Effective Health Care
Post-operative Treatment of Early Stage Breast Cancer Nomination Summary Document

Results of Topic Selection Process & Next Steps

- Post-operative radiation treatment of early stage breast cancer was found to be addressed by a 2011 meta-analysis by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) on long-term outcomes of radiation treatment, a 2009 systematic review by Offersen and colleagues on various radiation technologies, and a 2009 AHRQ review on radiation treatment in patients with ductal carcinoma in situ (DCIS). Given that the existing reviews cover this nomination, no further activity will be undertaken on this topic.
  - Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomized trials. The Lancet 2011; 378: 1707-16. PMID: 22019144
  - Offersen BV, Overgaard M, Kroman N, et al. Accelerated partial breast irradiation as part of breast conserving therapy of early breast carcinoma: a systematic review. Radiotherapy & Oncology 2009; 90: 1-13. PMID: 18783840
  - Virnig BA, Shamliyan T, Tuttle TM, Kane RL, Wilt TJ. Diagnosis and Management of Ductal Carcinoma in Situ (DCIS). Evidence Report/Technology Assessment No. 185. Rockville, MD: Agency for Healthcare Research and Quality. September 2009. http://www.ncbi.nlm.nih.gov/books/NBK32576/

Topic Description

Nominator: Organization

Nomination Summary: The nominator is seeking a systematic review to compare the effectiveness of alternative methods of post-operative radiation treatment following breast conserving surgery for adult women with early stage breast cancer who have a low risk of recurrence.

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Population(s): Adult women with breast cancer at low risk (for example, few positive lymph nodes, relatively small tumor size, older age, ER-positive tumors) of recurrence undergoing breast conserving surgery (e.g., <2 cm). Subgroups include minority women and those living farther (not defined) from treatment facilities.

Intervention(s): Accelerated partial breast irradiation (APBI) vs. whole breast irradiation technologies, including (1) interstitial brachytherapy; (2) balloon brachytherapy; (3) combined brachytherapy (interstitial and balloon); (4) external beam

radiotherapy, with either 3D-conformal or intensity-modulated methodologies; and (5) intraoperative radiotherapy. Accelerated vs. conventional whole breast irradiation (e.g., 3-week vs. 5-week schedule).
Comparator(s): See above
Outcome(s): Benefits include greater convenience with possibly greater use of radiation therapy, leading to increased disease-free and overall survival; improved cosmesis; reduced radiation-related side effects to the rest of the breast and nearby tissues. Harms include radiation-induced side effects; higher recurrence; reduced survival (overall, disease-free); adverse events associated with specific APBI methods (e.g., the need to explant the balloon brachytherapy device and use an alternative radiotherapy technique).

Key Questions from Nominator:

1. For patients with early stage breast cancer, what is the comparative effectiveness of alternative methods for post-lumpectomy radiation therapy (whole-breast vs. partial breast; accelerated versus conventional fractionation) in improving net health outcome?

Considerations

- The topic meets EHC Program appropriateness and importance criteria. (For more information, see http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/.)

- Radiotherapy in treatment of individuals with DCIS was found to be addressed by a 2009 AHRQ evidence review titled "Diagnosis and Management of Ductal Carcinoma in Situ (DCIS)." Key questions from this report are listed below. The bolded key question specifically focus on radiotherapy in treatment of DCIS.
  1. What are the incidence and prevalence of DCIS and its specific pathologic subtypes, and how are incidence and prevalence influenced by mode of detection, population characteristics, and other risk factors?
  2. How does the use of MRI or SLNB impact important outcomes in patients diagnosed with DCIS?
  3. How do local control and systemic outcomes vary in DCIS based on tumor and patient characteristics?
  4. In patients with DCIS, what is the impact of surgery, radiation, and systemic treatment on outcomes?
     a. Given that the lack of evidence that BCS+RT provides any mortality benefit and the number of local DCIS or invasive recurrences per 1,000 women treated is small, is there benefit in routine use of RT following BCS?
     b. What is the role of partial breast radiation? What is the preferred technique of partial breast radiation?
     c. Since RCTs show that RT after BCS does not remove the negative prognostic impact of positive margins, understanding the optimum management to counteract this effect is essential. What is the optimum definition of positive margins? Should patients with close margins undergo re-excision?
     d. The role of tamoxifen and aromitase inhibitors is of current interest and will be influenced by the ongoing NSABP trials. Is the benefit of tamoxifen and aromitase inhibitors to provide treatment for the primary DCIS or primary prevention for a future new primary DCIS or

invasive cancer? This question acknowledges that history of DCIS or invasive breast cancer is a risk factor for DCIS or invasive cancer incidence.

- A comparison of the various radiotherapy techniques was found to be addressed by a 2009 systematic review by Offersen and colleagues titled “Accelerated partial breast irradiation as part of breast conserving therapy of early breast carcinoma: a systematic review.” This review includes data from clinical trials and compares 3D CRT, interstitial brachytherapy, balloon brachytherapy, intraoperative radiotherapy, and intraoperative targeted radiotherapy.

- Long-term outcomes of radiotherapy were found to be addressed by a 2011 meta-analysis by EBCTCG titled “Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomized trials.” This analysis included only data from randomized controlled trials completed before 2000 because the outcomes of interest for the analysis are 10-15 year recurrence rates.