



Hypofractionated whole breast irradiation is cost-effective—but is that enough to change practice?

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Breast cancer is both the most commonly diagnosed new cancer and the most expensive cancer to treat in the United States (US) (1). It was estimated to account for the largest share of national cancer expenditures in 2010, at \$16.5 billion, and is projected to increase to \$20.5 billion by 2020 based on US population growth alone (2). In the current climate of unsustainable rising healthcare costs, breast cancer and its treatment present ample opportunities to favorably bend the cost curve while positively benefitting patients.

Alternative treatment regimens for breast cancer radiotherapy have emerged in the last 10–20 years that enable high-value care. Hypofractionated whole breast irradiation (HF-WBI) entails the adjuvant treatment of breast cancer in a course of 3 to 4 weeks and has been found to be equivalent to longer 5–7 weeks' courses of conventionally-fractionated whole breast irradiation (CF-WBI) in multiple large international randomized trials (3,4). Similarly, in the most favorable subset of breast cancer patients, accelerated partial breast irradiation (APBI) has been explored as a viable alternative to CF-WBI and is completed in anywhere from 1 to 10 days, using a variety of techniques including intraoperative radiation treatment (IORT), interstitial or balloon brachytherapy, or external beam radiotherapy (5,6).

It is intuitive that HF-WBI is cost-effective as hypofractionation both utilizes less resources and results in equivalent outcomes, yet until now there have been no formal cost-effectiveness analyses published between HF-WBI and CF-WBI. Further, HF-WBI has been objectively

shown to be less costly than CF-WBI (7,8), and yet most cost-effectiveness studies assessing APBI have used CF-WBI as the baseline comparator (9). Only two previous studies have compared APBI (both IORT) to HF-WBI, both within the context of the United Kingdom (UK) National Health Service, with disparate results (10,11).

In the current study, Deshmukh and colleagues are the first to analyze the cost-effectiveness of HF-WBI in comparison to CF-WBI (12). In addition they are the first to compare IORT to HF-WBI within the context of the US healthcare system. They developed a comprehensive model of early-stage breast cancer; model inputs for tumor control rates were based on the Canadian hypofractionation (4) and ELIOT (6) trials and costs were based on US Medicare reimbursement rates. Model utilities were derived from patient-reported outcomes from a randomized MD Anderson trial assessing differences in quality of life between HF-WBI and CF-WBI (13). Importantly, the authors used a lifetime horizon to capture lifelong disease states, which can continue to evolve well beyond 5 and 10 years (which are the most recent updates of the ELIOT and Canadian trials, respectively).

Their most significant finding is one that we have long surmised: that HF-WBI is more cost-effective (or of greater value) than CF-WBI. The finding that HF-WBI “dominates” CF-WBI shows that HF-WBI lowers costs while also improving quality of care—there is no trade-off between cost and effectiveness. Hypofractionation wins in every scenario. They additionally found that HF-WBI is cost-effective compared to IORT, even at low willingness-to-pay thresholds, under a wide variety of assumptions and

parameters using a thorough sensitivity analysis.

These results are a reflection of HF-WBI's positive impact on patients' quality of life. In the MD Anderson trial that was used to determine patient utilities, acute side effects of radiation treatment including dermatitis, pruritus, breast pain, hyperpigmentation, and fatigue were all reduced with HF-WBI as compared to CF-WBI (14). At 6 months following treatment, patients randomized to HF-WBI reported less fatigue and less trouble meeting family needs, although patients improved and reported similar functional outcomes at later time points in both arms (13,14). In the UK START trials, HF-WBI was associated with lower long-term rates of breast edema, telangiectasia, and breast shrinkage compared to CF-WBI (3).

Are these findings enough to change practice in the US? So far, despite the equivalent tumor control, modestly improved cosmetic outcomes, and added convenience of HF-WBI compared to longer fractionated regimens, its uptake in the US has been less than anticipated. In 2011, the American Society of Radiation Oncology (ASTRO) released practice guidelines endorsing HF-WBI for patients aged 50 years or older, with pT1-2 pN0 disease, who did not receive chemotherapy, and who were treated with radiation dose homogeneity within $\pm 7\%$ of the prescription dose in the central axis plane (15). The guidelines permitted, but did not endorse or oppose, the use of HF-WBI in patients who did not meet these criteria. In a study of commercial claims data covering 7.5% of all US female women, HF-WBI was only used in 34.5% of hypofractionation-endorsed patients and 21.2% of hypofractionation-permitted patients in 2013 (8). A National Cancer Database study supported these findings with overall HF-WBI usage among patients with invasive cancer at only 15.6% in 2013 (16).

Several explanations have been offered as to why US uptake of HF-WBI has been so slow. As the HF-WBI trials have about 10 years of follow-up data, providers may be apprehensive of late normal tissue effects, although there is little reason to believe there will be significant changes with longer follow-up. Some propose that with a largely overweight or obese population in the US, providers may have difficulty in meeting dose homogeneity constraints, although in the MD Anderson trial, half of all patients had hotspots above 107% (14). Others contend that the non-standardized use of tumor bed boosts in the randomized trials limit applicability to US practice, where boosts are commonly used. Finally, it is commonly agreed that the 2011 consensus guidelines were too conservative in their recommendations (which were published before additional

long-term data were available) and new 2018 ASTRO guidelines prefer HF-WBI as standard of care in most women with early-stage breast cancer (17).

However, a far more obvious reason for low HF-WBI uptake emerges when re-examining the perspective of cost-effectiveness studies. In the current study, the model employed both societal and health care sector perspectives, and in both perspectives HF-WBI was found to be cost-effective. What is not modeled (and would not be expected in a broad cost-effectiveness analysis) is the perspective of the radiation oncology practice, the level at which the costs and benefits of HF-WBI and CF-WBI are deliberated in daily practice. In the current US fee-for-service landscape, there is a clear disincentive to deliver high-value care, as fewer services (fractions) are billed for proportionally lower revenue. The UK and Canada have seen far broader adoption of HF-WBI (around 80% and 71%, respectively) (18,19), which can in part be attributed to the UK's nationalized adoption of HF-WBI and Canada's more flexible use of fee-for-service payments. It is estimated that a US hospital-based practice's adoption of a 70% HF-WBI rate would result in annual reductions of \$300,790 in technical revenues and 731 professional RVUs with current reimbursement policies (20), representing significant proportions of total practice income; therefore, it is not surprising that variation in HF-WBI utilization has been found to be related more to individual provider characteristics than clinical or demographic characteristics (21).

To address these shortcomings in the US healthcare system, Congress passed the Medicare Access and CHIP Reauthorization Act of 2015, which enabled ASTRO to develop the Radiation Oncology Advanced Payment Model (RO-APM). The RO-APM proposes to replace fee-for-service payments with episode-based payments for five primary disease sites, including breast cancer, that are constant regardless of the length of treatment, while also measuring and rewarding performance on quality metrics and adherence to practice guidelines (22). Thus the RO-APM incentivizes high-value, high-quality care, and it is expected to be approved by the Center for Medicare and Medicaid Services in the coming months. With successful implementation, the radiation oncology community would finally be able to fully embrace HF-WBI, realizing societal and health sector cost-effectiveness benefits that pass down to the individual practice level. Individual providers would have the opportunity to share in cost savings while maintaining stable revenue streams, and thus would be predicted to adopt high-value interventions such as HF-

WBI that make their own practices competitive.

Hypofractionation in breast cancer radiation treatment realizes the six goals of high-quality care as defined by the Institute of Medicine: safety, effectiveness, patient centeredness, timeliness, efficiency, and equity (23). Cost-effectiveness analyses help to highlight the high-value nature of HF-WBI as compared to other breast radiotherapeutic regimens. In the future, as HF-WBI regimens are more widely adopted, further shortened (24), and applied in the post-mastectomy setting (25), the cost-effectiveness of breast radiation treatment overall will increase. Once reimbursement models align provider incentives with best practices, all stakeholders will be able to take delight in providing high-value care that decreases national healthcare costs while providing timely, efficient, and safe patient care.

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