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Five-year outcomes of partial breast-proton beam therapy without lumpectomy for early-stage breast cancer: An interventional prospective study

Etsuyo Ogo

etsuogo@kurume-u.ac.jp

Kurume University School of Medicine: Kurume Daigaku Igakubu Daigakuin Igaku Kenkyuka
https://orcid.org/0000-0002-4909-0217

Takeshi Arimura
Therapy Institute

Takashi Ogino
Therapy Institute

Uhi Toh
Kurume University School of Medicine: Kurume Daigaku Igakubu Daigakuin Igaku Kenkyuka

Kenta Murotani
Kurume University - Asahimachi Campus: Kurume Daigaku

Ichiro Isomoto
Saint Francis Hospital

Makoto Kubo
Kyushu University: Kyushu Daigaku

Reiki Nishimura
Therapy Institute

Yusaku Miyata
Kurume University School of Medicine: Kurume Daigaku Igakubu Daigakuin Igaku Kenkyuka

Gen Suzuki
Kyoto Prefectural University of Medicine: Kyoto Furitsu Ika Daigaku

Yoshio Hishikawa
Therapy Institute

Shoshu Mitsuyama
Kitakyushu Municipal Medical Center: Kitakyushu Shiritsu Iryo Center

Ryoichi Nagata
Therapy Institute

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Abstract

Background

We report on our initial clinical experience with partial breast proton therapy (PB-PBT) without tumor resection as an alternative to partial mastectomy for low-risk early-stage breast cancer.

Methods

This trial commenced in 2015, and eligibility criteria included women with cT1N0M0 invasive ductal carcinoma, estrogen receptor positivity, human epidermal growth factor receptor type-2 negativity, age of 40–70 years, and a performance status of 0 or 1. In Phase I, PB-PBT was administered at 62.4 Gy in 26 fractions using the field-in-field technique. After confirming that no serious adverse events occurred, Phase II was conducted using the same dose. Follow-up evaluations were conducted every 3 months for the first year after irradiation and every 6 months thereafter.

Results

As of December 2025, 11 patients had completed a follow-up of ≥ 5 years. The median follow-up time was 82 months. Tumors exhibited immediate shrinkage post-PB-PBT, with morphological changes on ultrasonography and magnetic resonance imaging observed within 3–6 months. No recurrence was observed within the irradiated field in patients with > 5 years of follow-up. Dermatitis was Grade 1 in 55% of cases and Grade 2 in 45%; there were no cases of Grade ≥ 3. Grade 1 telangiectasia was observed in 36% of patients after 2 years, although most patients tolerated the treatment well.

Conclusion

Preliminary clinical observations suggest that PB-PBT without lumpectomy achieves results within specific criteria and that it could be an option for breast cancer treatment using radiation therapy alone.

Introduction

Breast-conserving therapy (BCT) involves performing tumor excision and sentinel lymph node biopsy (SLNB), followed by radiation therapy (RT). The 2022 Japanese Breast Cancer Society Clinical Practice Guidelines for Breast Cancer recommend that post-BCS RT be used for early breast cancer [1]. Post-BCT recurrences predominantly occur in the peritumoral bed, with rates of 68%–83% [2–4]. Patients with initial recurrences within 3 cm of the tumor bed have a lower survival rate and a higher incidence of distant metastases [2]. These findings suggest that targeting RT at the peritumoral bed might decrease the recurrence risk after partial breast resection [5].

The National Surgical Adjuvant Breast and Bowel Project B-39/Radiation Therapy Oncology Group reported 10-year intramammary recurrence rates of 3.9% and 4.6% in the whole breast irradiation (WBI) and accelerated partial breast irradiation (APBI) groups, respectively, reflecting a minimal difference [6]. Reports examining non-surgical curative stereotactic body radiation therapy and stereotactic ablative body radiation therapy for breast cancer indicate that these treatments are being administered in accordance with the American Society for Radiation Oncology criteria for APBI [7]. While primary treatment efficacy is expected, concerns remain regarding an increased risk of late toxicity and technical challenges [8]. Compared with conventional RT, proton beam therapy (PBT), a form of particle RT, facilitates precise radiation delivery to the target area while minimizing exposure to surrounding healthy tissues.

After BCS, RT to the conserved breast is associated with recurrence and mortality rates that are reduced by a half and sixth, respectively [9]. While research on post-BCS partial irradiation is well-established, investigations regarding partial irradiation without lumpectomy are scarce and its application remains confined to clinical trials. In Japan, although case studies have examined definitive RT using carbon-ion beams without surgery [10], none evaluated PBT. Furthermore, the optimal dose of PBT for patients with early-stage breast cancer who did not undergo breast-conserving surgery has not yet been established and no data are available. This study was designed as an observational interventional study to evaluate the safety and cosmetic outcomes [11] of PB-PBT for early-stage breast cancer in Japanese patients.

Materials and Methods

This study included a follow-up period of at least 5 years for low-risk patients.

Ethics

The research protocol was registered in the University Hospital Medical Information Network Clinical Trial Registry (UMIN000017579). This study was approved by the Ethics Committee and Institutional Review Board of Medipolis Proton Therapy and Research Center (MPTRC) (approval number 9; May 1, 2015) and Kurume University (approval number 16069; July 19, 2016) and conducted in accordance with the Declaration of Helsinki and Introduction to Clinical Research guidelines. The report was prepared in accordance with the TREND or CONSORT extension guidelines for non-randomized trials. Written informed consent for study participation and publication of de-identified data and images was obtained from all eligible patients by a radiation oncologist. Patient suitability was assessed through multidisciplinary consultation involving breast surgeons, radiation diagnosticians and oncologists, and Kyushu Particle Beam Study Group members. Four medical safety managers reviewed and approved the study protocol. Centralized, objective reviews were used for histopathological and imaging diagnoses.

Statistical analysis

Local control and overall survival were estimated using the Kaplan–Meier method, and the 5-year rates with 95% confidence intervals (CIs) were calculated. As no local recurrence events were observed during

the follow-up period, the CI for local control based on the Kaplan–Meier method was not estimable. Therefore, as a supplementary analysis, an exact 95% CI for the binomial proportion at 5 years was calculated using the Clopper–Pearson method.

Study oversight

This clinical trial began in May 2015. The protocol involved the generation of high-quality proton dose–volume histograms tailored for small breast cancers.

In Phase I, the recommended PB-PBT dose for early-stage breast cancer was calculated with reference to the biologically equivalent dose reported by Rosenstein [12]. Given that standard RT for cases with positive surgical margins following partial mastectomy is administered at 60 Gy in 30 fractions to the tumor bed and that the standard dose for chemoradiotherapy in unresectable advanced head and neck tumors is 70 Gy in 35 fractions, we estimated the optimal dose for treating early-stage (Stage I) breast cancer with RT alone based on the α/β ratio of breast cancer. Given that hypofractionated RT is as effective as standard fractionation and may result in fewer late toxicities, we also performed calculations using 25–26 fractions [13]. Since the α/β ratio for breast cancer tissue is 4 Gy and the tumor control effects are considered generally equivalent under the compared dose and fractionation conditions, this study focused on the effects on normal tissues and, as part of the bioequivalence assessment, examined equivalent doses with respect to adverse events such as dermatitis and fibrosis (Table 1). We concluded that the 62.4 Gy (RBE)/26 fractions were biologically appropriate for this Phase I trial.

Table 1
The α/β ratio for breast cancer tissue

2 Gy × 25 fr	**Fibrosis α/β=2Gy**	**Breast tumor control α/β=4 Gy**	**Erythema α/β=8Gy**	**Tumor control α/β=10 Gy**	**Desquamation α/β=11 Gy**
	100	**75**	**63**	**60**	**59**
2 Gy × 33 fr	132	99	83	79	78
2 Gy × 35 fr	140	105	87	84	82
2.4 Gy (RBE) × 26 fr	137	100	81	77	76
2.5 Gy (RBE) × 26 fr	146	105	85	81	79
2.7 Gy (RBE) × 26 fr	165	118	94	89	87
fr: fractions					

The study enrolled 4 patients in Phase I and at least 20 patients in Phase II. The enrollment period was 10 months for Phase I and 13 years for Phase II, with a follow-up period of 5 years (up to 10 years). Since this study is a proof-of-concept trial using proton therapy, a stopping rule was established regarding the planned number of cases for the Phase II trial. After the first 10 cases were enrolled in the Phase II trial, a report was submitted to the Kyushu Particle Beam Study Group and Ethics Committee for review to advise on whether the study should continue. Members of the group evaluated the appropriateness of the doses recommended in Phase I; in Phase II, the safety and efficacy of treatment were evaluated using the doses recommended in Phase I. The primary endpoints were the incidence and severity of complications. Secondary endpoints included intramammary recurrence-free survival, the correlation between the site of intramammary recurrence and clinical target volume (CTV), duration of local control, overall survival, and cosmetic outcomes.

In the results of the RTOG 0319 trial, the incidence of Grade 3 treatment-related adverse events in APBI using 3DCRT following BCS was 7.7% [4]. Therefore, in this study, PB-PBT was deemed acceptable on the condition that the incidence of Grade ≥ 3 complications did not exceed 7.7%.

Eligibility criteria

Inclusion criteria

Participants were women aged 40–70 years with Union for International Cancer Control stage I (T1N0) breast cancer. Tumors measured ≤ 2 cm along the longest diameter, had clear margins, and were clearly visible on ultrasonography or magnetic resonance imaging (MRI). MRI scans showed no extensive invasion or intraductal extension, and mammography showed no malignant calcification suggestive of widespread disease.

Tumors were located approximately 1 cm from the skin surface and ribcage, measured using vertical ultrasonography imaging, without excess compression, ensuring safe radiation delivery and minimizing exposure of adjacent normal tissue. No axillary lymph node metastases were permitted, as confirmed by imaging. Systemic imaging revealed no evidence of distant organ metastases.

The primary tumor was histopathologically confirmed as invasive ductal carcinoma. Hormone receptor status was considered; estrogen receptor (ER)-positive and human epidermal growth factor receptor type-2 (HER-2)-negative with progesterone receptor (PgR) positivity were considered favorable. Histological findings and receptor status were determined according to each institution’s criteria. Hormone receptor status was determined based on the Allred Score, HER2 status was determined using the immunohistochemistry method, and Ki67 cutoff values were set at 20% in accordance with each institution’s diagnostic criteria. Luminal A-type tumors were prioritized because of their favorable prognosis and responsiveness to adjuvant therapy.

The Eastern Cooperative Oncology Group performance status was 0 or 1. Before enrollment, patients were provided with an explanation of the trial and written informed consent was required, including acknowledgment of standard treatments recommended by the Japanese Breast Cancer Society Clinical Practice Guidelines. Additionally, consent included acknowledgment of the availability of salvage surgery for recurrence. All patients received approval for trial entry by the Institutional Cancer Board.

Exclusion criteria

Patients were excluded if they were receiving RT to the affected breast; had prior radiation to overlapping treatment fields; or had undergone previous surgery, chemotherapy, or molecular targeted therapy to the affected breast. The exclusion criteria further included severe infectious diseases or specific skin inflammatory disorders, severe diabetes mellitus, and pregnancy. Patients with multiple malignancies or those with synchronous bilateral breast cancer were also excluded. Any patient deemed unsuitable for participation by the treating physician was excluded.

Eligibility confirmation and treatment preparation

The overall study flowchart is presented in Fig. 1. Eligible patients underwent routine clinical staging. Subsequently, tumor sampling was performed using core-needle biopsy (minimum 14-gauge), followed by biomarker testing for hormone receptor evaluation, including assessments for ER and PgR, as well as the Ki-67 proliferation index. The biopsy puncture site was documented for treatment planning.

If the lesion was confirmed to be an isolated malignant tumor, an SLNB was performed and only patients with negative SLNB results were eligible for treatment. Typically, 10–14 days after SLNB, once a negative result was confirmed, approximately two metal markers were inserted into the breast tissue to serve as treatment targets. Approximately 5–7 days after the metal markers were inserted, the patient visited the MPTRC to undergo preparation for PB-PBT, which began approximately 10–14 days after the preparation was completed.

Fiducial marker placement for PBT

To accurately localize small breast tumors during PB-PBT, fiducial markers were implanted in the breast as landmarks. Various examinations and SLNB were performed to confirm the diagnosis. The marker was implanted after the indication was confirmed, approximately 1 month after the core needle biopsy. VISICOIL™ (IZI Medical Products, MD, USA), a flexible linear fiducial marker designed for precise image-guided RT, was used. Each marker measured 0.5 mm in diameter and 5 mm in length.

Markers were typically implanted near the posterior nipple line, 1.5–2.0 cm from the nipple center, with the exact placement adjusted based on tumor location and clinical trial office guidance. Subsequently, pre-treatment preparations, including the making of a breast fixation device, were completed and PB-PBT was initiated.

During daily irradiation, the position of the markers was verified using X-ray-guided image-guided radiation therapy.

PBT delivery and patient management

PB-PBT was conducted at the MPTRC, with patient selection, diagnosis, SLNB, VISICOIL™ marker insertion, and post-treatment follow-up examinations performed at Kurume University Hospital.

When using the breast immobilization system, the patient was first positioned supine with the torso secured, then rotated 180 degrees to a prone position, where a custom-made three-dimensional breast immobilization device was secured. Then, the patient was returned to the supine position and the breasts were secured in a slightly elevated position. After immobilization, the patient was transferred to the PB-PBT treatment table [14] (Fig. 2). Since the position of the breast tumor varies significantly with respiration, the treatment was performed using respiratory gating technology (gating at 1/10 of the inspiratory amplitude). The PB-PBT technique utilized the passive scattering method. Daily alignment was performed by using orthogonal X-rays to verify the position of the markers.

The treatment plan used computed tomography (CT) images (2-mm slice thickness) with a three-dimensional planning system (Xio-M, Elekta, Stockholm, Sweden; Hitachi, Tokyo, Japan). The gross tumor volume (GTV) referred to the area where the tumor clearly appeared on ultrasonography, MRI, and CT scans. CTV included GTV and a safety margin to encompass potential tumor spread into nearby mammary and lymph ducts, based on MRI scans. Using the field-in-field technique, a curative dose was delivered to the tumor site. Patients received irradiation once daily, 5 days per week. In breast-conserving surgery, the tumor is generally excised with a 1.5-cm margin, followed by postoperative RT to the residual breast tissue. Following this principle, the tumor identified on the images was used to define the GTV. Taking setup uncertainties into account, CTV1 (defined as the standard surgical resection margin) was set within a range of 1–1.5 cm around the GTV and 62.4 Gy (RBE) was delivered in 26 fractions. The remaining breast tissue (CTV2), defined as the area 1.5–2 cm around CTV1, was irradiated with 46.8 Gy (RBE) in 26 fractions. PTV1 and PTV2 were defined as 3-mm extensions of CTV1 and CTV2, respectively, and the overlap regions were adjusted individually. The dose evaluation point was set at the isocenter. Organ at risk was defined as follows: Skin Dmax: ≤110%; Ipsilateral lung: V20Gy < 3%: Heart (for the left side): Mean heart dose < 3 Gy.

Post-treatment monitoring and management

After PB-PBT completion, patients underwent ultrasonography and MRI at 3, 6, 12, 18, 24 months and every 6 months thereafter. Assessments included monitoring for recurrences, cosmetic outcomes, treatment-related toxicities, and patient satisfaction. Tumor size was measured and assessed using ultrasonography and MRI. On MRI scans, if tumor tissue taking up contrast agent remained, the contrast-enhanced area was measured. If there was no change in tumor size during follow-up or if enlargement was observed, recurrence was suspected and a biopsy was performed. If recurrence was confirmed, salvage surgery was performed. For local recurrence, the recurrent tumor was surgically removed, with

post-mastectomy breast reconstruction considered individually by the breast plastic surgeon. For any recurrence, a central histopathological review was performed to assess the correlation between previous irradiation and recurrence. Annual meetings of the Kyushu Breast Cancer Particle Therapy Study Group reviewed individual cases. Radiation-related local recurrence was defined as recurrence within the CTV1 or CTV2, and was distinguished from recurrence in other parts of the same breast, as well as regional lymph node recurrence and distant recurrence.

As all patients had luminal-type tumors, endocrine therapy was planned for approximately 5 years, aligning with standard breast cancer care under the supervision of the breast surgery department. Treatment was primarily based on anti-estrogen therapy for premenopausal patients and aromatase inhibitors for postmenopausal patients; chemotherapy was generally not administered.

The cosmetic evaluation was conducted using the Harvard/Harris Aesthetic Scale (Excellent/Good/Fair/Poor) [15].

Furthermore, regarding standard surveillance for cases managed conservatively, including contralateral breast cancer, periodic ultrasound, MRI, CT, and mammography were performed under the supervision of the breast surgery department.

Results

Twenty-two patients were enrolled until December 2025 (Fig. 3), including 4 in Phase I and 18 in Phase II. PB-PBT was completed in 21 patients. In all cases, a prescribed dose of 62.4 Gy was confirmed for the CTV1. No displacement of fiducial markers was observed during treatment, and fixation reproducibility was not an issue. All Phase I patients completed the therapy as planned. In Phase II, the following cases were excluded: one patient discontinued treatment immediately post-PB-PBT, one patient became untraceable 3 years and 9 months after the start of PB-PBT, and one patient underwent salvage surgery for a recurrence outside the irradiated field 4 years and 6 months after the start of PB-PBT; however, postoperative histopathological examination revealed no recurrent lesions within the radiation field. The results regarding the efficacy and safety of the treatment were analyzed for 11 patients who were followed up for > 5 years (Table 2).

Table 2
Charactaristics of the cases confirmed to have progressed for more than 5 years

Charactaristics		**Number Total (phase1)**
Age	40–49	5 (1)
(years old)	50–59	3 (1)
	60–69	3 (2)
Location	Right A	3
	B	1 (1)
	C	1
	D	1 (1)
	E	0
	Left A	1 (1)
	B	0
	C	4 (1)
	D	0
	E	0
Histological type	IDC	11 (4)
Subtype	ER(+)PgR(+)HER2(-)	
Tumor size	-10	3 (2)
(mm)	10–15	4 (2)
	15–20	4
SLNB	Positive	0
	Negative	11 (4)
Therapy after PBT	Hormone Therapy	5 (1)
	TAM	6 (3)
	AI	0
	Chemotherapy	
Adverse Events	Radiation dermatitis	G3 ≤ 0
Acute	Immediate – < 1M	G2 6 (2)
Late	The period during which Grade 2 becomes Grade 1	G1 5 (2)

Charactaristics		Number Total (phase1)
	Pigmentation	1M 4 (2)
		2M 2
	No	2
	G1	9 (4)
	Telangiectasia G1	4 (2)
	No	1
	1Y≤ <2Y	4
	2Y≤ <3Y	1 (1)
	3Y≤ <4Y	1 (1)
	4Y≤	
Cosmetic score	Excellent	10 (4)
(Harris method)	Good	1
at 5 years	Fair	0
	Poor	0

Patients were 40–65 years old, with tumor diameters of 7–16 mm. All patients had node-negative disease on SLNB (cT1N0M0) and were $ER^+/PgR^+/HER\text{-}2^-$, with tumors located in the left (n = 5) and right (n = 6) breasts. All cases were selected strictly according to the inclusion criteria. No local recurrences were observed in the irradiated field during the follow-up period. However, one patient was found to have ipsilateral axillary lymph node metastasis 18 months after PB-PBT and systemic chemotherapy was initiated; however, liver metastasis was confirmed 36 months later. Although chemotherapy was continued, liver metastases and intraperitoneal lymph node metastases progressed and the patient died of distant metastasis 5 years after PB-PBT. No local recurrence was observed at the PB-PBT site in this case.

Imaging findings showed tumor shrinkage within 6 months after PB-PBT. Ultrasound findings revealed the tumor as a hypoechoic lesion, which flattened and transformed into scar tissue within 6 months (Fig. 4a). The reduction rate of measurements including the structures on ultrasound was 20%–81% at 6 months after PB-PBT and 46%–87% at 12 months; no such structures were detectable after 42 months. Contrast-enhanced MRI scans confirmed the disappearance of contrast enhancement at 6 months post-treatment in all cases. In some cases, cord-like structures were observed at the site of the primary lesion. None of these structures showed contrast enhancement and were not considered tumors (Fig. 4b). The rate of volume reduction, including the structures visible on MRI, was 14%–100% at 6 months post-PBT and 36%–100% at 12 months. Cases in which the structures were still visible

accounted for 36% (4 cases) at 12 months and 9% (1 case) at 24 months; they were no longer detectable after 30 months. Although these lesions were closely monitored through imaging-based follow-up, no changes or enlargement were observed and they gradually decreased in size. Positron emission tomography-CT scans showed no accumulation at 12 months in any patient. No tumor recurrence was observed within the irradiated field during the follow-up period. Local control following PB-PBT was excellent. The 5-year local control rate was 100% (95% CI: not calculated), and the 5-year survival rate was 90.9% (95% CI: 50.8% – 98.7%) (Fig. 5).

Skin reactions varied in a manner related to tumor proximity to the skin, and Common Terminology Criteria for Adverse Events (CTCAE; v5.0) Grade ≤ 2 skin reactions were observed in all cases immediately after irradiation and 2 weeks after PB-PBT. However, when asked about it during examinations, the patients declared no changes in their quality of life. Appropriate local cooling, topical steroids, and moisturizers facilitated improvement without exacerbation. One month after PB-PBT treatment, the dermatitis had resolved.

Radiation dermatitis was observed in 6 cases (Grade 2); however, 4 cases improved to Grade 1 within 1 month, and 2 cases improved within 2 months. Adverse events included mild induration in 1 case, Grade 1 hyperpigmentation following PB-PBT in 9 cases, and telangiectasia in 7 cases. These were most frequently observed in patients in their 40s and early 50s. However, no patient reported discomfort.

As adjuvant therapy, while premenopausal patients received tamoxifen (5 cases) following PB-PBI, postmenopausal patients underwent hormone therapy with aromatase inhibitors (6 cases); all 11 patients with a follow-up period of ≥ 5 years were continuing hormone therapy at the time of writing.

Discussion

In this study, we selected patients according to strict eligibility criteria to mitigate the risk of missed positive margins and potential multifocal lesions. We also conducted rigorous follow-up to evaluate ipsilateral breast recurrence and recurrence within the irradiated field. In the eligible cases, no recurrence was observed within the irradiation field.

Recurrence sites in the ipsilateral breast post-BCT are typically within 3 cm of the original tumor bed, regardless of RT. For eligible patients, RT targeting the tumor bed area was deemed adequate to reduce recurrence risk after PB excision. The efficacy of APBI, which targets the tumor bed, is well-documented. According to the American Society of Radiation Oncology consensus statement, partial breast irradiation is recommended in Western settings for patients meeting all the following criteria: Stage I–II disease, ER-positivity, age ≥ 40 years, and tumor size ≤ 2 cm [16]. Several institutions have reported using PBT in prospective ABPI studies, noting improved dose distribution [17, 18]. These developments informed the current study design.

In a Phase I/II APBI trial, PBT showed cosmetic outcomes comparable to those of 3DCRT while effectively reducing lung and heart exposure [19]. In another PBT report [20], after an approximate 5-year

follow-up period, the recurrence-free survival rate was 97%, with no cases of Grade ≥ 3 acute skin reactions, while late skin reactions included Grade 1 telangiectasia in 7% of patients. PBT tends to cause more severe skin reactions compared to 3DCRT; reports indicate that 54% of patients treated with PBT experienced hyperpigmentation and 69% experienced telangiectasia [21]. During the follow-up period at our institution, compared with that seen in conventional WBI, PB-PBT-induced dermatitis tended to be more severe and prolonged. Acute radiation dermatitis (CTCAE Grade 2) developed during the second half of PB-PBT, although it resolved within 2 months after PB-PBT and did not affect the quality of life.

Late adverse events showed individual variation; at high-dose administration sites, hyperpigmentation Grade 1 occurred in approximately 80% of patients and telangiectasia in approximately 63%. Post-RT adverse events following PB removal include fatigue, dermatitis, breast swelling, xeroderma, radiation pneumonitis, upper arm edema and nerve damage, soft tissue necrosis, rib fractures, and cardiopathies [22, 23]. In BCT, Grade ≥ 3 adverse events associated with WBI occur in < 2%–3% of cases. In the present study, no cases of brachial plexus injury, rib fractures, soft tissue necrosis, pericarditis, symptomatic pneumonitis, and upper arm edema were observed over a follow-up period of 5–10 years. In our study, no Grade ≥ 3 adverse events were observed in follow-up imaging studies. Furthermore, the incidence of serious Organs At Risk toxicity (rib fractures, brachial plexus injury, pneumonia, among others) was zero, confirming the safety of PB-PBT. Patients generally tolerated any experienced changes well and did not express any dissatisfaction. The 5-year aesthetic scores were favorable, with 90% rated as “Excellent” and 10% as “Good.”

The optimal RT dose for breast cancer cases without lumpectomy remains undefined. In advanced breast cancer, administering standard RT doses (50–60 Gy) of post-neoadjuvant chemotherapy and subsequent tumor excision results in a histopathological complete response rate of approximately 30% [24, 25]. This estimate predates the use of trastuzumab deruxtecan, and the implications for systemic therapy may differ at present. In this trial, HER2 1+ (HER2-low) was considered “negative,” and trastuzumab deruxtecan was not used. This approach should be reviewed considering future changes in systemic therapy.

For locally advanced breast cancer, the radiation dose was set at 60 Gy (30 fractions). Mastectomy was performed following either neoadjuvant chemoradiotherapy or RT alone, and the pathological complete response rate was 29.1% in the chemoradiotherapy group and 19.4% in the radiotherapy-alone group [26]. A pioneering case report [10] from Japan's National Institute of Radiological Sciences introduced in 2014 carbon–iron radiotherapy with radical intent for stage 1 breast cancer, based on clinical early-stage breast cancer trials. While heavy ions (densely ionizing radiation) are known to have an energy- and charge-dependent increased RBE, PB should not be very different from photons. A slightly increased biological effectiveness is considered in PB treatment planning by assuming a fixed RBE of 1.1 for the whole radiation field [5]. Although it is presumed that there are limitations to tumor control with radiation alone, in this study, PB-PBT monotherapy was adopted for early-stage breast cancer and the tumor dose was set at 62.4 Gy (RBE) delivered in 26 fractions.

In this study, tumor shrinkage was observed in all cases within 6 months of PB-PBT treatment, with a shrinkage rate of 20%–81% achieved at 6 months. At 12 months, no contrast-enhancing tumors were detected on MRI scans and the scar tissue appeared flat and stable. During a follow-up period of up to 10 years, no local recurrences were reported and no changes in the condition of the scar tissue were observed. These findings indicate that tumor control exceeding 5 years is achievable in cases with a tumor diameter of ≤ 2 cm by administering 62.4 Gy (RBE) in 26 fractions. In this study, because endocrine therapy was administered after radiation, it is not possible to assess the efficacy of PB-PBT alone for achieving local tumor control. Endocrine therapy likely contributes to tumor suppression; however, evaluating this effect is challenging.

Patient immobilization remains the greatest challenge in partial breast irradiation. To address this challenge, this study developed a breast fixation technique that enables precise radiotherapy of tumors with 26 fractionated irradiations, yielding promising clinical results. In our study, the recurrence-free survival rate after > 5 years of follow-up was 100%.

Conclusion

This clinical trial addresses the major challenges associated with PB-PBT without breast-conserving surgery in the treatment of isolated early-stage luminal breast cancer measuring ≤ 2 cm. Although the number of cases was limited, no recurrences were observed during the follow-up period exceeding 5 years. This suggests that PB-PBT without lumpectomy may yield excellent treatment outcomes within defined criteria. We continue to enroll patients in accordance with our selection criteria and actively address challenges such as expanding the scope of indications.

Study limitations

This study focused on luminal A breast cancer, a subtype considered to have a relatively favorable prognosis among breast cancer histological types. Additional studies using larger sample sizes are required. Although patients were followed from 2015 to 2025 in this study, protocol revisions are likely in the future, as tests and treatments advance. The cost of PBT is high, and the breast fixation device used in this case is specialized, raising concerns regarding its clinical implementation and healthcare equity.

Declarations

Conflict of Interest

The authors declare that no conflicts of interest exist.

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Author Contributions:

Conceptualization: Etsuyo Ogo

Methodology: Etsuyo Ogo, Takeshi Arimura, and Takashi Ogino

Statistical Analysis: Kenta Murotani

Formal analysis and investigation: Etsuyo Ogo and Uhi Toh

Statistical Analysis: Kenta Murotani

Writing–original draft preparation: Etsuyo Ogo

Writing–review and editing: Etsuyo Ogo, Uhi Toh, Takeshi Arimura, Takashi Ogino, Gen Suzuki, Yusaku Miyata, Ichiro Isomoto, Makoto Kubo, Reiki Nishimura, Yoshio Hishikawa, Shoshu Mitsuyama, and Ryoichi Nagata

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Data Availability Statement:

All data generated and analyzed during this study are included in this published article (and its supplementary information files).

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Figures

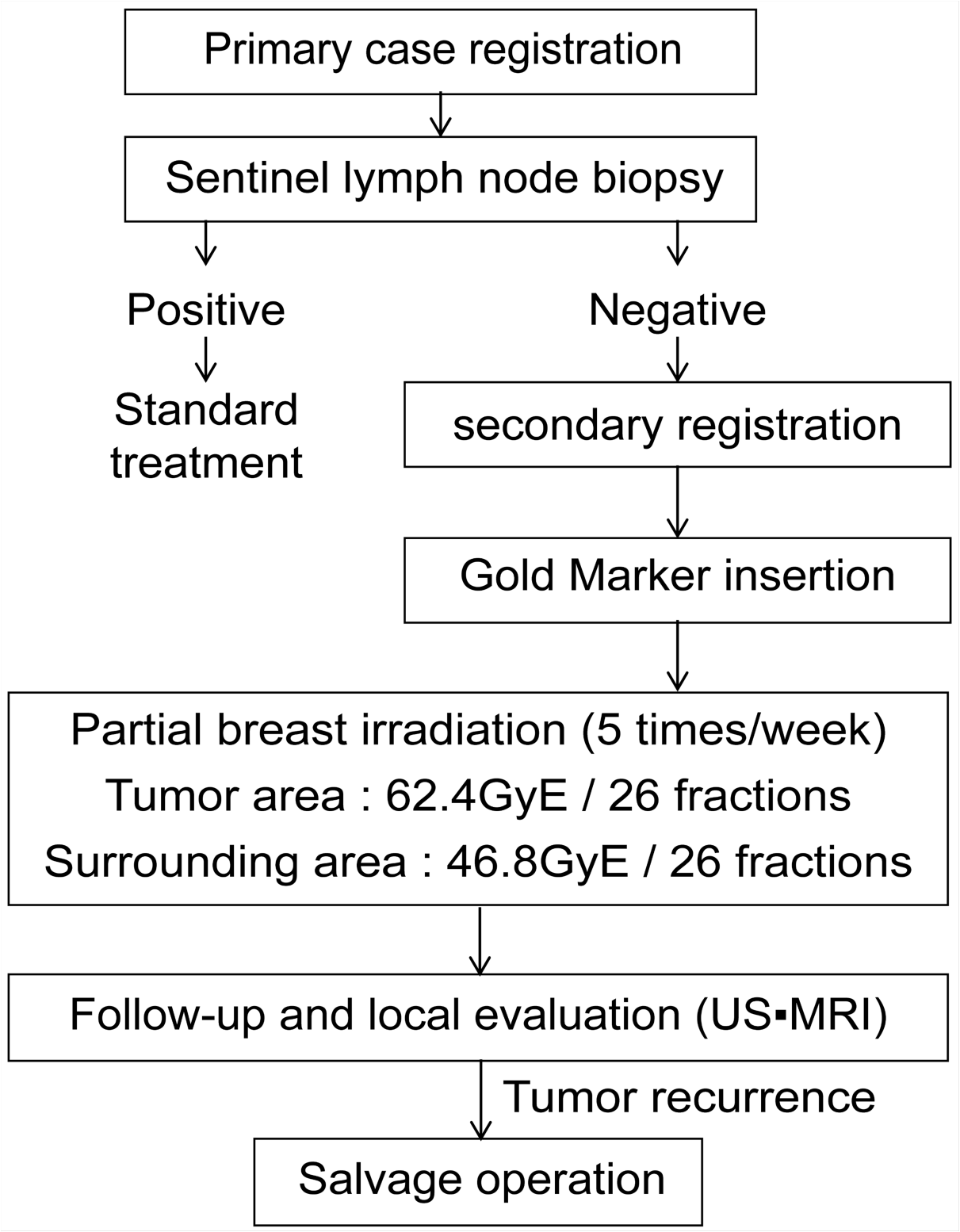


Figure 1

Flowchart of this study

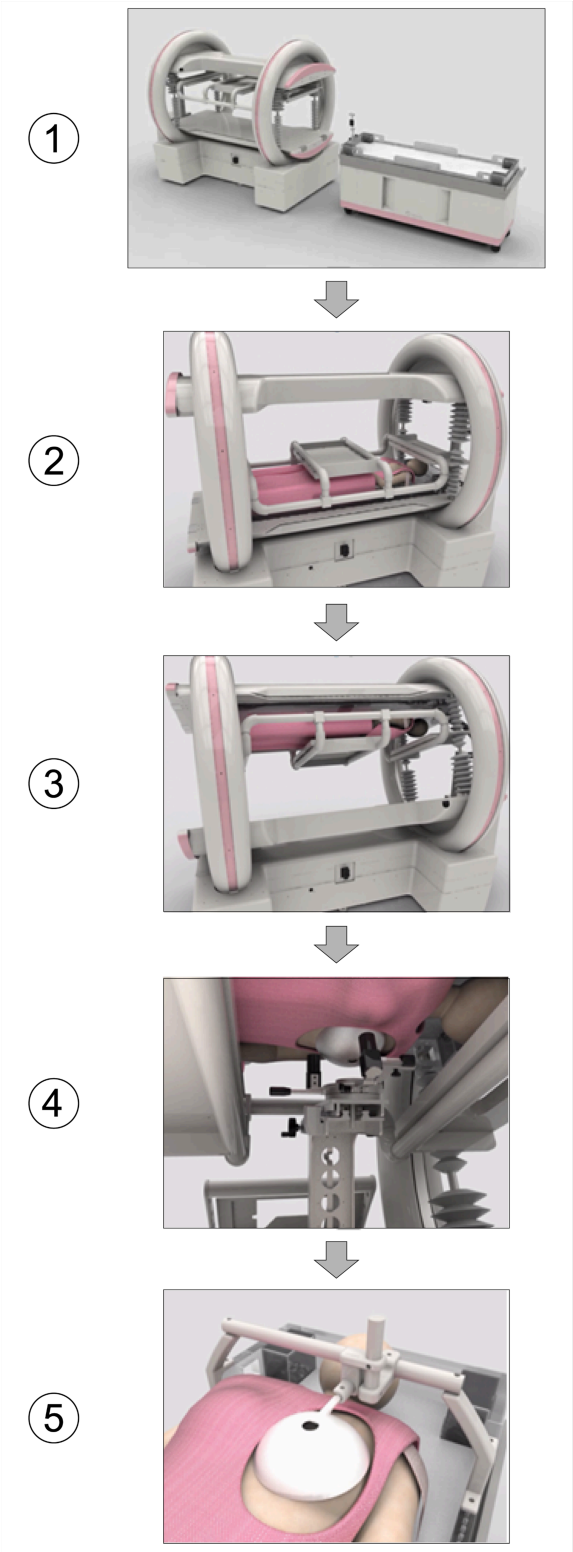


Figure 2

The immobilization for PB-PBI

 Overview of the device

 The patient is secured in a supine position on the device

 The device rotates 180 degrees, placing the patient in a prone position

 A specialized breast clamp is attached to the breast so that the opening aligns with the nipple

 The patient is returned to the supine position, and the breast is secured in a lifted position

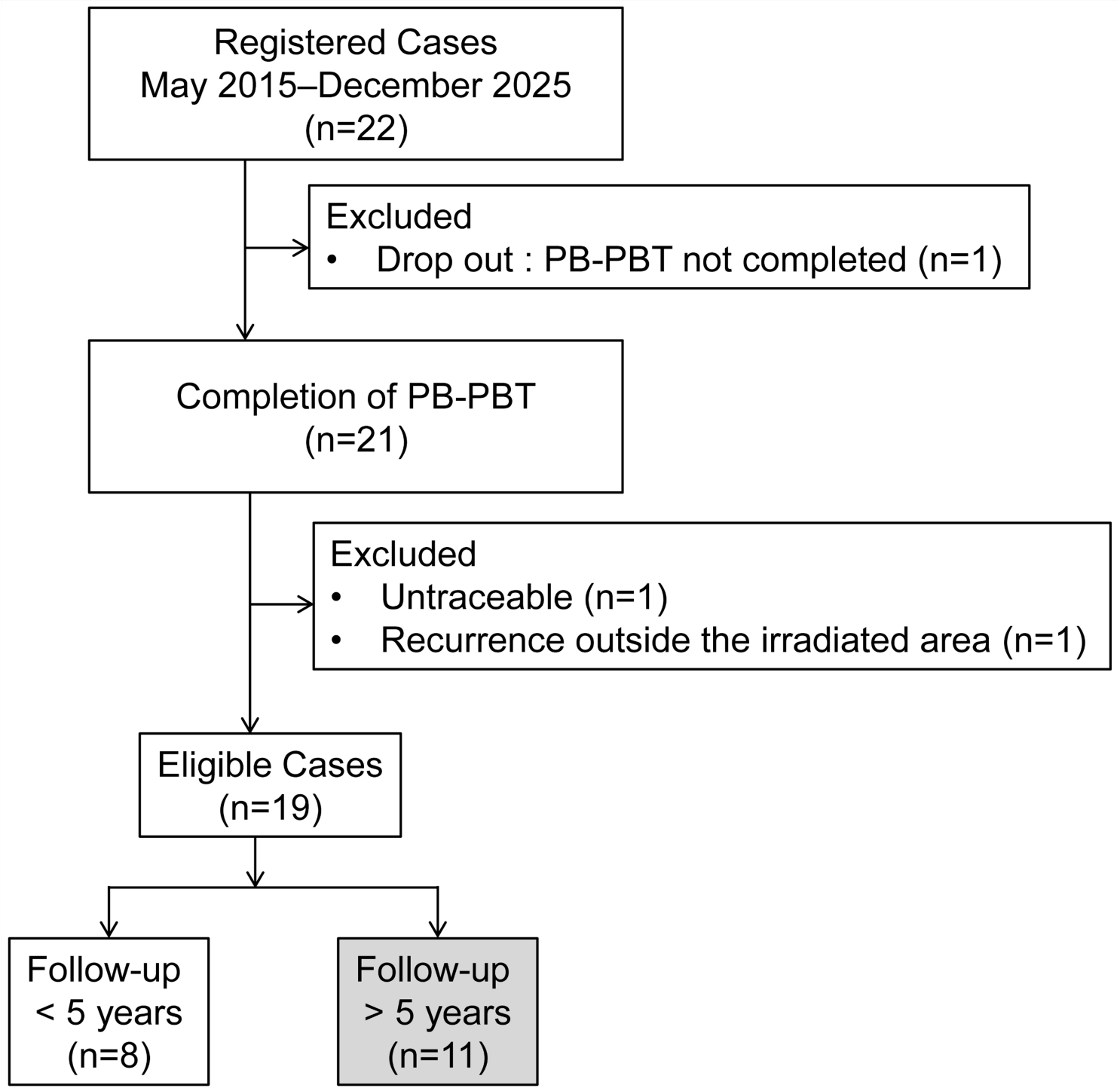


Figure 3

Participant Flow Diagram

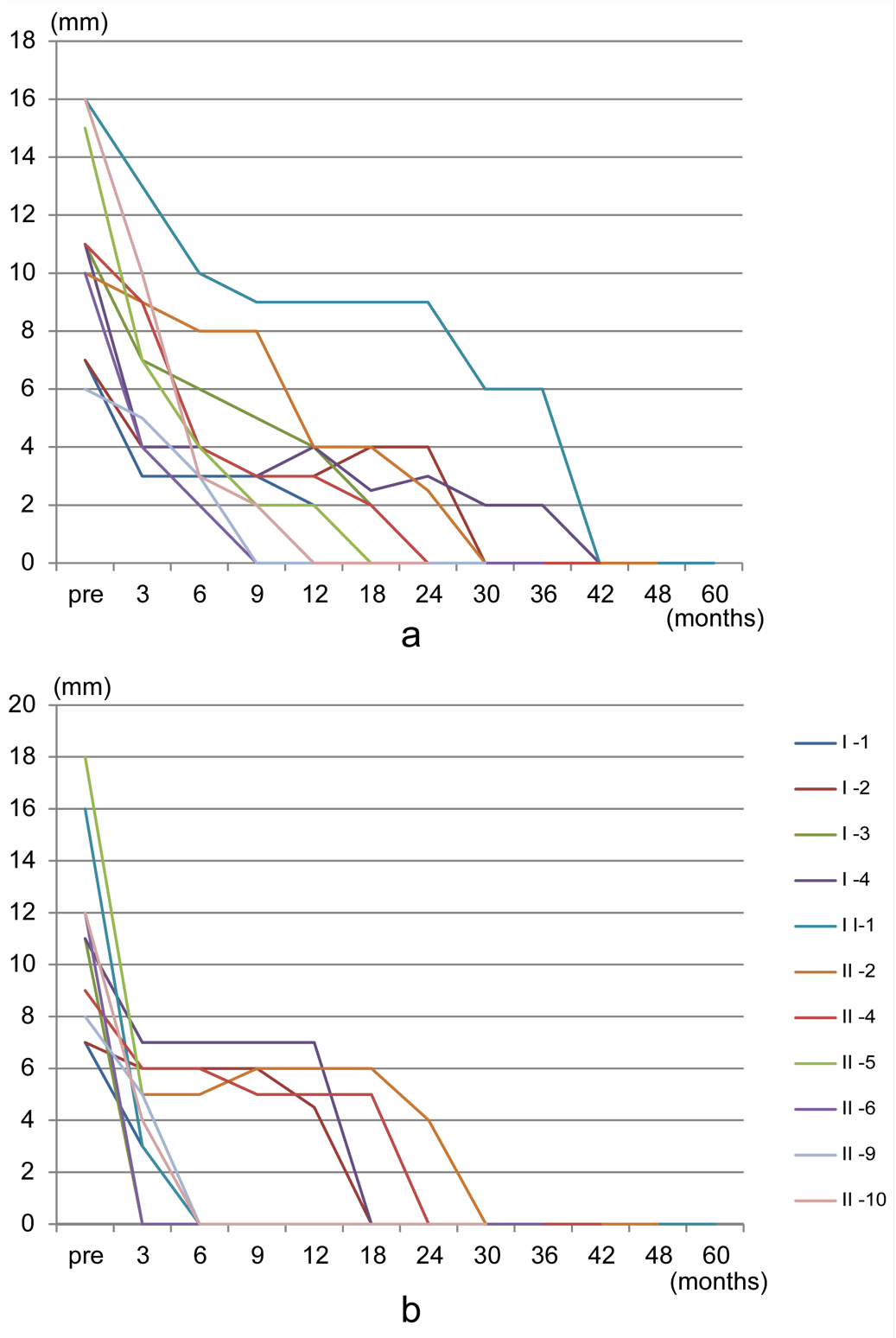


Figure 4

Tumor measurement using images

a. Ultrasound examination b. Contrast-enhanced MRI

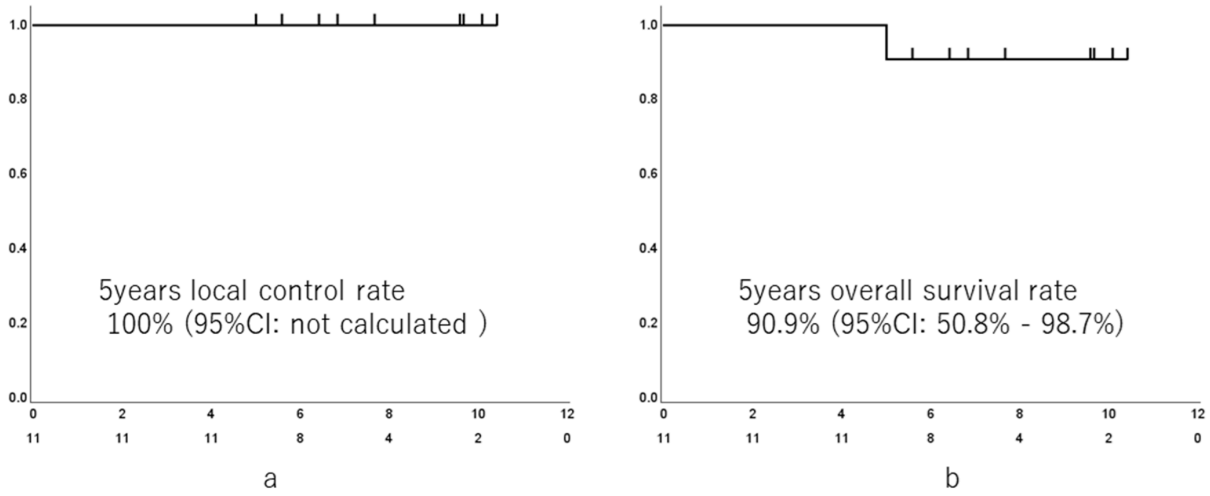


Figure 5

Confidence Interval Using the Clopper-Pearson Method

a. 5years local control rate b. 5years overall survival rate