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EDITORIAL

Postmastectomy Radiation Therapy for Inflammatory Breast Cancer: Is More Better?

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A recently published review of the literature on postmastectomy radiation therapy (PMRT) for inflammatory breast cancer (IBC) cited a range for 5-year locoregional control (LRC) after PMRT from 73% to 92% (1). Even examining only contemporary datasets, these rates of LRC are lower than those reported for non-IBC (ie, 97% at 5 years [2]), and some authors have shown directly that IBC presentation is associated with worse local control compared with non-IBC patients (3). This motivates interest in investigating whether varied approaches might be best to ensure LRC in this difficult circumstance.

The radiation treatment dose and techniques described across series reporting IBC outcomes vary. The University of Texas MD Anderson Cancer Center experience demonstrated improved local control with hyperfractionated dose escalation in high-risk subsets such as patients with poor response to chemotherapy, involved margins, and age <45 years (4). The Memorial Sloan-Kettering Cancer Center reported similar local control without dose escalation but incorporating daily bolus (5). The University of Pennsylvania reports excellent local control among contemporary patients using bolus every other day (6). The Cleveland Clinic Foundation recently reported local control outcomes in a contemporary era including taxanes and trastuzumab and reported higher LRC with doses >60.4 Gy using the MD Anderson Cancer Center twice daily regimen in 11 of 13 patients who received >60.4 Gy (7). In this issue of *International Journal of Radiation Oncology, Biology, Physics*, Brown et al (8) report a 5-year LRC rate of 81% for 49 IBC patients treated with neoadjuvant chemotherapy, modified radical mastectomy, and once-daily PMRT using daily bolus similar to the Memorial Sloan-Kettering Cancer Center experience.

Because there will likely never be a randomized trial of PMRT dose escalation in IBC it is helpful to consider empirical recommendations and what general principles can be ascertained from these studies. Because local failure in IBC can rapidly progress to carcinoma en cuirasse, representing a particularly distressing local problem, and is a disease characterized by local tumor cell migration through the skin and at times beyond field borders, careful attention to field design, pretreatment examination and imaging, and treatment regimen is warranted (9). Pretreatment medical photographs and cross-sectional imaging can be extremely valuable for field design and plan assessment, and every effort should be made to encourage this from the team that sees these patients at presentation. From the collective literature, including the report in this issue by Brown et al (8), local control is considered low by today's standards for non-IBC, even considering that most of these articles describe an aggressive local therapy approach including either thick daily or every other day bolus, hyperfractionation, or dose escalation tailored to the response to chemotherapy.

Specifically considering dose (Table 1), to date three reports describe a dose-response relationship with doses 60 Gy associated with improved LRC in select patients (4, 7, 10). Although Damast et al (5) report LRC on the higher side for these reports with most patients receiving 50 Gy, they do note none of the 11% who received a boost to 60 Gy experienced a locoregional recurrence, and 11

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Table 1 Relationship between dose and local control in inflammatory breast cancer

Center	Dose	5-y LRC (%)	Era	Notes
MDACC (4)	60-66 Gy, prn bolus (66 Gy bid)	91	1977-2004, N = 125*	66 Gy improved LRC for age <45 y, + margins, and poor CT response
Cleveland (7)	45-66 Gy, bolus NS	83	2000-2009, N = 104	
	≥60.4 Gy	100		11/13 pts received bid
Florida (10)	42-60 Gy, qd bolus	78	1982-2001, N = 61	≥60 Gy, MVA $P = .06$
MSKCC (5)	50 Gy, qd bolus	87	1995-2006, N = 107	100% LC @ 60 Gy
Mayo (8)	60-66 Gy, qd bolus	81	2000-2010, N = 49	PCR associated with better LRC
Penn (6)	46-50 Gy, qod bolus	88	1986-2006, N = 19†	Only pts with DLI had LRR
BCCA (11)	42.4 Gy (hypofx), bolus NS	63	1980-2000, N = 148	PCR associated with better LRC

Abbreviations: BCCA = British Columbia Cancer Agency; CT = chemotherapy; DLI = dermal lymphatic invasion; Florida = The University of Florida College of Medicine; hypofx = hypofractionation (equivalent to 50 Gy in standard fractionation); LRC = locoregional control; MDACC = MD Anderson Cancer Center; Mayo = The Mayo Clinic; MSKCC = Memorial Sloan Kettering Cancer Center; prn = as needed; MVA = multivariate analysis; NS = not stated; PCR = pathologic complete response; Penn = The University of Pennsylvania; pts = patients; qd = daily; qod = every other day.

* Data reported for those patients who had negative margins to skew the data toward the more contemporary cohort (5-y LRC of 60 pts with positive or unknown margins, 68%).

† Data reported for those with inflammatory breast cancer and DLI.

patients were not able to complete the prescribed treatment owing to acute dermatitis. Among the studies that used up to 66 Gy as in the present report by Brown et al (4, 7, 8), the reported LRC by Brown et al is on the lower side, and the case could be made for further intensifying therapy in this setting, potentially with twice-daily fractionation (8). Although the experiences reported by Damast et al (5) and Abramowitz et al (6) are encouraging with 50 Gy and aggressive bolus, 2 other reports using these doses have among the lowest local control rates reported (10, 11).

Whether acceleration, bolus, and/or total dose play the most important role in local control in this disease will likely not be established. This author's opinion is that one of these strategies is warranted in all IBC cases, and providers should select according to their own experience and comfort level, managing side effects to limit the possibility of treatment breaks. Certainly additional efforts to identify safe radiosensitizers for this population are needed. Although limited, the data favor increased LRC using doses of 60-66 Gy. Further consideration should then be given to individualized treatment, with increasing intensification for patients with high-risk factors such as poor response to chemotherapy.

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