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Short-Course Preoperative Breast Radiotherapy: A Strategy to Reduce Financial Toxicity in Early-Stage Breast Cancer

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Abstract

Financial toxicity is an increasingly recognized challenge in cancer care, with significant implications for patient outcomes and quality of life. Preoperative radiotherapy (PRT) offers a promising approach to mitigate this issue in the treatment of early-stage breast cancer (EBC). While hypofractionated whole-breast irradiation (HF-WBI) is the current standard of care, providing equivalent oncologic outcomes to conventional fractionation with shorter treatment duration, its implementation often requires daily treatments over several weeks, resulting in higher costs and greater patient burden, including travel, accommodation, time away from work, and caregiver demands. Short-course PRT may reduce normal tissue exposure, although assessment of delayed tumor response depends on the interval before surgery, and long-term oncologic efficacy and cosmetic outcomes require further investigation. Contemporary radiotherapy regimens include conventional fractionation (50 Gy in 25 fractions), moderate hypofractionation (40-42.5 Gy in 15-16 fractions), ultra-hypofractionation (26 Gy in 5 fractions), and accelerated partial breast irradiation (APBI), each differing in duration, cost, and resource utilization. Established postoperative regimens should be distinguished from investigational single-fraction and five-fraction PRT in selected patients. Existing literature highlights the economic advantages of shorter regimens, such as five-fraction APBI, which remain underutilized, particularly in underserved populations. PRT may address challenges in postoperative target delineation by targeting the intact tumor before surgery. However, whether PRT reduces financial toxicity remains uncertain. The preliminary, unpublished institutional savings estimate compares five-fraction PRT with 15-20-fraction postoperative treatment and has not been validated using time-driven activity-based costing (TDABC). Future prospective studies should incorporate TDABC to assess treatment delivery costs, including planning, imaging, quality assurance, and staffing, alongside clinical outcomes, cosmesis, patient-reported quality of life, time burden, and financial toxicity.

Categories: General Surgery, Radiation Oncology, Oncology
Keywords: accelerated partial breast irradiation (apbi), financial toxicity, preoperative partial breast rt, radiotherapy access, whole breast rt

Editorial

Short-course preoperative radiotherapy (PRT) has emerged as a promising strategy for patients with early-stage breast cancer (EBC), particularly in efforts to reduce treatment burden and financial toxicity [1]. Breast conservation therapy is the standard for EBC, with adjuvant radiotherapy (RT) playing a crucial role in reducing local recurrence and improving mortality rates [2].

Despite the American Society for Radiation Oncology (ASTRO) guidelines recommending hypofractionated whole-breast irradiation (HF-WBI), 40 Gy in 15 fractions or 42.5 Gy in 16 fractions over three to four weeks, regardless of age, tumor grade, or receptor status, as the preferred standard of care for eligible patients receiving WBI, many patients still receive prolonged conventional fractionation regimens of five to seven weeks of daily treatment [2]. Clinical trials and systematic evidence support the feasibility and efficacy of shorter RT regimens; the gap between recommendations and practice highlights an opportunity to reduce treatment burden [3].

The FAST-Forward trial compared a one-week HF-WBI course (26 Gy in 5 fractions) with the standard three-week regimen (40 Gy in 15 fractions). The 10-year analysis reported ipsilateral breast recurrence rates of 3.6% for the standard regimen versus 2.1% for the one-week group [4]. Similarly, the National Surgical Adjuvant Breast and Bowel Project Radiation Therapy Oncology Group (NRG/RTOG) 1005 phase III trial demonstrated that HF-WBI with a concurrent boost delivered over three weeks was noninferior to conventionally fractionated WBI with a sequential boost in patients with higher-risk EBC. At a median follow-up of 7.3 years, five-year in-breast recurrence rates were 1.9% and 2.1%, respectively (hazard ratio

(HR): 1.31, 90% confidence interval (CI): 0.84-2.04) [5]. Additional studies have supported the efficacy and safety of HF-WBI in EBC, including regimens delivered over 16 fractions [2,3,6,7]. The FLORENCE trial further demonstrated favorable long-term local control with intensity-modulated accelerated partial-breast irradiation (APBI) compared with WBI [8]. Collectively, these findings support shorter RT regimens as effective alternatives to conventional fractionation in appropriately selected patients, with the potential to reduce treatment burden and associated financial costs.

PRT can also be delivered using short-course regimens, substantially reducing the duration of RT before surgery. The single-arm phase II Single Pre-Operative Radiation Therapy (SPORT-CK) study enrolled women aged at least 60 years with unifocal, low-risk invasive ductal carcinoma (reported cohort: cT1N0, grade 1-2, estrogen-receptor positive, HER2-negative) and evaluated a single fraction of 20 Gy delivered via volumetric modulated arc therapy (VMAT), followed by breast-conserving surgery within 72 hours. No surgical complications were observed within the first 90 days [9]. Because surgery occurred within 72 hours, this study cannot reliably assess delayed pathological tumor response; the approach may minimize normal tissue exposure (mean planning target volume (PTV) of 44.7 cc) and deliver low radiation doses to critical structures, including the ipsilateral lung (0.64 Gy) and heart (0.22 Gy). Additionally, cosmetic outcomes were rated good to excellent by both physicians and patients, and no local, regional, or distant recurrences were observed at a median follow-up of 60 months [9]. These findings support further investigation of PRT in selected older patients with low-risk disease, although the small, nonrandomized study does not establish equivalence to postoperative treatment or applicability to younger patients or those with higher-risk disease. Further research is needed to evaluate its impact on financial toxicity compared with conventional three- to seven-week treatment courses.

Financial toxicity is a critical consideration in cancer care, significantly impacting patients' quality of life, treatment adherence, and healthcare systems. Studies have shown that cancer patients are 2.5 times more likely to declare bankruptcy compared to those without cancer [10]. A survey of breast cancer patients revealed that 47% reported financial distress, with 37% reducing spending on basic needs to afford treatment [11]. Additionally, financial hardship has been linked to decreased treatment compliance and worse overall survival rates [12]. Addressing financial toxicity through optimized treatment strategies is essential to improving clinical and economic outcomes. These burdens extend beyond direct medical expenses and include indirect costs related to transportation, accommodation, time away from work, childcare, and other demands associated with repeated treatment visits. Reducing the number of required RT visits may therefore decrease both healthcare costs and the economic burden on patients and their families. Shorter RT regimens, such as five fractions of APBI using intensity-modulated radiation therapy (IMRT), have been shown to be less costly than HF-WBI [13]. APBI delivers radiation to a limited portion of the breast surrounding the tumor bed rather than the entire breast as part of breast conservation therapy. It can be delivered with different techniques such as brachytherapy, three-dimensional (3D) conformal or intensity-modulated external beam radiation therapy (EBRT), stereotactic body radiation therapy (SBRT), or intraoperative radiation therapy (IORT). However, APBI adoption has been limited by concerns about local recurrence, poor cosmesis, and dose heterogeneity, particularly in patients with larger tumors or small breasts. Preoperative APBI (PAPBI) may address some of these limitations by targeting the intact tumor before surgery, potentially reducing treatment volume and normal tissue exposure.

Several studies have compared the outcomes of APBI with WBI. The FLORENCE trial reported no statistically significant difference in 10-year ipsilateral breast tumor recurrence (IBTR) between APBI with IMRT (3.7%) and WBI (2.5%) ($p = 0.4$), with reduced toxicity and improved cosmetic outcome [8]. The Electron Intraoperative Radiotherapy (ELIOT) trial found comparable overall survival but a significantly higher 10-year IBTR for IORT compared to WBI (8.1% vs. 1.1%, $p < 0.001$) [14]. The TARGeted Intraoperative radioTherapy Alone (TARGIT-A) trial reported a five-year local recurrence rate of 2.11% for IORT and 0.95% for WBI (difference: 1.16%, 90% CI: 0.32-1.99), demonstrating a modestly higher local recurrence risk with targeted IORT while supporting its potential role as an alternative treatment approach in appropriately selected patients [15]. Additionally, a study comparing external-beam APBI to WBI found lower rates of acute skin toxicity in the APBI group (51.4% vs. 94.9%, $p < 0.001$) and reduced incidence of late hyperpigmentation (0% vs. 17.9%, $p = 0.04$) [16]. Although APBI remains underutilized [17], postoperative treatment planning can be challenging when the surgical cavity is large or poorly defined. The German Society for Radiation Oncology (DEGRO) practical guidelines emphasize the importance of accurate target delineation, adequate target coverage, and adherence to dose-volume constraints to minimize irradiation of surrounding healthy tissues [18]. Innovative techniques, such as online adaptive radiation therapy (OART), are helping address this issue. Mariotto et al. demonstrated that OART improved APBI plan quality by enhancing target coverage and increasing compliance with planning objectives by 43.7% [19]. Adaptive plans were used in 86% of treatment fractions, achieving a 16% median reduction in gross tumor volume while optimizing coverage and sparing adjacent organs at risk. Despite slightly longer treatment times (median 31.3 minutes), OART shows promise for improving APBI feasibility [19]. This issue is particularly pronounced in certain underserved groups, including the Hispanic population, who experience disparities in accessing less toxic treatments such as APBI [20]. Barriers to RT access may also include travel distance, transportation limitations, and socioeconomic factors, which can make prolonged daily treatment difficult to complete. Shorter treatment courses may reduce these logistical burdens and improve access to RT, particularly for patients who face geographic barriers to care [21]. Shorter treatment courses, including PRT, may alleviate these burdens, although assessment of delayed tumor response requires an appropriate

interval before surgery.

Evaluating the economic implications of shorter RT regimens requires accounting for the resources used throughout treatment. Time-driven activity-based costing (TDABC) provides this framework by incorporating personnel, equipment, and treatment time. Using TDABC, Dziemianowicz et al. reported that accelerated WBI reduced costs compared with conventional fractionation, with repeated treatment delivery contributing to the difference [22]. Similarly, Nagra et al. examined costs across the breast cancer care pathway, identifying resource utilization by care component [23]. A prospective evaluation of PRT could apply this approach to compare preoperative treatment with 15-16-fraction and 5-fraction postoperative WBI or APBI, accounting for simulation, planning, quality assurance, treatment delivery, adaptive workflows, and surgical coordination. Provider delivery costs should be distinguished from reimbursement and patient expenses, while clinical outcomes, cosmesis, quality of life, time burden, and financial toxicity should be evaluated alongside costs.

Preliminary, unpublished institutional estimates from University of Pittsburgh Medical Center (UPMC) suggest that implementing 5-fraction PRT could potentially reduce direct medical costs by approximately $1,000 per patient compared with 15-20-fraction postoperative hypofractionated regimens. These estimates have not undergone peer review or formal TDABC validation and remain hypothesis-generating, as detailed costing methods are unavailable for independent verification. They do not establish patient out-of-pocket savings or superiority over 5-fraction postoperative treatment. Previous economic modeling in glioblastoma has also examined the relationship between RT duration and patient out-of-pocket expenses [24]. Given that UPMC treats approximately 1,000 patients with EBC annually, validated per-patient differences of this magnitude could be institutionally meaningful, although confirmation requires formal costing and assessment of patient eligibility for PRT.

As healthcare increasingly shifts toward value-based care, optimizing breast cancer treatment requires balancing clinical efficacy, patient convenience, and economic considerations. Short-course PRT may reduce treatment burden and resource utilization while improving access to care. Prospective studies are needed to establish its long-term clinical outcomes, economic value, and impact on equitable access to treatment.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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