

〈Case Report〉

Evaluation of intra-ductal cancer spread using contrast superb micro-vascular imaging (SMI) —a case report—

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ABSTRACT Currently, breast conserving surgery has been adopted to treat more than half of all breast cancer patients in Japan. When performing breast-conserving surgery, an appropriate margin needs to be determined for radical cure. The resection volume influences the esthetic outcome, but a cancer-positive resection stump is also important risk factor of local recurrence. Additionally, the degree of cancer progression influences the surgical method, so understanding the appropriate resection margin is necessary for the surgeons. We report here on a 50-year old patient whose intra-ductal cancer progression was shown, as predicted, by contrast SMI (superb micro-vascular imaging). A one-cm size tumor mass was palpable with a clear boundary. B-mode ultrasound confirmed the presence of a breast duct towards the nipple from the tumor mass. Using contrast SMI, an accelerated blood flow was detected around the duct, which suggested intra-ductal progression. The pathological results also showed intra-ductal progression to the nipple from the tumor. Around the progression area, a meandering vessel was found and the vessel was able to be visualized by contrast SMI.

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Key words : Contrast superb micro-vascular imaging, Breast cancer, Intra-ductal cancer

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INTRODUCTION

Both breast-conserving surgery and mastectomy are available to treat breast cancer, and currently breast-conserving treatment has been adopted to treat more than half of breast cancer patients in Japan¹⁾. When performing breast-conserving surgery, the resection volume influences the esthetic outcome. In 2016, the American Society of Clinical Oncology (ASCO) published a report that any resected margin larger than 2 mm for treating noninvasive/intra-ductal cancer using conserving treatment doesn't contribute to life prognosis²⁾. When the intra-ductal cancer spread is detected and understood in mm level detail, the resected margin can be minimized for performing better breast-conserving surgeries. We report here a case in which contrast superb micro-vascular imaging (SMI) proved to be useful to diagnose the intra-ductal cancer spread.

Patient

A fifty-year-old female. She discovered a tumor mass in her left breast and visited a doctor. She hadn't had any prior medical check for breast cancer.

Current medical history: A one-cm size tumor mass with good mobility was palpable in the upper inner quadrant of the left breast.

Mammography: Microlobulated round mass in the left M (middle) / O (outside) area. (Fig. 1)

Ultrasound: An 8 x 9 mm size irregular shaped

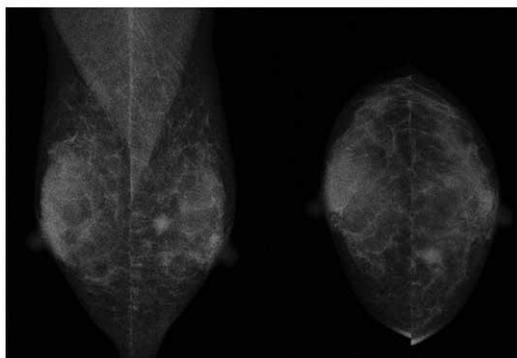


Fig. 1 Microlobulated round mass in the left M/O area

tumor mass was found with an unclear boundary in the lower outer quadrant of the left breast. The inner echo was even and the tumor mass was hypoechoic (Fig. 2-1). The blood flow measured by Doppler ultrasound was moderate (Fig. 2-2). The duct was enlarged from the tumor to the nipple, which suggested intra-ductal progression, however, this site showed a red signal by elastography, and the cancer progression could not be confirmed (Fig. 2-3). 0.0075ml/kg of Sonazoid was administered transvenously as an ultrasound contrast agent, which was flushed out with 10 ml of saline. The contrast SMI showed a meandering blood flow along the expanded duct site (Fig. 2-4).

Core Needle Biopsy: A finding of invasive ductal carcinoma. Having a fibrous stroma in the background, atypical cells infiltrated and proliferated in ductal and cribriform patterns. [ER (estrogen receptor) + (90%)], [PgR (progesterone receptor) + (5%)], [HER-2 (human epidermal growth factor receptor type2) :2+, FISH (fluorescence in situ hybridization) -], Ki-67 index 16%.

MRI: A 9 x 11 mm size tumor was found that had a rapid-washout of contrast effect in the upper inner quadrant of the left breast. Nodules were found in cords inside of the tumor mass (Fig. 3).

Preoperative diagnosis: Left breast cancer T1bN0M0 Stage I.

Operation method: Due to the positive result of the intra-operative rapid diagnosis, the left breast quadrantectomy was changed to a mastectomy with a sentinel lymph-node biopsy.

Macroscopic finding of resected specimen: A 8 x 7 mm size yellowish white nodule was found.

Pathology: Atypical cells infiltrated and proliferated in the fibrous connective tissues in the forms of cords, follicles and glandular ducts, thus diagnosed as scirrhous carcinoma. Also, the cancer cells progressed into a solid form, comedo type and cribriform from the area surrounding the tumor towards the nipple (Fig. 4-1, 2, 3). Venous invasion

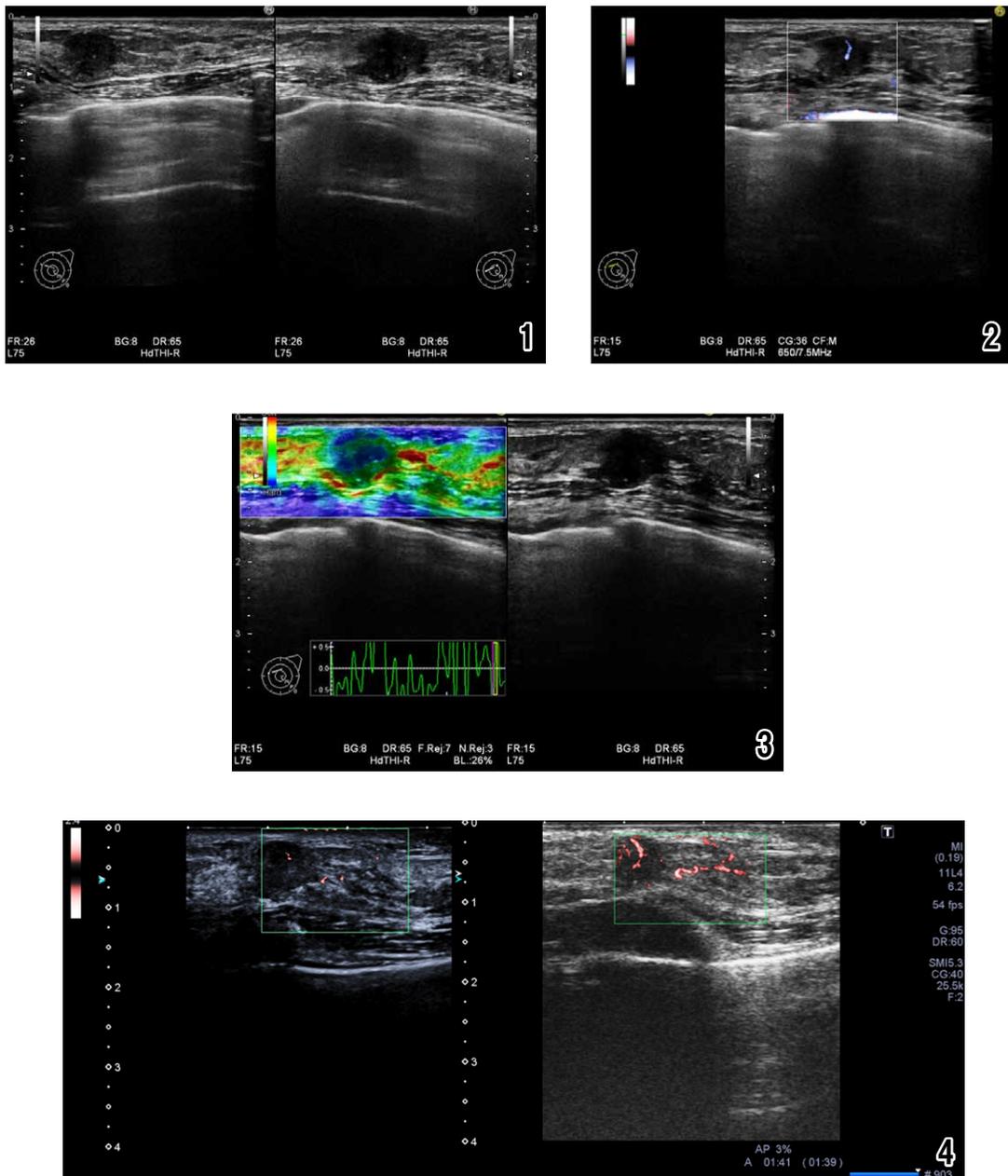


Fig. 2 An 8 x 9 mm size irregular shaped tumor mass was found with an unclear boundary in the A area of the left breast. Vascularity was moderate. The duct was enlarged from the tumor to the nipple, which suggested intraductal progression, however, this site showed a red signal by elastography, and the cancer progression could not be confirmed. The contrast SMI showed a meandering blood flow along the expanded duct site, and SMI didn't show them.

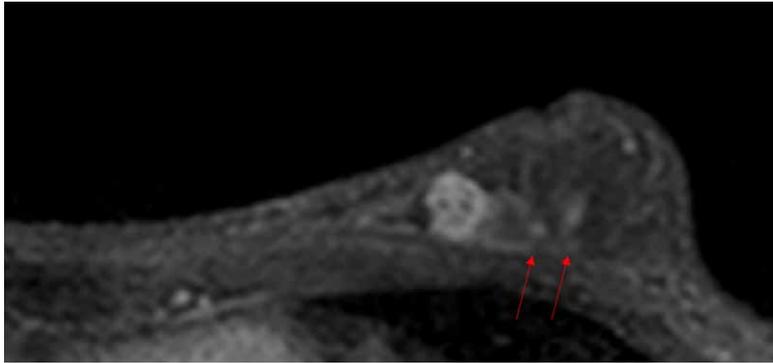


Fig. 3 A tumor was found that had a rapid-washout of contrast effect in the upper inner quadrant of the left breast. Nodules were found in cords inside of the tumor mass (Arrows).

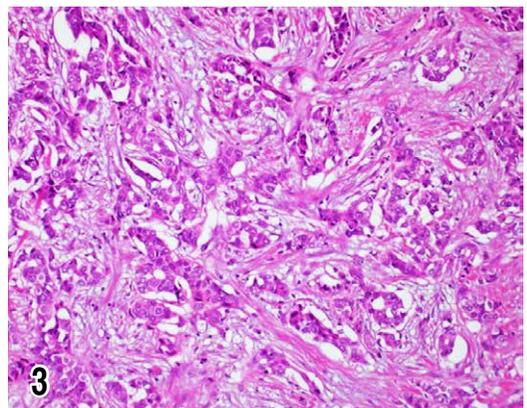
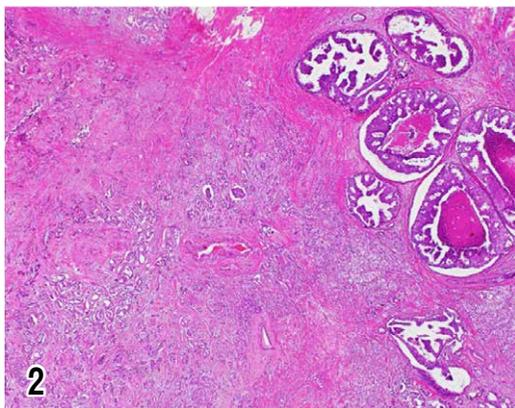
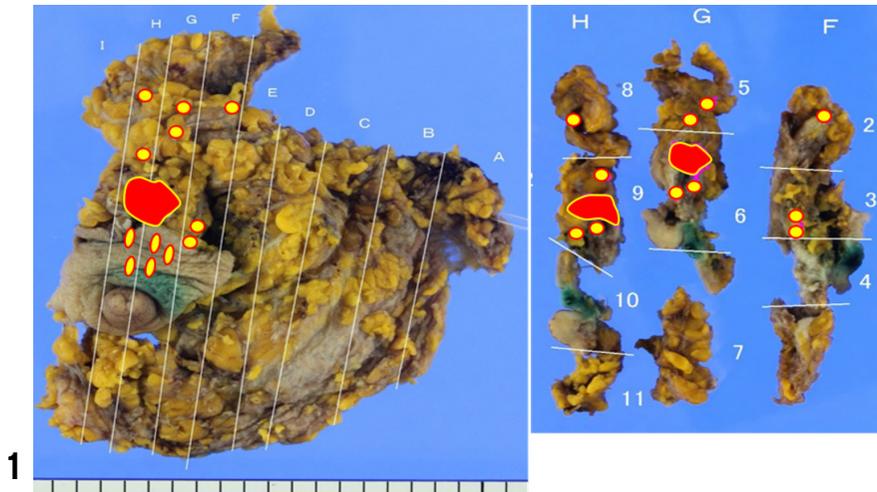
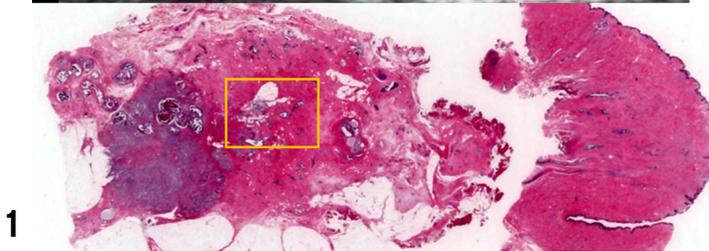
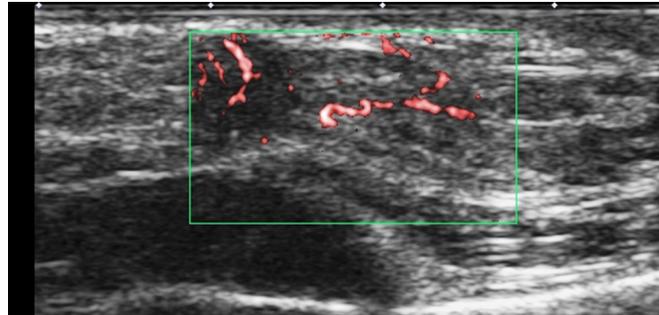


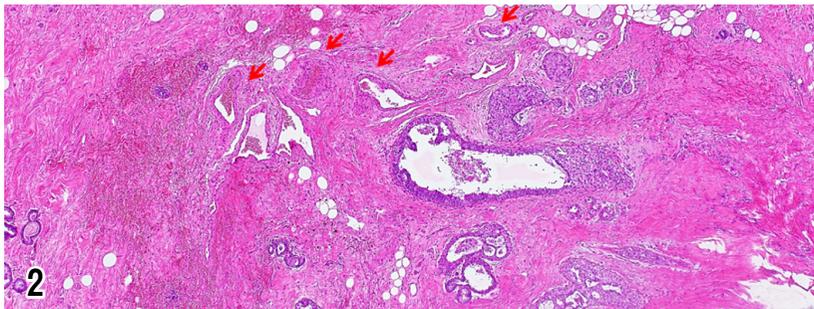
Fig. 4 Atypical cells infiltrated and proliferated in the fibrous connective tissues in the forms of cords, follicles and glandular ducts, thus diagnosed as scirrhous carcinoma. Also, the cancer cells progressed surrounding the tumor towards the nipple

was found but no lymph duct invasion was found. Estrogen receptor was 100% positive and progesterone receptor was 5% positive. HER2 was 2+ and Fish was negative. Ki67 was 15%.

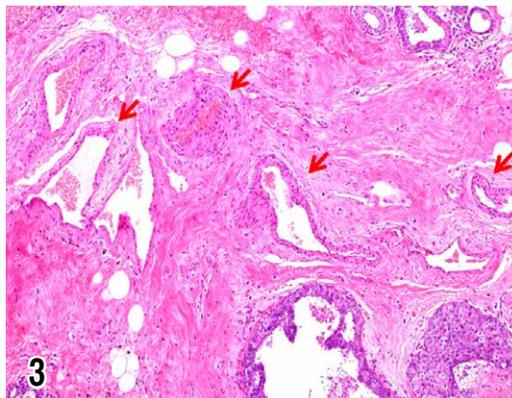
Intra-ductal progression was found from the tumor towards the nipple. A 100 μm meandering vessel was found around the tumor which was the same vessel detected by contrast SMI (Fig. 5-1, 2, 3).



1



2



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Fig. 5 1: Comparison of us image and pathological loupe image. 2, 3: Expanded within the frame of Fig. 5-1. Intra-ductal progression (Arrows) was found from the tumor towards the nipple same as vessel detected by contrast SMI.

DISCUSSION

Currently, breast-conserving surgery is being used for more than half of all breast cancer patients in Japan. When performing breast-conserving surgery, an appropriate margin needs to be determined for radical cure. The resection volume influences the esthetic outcome, but a cancer-positive resection stump is also important risk factor of local recurrence. In addition, the degree of cancer progression influences the surgical method, so determining the appropriate resection margin is necessary for the surgeons. It is difficult to understand the intra-ductal cancer spread precisely including intra-ductal progression. MRI is useful for diagnosing the intra-ductal spread of breast cancer, however, the contrasted range of the intra-ductal cancer spread could lead to overdiagnosis. Moreover, the patient's body position at the time of the MRI and the time of surgery are different, so it is difficult to reproduce the same precise resection margin marking for surgery. Ultrasound is relatively simple to perform even during surgery, so ultrasound is necessary for marking.

Tumor angiogenesis plays an important role in cancer growth and is also an independent prognosis factor for breast cancer³⁾. Blood flow in mammary ducts is usually evaluated with multiple modalities. Until recently, blood flow was evaluated using Doppler ultrasound and first generation ultrasound contrast agent, but observing precise and detailed tumor vessels proved difficult. Since 2012, Sonazoid, which is a second generation ultrasound contrast agent, has been available, and now even slow blood flow can be evaluated which was difficult to image using conventional Doppler ultrasound. Sonazoid is comprised of microbubbles that are as small as a few microns in diameter, and it is delivered to the targeted organ by the circulatory system. Due to Sonazoid's strong resonance and distribution in the blood, ultrasound signals can be greatly enhanced, and the evaluation of blood

flow does not need to rely on blood flow speed. Also, SMI can eliminate motion artifacts that were an obstacle for the conventional evaluation of blood flow and can also capture ultra-low blood flow. Contrast enhanced ultrasound (CEUS) was reported to be superior to MRI in terms of precision of benignancy or malignancy distinction during the second and third phases of Sonazoid clinical trials^{4, 5)}. Currently, there are reports of CEUS on the diagnosis of intra-ductal cancer spread and therapy evaluation, not only the distinction between benignancy and malignancy⁶⁾ and the same effect is expected with contrast SMI⁷⁾. Different from the enhancement effect of CEUS, contrast SMI can show vascular morphology sterically, which means it can show abnormal vascular morphology.

At our hospital, all the breast cancer patients who undergo a contrast enhanced ultrasound receive (breast) marking the day before surgery. The surgical method is decided based on the MRI information. This patient was suspected of having intra-ductal progression. B-mode detected successive ducts from the tumor mass towards the nipple and only the contrast SMI was able to show the increased vascularity around the ducts. There was no major change in the normal ducts towards the body both before and after performing the contrast SMI. From the above facts, the clearly accelerated blood flow shown by Sonazoid could have been caused by abnormal blood vessels. A meandering blood vessel that was about 100 μm long was running along the carcinoma according to the pathology results. Contrast SMI also predicted the intra-ductal progression. However, diagnosing only based on the blood flow could lead to an overdiagnosis of intra-ductal progression of a carcinoma and/or papilloma. Nakashima *et al.* reported that comprehensive ultrasound diagnosis^{8, 9)} can detect an intra-ductal lesion that is larger than 2 mm using elastography. By adding a contrast SMI, a more precise diagnosis can be expected.

CONCLUSION

We experienced a case in which contrast SMI was useful for evaluating intra-ductal progression.

Conflict of interest None declared.

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