JNCI J Natl Cancer Inst (2018) 110(2): djx177

doi: 10.1093/jnci/djx177
First published online September 13, 2017
Editorial

EDITORIAL

Interaction of Postmastectomy Radiation Treatment With Breast Reconstruction: Many Questions, Emerging Data

Lawrence J. Solin

Affiliation of author: Department of Radiation Oncology, Albert Einstein Healthcare Network, Philadelphia, PA.

Correspondence to: Lawrence J. Solin, MD, FACR, FASTRO, Department of Radiation Oncology, Albert Einstein Healthcare Network, 5501 Old York Road, Philadelphia, PA 19141 (e-mail: solin@einstein.edu).

In the increasingly complex landscape of breast cancer management, patients and physicians have a broad menu of treatment options. While this trend is overall positive, evaluating the subtle, and sometimes not so subtle, interaction of individual treatment components can be complicated. In this context, information on the interaction of postmastectomy radiation treatment (PMRT) and breast reconstruction has been limited, even though PMRT and breast reconstruction each benefit appropriately selected patients.

PMRT is indicated for a number of clinical settings, for example, pathologically positive axillary lymph nodes, inadequate margins of resection, or locally advanced or inflammatory breast cancer. For patients with four or more positive lymph nodes, adding PMRT has generally been accepted. For patients with one to three positive lymph nodes, adding PMRT has been the subject of considerable debate, although national guidelines allow for or even recommend strong consideration of adding PMRT (1–3). In the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis of the randomized trials of radiotherapy after mastectomy, adding radiotherapy improved the 10-year risk of local-regional recurrence and 20-year breast cancer mortality rate in the setting of both one to three positive lymph nodes and four or more positive lymph nodes (all $P \leq .04$) (4).

The options for breast reconstruction after mastectomy continue to increase. Patient-related factors and patient and physician preferences strongly influence the type and timing of breast reconstruction (5,6). The type of reconstruction is generally characterized as an implant reconstruction or an autologous tissue reconstruction, and the timing as immediate (ie, at the time of the mastectomy) or delayed (ie, after the mastectomy). A number of different types of autologous tissue reconstructive options are now available.

Notwithstanding the value of both PMRT and breast reconstruction, analysis of their interaction has been limited. In this issue of the Journal, Jagsi et al. provide valuable and clinically relevant information on two-year outcomes for the interaction of PMRT and breast reconstruction (7). The authors evaluated 2247 patients (622 with and 1625 without PMRT) prospectively accrued in the multicenter Mastectomy Reconstruction Outcomes Consortium (MROC).

Major findings from this study were that adding PMRT was associated with a higher two-year risk of complications and lower patient-reported quality of life for implant reconstruction, but not for autologous reconstruction (7). These differences were statistically significant and clinically meaningful. The two-year rates of any complication were 38.9% for implant reconstruction with radiation, 25.6% for autologous reconstruction with radiation, 21.8% for implant reconstruction without radiation, and 28.3% for autologous reconstruction without radiation. There was a statistically significant interaction for the type of reconstruction and use of radiation (odds ratio [OR] = 2.64, 95% confidence interval [CI] = 1.77 to 3.94, $P < .001$, for radiation vs no radiation for implant reconstruction; OR = 1.12, 95% CI = 0.66 to 1.92, $P = .67$, for radiation vs no radiation for autologous reconstruction). The respective two-year rates of reconstruction failure were 18.7%, 1.0%, 3.7%, and 2.4%. Patient-reported satisfaction with the breast and with the overall reconstructive outcome were also less satisfactory for implant reconstruction plus radiation compared with the other groups.

Strengths of this study include the large number of patients evaluated, with detailed information collected. Even though not randomized, the data were prospectively collected. While selection bias cannot be excluded, the authors provide in-depth statistical analyses to support their findings and conclusions.

Received: July 25, 2017; **Accepted:** August 2, 2017

Although the data by Jagsi et al. provide valuable information, many questions remain. With the relatively short two-year follow-up, the reported findings could change over time. Based on other studies with longer follow-up, the irradiated patients might have further complications and worsening cosmetic outcomes with longer follow-up. Other clinically relevant details to be considered include the grade and type of various complications, the extent of the radiotherapy fields used, the type of systemic therapies given, the specific types of reconstructions used, and pedicle vs free flaps.

Large, high-quality, nonrandomized studies such as MROC provide needed data for informing patients and clinical decision-making. In addition to the study by Jagsi et al. (7), other published studies from MROC have examined various other issues related to breast reconstruction (8–15).

Interpreting the literature on the interaction of PMRT and breast reconstruction is difficult at best. In view of the lack of randomized trial data, most reported evidence comes from retrospective, institutional studies. A number of different outcomes can be measured, including oncologic events (eg, local-regional recurrence), cosmetic outcomes, complications, and patient-reported quality of life. Retrospective studies often have small numbers of patients and vary in detail relative to treatment of individual patients, and hence are subject to selection bias. PMRT is typically given last in sequencing oncologic treatments (ie, after surgery and after systemic therapy). Other limitations of retrospective studies include varying types and sequences of reconstructions, sequencing of treatment modalities, differences in systemic therapies (including use and type of chemotherapy), and institutional preferences. Finally, most retrospective studies have relatively short follow-up, which is particularly important as late radiation complications and differences between management approaches may not become evident until years, or even decades, after irradiation (16,17).

The interaction of the technical aspects of surgical reconstruction and PMRT is another potential area for future research. While the impact of the technical approach and expertise is well recognized for surgical procedures, the impact of the technical approach and expertise for radiotherapy is equally important. For example, in the EBCTCG meta-analysis of radiotherapy after mastectomy for node-positive disease, the gains in breast cancer mortality and overall mortality were limited to those patients irradiated to the chest wall and regional lymph nodes (both $P < .00001$) and were not seen in those patients irradiated to the regional lymph nodes only, without the chest wall (both $P > .1$) (4). Increasing radiation dose to the heart has been directly linked to an increasing risk of cardiac events (18,19). In two randomized trials evaluating extended field radiation, improvements in disease-free and distant disease-free survival were seen (all $P \leq .04$), although at the cost of increased complications, for example, pneumonitis and arm lymphedema (20,21).

In summary, the study by Jagsi et al. provides patients and physicians with clinically important information to help guide decision-making in the setting of PMRT and breast reconstruction. In this study, implant reconstruction plus radiation was associated with worse outcomes for complications and patient-reported quality of life. While these findings represent a major step forward, more research will be needed to further evaluate the complex interaction of PMRT and breast reconstruction.

Note

The author has no conflicts of interest to declare.

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