

## Significance of the Ultrasonic Diagnosis for the Decision of the Appropriate Extent of Resection in Breast Conserving Surgery

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"Surgical margin (SM) positive" is the most significant recurrence risk factor in breast conserving surgery, which makes accurate preoperative diagnosis quintessential to avoid this risk.

The objective of the present study was to examine the significance of ultrasonic (US) diagnosis for the decision of the appropriate extent of resection in breast conserving surgery. Of the 300 cases of primary breast cancers for which surgery was performed in our department for the past two years, 189 cases (63%) were for tumors 3 cm or less in diameter. In the preoperative US examination of 189 cases, 124 cases were (65.6%) diagnosed as indicating breast conserving surgery, and breast conserving surgery was performed on 104 cases of those 189 cases (55%), excluding 16 cases of patients who did not want breast conserving and the 4 cases of advanced lymph node metastasis. As a result, the SM-positive ratio was low (6 of 104 cases, 5.8%), an outstanding result.

US examinations are useful for determining the appropriate extent of resection in breast conserving surgery, and although there are limitations, a US examination is necessary to avoid leaving cancer cells and to reduce the risk of local recurrence.

**Key words:** breast conserving surgery, ultrasonic examination, ductal spreading, surgical margin

### Introduction

Breast conserving surgery for patients with breast cancer is increasing year by year. Mastectomy and breast conserving surgery are the two major pillars of primary breast cancer treatment. However, it is undeniable that with breast conserving surgery the risk of cancer remaining in the conserved breast is becoming higher. Of the risk factors related to the recurrence of cancer after breast conserving surgery, "surgical margin (SM) positive" is widely recognized as the most important. To reduce this risk, it is imperative to preoperatively accurately diagnose the area of cancerous spreading and to appropriately determine the extent of the resection with an adequate SM.

In this regard, the diagnosis of the area of the cancerous spreading is made using various modalities of diagnostic imaging. We have successfully

been using, to our patients' great benefit, US examinations to determine the extent of resection in breast conserving surgery. In this paper, we examined the significance of this diagnostic technique to determine the appropriate extent of resection of the mammary gland based on our recent studies.

### Patients and Methods

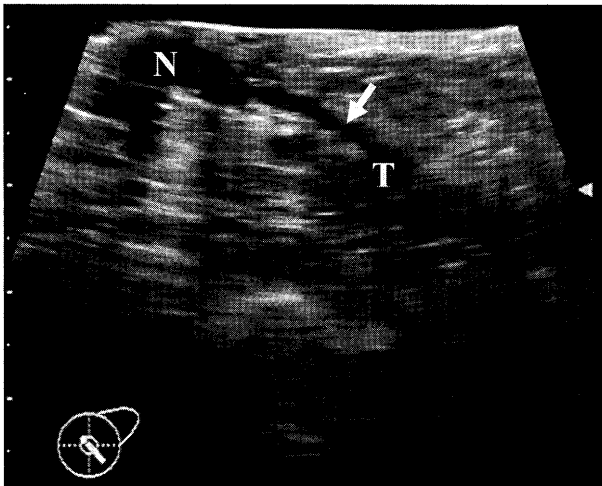
Of 300 cases of primary breast cancer in our surgical department in the past 2 years (from May 2004 through April 2006), there were 189 cases (63%) of tumors of 3 cm or less in diameter in the present study (Table 1). Patients are generally recommended to undergo breast conserving surgery when their tumors are 3 cm or less in diameter.

The ultrasonographic device used was ALOKA SSD 2000 and the probe used was a 10 MHz annular array (ASU-36WIL-10). The scanning is conducted thoroughly over the entire breast. Scanning was

**Table 1** Tumor size variations

Size (cm)	n	%
0	37	12.3
0.1-1.0	17	5.7
1.1-2.0	76	25.3
2.1-3.0	59	19.7
3.1-4.0	36	12.0
4.1-5.0	29	9.7
5.1-	46	15.3
Total	300	100

(May 2004 – April 2006)

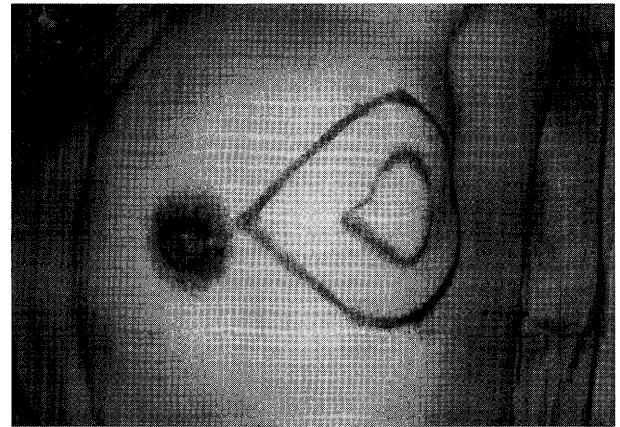
**Fig. 1** US image of ductal spreading

Ductal spreading of cancer cells (arrow) is seen from the tumor (T) to the nipple (N).

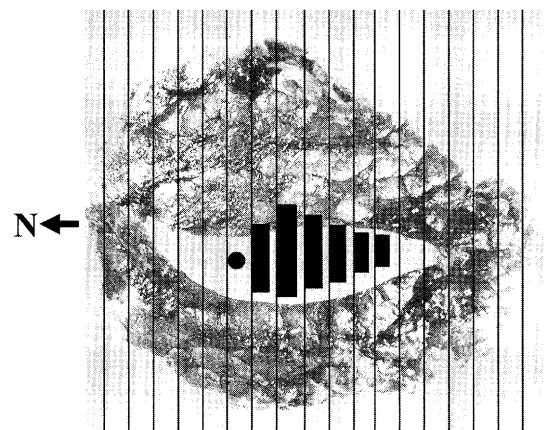
done, however, the scanner was moved 360 degrees around the tumor, while being especially careful to make the diagnosis for ductal spreading (Fig. 1).

First the US diagnosis was made to decide whether or not breast conserving surgery was indicated. Cases in which there was ductal spreading or direct invasion of cancer cells in and/or proximal (<1 cm) to the nipple or multiple tumors were determined to be outside the scope of breast conserving surgery and therefore indicated mastectomy.

Breast conserving surgery was indicated for all other cases. The extent of the cancerous spreading was marked on the skin using preoperative US examinations. We concentrated on the images of ductal spreading, and detailed images were examined to determine the extent of resection. Furthermore, the extent of resection was determined 2cm outside the marks, and if at all possible, up to 3cm in the di-

**Fig. 2** The area of cancerous spreading and marked extent of resection

After marking the area of the cancerous spreading (inner line) using ultrasonography, the extent of resection (outer line) is determined and, at key points on the demarcation, a mixture of pyoktanin and xylocaine jelly® is injected.

**Fig. 3** Complete slicing of resection specimen and cancer mapping

On a line from the nipple (N) through the center of the tumor to the outer edge of the resected specimen, perpendicular slices at 5-mm intervals are made to map the extent of cancerous tissue. ●: ductal carcinoma in situ; ■: invasive ductal carcinoma.

rection of the nipple, however when less than 3cm was available, the resection was made from just under the nipple. In order to make the resection, at key points along this line, a mixture of pyoktanin and xylocaine jelly® was injected. The mammary gland was then resected along this demarcation (Fig. 2).

The histopathologic evaluation of the resected specimen was done by making perpendicular sliced

**Table 2** Relation between US findings and operation methods of breast cancer diameter  $\leq 3$  cm

US findings	Operation	n	%
Ductal spreading or direct invasion in and/or proximal to the nipple (Indication of mastectomy)	Mastectomy	50	26.5
Multiple tumors (Indication of mastectomy)	Mastectomy	15	7.9
Single tumor with no ductal spreading or direct invasion in and/or proximal to the nipple (Indication of breast conserving surgery)	Mastectomy (Breast conserving surgery not elected)	16	8.5
	Mastectomy (Advanced lymph node metastasis)	4	2.1
	Breast conserving surgery	104	55.0
Total		189	100

US: ultrasonic.

**Table 3** Histopathological diagnosis of surgical margin

Surgical margin	n	%
Negative	98	94.2
Positive	6	5.8
Total	104	100

sections at 5-mm intervals along the line from the nipple through the center of the tumor to the outside edge of the resection. Then, a map of sections of the tumor was made (Fig. 3), and, if no cancer cells were found within 5 mm of the SM, it was judged as "SM negative", and if cancer cells were found within 5 mm of the SM, it was judged as the "SM positive".

The negative and positive ratios of the SM were calculated and examined for effectiveness and limitations of the US diagnostic determination of the extent of the resection.

### Results

Detailed US diagnoses were made on 189 cases of tumors 3 cm or less in diameter, and there were 50 cases (26.5%) of cancerous spreading in and/or proximal to the nipple ( $<1$  cm) and 15 cases (7.9%) of multiple tumors for which mastectomy was indicated and performed (Table 2). In the other 124 cases (65.6%), the cancer was a single tumor with no ductal spreading or direct invasion in and/or proximal to the nipple, in which cases breast conserving surgery was indicated. Of these cases, however, 16 patients did not want breast conserving treatment, therefore, mastectomy was performed. There were also 4 cases of advanced lymph node metastasis in which a mastectomy was performed.

Breast conserving surgery was conducted on a total of 104 of 189 cases (55%) of breast cancers 3 cm or less in diameter.

In the histopathological evaluation of the SM, there were 98 SM negative cases of 104 cases (94.2%). And there were 6 cases (5.8%) of SM positive, outstanding results (Table 3). Of the SM positive cases, there were 2 cases of nonpalpable, noninvasive ductal carcinoma with microcalcifications, 2 cases of invasive lobular carcinoma, 1 case of mucinous carcinoma, and 1 case of scirrhous carcinoma (Table 4). There were 5 cases of cancerous spreading and 1 case of multiple tumors which were the cause of the positive SM. Surgery was conducted again on all of the 6 SM positive cases, and we confirmed remnant cancer in 5 of 6 cases (83.3%). In cases that indicated mastectomy, the diagnoses were correct in 64 of 65 cases (98.5%) (Table 5).

### Discussion

As the frequency of breast conserving surgery increases, the "SM positive" risks also increase. According to Takahashi et al<sup>1)</sup>, breast conserving surgery after 1998 was seen in almost 50% of all breast cancer cases. Of these, the SM positive ratio was 45-49%. The ratio of the SM negative cases in all breast cancer cases was about 25-27%. As for the evaluation method of the SM, there is no uniform international standard for the width of the margin which is 0-5 mm<sup>2)3)</sup>.

In Western countries, however, in the majority of cases, the only positive cases are those of exposed tumors on the resected surface. When making diagnoses in this manner, the rate of positive SM will naturally be lower. However, histopathologically,

**Table 4** Characteristics of surgical margin positive cases

Case	Size (cm)	Histopathological type	Microcalcifications	Cause
1	0	Noninvasive ductal Ca	+	Ca S
2	0	Noninvasive ductal Ca	+	Ca S
3	0.5	Invasive lobular Ca	—	Ca S
4	1.5	Invasive lobular Ca	—	Ca S
5	1.7	Mucinous Ca	—	Multiple tumors
6	2.7	Scirrhou Ca	+	Ca S

Ca: carcinoma, Ca S: cancerous spreading.

**Table 5** Relation between US and histopathological findings in cases indicating mastectomy

US findings	Histopathological findings	n	%
Ductal spreading or direct invasion in and/or proximal to the nipple	Cancer cells in and/or proximal to the nipple	49	75.4
	Single tumor with no cancer cells in and/or proximal to the nipple	1	1.5
Multiple tumors	Multiple tumors	15	23.1
Total		65	100

US: ultrasonic.

making diagnoses in this manner does not ensure that the cancer tissues have been completely resected. In the guidelines for breast conserving treatment in Japan, the most essential and unyielding point is for the definition of SM positiveness in which there are cancer cells within 5 mm of the resected surface. The results of Takahashi et al were obtained by strictly following these principles, which we also do.

Since “SM positive” is the most important risk factor for recurrence of cancer in the remnant part of the conserved breast<sup>4)</sup>, to reduce the rate of recurrence, it is important to increase the “SM negative” rate<sup>5)~7)</sup>. It is estimated that there is about 30% of the total breast cancer cases where the cancer can be completely removed by breast conserving surgery<sup>1)</sup>. The keys to avoiding recurrence of cancer within the breast are making the initial judgment correctly of whether or not to perform breast conserving surgery, in about 30% of the preoperative breast cancer cases, and to accurately determine the extent of resection.

In our department, we have always endeavored to perform breast conserving surgery with the intent of an “SM negative” outcome after surgery. We have also been making rigorous histopathological SM evaluations. In the process, we developed

imaging methods on ductal spreading of breast cancer using ultrasonography<sup>8)</sup>. We have concurrently been promoting US diagnosis for ductal spreading of breast cancer<sup>9)</sup>. Examining the results of US diagnosis on the extent of resection in breast conserving surgery, the SM positive ratio was as low as 5.8%, an excellent result. Breast conserving surgery (excluding cases of mastectomy due to SM positive results) was performed in 32.7% of the total breast cancer cases, which is slightly more than the 30% considered as the limit of breast conserving surgery aimed at SM negative results. This proves the effectiveness of US diagnosis of the indication of breast conserving surgery and the accurate determination of the resection extent. There are still limits to diagnose lesions with microcalcifications, invasive lobular carcinoma and others.

Nonpalpable, noninvasive ductal carcinomas with microcalcifications are detected by the US images, such as those of ducts with calcifications and low-echoic area with calcifications. Using these as indices, it is possible to diagnose the ductal spreading. As with these two cases in this study, however, that proved to be SM positive, which have a few and sporadic calcifications, it was difficult to make accurate diagnoses because ducts and low-echoic areas with microcalcifications were rarely demonstrated.

Invasive lobular carcinoma presents similar US images as scirrhous carcinoma and diagnosing it is usually rather easy. Some invasive lobular carcinomas, however, do not form into a singular tumor. Instead, they may spread to wider areas multifocally or multicentrically. These are considered to be the causes for these two SM positive cases this time. One case was of a mucinous carcinoma which had another minute tumor 0.3 cm in diameter in the SM. It might have been possible to detect this minute tumor if more careful scanning had been done. One case of scirrhous carcinoma with ductal spreading in the area surrounding the primary tumor was SM positive because there were a few and sporadic calcifications and the images of the duct and the low-echoic areas were not clear. The major tasks in the future, therefore, will be to make improvements in the accuracy of diagnoses and determine the limits of these diagnoses.

Diagnoses of the areas of cancerous spreading are also made with mammography, MRI, and CT. With a mammography, it is difficult to detect ductal spreading without the appearance of microcalcifications. If there are broad microcalcifications, however, it can be easily surmised that possibilities are high for SM positive after breast conserving surgery. It is recognized that mammography is effective to select cases not indicated for breast conserving surgery<sup>10)</sup>. Nakahara et al<sup>11)</sup> made CT vs. MRI comparisons of 50 cases against the histopathological diagnoses. They found the sensitivity, specificity, and accuracy of CT examinations to be 71.9, 83.3 and 76.0% respectively. The respective percentages with MRI were 87.5, 61.1 and 78.0%. With the advent of these techniques, by using them in combination with various modalities and US examinations, the expectation is high for making contributions in the increased diagnostic accuracy of cancerous spreading.

The goal of breast conserving treatment is, first and foremost, no recurrence and for the surgical result to be aesthetically pleasing to the patient. In order to achieve this goal, it is most important to perform complete breast conserving surgery based on

accurate diagnosis. US diagnosis is the quintessential examination method for achieving this objective.

### Conclusions

In breast conserving surgery, it is imperative to preoperatively accurately assess the extent of cancerous spreading to avoid leaving any remnant cancerous tissue. US diagnosis is useful to determine the extent of resection in breast conserving surgery so that there is no postoperative remnant cancer. It is expected that US examinations will play more important roles with the advent of the social trend in favor of breast conserving treatment.

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## 乳房温存手術における超音波を用いた乳腺切除範囲診断の意義

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乳癌に対する乳房温存療法の頻度の増加に伴い、残存乳房内への癌遺残リスクも上昇している。“切除断端陽性”は、乳房温存手術後の最も重要な再発リスク因子であるため、これを回避するための術前診断が極めて重要となる。

今回われわれは、最近2年間に当科で手術を施行した原発性乳癌症例300例のうち、腫瘍径3cm以下の189例(63.0%)を対象として、乳房温存手術における超音波検査を用いた乳腺切除範囲診断の意義について検討した。術前の超音波検査で、乳房温存手術の適応ありと診断した症例は189例中124例(65.6%)であり、このうち乳房温存を希望しない症例および高度のリンパ節転移を認めた20例を除く104例(189例中55.0%)に乳房温存手術を施行した。この結果、断端陽性率は104例中6例、5.8%と非常に低く、極めて良好な成績が得られた。断端陽性例のうち2例は微細石灰化を伴う非触知の非浸潤性乳管癌であり、2例は浸潤性小葉癌であった。一方、術前超音波検査で、乳頭近傍(1cm以内)への癌の広がり、あるいは多発癌を認め乳房切除術の適応であると診断された症例は189例中65例(34.4%)であり、このうち64例、98.4%で病理組織学的診断との一致が得られた。

超音波検査は、乳房温存手術における適切な乳腺切除範囲の診断に極めて有用である。限界はあるものの、癌遺残を回避し局所再発リスクを軽減する上で必須の検査法であり、今後、新たな装置の開発と診断技術の向上に伴い一層重要な役割を担うものと期待される。