarily confirm the clinical feasibility and effectiveness of this novel technology [12]. However, a BSG made with MRI data in the supine position may be more appropriate and can potentially lead to better clinical outcomes because the patient is generally placed in the supine position during surgery. In the current case, to imitate the patient's position during surgery and to increase the accuracy of tumor localization, we performed supine MRI in addition to the conventional prone MRI examination and customized the BSG according to breast shape on supine MRI and tumor range on both prone and spine MRI. This differs from our previously reported 3D-printed BSG cases using only prone MRI [12]. The use of 3D-printed BSGs has the advantage of being able to mark a tumor area directly on the breast, and even if the residual area is well defined, it is possible to confirm and target the tumor area in the previous MRI before treatment.

In the case reported here, the initial tumor showed substantial remission after NACT on both ultrasonography (2.9 cm to 0.9 cm in the longest tumor diameter) and MRI (4.5 cm to

1.3 cm). However, in the final pathology result, the long axis of the tumor was 3.7 cm, which is different from the residual cancer area predicted by ultrasonography or MRI. A patient-specific 3D-printed BSG based on MRI data was used to directly mark the original tumor bed on the affected breast skin. The tumor was removed with clear resection margins. In this case, if conventional ultrasonography-guided localization had been used instead of the MRI-based BSG, it would have been difficult to accurately determine the boundary of the resection area and may have potentially resulted in an increased likelihood of margin positivity and re-excision. In addition to potentially improving the precision of patient care and surgical outcomes, the current technique is less invasive than conventional localization methods and has some advantages, such as not requiring radiation exposure and being pain-free, as well as a shorter procedure duration [12]. We plan to continue using 3D-printed BSGs for more patients and establish the safety and effectiveness of this technique in the NACT setting.

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