Accelerated Partial Breast Irradiation Consensus Statement from the American Society for Radiation Oncology (ASTRO)

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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] 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 longterm 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. APBI 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. But 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) breast brachytherapy catheter.[2] In past years, few data were available to define which patients could be safely treated with APBI and which patients should receive WBI. But in light of increasing evidence that WBI improves longterm overall survival,[1] 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 about 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. An excerpt of this consensus statement is presented here. The complete consensus statement is published in the *International Journal of Radiation Oncology, Biology, and Physics* 2009.

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METHODS

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 about APBI

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Abbreviations and Acronyms

APBI = Accelerated partial breast irradiation
ASTRO = American Society for Radiation Oncology
DCIS = Ductal carcinoma in situ
EIC = Extensive intraductal component
ER = Estrogen receptor
IBTR = Ipsilateral breast tumor recurrence
LVSI = Lymph-vascular space invasion
NSABP = National Surgical Adjuvant Breast and Bowel Project
RTOG = Radiation Therapy Oncology Group
WBI = whole breast irradiation.

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 longterm 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 (BDS) searched for English-language citations in the National Library of Medicine's PubMed database through May 30, 2008, using the MeSH heading "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, 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).[3-9] 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 (BDS) and abstracted for inclusion criteria, radiotherapy methods, clinical outcomes, and toxicity.

Table 1. Published Prospective Studies Identified by a Systematic Literature Review

Study	Full name	First author	Year	Reference
Christie Hospital	Christie Hospital, Manchester UK	Ribeiro	1993	3
		Ribeiro	1990	4
NIC Hungary	National Institute of Cancer, Hungary	Polgar	2007	5
		Lovey	2007	6
		Polgar	2002	7
TARGIT	Targeted Intraoperative Radiation Therapy	Holmes	2007	8
YBCG	Yorkshire Breast Cancer Group	Dodwell	2005	9

RESULTS

Clinical questions

Which patients may be considered for accelerated partial breast irradiation outside of a clinical trial?

Consensus statement. All patients considered for APBI should be candidates for breast-conserving therapy (no earlier radiation therapy, no history of certain collagen vascular diseases, and not pregnant) and should be committed to longterm followup to evaluate for recurrence, second primary cancers, and treatment toxicity. Table 2 presents the Task Force's consensus for the following: a "suitable" group, for whom treatment with APBI is considered acceptable outside of a clinical trial; 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; and 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 this table provides 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 into the Radiation Therapy and 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. But 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