: 4160-90-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Partial Breast Irradiation for Breast Cancer

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Supplemental Evidence and Data Submissions.

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review on *Partial Breast Irradiation for Breast Cancer,* which is currently being conducted by the AHRQ's Evidence-based Practice Centers (EPC) Program. Access to published and unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES:

E-mail submissions: epc@ahrq.hhs.gov

Print submissions:

Mailing Address:

Center for Evidence and Practice Improvement

Agency for Healthcare Research and Quality

ATTN: EPC SEADs Coordinator

5600 Fishers Lane

Mail Stop 06E53A

Rockville, MD 20857

Shipping Address (FedEx, UPS, etc.):

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5600 Fishers Lane

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FOR FURTHER INFORMATION CONTACT:

Jenae Benns, Telephone: 301-427-1496 or Email: epc@ahrq.hhs.gov.

SUPPLEMENTARY INFORMATION:

The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Centers (EPC) Program to complete a review of the evidence for *Partial Breast Irradiation for Breast Cancer*. AHRQ is conducting this technical brief pursuant to Section 902 of the Public Health Service Act, 42 U.S.C. 299a.

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on *Partial Breast Irradiation for Breast Cancer,* including those that describe adverse events. The entire research protocol is available online at:

https://effectivehealthcare.ahrq.gov/products/accelerated-partial-breast-irradiation/protocol

This is to notify the public that the EPC Program would find the following information on *Partial Breast Irradiation for Breast Cancer* helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number*.
    - *For completed studies that do not have results on ClinicalTrials.gov*, a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions,

inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.

- *A list of ongoing studies that your organization has sponsored for this indication*. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute *ALL Phase II and above clinical trials* sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: https://www.effectivehealthcare.ahrq.gov/email-updates.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.

Key Questions (KQ)

KQ 1. In adult women with early stage breast cancer, what are the comparative effectiveness, adverse events, and cosmetic outcomes of partial breast irradiation compared to whole breast irradiation?

KQ1a. How does effectiveness of partial breast irradiation vary by clinical-pathologic characteristics?

KQ1b. How do the effectiveness, adverse events, and cosmetic outcomes of partial breast irradiation vary by target volumes, dose-fractionation schemes, motion management, and planning parameters?

KQ 2. In adult women with early stage breast cancer, what are the comparative effectiveness, adverse events, and cosmetic outcomes of different partial breast irradiation modalities (including multicatheter interstitial brachytherapy, single-entry catheter brachytherapy, 3-dimensional conformal external beam radiation therapy, intensity modulated radiation therapy, proton radiation therapy, and intraoperative radiotherapy)?

*KQ 2a***.** When there are no eligible comparative studies to address KQ2 for a particular PBI modality, what are the rates of adverse events in noncomparative series of such modality?

*KQ 2b***.** When there are no eligible comparative studies to address KQ2 for a particular PBI modality, what are the rates of long-term (> 5 years) effectiveness outcomes and cosmesis in noncomparative series of such modality?

Contextual Question (CQ)

CQ 1. In adult women with early stage breast cancer, to what extent does financial toxicity differ between partial and whole breast irradiation?

PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, and Settings)

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
Population	• Adult women (i.e., 18 years and older) with early stage breast cancer (i.e., a small tumor less than or equal to 3 cm that has minimal or no lymph node involvement (N0/1))	• Animals • Children (i.e., age <18 years) • Men • Recurrent breast cancer

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
Interventions	For all KQs and CQ1, PBI includes the following modalities: • Multicatheter interstitial brachytherapy • Single-entry catheter brachytherapy • 3-dimensional conformal external beam radiation therapy • Intensity modulated radiation therapy • Proton radiation therapy • Intraoperative radiotherapy	• Combination of PBI and WBI
Comparators	KQ 1, CQ 1: WBI KQ 2: A different PBI modality • Multicatheter interstitial brachytherapy • Single-entry catheter brachytherapy • 3-dimensional conformal external beam radiation therapy • Intensity modulated radiation therapy • Proton radiation therapy • Intraoperative radiotherapy KQ 2a and 2b: No comparator	None

Outcomes	KQ 1 and 2:
	• Ipsilateral breast cancer recurrence (i.e., tumor bed ipsilateral breast cancer recurrence, elsewhere ipsilateral breast cancer recurrence)
	• Mastectomy-free survival
	• Overall survival
	• Cancer-free survival
	• Contralateral breast cancer recurrence
	• Distant breast cancer recurrence
	• Regional breast cancer recurrence
	• Any breast cancer recurrence
	• Breast conservation
	• Quality of life (e.g., BCTOS, FACT-B, SF-36, Breast Q scale)
	• Patient-reported and physician-assessed cosmesis (e.g., including Harvard Breast Cosmesis Scale, Global Cosmesis Scale, or the EORTC breast cancer cosmetic rating system)
	• Sexual health
	• Adverse events, including scales measuring radiation toxicity:
	  ○ RTOG/EORTC scores
	  ○ LENT-SOMA scales
	  ○ CTCAE scores
	CQ 1: Contextual information about the construct of financial toxicity (i.e., financial distress and hardship)
		None

Timing	At the following intervals: For effectiveness and cosmetic outcomes • >=1 year to 5 years • >5 years to 10 years • >10 years For adverse events • <3 months • >=3 months	None
Settings	Any	None

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
Study design	KQ1: • RCTs KQ 2: • RCTs • Comparative observational studies KQ 2a: • Single-arm observational studies (>=50 patients) KQ 2b: • Single-arm observational studies (>=50 patients and >=5 year followup) CQ 1: • RCTs • Comparative observational studies • Qualitative studies • Cost-benefit analyses • Surveys All KQs and CQ 1: • Relevant systematic reviews or meta-analyses (used for identifying additional studies)	• In vitro studies • Nonoriginal studies (e.g. narrative reviews, editorials, letters, or erratum), • Cross-sectional (i.e., nonlongitudinal) studies

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
Subgroup analysis	KQ 1 and 2: • Age • Treatment schedule (i.e., accelerated, nonaccelerated) • Race/ethnicity • Socioeconomic status • Area Deprivation Index • DCIS vs. invasive disease • Breast size • BMI • Cup size • Breast implants • Mental health comorbidities • Menopausal status • Receipt of systemic therapy (i.e., none, endocrine therapy, and/or chemotherapy, both) • Histologic subtype (e.g., invasive ductal carcinoma, invasive lobular carcinoma, DCIS, other) • Nodal status (i.e., N0, N1, NX, number of positive nodes) • Nodal assessment (i.e., sentinel lymph node biopsy, axillary lymph node dissection, none) • Tumor grade • Tumor size (i.e., <1 cm, 1-2 cm, 2-3 cm, >3 cm) • Focality (unifocal vs multifocal) • Margin status (i.e., positive, <2 mm, 2-3 mm, >3 mm) • Extensive intraductal component • Ki-67 (<20% vs. >= 20%) • ASTRO or ESTRO risk category (i.e., suitable, cautionary, unsuitable; low, intermediate, high) • Germline genetic mutation (e.g., *BRCA1, BRCA2, CHEK2, PALB2, ATM,* etc.) • Cancer-predisposing syndrome • Estrogen receptor status • Progesterone receptor status • Hormone receptor status • Lymphovascular invasion • HER2 status • Prior chemotherapy • Monoelectron therapy • Dermatologic Rheumatologic conditions (i.e., lupus, scleroderma, rheumatoid arthritis) • Dose-fractionation schemes (i.e., accelerated, nonaccelerated, daily vs every other day vs twice daily, total dose, EQD2) • Target volumes (i.e., size of expansion on cavity, diameter of the inflated balloon, size of the planning target volume) • Motion management • Planning parameters (i.e., the diameter of the inflated balloon, the planning target volume, and the dose distribution organ-at-risk constraints and dose received [such as ipsilateral breast V50 and V100], number of beams, PTV coverage goals and constraints) • Number of treatment fields • Image guidance (i.e., MV imaging, kV imaging, cone beam CT, use of clips for localization) • Risk of bias (i.e., low, moderate, high)	None
Publications	• Studies published in English as peer reviewed full text • Published after Year 2000	• Foreign language studies • Conference abstracts

Abbreviations: ASTRO = American Society for Radiation Oncology; *ATM* = ataxia telangiectasia mutated; BCTOS = Breast Cancer Treatment Outcomes Scale; BMI = body mass index; *BRCA1* = breast cancer 1; *BRCA2* = breast cancer 2; *CHEK2* = checkpoint kinase 2; cm = centimeter; CQ = contextual question; CT = computed tomography; CTCAE = Common Terminology Criteria for Adverse Events; DCIS = ductal carcinoma in situ; EORTC = European Organisation for Research and Treatment of Cancer; ESTRO = European Society for Radiotherapy and Oncology; FACT-B = Functional Assessment of Cancer Therapy-

Breast; EQD2 = Equivalent Dose in 2 Gy fractions; HER2 = human epidermal growth factor receptor 2; KQ = key question; kV = kilovoltage; LENT-SOMA = Late Effects Normal Tissue Task Force- Subjective, Objective, Management, Analytic; mm = millimeter; MV = megavoltage; N0 = no involved lymph nodes; N1 = 1-3 involved lymph nodes; NX = lymph nodes not assessed; *PALB2* = partner and localizer Of *BRCA2*; PBI = partial breast irradiation; PICOTS = populations, interventions, comparators, outcomes, timing, and settings; PTV = planning target volume; RCT = randomized controlled trial; RTOG = Radiation Therapy Oncology Group; SF-36 = Short Form (36) Health Survey; V50 = volume (%) receiving >= 50% of the prescription dose; V100 = volume (%) receiving >= 100% of the prescription dose; WBI = whole breast irradiation

Dated: November 2, 2021.

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Associate Director.

[FR Doc. 2021-24403 Filed: 11/8/2021 8:45 am; Publication Date: 11/9/2021]