Title

Evaluation of background parenchymal enhancement in breast contrast-enhanced ultrasound with Sonazoid®

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Abstract

Purpose

The objective of this study was to retrospectively evaluate the association between background parenchymal enhancement (BPE) on contrast-enhanced ultrasound (CEUS) with Sonazoid® and patient characteristics. Additionally, background parenchymal tissues with the high-contrast effect were pathologically observed compared to those showing the low-contrast effect.

Methods

A total of 65 patients who underwent breast CEUS with Sonazoid® between January 2010 and November 2013 were enrolled. Regions of interest (ROIs) were put on the tumor and on the background parenchymal tissue. The dB values during the nonenhanced time and at peak contrast enhancement were measured based on the time intensity curve (TIC) drawn by the ROI. The differences in the dB values of pre- and post-enhanced time were obtained separately for ROIs on the tumor and ROIs on the parenchymal tissue. The patient characteristics studied were age, menstrual status, mammographic density, BPE on magnetic resonance imaging (MRI), and pathological diagnoses of breast tumors.

Results

There was a weak negative correlation between BPE on CEUS and age. As for the contrast effect of parenchymal tissue, there was a significant difference between the menstruating and menopausal groups. There was no significant difference among the

levels of mammographic density, and among the degrees of contrast effect on MRI. BPE on CEUS was the same between those with a malignant tumor and those with a benign tumor in each menstrual status. The parenchymal tissue with the low-contrast effect showed pathological atrophy.

Conclusion

The degree of BPE on CEUS appeared related to age, menstruating or menopausal, and atrophy of breast tissue. BPE on CEUS was the same between those with a malignant tumor and those with a benign tumor in each menstrual status.

Keywords

breast, US, background parenchymal enhancement (BPE), Sonazoid®, pathology

Introduction

CEUS with Sonazoid® has a high sensitivity for detecting vascular flow and is a reliable modality to assess detailed hemodynamics in real time. There have been some studies showing that CEUS is useful for distinguishing benign breast tumors from malignant breast tumors [1,2], evaluating the response of breast cancers after neoadjuvant chemotherapy [3,4], and evaluating the involved regions of breast tumors [5,6]. However, there have been no reports of the contrast effect of breast parenchymal tissue on CEUS.

The objective of the present study was to evaluate retrospectively the association between BPE on CEUS using Sonazoid® and patient clinical and radiological characteristics: age, menstruating or menopausal, mammographic density, BPE on MRI, pathological diagnoses of breast tumors, and enhancement of breast tumors themselves. Additionally, background parenchymal tissues with the high-contrast effect were examined pathologically and compared to tissues showing the low-contrast effect.

Materials and Methods

Patients

This study was approved by the Institutional Review Board (No. 1751). A total of 113 patients who underwent breast CEUS with Sonazoid® were recruited with informed consent between January 2010 and November 2013. Cases in which it was possible to evaluate the background parenchymal tissues and the breast tumors on the same US screen in real time were chosen. Patients who had been examined for follow-up after chemotherapy (n = 21), whose tumors were bigger than the US screen (n = 11), whose tumors could not be observed in real time (n = 7), who had received neoadjuvant chemotherapy before initial CEUS (n = 6), who were male (n=1), whose tumor was axillary lymph node swelling (n=1), and who had surgery in another hospital (n = 1) were excluded. The remaining 65 patients (mean age 55.7 years, range 22–79 years) were enrolled. The examinations were performed in the order of mammography, MRI, and CEUS. Finally, pathological diagnoses were obtained by mammotome biopsy or surgery. Twelve breast tumors that were clearly benign on US were ultimately diagnosed by mammotome biopsy. All other tumors were removed by surgery. The median number of days before CEUS that mammography was performed was 42.3 days. The median number of days before CEUS that MRI was performed was 20.7 days. The median number of days that CEUS was performed before biopsy or surgery was 74.2 days. The number of days from CEUS to biopsy or surgery varied by benign or malignant tumor, and with or without neoadjuvant chemotherapy (benign tumor: 15.6 days, malignant tumor without neoadjuvant chemotherapy: 24.2 days, malignant tumor with neoadjuvant chemotherapy: 449.5 days).

Clinical information

Patient age, menstruating or menopausal, and pathological diagnoses were retrospectively reviewed. The dates of the menstrual cycle of the menstruating patients were not recorded in the medical records, so the effects of the menstrual cycle could not be investigated.

Mammography

Mammograms were available for all patients. Mammography in two standard imaging planes (mediolateral oblique and craniocaudal) was done with the use of a Selenia I-IV system (Lorad, St. Petersburg, FL, USA). The mammograms were retrospectively reviewed for overall breast density of the contralateral normal breast according to the Breast Imaging Reporting and Data System (BI-RADS) classification. This density scoring system consisted of four categories: a predominantly fatty breast, a scattered fibroglandular fatty breast, a heterogeneous dense breast, and an extremely dense breast.

MRI

Breast MRI was available for 59 patients. Six patients did not undergo MRI due to asthma (n=4), previous history of an allergic reaction to the contrast agent (n=1), and pacemaker placement (n=1). Breast MRI was performed on a 3.0-T MR system (Achieva; Philips Medical Systems, Best, The Netherlands). Patients were placed in the prone position on a dedicated bilateral breast coil. The contrast-enhanced images were acquired before and immediately after bolus injection of 0.1 mmol/kg body weight of gadolinium contrast agent (Omniscan; GE Healthcare, Oslo, Norway) using an automatic injector. Japan Association of Breast Cancer Screening recommends that

breast MRI be performed according to the menstrual cycle. In this study, all MRI in premenopausal women was performed between the 5th and 12th days of the menstrual cycle (the first day of menstruation is referred to as the beginning of the cycle). BPE on breast MRI was classified into the following four categories according to the percentage of glandular tissue demonstrating enhancement: minimal (<25%), mild (25-50%), moderate (>50-75%), and marked (>75%).

CEUS

CEUS was available for all patients. The LOGIQ E9 (GE Healthcare, Tokyo, Japan) ultrasound system with the 9L and ML6-15 linear probes was used. The CEUS mode was Amplitude Modulation, and the parameters were 0.2 for the mechanical index and 12–16 frames per second for the frame rate. The focus was set below the deepest portion of the tumor of interest. Sonazoid® (perflubutane, 0.01 ml/kg; Daiichi Sankyo, Tokyo, Japan) was administered into the antebrachial vein followed by a 10-ml flush of normal saline. The probe was held at a section that visualized both parenchymal tissue and the tumor. Early enhanced images obtained from before injection to 40 s after the injection of Sonazoid® were saved as raw data on the system's hard disk drive. An ROI of 3 mm in diameter was put on the background parenchymal tissue at the same depth as the tumor with the saved movie data offline. A TIC was drawn by the ROI using the software program built into the system. The dB value of the tumor during nonenhanced time was defined as T-baseline, and the dB value of the tumor at peak contrast-enhanced time was defined as T-max. Likewise, the dB value of the parenchymal tissue during nonenhanced time was defined as PT-baseline, and the dB value of the parenchymal tissue at peak contrast-enhanced time was defined as PT-max.

The contrast effect of the tumor was obtained by the difference between T-max and T-baseline. The contrast effect of the parenchymal tissue was obtained by the difference between PT-max and PT-baseline (Figure 1).

Statistical analysis

The categorical variables are presented as frequencies. Pearson's product-moment correlation coefficient was used to evaluate the correlation between BPE and age based on a scatter diagram.

Student's *t*-test was used to assess the association between the menstruating and menopausal groups. Student's *t*-test was also used to assess the association between the contrast effect of parenchymal tissue in those with a benign tumor and that in those with a malignant tumor. Student's *t*-test was also used to assess the association between BPE and breast tumor enhancement.

Comparisons among multiple categories, such as the degree of contrast effect on MRI and the mammographic density, were analyzed as follows. If normality and equal variance were confirmed, one-way analysis of variance was used; if they were not confirmed, the Kruskal-Wallis test was used. $P<0.05$ was considered significant. R (The R Foundation for Statistical Computing, Version 3.4.2; Vienna, Austria) was used for statistical analysis.

Results

The association between age and BPE on CEUS is shown in Figure 2. There was a weak negative correlation between BPE on CEUS and patient age ($r=0.313$).

The relationships between BPE on CEUS and patient clinical and radiological

characteristics are shown in Table 1. A total of 24 patients were menstruating, and 41 were menopausal. As for BPE on CEUS, there was a significant difference in the average between the menstruating and menopausal groups (p=0.042).

On mammography, two cases were classified as predominantly fatty breasts, 26 cases were scattered fibroglandular fatty breasts, 31 cases were heterogeneous dense breasts, and six cases were extremely dense breasts. There were no significant differences in BPE on CEUS among the mammographic density groups (p=0.134).

A total of 59 patients underwent contrast-enhanced MRI, and 32 patients were categorized as minimal, 16 as mild, 11 as moderate, and none as marked. There were also no significant differences in BPE on CEUS among the degrees of contrast effect on MRI in this study (p=0.283).

The breast tumors were benign in 18 cases and malignant in 47 cases. The benign tumors were fibroadenomas (n=9), fibrocystic changes (n=5), phyllodes tumors (n=2), intraductal papilloma (n=1), and panniculitis (n=1). The malignant tumors were invasive carcinomas of no special type (NST) (n=33), ductal carcinomas in situ (n=8), invasive lobular carcinomas (n=3), solid papillary carcinoma (n=1), mucinous carcinoma (n=1), and Paget's disease of the nipple (n=1). Neoadjuvant chemotherapy was given to eight patients with malignant tumors. As for BPE on CEUS, there was a significant difference in the average between the benign and malignant tumor groups (p=0.031). The relationships between benign or malignant tumor and menstrual status are shown in Table 2. The benign tumor group included younger women, with a larger number of premenopausal women. Therefore, the patients were divided into two groups, before menopause and after menopause. The statistical difference between BPE in those with a benign tumor and that in those with a malignant tumor by each group was

additionally analyzed. There was no significant difference between BPE in those with a benign tumor and that in those with a malignant tumor before menopause ($p=0.175$). There was also no significant difference between BPE in those with a benign tumor and that in those with a malignant tumor after menopause ($p=0.976$) (Figure 3, Table 3). Although there was no statistically significant difference, BPE in those with a benign tumor before menopause tended to be higher than other BPE.

The statistical difference between BPE and contrast effect of benign or malignant tumor itself by each group was also analyzed. A graph of the contrast effect of parenchymal tissue, malignant tumor, and benign tumor in each group is shown in Figure 4. The background parenchymal tissues were divided into two groups, those with a benign tumor and those with a malignant tumor. Table 3 shows the relationships between BPE in those with a benign tumor and benign tumor enhancement, and between BPE in those with a malignant tumor and malignant tumor enhancement separately before menopause and after menopause. The background parenchymal tissue in those with a benign tumor had a lower contrast effect than benign tumor enhancement before menopause ($p<0.001$). The background parenchymal tissue in those with a malignant tumor also had a lower contrast effect than malignant tumor enhancement before menopause ($p<0.001$). There was a significant difference between BPE in those with a malignant tumor and malignant tumor enhancement after menopause ($p<0.001$). There was no significant difference between BPE in those with a benign tumor and benign tumor enhancement after menopause ($p=0.364$). (Table 3). In addition, benign tumor enhancement after menopause had a lower contrast effect than that before menopause ($p=0.025$).

All of the cases whose background parenchymal tissues had a higher contrast effect than the breast tumors at peak contrast-enhanced time turned out to be benign (Figure 5). Of these four cases, two were in the premenopausal group and two were in the postmenopausal group. The difference between BPE and breast tumor enhancement at peak time was the same irrespective of the tumor being benign or malignant before menopause ($p=0.073$). The difference between BPE and malignant tumor enhancement at peak time was bigger than the difference between BPE and benign tumor enhancement after menopause ($p<0.001$), suggesting that malignant tumors in postmenopausal women are more easily detected by CEUS.

Next, pathological evaluation of the parenchymal tissue was performed. In 11 cases (mean age, 45.5 years; range, 33-59 years; five benign tumors and six malignant tumors), CEUS showed background parenchymal tissues having a contrast effect greater than 13 dB. Patients whose tumors were ultimately diagnosed by mammotome biopsy or mass resection (n=5) and who had neoadjuvant chemotherapy after CEUS (n=2) were excluded. Pathological images of the remaining four cases were reviewed with a pathologist. The median number of days before surgery that CEUS was performed was 28 days. Case 1 was a 52-year-old woman with invasive carcinoma with NST. Breast tissue showed pathological atrophy. Mammotome biopsy revealed widespread scarring and hemorrhage around the tumor. Therefore, there were many blood capillaries and granulation tissues. Case 2 was a 39-year-old woman with invasive carcinoma with NST. On pathology, there were terminal duct lobular units (TDLUs) with their shape maintained and dilated vessels (Figure 6). Case 3 was a 33-year-old woman with ductal carcinoma in situ. There were pathologically well-developed lobules and dilated vessels lying between the lobules. Case 4 was a 56-year-old woman with invasive carcinoma

with NST. On pathology, there was atrophy of breast tissue but no blood vessels.

Meanwhile, in six cases (mean age, 62.8 years; range, 50-74 years, one benign tumor and five malignant tumors), CEUS showed background parenchymal tissues having a contrast effect less than 4 dB. Patients whose tumor was diagnosed by mammotome biopsy (n=1), who had neoadjuvant chemotherapy after CEUS (n=1), and who had widespread hemorrhage according to mammotome biopsy after CEUS (n=1) were excluded. Pathological images of the remaining three cases were examined. The median number of days before surgery that CEUS was performed was 19 days. Case 1 was a 61-year-old woman with invasive carcinoma with NST, case 2 was a 67-year-old woman with invasive carcinoma with NST, and case 3 was a 74-year-old woman with solid papillary carcinoma. Breast tissues were atrophied on pathology in all three patients (Figure 7).

Discussion

The first description below refers to the relationships among background parenchymal tissue, age, and menopause. Breast tissue consists of fat and fibroglandular tissue. BPE on contrast-enhanced MRI reflects the enhancement of normal breast parenchyma. It has been well known that BPE on MRI fluctuates with variations in hormones, particularly estrogen levels [7]. Therefore, it has been reported that there are significant differences between menstruating and menopausal groups in the distribution of BPE on MRI [8]. In addition, previous studies have also reported a significant association between ultrasonographic background echotexture and BPE on MRI in menstruating and menopausal groups [8,9]. This suggests that heterogeneous echotextures are found in premenopausal women because of abundant lobules and intralobular stroma, while homogeneous echotextures are found in postmenopausal women because of the small percentage of lobules and intralobular stroma affected by breast hormonal changes. On mammography, fibroglandular tissue is characterized as areas of breast tissue that are denser than fat. It has been reported that there are significant differences between the menstruating and menopausal groups in the distribution of mammographic density [8]. This may indicate that fibroglandular tissue has been gradually replaced by fat. In the present study, there was a weak negative correlation between BPE on CEUS and patient age. Moreover, as for BPE on CEUS, there was a significant difference between the menstruating and menopausal groups. This indicates that BPE on CEUS is also affected by hormonal changes. BPE on CEUS is decreased by diminution in the number of blood vessels because of the small percentage of lobules and intralobular stroma affected by breast hormonal changes.

Next, the relationship between background parenchymal tissue and breast cancer was

examined. A significant correlation between moderate and marked BPE on MRI and an increased risk of breast cancer has been reported [10]. It has been reported that BPE on MRI is a marker of physiologically active breast tissue that is more likely to undergo malignant transformation, perhaps specifically identifying areas of increased inflammation that recently have been linked to malignant breast tumorigenesis [11]. Besides, it has been known that increased mammographic density is correlated with breast cancer risk [10]. It has also been well known that increased mammographic density decreases the detection rate of breast cancer [12]. In this study, there was no significant difference between BPE in those with a benign tumor and that in those with a malignant tumor on CEUS. This suggests that the degree of BPE on CEUS does not express the risk of breast cancer. Additional studies to assess the relationship between BPE on CEUS and breast cancer are needed.

According to some previous studies, BPE on MRI did not show a significant correlation with mammographic density [8,9,13]. As for BPE on CEUS in the present study, there was no significant difference among the mammographic density groups, and among the degree of contrast effect on MRI groups. The reason for this was that the CEUS contrast agent, Sonazoid®, reflected proliferation of blood vessels. Furthermore, the MRI contrast agent, gadolinium, reflected absorption into the fibrillary element. The mammographic density reflected the amount of tissue present in the breast.

There have been a few reports comparing CEUS images and pathological findings. It has been reported that enhancement regions with SonoVue® (Bracco Spa, Milan, Italy) pathologically reflects high microvessel density, high cellular density, and inflammatory cell infiltration [14]. Moreover, it has also been reported that nonenhanced regions pathologically reflect low microvessel density, low cellular density, fibrous stroma,

dilated breast duct, degeneration, fibrotic response, and necrosis [14]. Mitsuzuka et al. reported that the findings of enhancement extending outward beyond the expected borders of malignant tumors with Sonazoid® reflected proliferation of blood vessels in the infiltrated region [15]. Mitsuzuka et al. also reported that nonenhanced or low-contrast effect lesions with Sonazoid® after neoadjuvant chemotherapy reflected hemorrhage, necrosis, and persisting scarred tissue [16]. In the present study, atrophy of breast tissue was shown in the cases with a contrast effect less than 4 dB. In addition, many blood capillaries, granulation tissues, and dilated vessels were seen in the cases with a contrast effect more than 13 dB. The result is not inconsistent with previous studies.

Finally, BPE on CEUS and breast tumor enhancement were compared. Previous studies demonstrated that natural and gently curved vessels along the margin of the tumor indicated a benign tumor, and tortuous and irregular vessels focusing on the peripheral tumor indicated a malignant tumor [17-20]. These findings reflected neoangiogenesis, cellular proliferation, and infiltration. In the present study, BPE on CEUS was lower than the enhancement of almost all tumors. This indicates the tumors' increased blood flow, as in the previous study. All of the cases whose background parenchymal tissues had a higher contrast effect than the breast tumors at peak contrast-enhanced time turned out to be benign. The results were consistent with those of a previous study that showed that some benign tumors showed low homogeneous enhancement of the entire lesion [1]. In addition, benign tumors after menopause had a lower contrast effect than those before menopause. The present result suggests that the pathological tissue of benign tumors varies with menopause. The number of benign tumor cases after menopause was small; thus, further studies are needed to confirm this.

There are a few limitations to this study. First, it was a single-site, single-reader, retrospective study. Second, in most cases of background parenchymal tissue with a high-contrast effect, the breast tumors were benign. The benign tumors were diagnosed by mammotome biopsy or mass resection; therefore, the background parenchymal tissue could not be evaluated pathologically. Finally, the menstrual cycle phase at the time of CEUS was not recorded in the medical records. The menstrual cycle should be evaluated as it may be an important factor related to BPE on CEUS. Additional studies are needed to determine BPE on CEUS.

Conclusion

BPE on CEUS was lower than enhancement of the malignant breast tumors. The degree of BPE on CEUS is possibly related to age, menstrual status, and atrophy of breast tissue. BPE on CEUS was the same between those with a malignant tumor and those with a benign tumor in each menstrual status.

Ethical statements

This study was approved by Nara Medical University.

Conflict of interest

The authors declare that they have no conflicts of interest.

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Figure legends

Figure 1. A 45-year-old woman with a palpable tumor in the outer upper quadrant of the left breast. This tumor was pathologically diagnosed as a phyllodes tumor.

(a) Gray-scale image showed a hypoechoic tumor. The background parenchymal tissue around the tumor showed a heterogeneous echotexture.

(b) Contrast-enhanced image showed a heterogeneously hyperenhanced lesion. The background parenchymal tissue showed an enhanced region.

(c) ROI was set at 3 mm. ROIs were put on the tumor and on the background parenchymal tissue at the same depth. A TIC was drawn by locating the ROI. The dB value of the tumor during the nonenhanced time was defined as T-baseline, and the dB value of the tumor at the peak contrast-enhanced time was defined as T-max. Likewise, the dB value of the parenchymal tissue during the nonenhanced time was defined as PT-baseline, and the dB value of the parenchymal tissue at the peak contrast-enhanced time was defined as PT-max. The contrast effect of the tumor was obtained by the difference between T-max and T-baseline. The contrast effect of the parenchymal tissue was obtained by the difference between PT-max and PT-baseline.

Figure 2. Scatter plot of the association between age and BPE. There was a weak negative correlation between BPE on CEUS and patient age.

Figure 3. Graph of the contrast effect of parenchymal tissue in those with a benign tumor and that in those with a malignant tumor. (a) Before menopause, (b) After menopause

BPE on CEUS was the same between those with a benign tumor and those with a malignant tumor in each menstrual status.

Figure 4. Graph of the contrast effect of parenchymal tissue, malignant tumor, and benign tumor. (a) Before menopause, (b) After menopause
The background parenchymal tissue had a lower contrast effect than the malignant and benign breast tumors before menopause. The background parenchymal tissue also had a lower contrast effect than malignant breast tumors after menopause.

Figure 5. Scatter plot of the difference between BPE and breast tumor enhancement at peak time. All of the cases whose background parenchymal tissues had a higher contrast effect than the breast tumors at peak contrast-enhanced time turned out to be benign.

Figure 6. Histopathological images of background parenchymal tissue. (a: hematoxylin and eosin (HE) stain, b: Elastica van Gieson (EVG) stain ×2.5)
Terminal duct lobular units (TDLUs) with their shape maintained and dilated vessels are shown.

Figure 7. Histopathological images of background parenchymal tissue. (a: HE stain, b: EVG stain ×2.5). Atrophy of breast tissue is shown.

Tables

Table 1. Relationships between contrast effect of breast tissue on CEUS and patient clinical and radiological characteristics

	Background parenchymal enhancement (dB)	P value
Menstrual status		0.042
Premenopausal group (n=24)	9.80 ± 4.22	
Postmenopausal group (n=41)	7.91 ± 3.07	
Mammographic density		0.134
Predominantly fatty breast (n=2)	8.40 ± 4.41	
Scattered fibroglandular fatty breast (n=26)	7.44 ± 3.30	
Heterogeneous dense breast (n=31)	9.66 ± 3.80	
Extremely dense breast (n=6)	8.31 ± 3.00	
Enhancement on MRI		0.283
Minimal (n=32)	8.17 ± 3.32	
Mild (n=16)	9.98 ± 4.47	
Moderate (n=11)	8.81 ± 3.08	
Marked (n=0)		
Breast tumor		0.031
Benign (n=18)	10.17 ± 4.39	
Malignant (n=47)	8.01 ± 3.13	

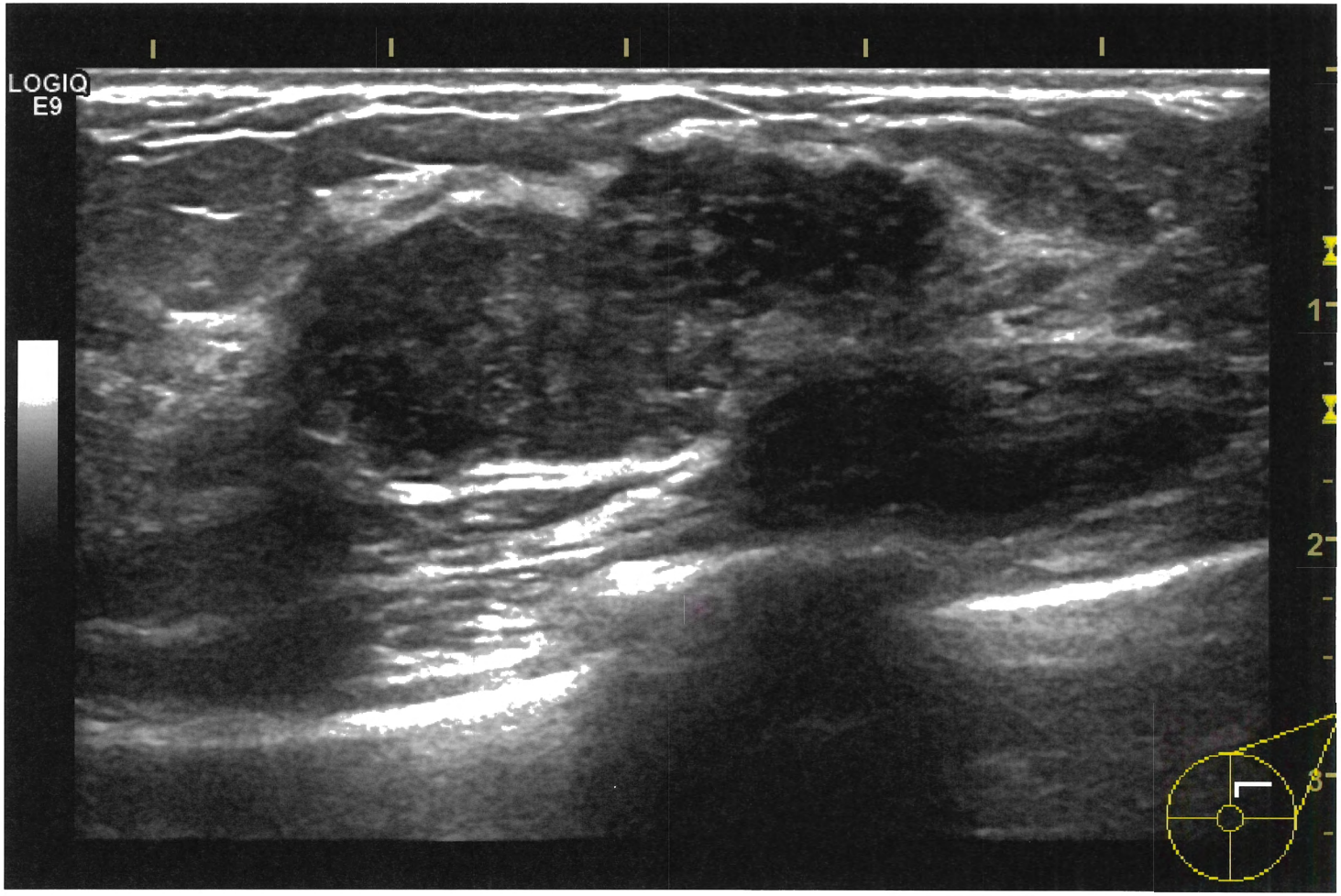
Table 2. Relationships between benign or malignant tumor and menstrual status

	Before menopause (n)	After menopause (n)	Total (n)
Benign (n)	14	4	18
Malignant (n)	10	37	47
Total (n)	24	41	65

Table 3. Relationships among contrast effect of background parenchymal tissue in those with a benign tumor, background parenchymal tissue in those with a malignant tumor, benign tumor, and malignant tumor in premenopausal group and postmenopausal group.

	Contrast effect (dB)	P value [95% CI*]
Before menopause		
Parenchymal tissue in those with benign tumor (n=14) / Parenchymal tissue in those with malignant tumor (n=10)	10.80 ± 4.58 / 8.40 ± 3.38	0.175 [-1.15, 5.94]
Parenchymal tissue in those with benign tumor (n=14) / Benign tumor (n=14)	10.80 ± 4.58 / 17.69 ± 4.88	<0.001 [-10.57, -3.21]
Parenchymal tissue in those with malignant tumor (n=10) / Malignant tumor (n=10)	8.40 ± 3.38 / 16.59 ± 3.19	<0.001 [-11.27, -5.09]
After menopause		
Parenchymal tissue in those with benign tumor (n=4) / Parenchymal tissue in those with malignant tumor (n=37)	7.96 ± 3.14 / 7.91 ± 3.10	0.976 [-3.26, 3.36]
Parenchymal tissue in those with benign tumor (n=4) / Benign tumor (n=4)	7.96 ± 3.14 / 10.81 ± 4.90	0.364 [-9.98, 4.26]
Parenchymal tissue in those with malignant tumor (n=37) / Malignant tumor (n=37)	7.91 ± 3.10 / 19.41 ± 4.16	<0.001 [-13.21, -9.81]

CI* : Confidence interval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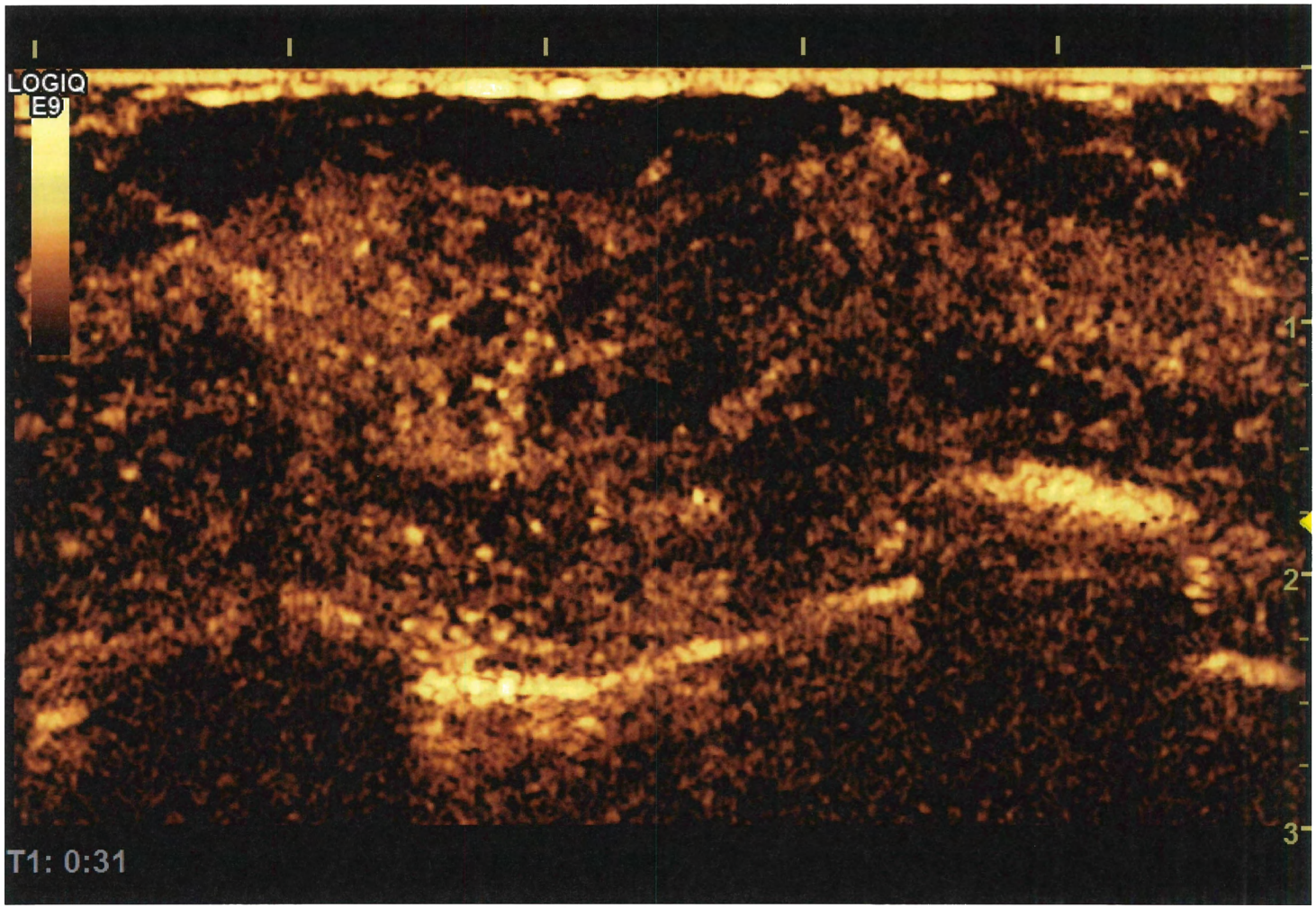
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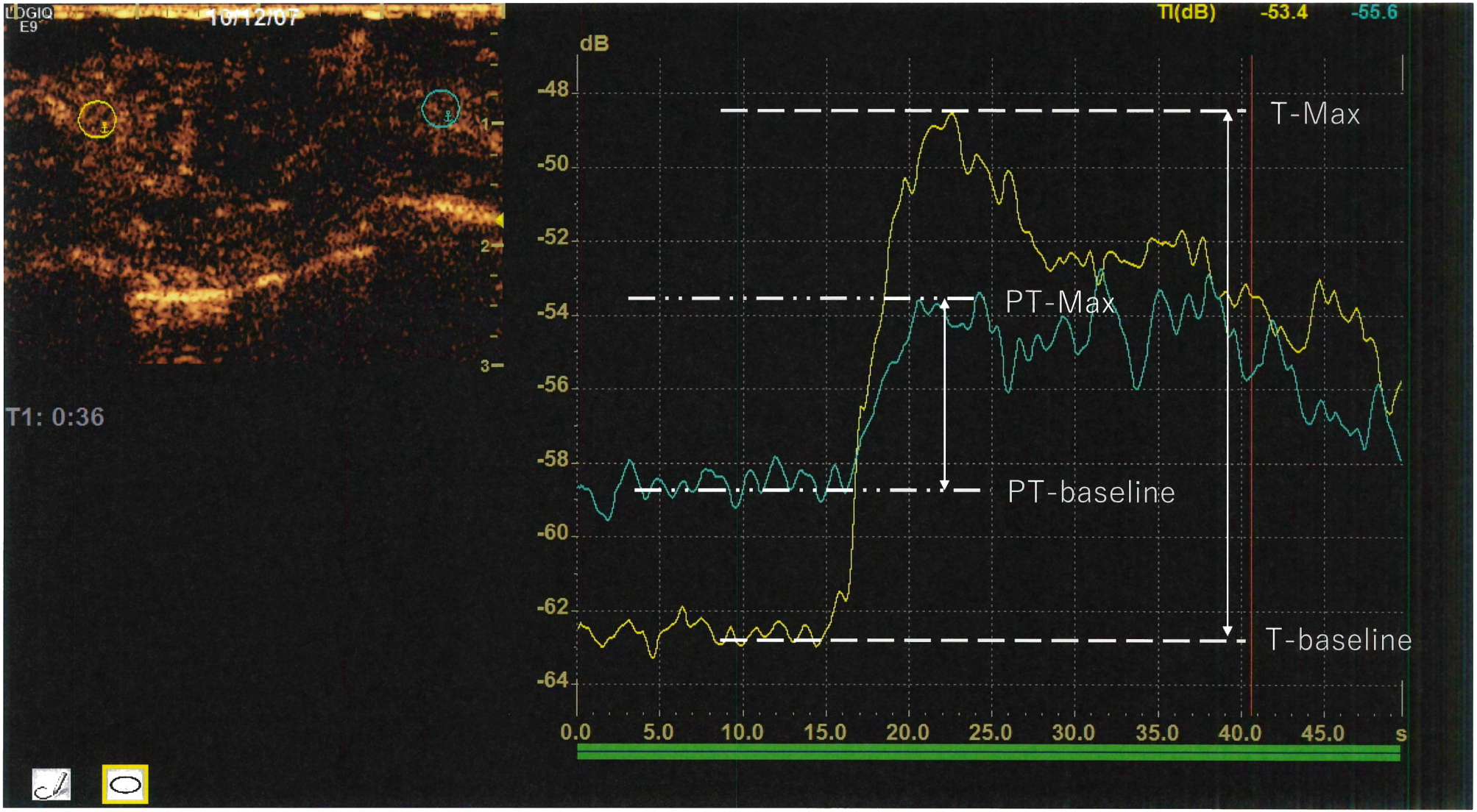
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T-Max
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PT-baseline
T-baseline
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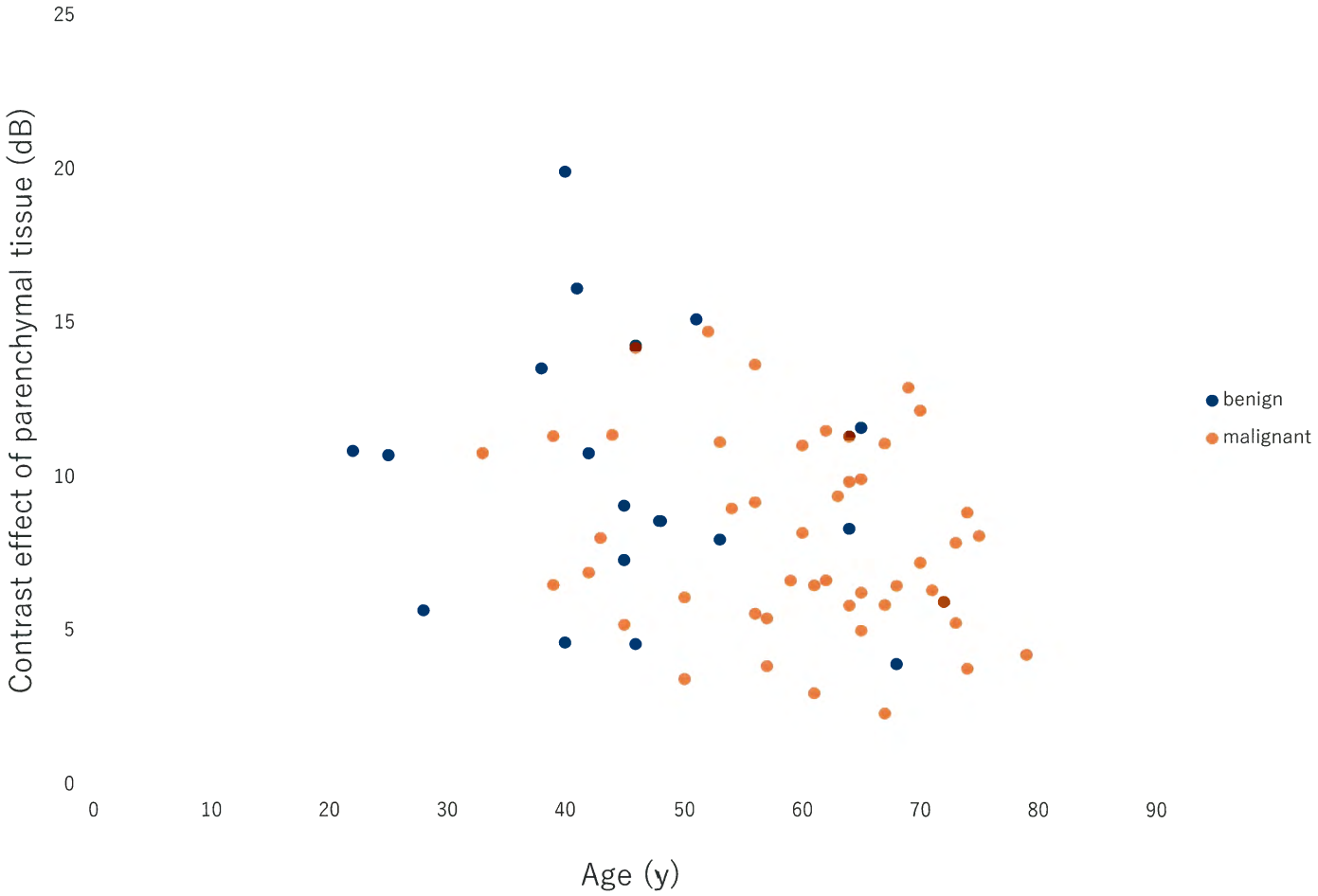
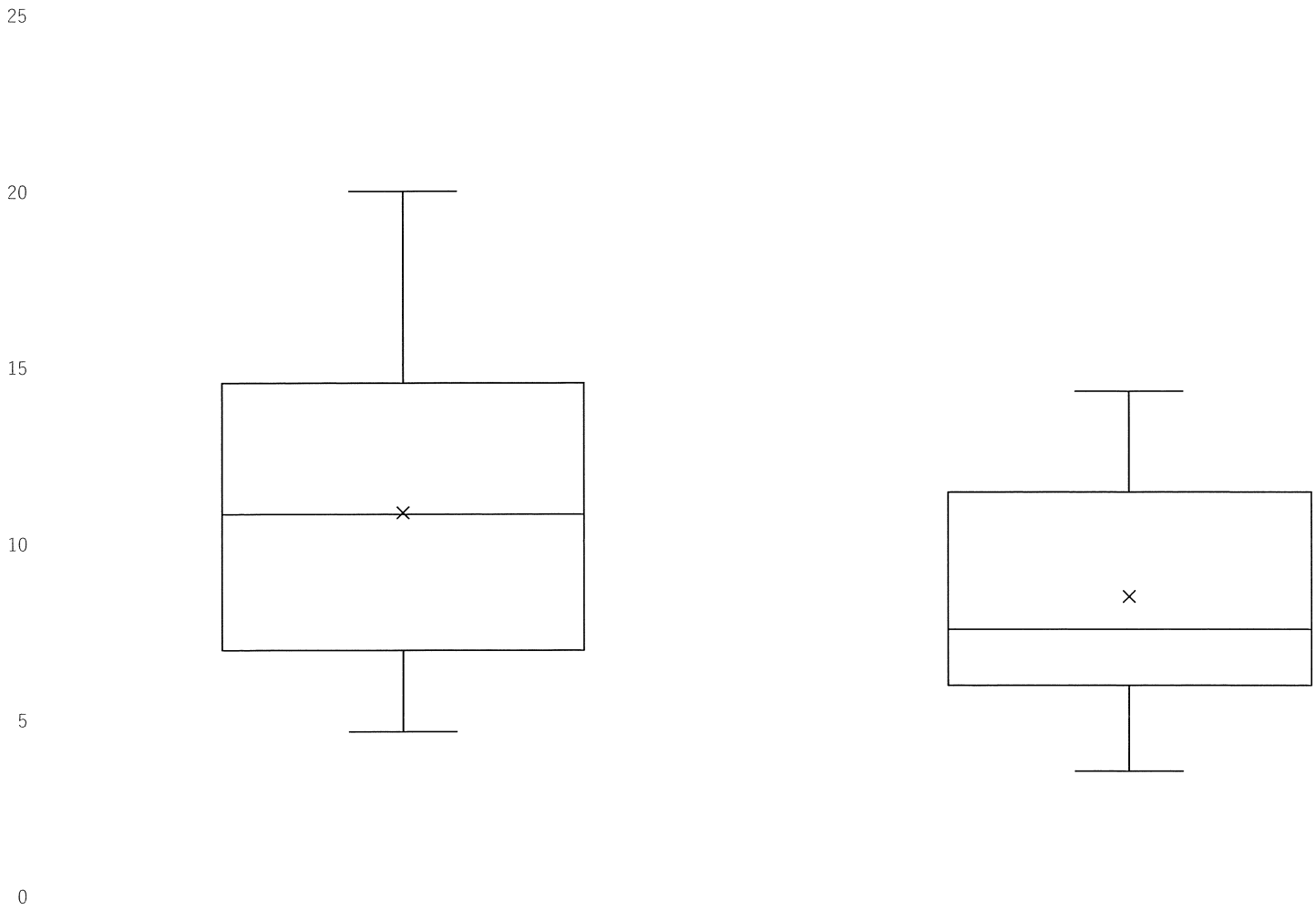
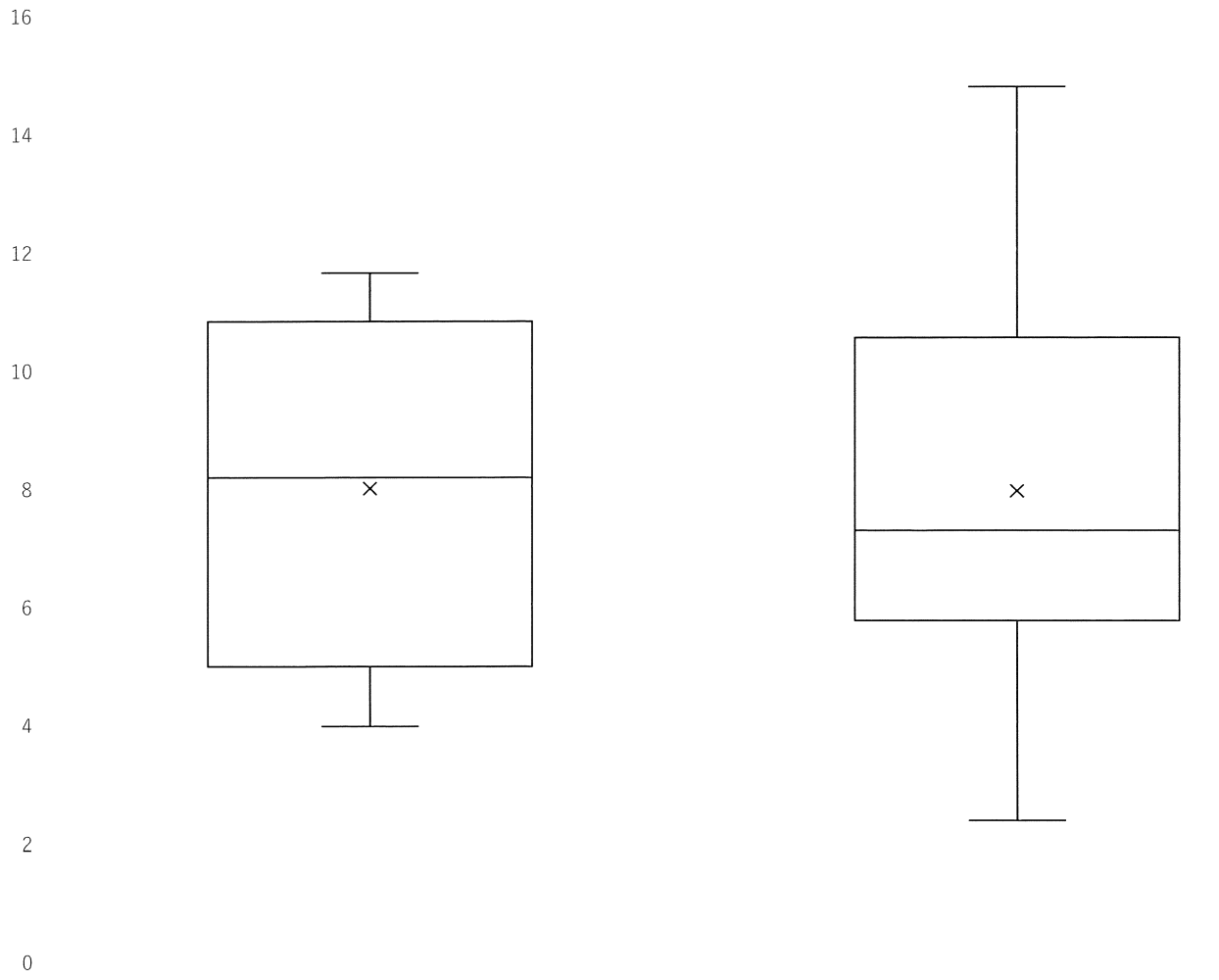
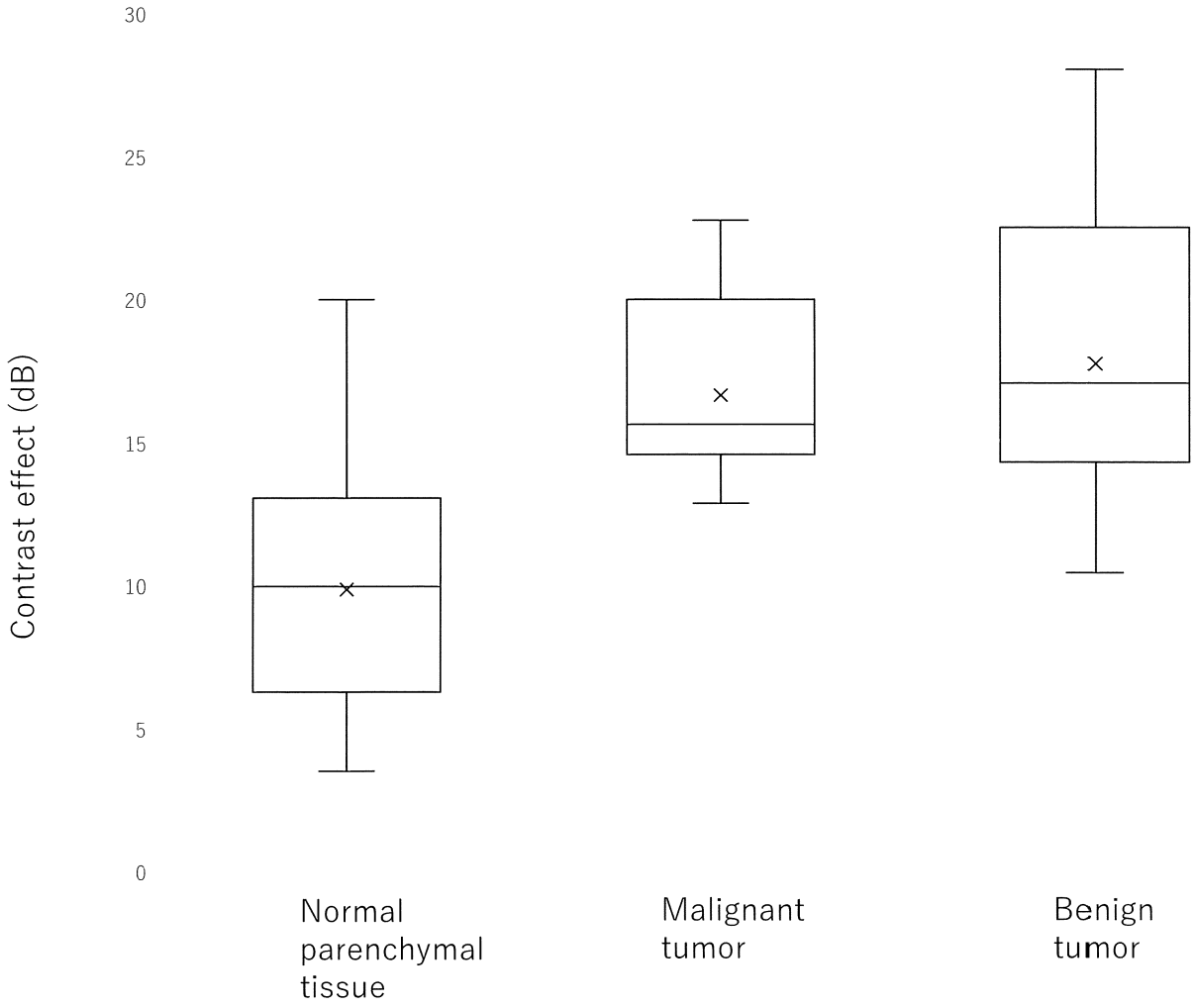
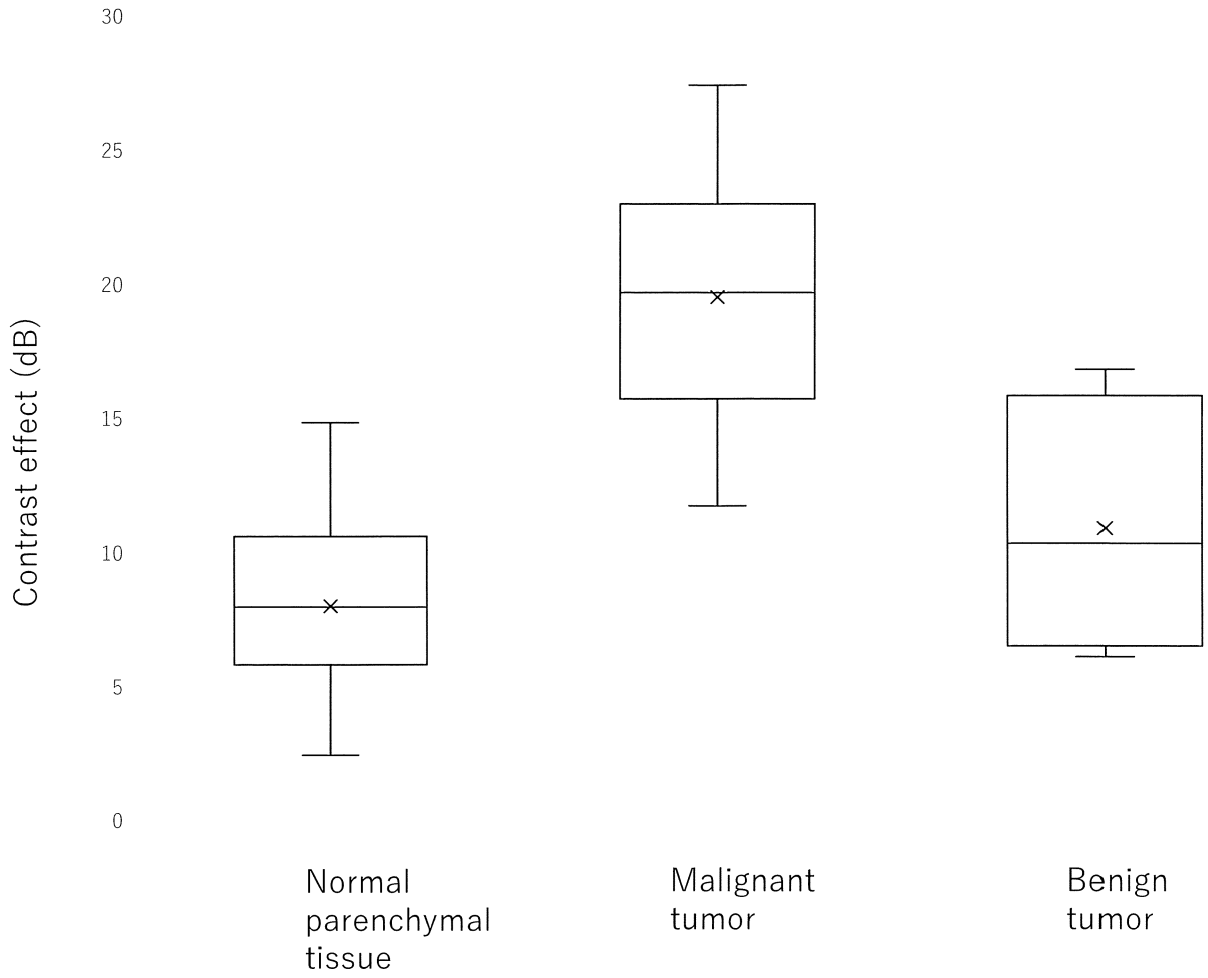
20.0
25.0
30.0
35.0
40.0
45.0
s

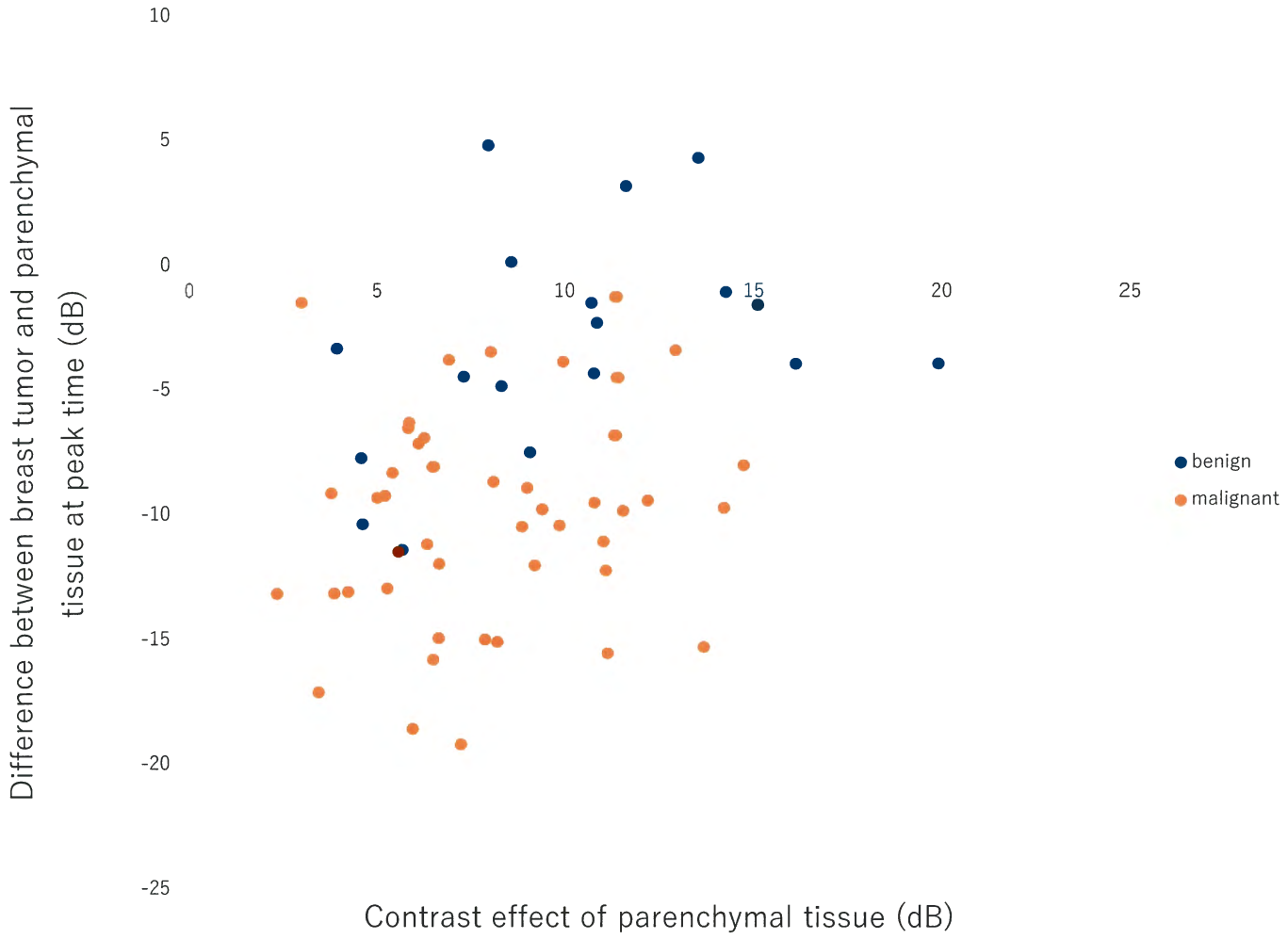

Contrast effect of parenchymal tissue (dB)
25
20
15
10
5
0
0
10
20
30
40
50
60
70
80
90
Age (y)
benign
malignant


25
20
15
10
5
0
Background parenchymal tissue with benign tumor
Background parenchymal tissue with malignant tumor


16
14
12
10
8
6
4
2
0
Background parenchymal tissue with benign tumor
Background parenchymal tissue with malignant tumor


Contrast effect (dB)
30
25
20
15
10
5
0
Normal parenchymal tissue
Malignant tumor
Benign tumor


Contrast effect (dB)
30
25
20
15
10
5
0
Normal parenchymal tissue
Malignant tumor
Benign tumor


Difference between breast tumor and parenchymal tissue at peak time (dB)
10
5
0
-5
-10
-15
-20
-25
0
5
10
15
20
25
Contrast effect of parenchymal tissue (dB)
benign
malignant