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CONSENSUS STATEMENT

ACCELERATED PARTIAL BREAST IRRADIATION CONSENSUS STATEMENT FROM THE AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO)

Benjamin D. Smith, M.D.,[*†] Douglas W. Arthur, M.D.,[‡] Thomas A. Buchholz, M.D.,[†] Bruce G. Haffty, M.D.,[§] Carol A. Hahn, M.D.,[‖] Patricia H. Hardenbergh, M.D.,[¶] Thomas B. Julian, M.D.,[#] Lawrence B. Marks, M.D.,[**] Dorin A. Todor, Ph.D.,[‡] Frank A. Vicini, M.D.,[††] Timothy J. Whelan, M.D.,[‡‡] Julia White, M.D.,[§§] Jennifer Y. Wo, M.D.,[‖‖] and Jay R. Harris, M.D.[¶¶]

[*] Radiation Oncology Flight, Wilford Hall Medical Center, Lackland AFB, TX; [†] Department of Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX; [‡] Department of Radiation Oncology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA; [§] Department of Radiation Oncology, University of Medicine and Dentistry of New Jersey – Robert Wood Johnson Medical School, New Brunswick, NJ; [‖] Department of Radiation Oncology, Duke University Medical School, Durham, NC; [¶] Shaw Regional Cancer Center, Veil, CO; [#] Department of Human Oncology, Allegheny General Hospital, Pittsburgh, PA; [**] Department of Radiation Oncology, University of North Carolina Medical School, Chapel Hill, NC; [††] Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, MI; [‡‡] Department of Radiation Oncology, Juravinski Cancer Center, Hamilton, ON, Canada; [§§] Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI; [‖‖] Harvard Radiation Oncology Residency Program, Boston, MA; and [¶¶] Department of Radiation Oncology, Dana-Farber Cancer Institute and Brigham and Women's Hospital, Boston, MA

Purpose: To present guidance for patients and physicians regarding the use of accelerated partial-breast irradiation (APBI), based on current published evidence complemented by expert opinion.

Methods and Materials: A systematic search of the National Library of Medicine's PubMed database yielded 645 candidate original research articles potentially applicable to APBI. Of these, 4 randomized trials and 38 prospective single-arm studies were identified. A Task Force composed of all authors synthesized the published evidence and, through a series of meetings, reached consensus regarding the recommendations contained herein.

Results: The Task Force proposed three patient groups: (*1*) a "suitable" group, for whom APBI outside of a clinical trial is acceptable, (*2*) a "cautionary" group, for whom caution and concern should be applied when considering APBI outside of a clinical trial, and (*3*) an "unsuitable" group, for whom APBI outside of a clinical trial is not generally considered warranted. Patients who choose treatment with APBI should be informed that whole-breast irradiation (WBI) is an established treatment with a much longer track record that has documented long-term effectiveness and safety.

Reprint requests to: Benjamin D. Smith, M.D., 2200 Bergquist Drive, Suite 1, Lackland AFB, TX 78236. Tel: (210) 292-5589; Fax: (210) 292-3773; E-mail: benjamin.smith@lackland.af.mil

Supplementary material for this article can be found at www.redjournal.org.

This document was prepared by the Accelerated Partial Breast Irradiation Consensus Statement Task Force of the Health Services Research Committee of the American Society for Radiation Oncology (ASTRO).

Before initiation of this Consensus Statement, all members of the Task Group writing the Statement were required to complete conflict of interest statements. These statements are maintained at ASTRO Headquarters in Fairfax, VA, and pertinent conflict information is published with the report. Individuals with disqualifying conflicts have been recused from participation in this Consensus Statement.

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Adherence to the guidelines set forth in this Consensus Statement will not ensure successful treatment in every situation. Furthermore, these guidelines should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific therapy must be made by the physician and the patient in light of all the circumstances presented by the individual patient. ASTRO assumes no liability for the information, conclusions, and findings contained in its consensus statements. In addition, these guidelines cannot be assumed to apply to the use of these interventions performed in the context of clinical trials, given that clinical studies are designed to evaluate or validate innovative approaches in a disease for which improved staging and treatment are needed or are being explored.

This Consensus Statement was prepared on the basis of information available at the time the Task Group was conducting its research and discussions on the topic. There may be new developments that are not reflected in this Statement, and that may, over time, be a basis for ASTRO to consider revisiting and updating the Statement.

Conflict of interest: D. W. Arthur, T. B. Julian, D. A. Todor, and F. A. Vicini have served as consultants to SenoRx, Irvine, CA.

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Conclusion: Accelerated partial-breast irradiation is a new technology that may ultimately demonstrate long-term effectiveness and safety comparable to that of WBI for selected patients with early breast cancer. This consensus statement is intended to provide guidance regarding the use of APBI outside of a clinical trial and to serve as a framework to promote additional clinical investigations into the optimal role of APBI in the treatment of breast cancer.

Accelerated partial-breast irradiation, Breast cancer, Consensus statement.

INTRODUCTION

For several decades, whole-breast irradiation (WBI) has been used to reduce the risk of ipsilateral breast tumor recurrence (IBTR) after breast-conserving surgery for early breast cancer. Multiple randomized clinical trials and meta-analyses have demonstrated the effectiveness and safety of WBI (1, 2). The use of WBI after breast-conserving surgery has been shown to substantially reduce the risk of recurrence in the affected breast and increase the likelihood of long-term survival.

Over the past several years, there has been growing interest in the use of accelerated partial-breast irradiation (APBI) as an alternative to WBI. Accelerated partial-breast irradiation offers decreased overall treatment time and several theoretical advantages over WBI, including a decrease in the radiation dose delivered to uninvolved portions of the breast and adjacent organs. However, there are several theoretical disadvantages to APBI, principally the possibility that occult foci of cancer exist elsewhere in the breast and will not be treated. Given the interest in APBI, several multicenter, randomized clinical trials have been initiated to compare the effectiveness and safety of APBI and WBI.

The use of APBI outside the framework of a clinical trial has markedly increased, even as we await the results of randomized clinical trials comparing APBI with conventional WBI. For example, to date more than 32,000 women in the United States have been treated with the MammoSite (Cytyc, Marlborough, MA) breast brachytherapy catheter (3). In past years, few data were available to define which patients could be safely treated with APBI and which patients should receive WBI. However, in light of increasing evidence that WBI improves long-term overall survival (1, 2), it has become clear that conservative patient selection criteria for APBI should be followed until additional data indicate otherwise.

Given these issues, the American Society for Radiation Oncology (ASTRO) Health Services Research Committee convened a Task Force of experts in the field of breast cancer to develop a consensus statement regarding patient selection criteria and best practices for the use of APBI outside the context of a clinical trial. Recommendations were based on the results of a systematic literature review and were supplemented by the expert opinions of the Task Force members. This consensus statement is presented herein.

METHODS AND MATERIALS

Process

The Health Services Research Committee, in accordance with established ASTRO policy, recruited a Task Force composed of recognized experts in the fields of breast cancer radiation oncology, breast cancer surgery, and radiation physics, in addition to representatives from radiation oncology private practice and residency. The Task Force was asked to provide guidance on the use of APBI for patients and physicians who may be considering this treatment option and to define which patients are suitable candidates for the off-protocol use of APBI before the availability of mature results from randomized clinical trials. The Task Force was also charged with providing guidelines for proper APBI dosimetry and for informed consent.

In June 2008, the ASTRO Board of Directors approved a proposal to develop a consensus statement regarding APBI and also authorized the membership of the Task Force. Subsequently, the Task Force participated in a series of conference calls and face-to-face meetings to compose the consensus statement. The members of the Task Force acknowledged at the outset the limitations in the scope of current knowledge and the lack of long-term data inherent in most APBI studies and further acknowledged that this consensus statement will require updating as additional information is obtained. The initial draft of the consensus statement was sent to external reviewers and posted on the ASTRO web site for public comment. The ASTRO Board of Directors integrated this feedback and approved the final document in January 2009.

Literature search

Whenever possible, this consensus statement relied on an evidence-based approach using a formal systematic literature review. One author (B.D.S.) searched for English-language citations in the National Library of Medicine's PubMed database through May 30, 2008 using the Medical Subject Heading term ''Breast Neoplasms/Radiotherapy,'' limiting results to articles whose major focus was this topic. Studies published only in abstract form were not eligible. Of 3,831 articles initially identified, a total of 645 original research articles contained any one of the following key words: accelerated, balloon, brachytherapy, catheter, implant, implantation, interstitial, intraoperative, limited, partial, MammoSite, or Savi. Of this sample, we identified four published randomized clinical trials and 38 prospective single-arm studies (Table 1) (4–76).

Bibliographies of candidate studies were also reviewed to ensure that all eligible studies were included. A total of six clinical studies were purely retrospective in nature and were not included. All prospective clinical studies were reviewed by one author (B.D.S.) and abstracted for inclusion criteria, radiotherapy methods, clinical outcomes, and toxicity.

RESULTS

Which patients may be considered for APBI outside of a clinical trial?

Consensus statement. All patients considered for APBI should be candidates for breast-conserving therapy (no prior radiotherapy, no history of certain collagen vascular diseases, and not pregnant) and should be committed to long-term follow-up to evaluate for recurrence, second primary cancers,

Table 1. Published prospective studies identified by a systematic literature review

Study	Full name	First author	Year	Reference
Randomized clinical trials				
Christie Hospital	Christie Hospital, Manchester, UK	Ribeiro	1993	4
		Ribeiro	1990	5
NIC Hungary	National Institute of Cancer, Hungary	Polgar	2007	6
		Lovey	2007	7
		Polgar	2002	8
TARGIT	Targeted Intraoperative Radiation Therapy	Holmes	2007	9
YBCG	Yorkshire Breast Cancer Group	Dodwell	2005	10
Prospective single-arm clinical trials				
Australia	St. Vincent's Hospital, Sydney, Australia	Stevens	2006	11
Beaumont 3D-CRT	William Beaumont Hospital 3-Dimensional Conformal Radiotherapy	Vicini	2007	12
		Vicini	2003	13
		Baglan	2003	14
Beaumont Interstitial	William Beaumont Hospital Interstitial Brachytherapy	Vicini	2007	15
		Chen	2006	16
		Benitez	2004	17
		Vicini	2003	18
		Baglan	2001	19
		Vicini	1999	20
		Vicini	1997	21
Beaumont MammoSite	William Beaumont Hospital MammoSite Brachytherapy	Chao	2007	22
Colorado	Four institutions within the Denver-Boulder, CO area	Leonard	1997	23
Czech Republic	Masaryk Memorial Cancer Institute, Czech Republic	Slampa	2005	24
ELIOT	Intraoperative Radiotherapy with Electrons, European Institute of Oncology, Milan, Italy	Luini	2005	25
		Veronesi	2005	26
		Intra	2005	27
		Veronesi	2003	28
		Veronesi	2001	29
European MammoSite	Multicenter European MammoSite Study	Niehoff	2006	30
Florence	Florence, Italy	Livi	2005	31
German-Austrian	Erlangen, Leipzig, Linz, and Vienna Phase II Trial	Ott	2007	32
		Ott	2004	33
German-Hungarian	Kiel and National Institute of Oncology, Hungary Phase II Trial	Niehoff	2006	34
Guy's Cesium	Guy's Hospital Cesium Study	Fentiman	2004	35
Guy's Iridium	Guy's Hospital Iridium Study	Fentiman	1996	36
		Fentiman	1991	37
Harvard 3D-CRT	Dana-Farber/Harvard Cancer Center, three-dimensional conformal radiotherapy dose-escalation protocol 03-179	Taghian	2006	38
Harvard Proton	Dana-Farber/Harvard Cancer Center, three-dimensional conformal radiotherapy dose-escalation protocol 03-179	Kozak	2006	39
		Taghian	2006	40
Hungarian Cobalt	Uszoki Hospital, Budapest, Hungary	Poti	2004	41
Hungarian Interstitial	National Institute of Cancer, Hungary	Polgar	2004	42
		Polgar	2002	8
		Polgar	1999	43
Kaiser	Kaiser Permanente Los Angeles Medical Center	Tsai	2006	44
Kansas	University of Kansas Medical Center	Krishnan	2001	45
Loma Linda	Loma Linda Proton Therapy Study	Bush	2007	46
MammoSite Prospective	MammoSite Multicenter Prospective Study	Benitez	2007	47
		Benitez	2006	48
		Keisch	2003	49
MammoSite Registry	American Society of Breast Surgeons MammoSite Breast Brachytherapy Registry Trial	Vicini	2008	50
		Jeruss	2006	51
		Vicini	2005	52
MCV	Medical College of Virginia	Wazer	2006	53
		Arthur	2003	54
MGH Interstitial	Massachusetts General Hospital Interstitial Brachytherapy Protocol	Lawenda	2003	55

(*Continued*)

Table 1. Published prospective studies identified by a systematic literature review (*Continued*)

Study	Full name	First author	Year	Reference
MSKCC	Memorial Sloan-Kettering Cancer Center Intraoperative Study	Beal	2007	56
NYU	New York University Phase II Prone Partial Breast Trial	Formenti	2004	57
NYU Pilot	New York University Pilot Prone Partial Breast Trial	Formenti	2002	58
Ochsner	Ochsner Clinic, New Orleans, LA	King	2000	59
Ontario	London Health Sciences Center, London, Ontario, Canada	Perera	2005	60
		Perera	2003	61
		Perera	1997	62
Osaka	Osaka Medical Center, Japan	Nose	2006	63
RTOG 0319	Radiation Therapy and Oncology Group 0319	Vicini	2005	64
RTOG 9517	Radiation Therapy and Oncology Group 9517	Kuske	2006	65
		Arthur	2008	66
Rush	Rush University Medical Center, Montgomery Cancer Center, and Lansche Breast Center	Dowlatshahi	2004	67
Santa Chiara	Santa Chiara Hospital, Trento, Italy	Mussari	2006	68
St. Vincent's	St. Vincent's Comprehensive Cancer Center, New York, NY	Richards	2004	69
Tufts	Tufts-New England Medical Center and Rhode Island Hospital	Kaufman	2007	70
		Wazer	2006	53
		Evans	2006	71
		Shah	2004	72
		Wazer	2002	73
		Wazer	2001	74
UNC	University of North Carolina	Ollila	2007	75
Wisconsin	University of Wisconsin	Patel	2008	76

and treatment toxicity. Table 2 presents the Task Force's consensus for a ''suitable'' group, for whom treatment with APBI is considered acceptable outside of a clinical trial. Table 3 presents the Task Force's consensus for a ''cautionary'' group, for whom caution and concern in the use of APBI should be exercised at this point in time because of limited data. Table 4 presents the Task Force's consensus for an ''unsuitable'' group, for whom APBI is not generally considered warranted outside of a clinical trial. To help accurately determine pathologic selection criteria, consultation with a specialist in breast pathology should be considered. Although these tables provide guidance in selecting patients who may be appropriate for APBI outside the context of a clinical trial, the Task Force strongly endorsed enrollment of all eligible patients considering APBI onto the Radiation Therapy Oncology Group (RTOG) 0413/National Surgical Adjuvant Breast and Bowel Project (NSABP) B-39 randomized trial and encouraged enrollment of other patients considering APBI, particularly those not in the ''suitable'' group, into prospective clinical studies to address many of the unanswered questions in APBI.

Narrative. The primary purpose of selection criteria for APBI is to identify a subset of patients with a very low risk of clinically occult disease remote from the lumpectomy cavity. However, few data were identified from pathologic studies or prospective clinical studies of APBI to define this subgroup of breast cancer patients. As a result, the proposed clinical–pathologic selection criteria for the ''suitable'' group (Table 2) were derived from the inclusion criteria and characteristics of patients enrolled in prospective single-arm studies of APBI that had a minimum of 4 years' follow-up and reported a low risk of IBTR (Table 5) (77); these data were supplemented by the Task Force's general knowledge of risk factors for IBTR after WBI. (There may be other groups of patients for whom APBI will prove to be suitable, but the Task Force believed that there was insufficient evidence to identify them at this time.) The ''cautionary'' group included those patients for whom the Task Force expressed uncertainty regarding the appropriateness of APBI, although at least some patients in this group have been included in single-arm, prospective trials. The ''unsuitable'' group included those patients for whom there was very limited evidence from clinical trials to support the use of APBI. Furthermore, the Task Force strongly suggested that those patients who remain eligible for the ongoing RTOG 0413/NSABP B-39 randomized clinical trial (patients aged <50 years or any age with estrogen receptor [ER]-negative tumor or any age with pN1 tumor) should be strongly encouraged to participate in this important trial (78).

Regarding patient characteristics, age ≥60 years was selected as the delimiting age for the ''suitable'' group, because the median age of patients treated in most single-arm, prospective APBI trials was ≥60 years, and studies have shown that older patients experienced a lower risk of IBTR than younger patients when treated with WBI (79, 80) or MammoSite (22). In addition, because data from the Early Breast Cancer Trialists' Collaborative Group suggested that WBI did not improve survival for women aged ≥60 years (1), the Task Force felt comfortable accepting APBI as an alternative to WBI for this patient group. Women aged 50–59 years were included in the ''cautionary'' group because, although many prospective single-arm trials have attempted to include

Table 2. Patients ''suitable'' for APBI if all criteria are present

Factor	Criterion
Patient factors	
Age	≥60 y
BRCA1/2 mutation	Not present
Pathologic factors	
Tumor size	≤2 cm*
T stage	T1
Margins	Negative by at least 2 mm
Grade	Any
LVSI	No†
ER status	Positive
Multicentricity	Unicentric only
Multifocality	Clinically unifocal with total size ≤2.0 cm‡
Histology	Invasive ductal or other favorable subtypes§
Pure DCIS	Not allowed
EIC	Not allowed
Associated LCIS	Allowed
Nodal factors	
N stage	pN0 (i^-, i^+)
Nodal surgery	SN Bx or ALND‖
Treatment factors	
Neoadjuvant therapy	Not allowed

Abbreviations: APBI = accelerated partial-breast irradiation; LVSI = lymph–vascular space invasion; ER = estrogen receptor; DCIS = ductal carcinoma *in situ*; EIC = extensive intraductal component; LCIS = lobular carcinoma *in situ*; SN Bx = sentinel lymph node biopsy; ALND = axillary lymph node dissection.

Criteria are derived from data (when available) and conservative panel judgment.

* The size of the invasive tumor component as defined by the American Joint Committee on Cancer (81).

† The finding of possible or equivocal LVSI should be disregarded.

‡ Microscopic multifocality allowed, provided the lesion is clinically unifocal (a single discrete lesion by physical examination and ultrasonography/mammography) and the total lesion size (including foci of multifocality and intervening normal breast parenchyma) does not exceed 2 cm.

§ Favorable subtypes include mucinous, tubular, and colloid.

‖ Pathologic staging is not required for DCIS.

such patients, relatively few patients of this age have actually enrolled in such trials. Therefore, the Task Force thought that the data were too limited to determine this age cohort's suitability. Few women aged <50 years have been treated with APBI in prospective single-arm studies, and thus, the Task Force strongly recommended against APBI outside of a clinical trial for this patient group at this time. It was noted that data from the University of Wisconsin prospective single-arm study indicated that the risk of IBTR may not be excessively high among appropriately selected women aged <50 years (76); however, there were only 70 patients aged <50 years in this study, and the median follow-up time was only 48.5 months. Therefore, the panel thought that confirmatory data were required before endorsing off-protocol APBI for this younger patient group. Finally, the Task Force recommended that carriers of deleterious *BRCA1* or *BRCA2* mutations, or individuals with a personal or family history

Table 3. ''Cautionary'' group: Any of these criteria should invoke caution and concern when considering APBI

Factor	Criterion
Patient factors	
Age	50–59 y
Pathologic factors	
Tumor size	2.1–3.0 cm*
T stage	T0 or T2
Margins	Close (<2 mm)
LVSI	Limited/focal
ER status	Negative†
Multifocality	Clinically unifocal with total size 2.1–3.0 cm‡
Histology	Invasive lobular
Pure DCIS	≤3 cm
EIC	≤3 cm

Abbreviations as in Table 2.

* The size of the invasive tumor component as defined by the American Joint Committee on Cancer (81).

† Patients with ER-negative tumors are strongly encouraged to enroll in the National Surgical Adjuvant Breast and Bowel Project B-39/Radiation Therapy and Oncology Group 04-13 clinical trial (78).

‡ Microscopic multifocality allowed, provided the lesion is clinically unifocal (a single discrete lesion by physical examination and ultrasonography/mammography) and the total lesion size (including foci of multifocality and intervening normal breast parenchyma) falls between 2.1 and 3.0 cm.

consistent with the presence of a mutation, should not receive APBI outside of a clinical trial because of the absence of literature supporting the use of APBI in this setting.

Regarding pathologic characteristics, the Task Force recommended measuring the maximum size of the invasive

Table 4. Patients ''unsuitable'' for APBI outside of a clinical trial if any of these criteria are present

Factor	Criterion
Patient factors	
Age	<50 y
BRCA1/2 mutation	Present
Pathologic factors	
Tumor size*	>3 cm
T stage	T3-4
Margins	Positive
LVSI	Extensive
Multicentricity	Present
Multifocality	If microscopically multifocal >3 cm in total size or if clinically multifocal
Pure DCIS	If >3 cm in size
EIC	If >3 cm in size
Nodal factors	
N stage	pN1, pN2, pN3
Nodal surgery	None performed
Treatment factors	
Neoadjuvant therapy	If used

Abbreviations as in Table 2.

If any of these factors are present, the Task Force recommends against the use of APBI outside of a prospective clinical trial.

* The size of the invasive tumor component as defined by the American Joint Committee on Cancer (81).

tumor in accordance with the definition used by the American Joint Committee on Cancer (AJCC) staging manual (81). On the basis of the characteristics of patients treated with APBI in prospective studies (Table 3), and using the AJCC definition, we selected a maximum tumor size of 2 cm for the ''suitable'' group, 2.1–3 cm for the ''cautionary'' group, and ≥3.1 cm for the ''unsuitable'' group. We also recommended patients with clinical and pathologic Stage T1 tumors for the ''suitable'' group, whereas patients with Stage T0 (ductal carcinoma *in situ* [DCIS]) or T2 tumors were recommended for the ''cautionary'' group. Patients with T3 or T4 tumors should not receive APBI. Patients with pure DCIS were placed in the ''cautionary'' group because of a lack of current data: 7 of the 10 prospective single-arm APBI trials with follow-up ≥4 years and a low risk of IBTR excluded such patients. Thus, the Task Force recommended that only patients with small (≤3 cm) DCIS tumors be included in the ''cautionary'' group and that patients with more extensive DCIS be placed in the ''unsuitable'' group. Along with small, pure DCIS tumors, we included small invasive tumors with an extensive intraductal component (EIC) in the ''cautionary'' group because these types of lesions are similar. Supporting this approach, the MammoSite registry study showed a potential association between EIC and a higher risk of IBTR (50). We therefore included patients having EIC not exceeding 3 cm (including the invasive and *in situ* components) in the ''cautionary'' group and placed patients having EIC >3 cm in the ''unsuitable'' group.

Regarding other pathologic features, the Task Force recommended that patients with invasive lobular histology be included in the ''cautionary'' group because the Christie Hospital randomized clinical trial showed that lobular histology was associated with a higher risk of IBTR than was ductal histology among patients treated with APBI (4, 5) and because 6 of the 10 prospective single-arm trials having ≥4 years' follow-up and low recurrence rates excluded patients with lobular histology altogether (Table 3). There were limited data with which to define whether patients with close but negative margins could safely be treated with APBI. (Margin distance should be measured from the inked surgical margin to the closest invasive or associated *in situ* tumor.) As a conservative measure, the Task Force included in the ''suitable'' group only those patients with negative surgical margins of at least 2 mm. Patients with ''close'' but negative margins (<2 mm) were included in the ''cautionary'' group, and patients with positive margins were included in the ''unsuitable'' group.

The presence of lymph–vascular space invasion (LVSI) seems to be a marker for a higher burden of residual disease within the breast after breast-conserving surgery, although there were no data to define the importance of LVSI in patients treated with APBI. Given this uncertainty, the Task Force recommended inclusion of patients without LVSI in the ''suitable'' group, patients with focal or limited LVSI in the ''cautionary'' group, and patients with extensive LVSI in the ''unsuitable'' group. Questionable or suspicious LVSI should be disregarded.

Because the vast majority of tumors treated to date with APBI have been ER positive, and because patients with ER-negative tumors remain eligible for the RTOG 0413/NSABP B-39 randomized clinical trial, the Task Force recommended inclusion of only those patients with ER-positive tumors in the ''suitable'' group and inclusion of patients with ER-negative tumors in the ''cautionary'' group, with the caveat that patients with ER-negative tumors should be strongly encouraged to participate in the RTOG 0413/NSABP B-39 trial.

Patients with multicentric tumors (defined as the presence of separate foci of cancer in different quadrants) should not receive APBI because the extent of disease cannot be encompassed using partial-breast irradiation techniques. Therefore, only patients with unicentric tumors were included in the ''suitable'' group, and patients with multicentric tumors were included in the ''unsuitable'' group. Patients with multifocal tumors (defined as separate foci of cancer within the same quadrant or vicinity) may potentially receive APBI if the entire extent of disease can be encompassed using partial-breast irradiation techniques; however, there were no published data regarding outcomes in this cohort. The Task Force therefore suggested that patients with clinically unifocal (only one discrete cancer identified by physical examination and ultrasonography/mammography) but pathologically multifocal tumors with a total tumor size (including foci of multifocality and intervening normal breast parenchyma) no greater than 2 cm be included in the ''suitable'' group, whereas patients with a total tumor size between 2.1 and 3.0 cm be included in the ''cautionary'' group. Patients with clinically detected multifocality or microscopic multifocality of >3 cm were included in the ''unsuitable'' group. Finally, the Task Force thought that tumor grade and associated lobular carcinoma *in situ* should be disregarded as selection criteria because most prospective single-arm trials have not considered these factors as eligibility criteria.

The majority of patients who have been treated on prospective single-arm APBI trials had pathologically node-negative disease. In addition, 2 of 3 patients with pN1 tumors treated on the Tufts APBI single-arm trial developed an IBTR, providing anecdotal evidence that patients with pN1 disease may experience a higher risk of IBTR than patients with pN0 disease after APBI (53, 70–74). Furthermore, patients in the Christie Hospital (4, 5) and Yorkshire Breast Cancer Group (YBCG) (10) randomized clinical trials did not undergo complete pathologic lymph node assessment, and these studies reported a higher risk of IBTR (4, 5) and locoregional recurrence (10) among patients treated with APBI than among patients treated with WBI. Therefore, the Task Force recommended that the ''suitable'' group include only those patients who have undergone either sentinel lymph node biopsy or Level I to II axillary lymph node dissection to document pathologic nodal status. Patients with foci of isolated tumor cells (<0.2 mm) should be considered node negative in accordance with the AJCC definition (81). Patients who do not undergo surgical nodal assessment or who have

Table 5. Inclusion criteria for prospective studies

Study	Age (y)	Tumor size (cm)	T stage	Margin	Grade	ER	Multicentric	Multifocal	Invasive lobular	Pure DCIS	EIC	LCIS*	N stage	LVSI	IBTR (%)	Time (y)
Guy's Iridium	<70	0–4	.	.	.	.	No	.	Yes	No	.	.	.	.	37	6
Hungarian Cobalt	.	0–5	pT1–2	.	.	.	No	No	Yes	Yes	.	.	.	.	24	12
Christie Hospital	<70	0–4	cT1–2	.	.	.	No	.	.	No	.	.	cN0	.	19.6	7
Guy's Cesium	>40	0–4	.	.	.	.	No	No	Yes	No	.	.	.	.	18	8.3
Ontario	.	.	cT1–2	Neg	.	.	.	.	No	No	Yes	.	cN0	.	18	8
YBCG	.	0–5	pT1/2	Neg	.	.	.	.	.	No	.	.	pN0–1	.	12	8
Hungarian Interstitial†		0–2	pT1	Neg	1 or 2	.	No	No	No	No	No	.	pN0–1mic	.	9	7
Tufts†	.	0–5	pT1–2	≥1 mm	.	.	No	No	No	No	Yes	No	pN0–1	.	9	7
Osaka†	>20	0–2.9	.	.	.	.	.	.	Yes	Yes	.	.	cN0	.	5	4.3
Czech Republic	≥40	0–3	cT1–2	Neg	.	.	.	.	No	No	.	.	pN0–1	.	5	0.9
NIC Hungary†	≥40	0–2	pT1	Neg	1 or 2	.	.	No	No	No	No	.	pN0–1mic	.	4.7	5
RTOG 9517†	.	0–3	pT1–2	Neg	.	.	No	No	No	No	No	.	pN0–1	.	4	5
Beaumont Interstitial†,‡	>40	0–2.9	.	≥2 mm	.	.	.	.	No	No	No	No	pN0	.	3.8	10
Wisconsin†	≥18	0–3	pT0–2	≥2 mm	.	.	No	Yes	Yes	Yes	.	.	pN0–1	.	3	4.0
Beaumont MammoSite	>40	0–3.0	cTis–T2	Neg	.	.	.	.	Yes	Yes	.	.	pN0–1	.	2.90	3
Ochsner†	.	0–4	cTis–T2	Neg	.	.	No	.	.	Yes	.	.	pN0–1	.	2	6.3
MammoSite Registry	>45	0–2	.	Neg	.	.	.	.	No	No	Yes	.	pN0	.	1.04	2
ELIOT	>48	0–2.5	.	.	.	.	No	No	Yes	.	.	.	.	.	1	2
German-Austrian	≥35	0–3	.	≥2 mm	1 or 2	+	No	.	Yes	No	No	.	pN0–1mic	No	0.4	3
MammoSite Prospective†	≥45	0–2	.	Neg	.	.	No	No	No	No	No	.	pN0	.	0	5.5
Santa Chiara†	>45	0–2	cT1	Neg	1 or 2	+	No	No	Yes	No	No	.	cN0	.	0	4
Kansas	≥60	0–2	pT1	Neg	1 or 2	.	.	.	Yes	No	No	.	pN0	.	0	3.9
MCV	.	0–4	.	Neg	.	.	No	No	.	No	No	.	pN0	.	0	3.5
NYU Pilot	Post	0–2	pT1	≥2 mm	.	+	.	.	.	No	No	.	cN0	.	0	3
Beaumont 3D-CRT	≥50	0–3.0	cT1–2	Neg	.	.	.	.	No	No	No	.	pN0	.	0	2
MGH Interstitial	>18	0–2	cT1	Neg	.	.	No	.	Yes	No	No	.	pN0	No	0	2
MSKCC	≥60	0–2	cT1	Neg	.	.	No	No	No	No	.	.	cN0	.	0	1.8
German-Hungarian	≥60	0–1.9	.	≥5 mm	1 or 2	.	No	No	No	No	No	.	.	.	0	1.7
NYU	Post	0–2	pT1	≥5 mm	.	+	No	No	.	No	No	.	pN0	.	0	1.5
Kaiser	≥45	0–2	.	Neg	.	.	.	.	No	No	No		pN0–1	.	0	1.3
European MammoSite	≥60	0–2	.	≥5 mm	.	+	No	No	No	No	No	.	.	.	0	1.2
Harvard Proton	.	0–2	pT1	≥2 mm	.	.	No	No	No	No	No	.	.	No	0	1.0
Colorado	≥40	0–2	pTis–T1	≥2 mm	.	.	.	.	.	Yes	.	.	pN0	.	0	0.8
Florence	Post	0–2.5	.	≥5 mm	.	.	.	.	No	No	No	.	.	.	0	0.5
UNC	≥55	0–3	.	.	.	.	No	.	No	No	.	.	.	.	.	0.5
RTOG 0319	.	0–5	pT1–2	>2 mm	.	.	No	No	No	No	No	.	pN0–1	.	.	.
Rush	.	0–5	pTis–2	Neg	.	.	.	.	Yes	Yes	.	.	pN0–1	.	.	.
St. Vincent's	≥45	0–2	.	≥2 mm	.	.	.	.	.	No	No	.	pN0–1	.	.	.
Harvard 3D-CRT	≥18	0–2	pT1	≥2 mm	.	.	No	No	No	No§	No	.	pN0	No	.	.
Loma Linda	.	0–3	.	Neg	.	.	.	.	No	No	.	.	pN0	.	.	.
TARGIT	≥35	.	T1–3	.	.	.	No	No	No	No	No	.	pN0–1	.	.	.

Abbreviations: IBTR = ipsilateral breast tumor recurrence; Neg = negative; Post = postmenopausal. Full trial names are shown in Table 1. Other abbreviations as in Table 2.

A period (.) indicates that the criterion was not mentioned by the study. ''No'' indicates that patients with the criterion were excluded. ''Yes'' indicates that patients with the criterion were specifically included. Australia study used American Brachytherapy Society Criteria (77). Studies sorted by reported risk of IBTR.

* LCIS associated with an invasive tumor or with DCIS.

† Studies with 4 or more years' follow-up and IBTR risk less than 10% are identified.

‡ Forty-one of 199 patients did not meet all eligibility criteria.

§ After accruing 100 patients, pure Grade 1 and 2 DCIS were allowed on this study.

pathologic evidence of nodal metastasis should not receive APBI outside of a clinical trial.

Regarding other treatment issues, there has been only limited study of APBI in patients receiving neoadjuvant or concurrent chemotherapy, and therefore such patients should not receive APBI outside of a clinical trial. Additionally, the groups proposed in Tables 2, 3, and 4 are not intended to apply to patients who receive intraoperative radiotherapy, for whom complete pathologic assessment cannot be performed before treatment. Determination of selection criteria for intraoperative radiotherapy is beyond the scope of this consensus statement.

What constitutes proper informed consent for patients treated with APBI outside of a clinical trial?

Consensus statement. Patients who choose treatment with APBI should be informed that WBI is an established treatment with a much longer track record that has documented long-term effectiveness and safety. In contrast, APBI is a relatively new method with a limited track record, and thus its long-term effectiveness and safety are not fully known. Treatment with APBI may lead to an increase in the risk of IBTR, which may require mastectomy and possibly chemotherapy and could be associated with an increased risk for distant metastasis and death. Accelerated partial-breast irradiation could also lead to an increased risk of toxicity, including local fibrosis or poor cosmesis, but may also improve cosmetic outcomes by treating a smaller volume of breast tissue. Patients in the ''cautionary'' group should be further informed that relatively little is known regarding long-term outcomes of APBI for this patient group, and thus even greater uncertainty exists.

Narrative. Radiotherapy to the whole breast after breast-conserving surgery has been the treatment of choice since breast-conserving surgery was initiated in the 1970s (82). The Early Breast Cancer Trialists' Collaborative Group conducted a meta-analysis using 10 randomized clinical trials that included 7,311 patients, many of whom were followed for at least 15 years (1). This landmark study demonstrated that after breast-conserving surgery, WBI lowered the relative risk of IBTR by 69% at 5 years and conferred a 16% relative reduction in the risk of death at 15 years compared with no radiotherapy (1). Data from large NSABP trials have demonstrated that the absolute risk of IBTR after WBI is approximately 6–9% at 10 years (83, 84). (Appropriate informed consent for WBI is beyond the scope of this consensus statement.)

Available Level I evidence concerning the efficacy of APBI is limited in quantity and quality. Randomized clinical trials that have compared APBI with conventional WBI are presented in Table 6. The National Institute of Cancer, Hungary randomized clinical trial compared APBI with WBI in a cohort of 258 patients and reported similar 5-year rates of IBTR and overall survival in both arms (6). In contrast, the Christie Hospital and YBCG randomized clinical trials demonstrated a higher risk of IBTR (4, 5) and locoregional recurrence (10) in patients treated with APBI. However, these two trials included many patients who would not be considered ''suitable'' or even ''cautionary'' candidates in this consensus statement, and given the available technologies at the time of these studies, it is possible that there was greater uncertainty in identifying the tumor bed in radiation treatment planning. Therefore, the results of the Christie Hospital and YBCG studies may not be applicable to appropriately selected patients treated with the current APBI techniques. In addition, long-term toxicity data were not uniformly reported in these trials. Finally, a number of prospective single-arm clinical trials (see Table 5 and Table E1) have demonstrated a low risk of IBTR after 4 or more years of follow up. Although these prospective single-arm trials provide reassurance that patients treated with APBI may experience a low risk of IBTR, they do not prove an equivalence of APBI to WBI. As noted above, the large majority of patients entered into these single-arm trials had characteristics corresponding to the ''suitable'' candidates.

Regarding toxicity, the National Institute of Cancer, Hungary randomized trial did not show an increased risk of poor cosmetic outcome or fat necrosis in patients treated with APBI (7), and most prospective single-arm APBI trials have reported good to excellent cosmetic results in 80–95% of patients. Nevertheless, in some prospective single-arm studies, the risks of fibrosis, fat necrosis, and telangiectasia due to APBI have been significant and seem to be higher than those seen using WBI (16, 39, 41, 42, 65, 68, 70). For brachytherapy approaches, there may also be an increased risk of breast cellulitis or abscess, with the risk of infection ranging from 2% to 16% in reported studies (59, 69). For external-beam–based approaches, there is preliminary concern that a minority of patients treated with APBI may be susceptible to severe soft-tissue fibrosis or pulmonary toxicity (85–87). However, preliminary data from the RTOG 0413/NSABP B-39 randomized clinical trial including 3,311 patients with a mean follow-up of 19 months have not demonstrated an increased risk of severe toxicity in patients treated with external-beam–based approaches (88). Given the current state of evidence, mature results of randomized clinical trials are needed to provide a comprehensive comparison of the toxicities of APBI and WBI.

The Task Force recommended that patients interested in APBI should be strongly encouraged to participate in available clinical trials. However, if clinical trials are not available, patients in the ''suitable'' or ''cautionary'' groups who elect treatment with APBI should be thoroughly counseled regarding the known effectiveness and safety of both WBI and APBI. Patients in the ''cautionary'' group should also be counseled regarding the specific limitations of the data and the greater uncertainty for this patient subgroup.

Which diagnostic imaging tests are needed for patients treated with APBI?

Consensus statement. Patients treated with APBI should undergo standard imaging assessment, which typically includes diagnostic mammography and breast ultrasonography (89). At present there are insufficient data to justify routine

Table 6. Randomized trials comparing whole-beast irradiation with APBI

Trial	*N*	Median follow-up (y)	Lumpectomy cavity definition	Arms	IBTR	Tumor bed failure	LRF	CSS	OS
TARGIT	779	0.98	Intraoperative assessment	(*1*) Whole-breast RT*	.	.	.	.	.
				(*2*) APBI: IORT delivering 20 Gy to cavity surface with 50-kV photons	.	.	.	.	.
NIC, Hungary	258	5.5	Surgical clips	(*1*) Whole-breast RT: 50 Gy in 25 fractions using either Cobalt-60 (n =29) or 6–9-MV photons (n = 100)†	3.4% (4/130)	1.7% (2/130)	.	96%	91.8%
				(*2*) APBI: HDR interstitial implant to 36.4 Gy in 7 fractions b.i.d. (n = 88) or external-beam RT with electrons to 50 Gy in 25 daily fractions (n = 40).‡ PTV defined as lumpectomy cavity + 2 cm	4.7% (6/128) At 5 y p = 0.50	1.6% (2/128) At 5 y p = NR	.	98.3% At 5 y p = NR	94.6% At 5 y p = NR
YBCG	174	8	''A combination of preoperative information if available, scar position, and patient recollection''	(*1*) Whole-breast RT: 40 Gy in 15 fractions followed by boost of 15 Gy in 5 fractions	4% (4/90)	.	9% (8/90)	.	73%
				(*2*) APBI: 55 Gy in 20 fractions using external-beam techniques.§ PTV not defined	12% (10/84) At 8 y p = 0.07	8% (7/84) At 8 y p = NR	24% (20/84) At 8 y p = 0.05¶	.	70% At 8 y p = 0.75
Christie Hospital	708	5.4	Not specified	(*1*) Whole-breast RT: 40 Gy in 15 fractions without a boost	11.0% (24/355)	.	.	.	71%
				(*2*) APBI: 40–42.5 Gy in 8 fractions using 8–14-MeV‖ electrons to an average field size of 8 × 6 cm. PTV constituted the entire quadrant of the index lesion	19.6% (52/353) At 7 y p < 0.001¶	.	.	.	73% At 7 y p = NR

Abbreviations: LRF = local–regional failure; CSS = cause-specific survival; OS = overall survival; IORT = intraoperative radiotherapy; RT = radiotherapy; HDR = high-dose-rate; NR = not reported; PTV = planning target volume. Full trial names are shown in Table 1. Other abbreviations as in Tables 2 and 5.

A period (.) indicates that data were not available.

* Details of whole-breast RT not specified.

† One patient received a 16-Gy electron boost, and 22 received a dose <50 Gy.

‡ Seven patients received a dose <50 Gy. Although patients treated with electrons received partial-breast irradiation, treatment was given using conventional fractionation and thus was not accelerated.

§ External-beam techniques included tangents, appositional Cobalt-60 or Cesium-137 teletherapy, or en face electrons (energy not reported).

‖ Electron energy was 10 MeV for most patients and 14 MeV for patients with ''large breasts.''

¶ Statistically significant comparison.

Table 7. Comparison of clinical studies by APBI treatment technique

Treatment technique	Total patients	Total follow-up (patient-years)	Average follow-up (y)
Interstitial	1,321	7,133	5.4
MammoSite	1,787	4,110	2.3
Intraoperative	681	1,430	2.1
External beam			
3D-CRT/IMRT	319	335	1.0
Protons	40	20	0.5

Abbreviations: 3D-CRT = three-dimensional conformal radiotherapy; IMRT = intensity-modulated radiotherapy. Other abbreviation as in Table 2.

Data are derived from prospective single-arm studies as listed in Table E1, with the average follow-up reflecting the average of the reported median follow-up times weighted by sample size.

use of breast magnetic resonance imaging (MRI) in patients selected for APBI.

Narrative. To date, only one published study has assessed the potential utility of breast MRI in a cohort of patients who met at least some of our inclusion criteria for APBI. In this study involving 79 women, MRI identified occult foci of pathologically confirmed multicentric disease in 10% of patients and multifocal disease in an additional 28% of patients (90). At present there are no data to suggest that incorporation of breast MRI for patients treated with APBI will result in a lower risk of IBTR. The Task Force agreed that there were insufficient data to justify recommendation of routine breast MRI for patients selected for APBI. Nevertheless, the Task Force acknowledged that future studies may demonstrate a benefit derived from breast MRI and that some patients and physicians may elect to pursue MRI despite the limited data currently available.

For patients receiving APBI, how should multidisciplinary care be integrated with surgery and medical oncology?

Consensus statement. The decision regarding conventional WBI vs. APBI should be made only after the patient's consultation with a radiation oncologist and a complete pathologic evaluation of the lumpectomy specimen. For patients who will receive adjuvant chemotherapy, it is recommended that APBI be performed first and that there should be an interval of at least 2 to 3 weeks between completion of APBI and initiation of chemotherapy.

Narrative. To promote appropriate multidisciplinary cancer care, the Task Force strongly recommended that the decision to treat a patient with APBI should be made only after the patient's consultation with a radiation oncologist and review of the final pathology specimen. Committing a patient to APBI by, for example, placing a brachytherapy catheter in the breast at the time of breast-conserving surgery, precludes the fully informed consent that is needed when using APBI. Furthermore, multiple prior studies have demonstrated that placement of the brachytherapy catheter in the lumpectomy cavity at the time of breast-conserving surgery approximately doubles the risk of seroma formation (22, 47–50, 52).

For patients who will be receiving adjuvant chemotherapy, a retrospective analysis from the MammoSite registry single-arm trial reported an association between initiation of adjuvant chemotherapy within 3 weeks of the last MammoSite treatment and an increased risk of both radiation recall skin reaction and suboptimal cosmesis (91). Although this finding requires validation, the Task Force believed these data were sufficient to recommend a 2- to 3-week interval between completion of APBI and the initiation of systemic chemotherapy. There were no data regarding timing of adjuvant endocrine therapy with APBI and, as with conventional WBI, sequential or concurrent irradiation and endocrine therapy seem to be reasonable options.

According to published clinical and dosimetric data, how do the various techniques for APBI compare?

Consensus statement. Interstitial brachytherapy is the technique with the longest follow-up reported, whereas follow-up data for other APBI techniques remain limited. At present there are insufficient clinical and dosimetric data to determine the optimal technique for APBI delivery.

Narrative. As shown in Table 7, interstitial brachytherapy was identified as the APBI technique having the longest period of follow-up data (an average of 5.4 years). In contrast, average follow-up was 2.3 years for MammoSite, 2.1 years for intraoperative radiotherapy, and 1.0 years for three-dimensional conformal radiotherapy/intensity-modulated radiotherapy (3D-CRT/IMRT). Reported risks of IBTR by treatment technique are presented in Fig. E1. At present the Task Force believes that there are insufficient data to compare the different treatment techniques with respect to their effectiveness or toxicity.

Regarding technical and dosimetric issues, there are clear differences between the available modalities. Because of their noninvasive nature, external-beam–based approaches seem to minimize the risk of seroma formation and infection compared with brachytherapy approaches (12, 39, 57, 58, 64). Three-dimensional conformal radiotherapy offers excellent target coverage and dose homogeneity, but at the potential expense of inferior conformality and increased doses to the uninvolved ipsilateral breast, heart, and lung (92–96). Intensity-modulated radiotherapy and TomoTherapy (TomoTherapy Incorporated, Madison, WI) (TomoTherapy may be considered computed axial tomography [CT]-guided IMRT) improve upon 3D-CRT approaches by enhancing conformality, with a possible reduction in high doses of radiation delivered to the uninvolved ipsilateral breast, heart, and lung. However, IMRT and TomoTherapy may result in a modest decrease in planning target volume (PTV) coverage (92–95), and the panel expressed concern that certain applications of these treatment approaches might also increase the volume of adjacent organs exposed to low doses of radiation, depending on the beam arrangement selected. Compared with photon therapy, proton therapy may decrease the dose to the uninvolved ipsilateral breast, heart, and lung

but may result in a modest decrease in PTV coverage (46, 97) and an increased risk of skin toxicity (39).

Brachytherapy techniques may deliver lower doses of radiation to the uninvolved ipsilateral breast, heart, and lung than do external-beam radiation techniques (93, 95, 96). The PTV used for brachytherapy planning is typically smaller than the PTV for external-beam techniques (96) because brachytherapy does not require expansion of the clinical target volume (CTV) to account for setup error or tumor motion. As a result, the integral dose to the patient treated with brachytherapy is lower than the integral dose to the patient treated with external-beam irradiation. (Integral dose is defined as the integral of the dose delivered multiplied by the volume treated and may be thought of as the total energy deposited in the patient.) However, brachytherapy results in significant dose inhomogeneity, with maximal doses that can exceed the prescribed dose by more than 200% (98). In addition, brachytherapy may result in PTV coverage inferior to that seen in external-beam irradiation (96). Finally, the skin dose from brachytherapy can markedly exceed the skin dose with external-beam techniques, and thus great care is required to ensure adequate source-to-skin distance in patients treated with brachytherapy (60). Because of this requirement, brachytherapy may not be a viable treatment option for patients with superficial tumors or small breasts.

Whereas the external-beam and brachytherapy approaches discussed above are all delivered in the postoperative setting, intraoperative radiotherapy represents a fundamentally different approach, whereby the complete course of radiotherapy is delivered as a single fraction at the time of definitive cancer surgery. Phase II investigations of this approach have yielded promising results (25–29, 56, 68, 75), and randomized trials to evaluate intraoperative radiotherapy are currently ongoing in Europe (9). Despite growing clinical data regarding intraoperative radiotherapy, the systematic literature review did not identify any studies that compared dosimetric parameters of intraoperative radiotherapy with other APBI techniques in patients with breast cancer.

The determination of when a new treatment technique can be introduced into ''off-protocol'' use was discussed but was believed to be outside the scope of this consensus panel. However, all agreed that physicians should recognize that the farther a new technique varies in its treatment approach and dosimetric profile from those techniques that have been evaluated through various forms of clinical trials, the more rigorously it should be tested before ''off-protocol'' use. Within this context, the Task Force agreed that proton therapy as a technique to deliver APBI requires additional study in clinical trials before ''off-protocol'' use because of limited clinical data published to date (39) and the marked differences in dosimetry between protons and photons. In addition, the Task Force believed that a thorough recommendation regarding selection criteria, clinical indications, and technical specifications for intraoperative radiotherapy was beyond the scope of this document and recommended caution in the adoption of this technique until more data become available.

What are the minimum requirements for APBI treatment planning and dosimetry?

Consensus statement. Treatment with APBI requires technical expertise encompassing the tools needed to evaluate and ensure the delivery of a safe and effective dose to a specific target. Use of any APBI technique requires the ability to (*1*) delineate a treatment target, (*2*) deliver the prescription dose to the target, (*3*) optimize dose homogeneity, (*4*) limit dose to nontarget tissue, and (*5*) use a quality assurance program to verify that the prescribed dose is delivered accurately.

Narrative. The Task Force elected not to address details of treatment planning specific to any particular technique for delivery of APBI, because technical aspects vary widely between the currently available APBI techniques, new techniques continue to emerge, and the present understanding of optimal treatment planning parameters continues to evolve as longer follow-up data become available. Nevertheless, the Task Force agreed that use of any APBI technique requires all five elements listed above.

Delineation of the treatment target requires the individual expertise of the treatment team for intraoperative techniques and a CT scan for postoperative techniques. For postoperative techniques, the CTV should be defined, at a minimum, by identifying the limits of the lumpectomy cavity and then expanding it to include at least 1 cm, but no more than 2 cm, of surrounding breast tissue. Furthermore, the PTV is an expansion of the CTV to account for breathing motion and setup error. As it relates to brachytherapy, the CTV equals PTV as a result of the fixed relationship between the interstitial or intracavitary brachytherapy devices and the CTV. Details of PTV expansion for external-beam treatment approaches will vary according to the specifics of the treatment technique and the influence of institutional experience. The Task Force emphasized the importance of including some PTV expansion for nonbrachytherapy APBI techniques and that conservative principles should be applied in off-protocol use until boundaries are better determined through reported treatment outcome studies.

The projected ability to deliver the prescription dose to the target with acceptable dose homogeneity depends on the specific technique used and the target size, shape, and location within the breast. A general baseline rule is that at least 90% of the target should be covered by at least 90% of the prescription dose (78). However, until additional data are available, CT-based evaluation of target coverage is recommended, with the goal of maximal dosimetric target coverage while balancing dose homogeneity and nontarget tissue dose criteria. Prescription doses used in published studies are presented in Table 6 and Table E1. Until additional data become available, the doses recommended by the RTOG 0413/NSABP B-39 national Phase III trial represent a reasonable standard of care; for MammoSite and interstitial brachytherapy, this dose/fractionation is 34 Gy in 10 fractions delivered twice daily over 5–7 days with interfraction interval ≥6 h, and for 3D-CRT this dose/fractionation is 38.5 Gy in 10 fractions delivered twice daily over 5–7 days with interfraction interval ≥6 h (78). Alternative fractionation schemes that deliver biologically equivalent

Table 8. NSABP B-39/RTOG 04-13 guidelines for target and normal tissue constraints

Treatment technique	Determination factors	Dose constraints
Interstitial brachytherapy	Dose homogeneity	DHI $\geq$0.75
		DHI = $(1 - V_{150\%}/V_{100\%})$
		$V_{150\%}$ $\leq$70 cm^3
		$V_{200\%}$ $\leq$20 cm^3
	Skin	Skin D_{max} $\leq$100%
	Ipsilateral breast*	$V_{\geq 50\%}$ $\leq$60%
	Target	$\geq$90% of the prescription dose covers $\geq$90% of the PTV_EVAL
MammoSite	Tissue-balloon conformance	Volume of trapped air/PTV_EVAL <10%
	Balloon symmetry	Deviation of $\leq$2 mm from expected dimensions
	Minimum balloon surface–skin distance	Ideal: $\geq$7 mm
		Acceptable: 5–7 mm if D_{max} to skin $\leq$145%
	Ipsilateral breast*	$V_{150\%}$ $\leq$50 cm^3
		$V_{200\%}$ $\leq$10 cm^3
		$V_{\geq 50\%}$ $\leq$60%
	Target	$\geq$90% of the prescription dose covers $\geq$90% of the PTV_EVAL (after accounting for volume of trapped air)
External beam	Ipsilateral breast*	$V_{\geq 50\%}$ $\leq$60%
		$V_{100\%}$ $\leq$35%
	Contralateral breast	D_{max} $\leq$3%
	Ipsilateral lung	$V_{30\%}$ <15%
	Contralateral lung	$V_{5\%}$ <15%
	Heart (right-sided tumors)	$V_{5\%}$ <5%
	Heart (left-sided tumors)	$V_{5\%}$ <40%
	Thyroid	D_{max} $\leq$3%
	Target	D_{max} $\leq$120%
		$\geq$90% of the prescription dose covers $\geq$90% of the PTV_EVAL

Abbreviations: DHI = Dose homogeneity index; PTV_EVAL = planning target volume used to evaluate dose coverage.
Data from reference 78.
* For purposes of this calculation, the ipsilateral breast volume includes the target volume and encompasses all tissue superficial to the chest wall–lung interface that falls within the borders of a conventional whole-breast radiotherapy treatment field.

doses may also be acceptable; however, the largest experiences published to date have used the RTOG 0413/NSABP B-39 twice-daily schedule.

When using APBI, limiting the dose delivered to nontarget tissue is critically important. Specific guidelines regarding maximum dose and volume limitations have been slow to emerge, because extended follow-up is necessary. However, the dose delivered to the skin, chest wall/rib, volume of normal breast tissue, and volume of adjacent critical organs should, at a minimum, be calculated, evaluated, and recorded before treatment delivery. Until additional outcome data are available, the Task Force recommended adherence to the dosimetric guidelines outlined in the RTOG 0413/NSABP B-39 national Phase III trial (Table 8).

All treatment techniques should have a clear quality assurance program established to ensure the plan of treatment is thoroughly evaluated before delivery and that the treatment is delivered accurately for every fraction of the treatment. This should include patient positioning setup and, if applicable, appropriate brachytherapy device assessment before each dose delivery.

CONCLUSIONS

Accelerated partial-breast irradiation is a new technology that provides faster, more convenient treatment after breast-conserving surgery and that may ultimately demonstrate long-term effectiveness and safety comparable to that of WBI for selected patients with early breast cancer. It is important to recognize that APBI is unlikely to replace WBI for all or even most patients treated with breast-conserving surgery. It is hoped that the recommendations contained within this consensus statement will help to provide guidance regarding the use of APBI outside of a clinical trial and will serve as a framework to promote additional clinical investigations into the optimal role of APBI in the treatment of breast cancer. Because knowledge regarding APBI is rapidly evolving, this consensus statement will require frequent updates and modifications to account for ongoing research findings.

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