IMRT for Breast Cancer—Balancing Outcomes, Patient Selection, and Resource Utilization

Lisa A. Kachnic, Simon N. Powell

Over the past decade, there has been a rapid rise in the utilization of advanced radiation delivery technologies for the intended curative management of many solid cancers. For breast cancer, radiation practice patterns have shifted from conventional two-dimensional therapy based on fluoroscopy and bony anatomy to a more refined three-dimensional approach utilizing computed tomography planning. Three-dimensional radiation provides the oncologist with precise information concerning the radiation dose to all areas of the affected breast, regional nodes, and adjacent normal tissues and therefore may offer reduced morbidity and improved long-term breast cosmesis, whereas maintaining local tumor control. The current question is whether further improvements in target dose coverage and normal organ sparing, both of which are provided by a more advanced form of radiation delivery called intensity-modulated radiation therapy (IMRT), produce a measurable improvement in treatment outcomes over three-dimensional radiation delivery.

In this issue of the Journal, Smith et al. (1) report on the increased use of IMRT for the adjuvant therapy of breast cancer in the United States. Improvements in radiation-induced morbidity have been described in patients with head and neck and prostate cancers treated with IMRT (2,3). Small randomized studies in early-stage breast cancer also suggest that a reduction in acute toxicity can be achieved (4–6). However, in this era of rapidly evolving radiation technology, there is a concern that IMRT is being widely implemented without evidence-based knowledge of its effects on long-term efficacy and morbidity. Moreover, IMRT is associated with a substantially greater cost to the patient (or insurance company) because of the increased physician and physicist workload to generate IMRT plans and provide the necessary quality assurance for such plans. With the recent emphasis on cost-effective quality care in the United States, we must understand the potential benefits of this new technology and balance them with an appropriate selection of patients, as well as best use of resources, before IMRT can be adopted for the adjuvant management of breast or other cancers.

Smith et al. (1) analyzed Surveillance Epidemiology and End Results–Medicare records of care and outcomes for 26,163 women aged 66 years or older who were treated with surgery and adjuvant radiation for nonmetastatic breast cancer between 2001 and 2005. They found that in 2001, there was a prevalence of IMRT use of 0.9%, which rose to 11.2% by 2005, reflecting a greater than 10-fold increase in use for a potentially large population of patients. Notably, the use of IMRT more than doubled the cost of radiation treatment, and the overall cost of treatment increased by more than 30% during this 5-year period. Unfortunately, these data do not provide insight into potential clinical scenarios in which IMRT may improve treatment results and perhaps justify its increased cost. Tumor characteristics were not strongly associated with an increased use of IMRT, suggesting that it was not being adopted to address a perceived medical concern. Even the higher prevalence of using IMRT for left-sided breast cancers (where there is concern over the radiation dose to the underlying lung and heart) was only 6.5%, as compared with 5.5% on the right. Notably, what we do learn from Smith et al (1) is that the largest increase in IMRT utilization is in regions where Medicare pays for it. As such, the major conclusion from the analysis is that IMRT is being adopted for the adjuvant management of localized breast cancer within areas of the United States where it is reimbursed. This conclusion would appear to confirm the suspicion of many, both within and outside of the healthcare industry, that medical decision making is too heavily influenced by reimbursement rather than medical necessity.

So does this analysis signal the end of IMRT for the treatment of breast cancer? We think the answer to this question is no, but radiation oncologists must first undertake trials of IMRT vs conventional radiation to determine the appropriate clinical indications for this advanced technology (7). In the three published randomized trials of IMRT in breast cancer (4–6), the focus was on the treatment of early-stage disease, such that the radiation target volume was breast only. In that setting, the only major advantage of IMRT is increased radiation dose homogeneity—the elimination of significant hotspots of radiation in the breast that would occur in wedge-based two- or three-dimensional plans. Such improved radiation dosimetry may be associated with improvements in acute radiation reactions, such as skin dermatitis, and in overall breast cosmesis. Accordingly, the results of these three breast IMRT trials (4–6) have shown modest but potentially useful improvements in these endpoints.

Two important issues not addressed by these studies (4–6) were the ability of IMRT to provide improved dosimetric coverage of the elective nodal groups at risk and the potential of IMRT to generate improved differential radiation dose gradients between the target volume and the adjacent underlying lung and heart. Both of these IMRT attributes may result in clinically meaningful improved outcome or reduced toxicity. The most likely beneficial application of IMRT may be for the treatment of node-positive breast cancer, particularly when the internal mammary nodal regions require treatment (8). Using non-IMRT techniques, the actual coverage of the internal mammary nodes can be marginal,
particularly at the superior aspect of the nodal chain, where the target is lateral and deep to the manubrium (9). For high-risk patients, the internal mammary nodes are a legitimate target in which local recurrences can be observed, even though they are underreported in the literature (10). Proving improved local control with IMRT, even in very high-risk patients, will be difficult and needs to be analyzed prospectively in large trials to have any chance of observing an impact of the improved target coverage.

It may be possible to address whether IMRT for breast cancer can reduce pulmonary and cardiac toxicity. For lung morbidity, because the incidence of clinically significant radiation pneumonitis is relatively low (11), we need to adopt a lower threshold for detecting symptoms by using patient-reported questionnaires and by measuring pulmonary function. The primary question is whether changing the ipsilateral lung dose-volume histogram from high-dose to low-dose with IMRT will make a measurable difference in pulmonary symptoms. There are a number of ongoing studies that are addressing these questions, and we eagerly await the results. For left-sided breast cancers, given the concerning association between radiation and ischemic heart disease and the use of cardiotoxic drugs, such as Adriamycin and trastuzumab, making sure that the radiation dose conforms to the chest wall and keeps away from the heart also has potential for reducing late cardiac morbidity (12–14). However, the incidence of late cardiac events after radiotherapy for breast cancer has been substantially reduced with the elimination of the use of anterior photon fields, so proving additional clinically meaningful improvements in cardiac morbidity with the use of IMRT would also require large randomized trials.

There are also “quick versions” of IMRT that are not labor intensive, such as the use of a few segments of IMRT exposure within the same tangentially arranged three-dimensional fields to produce and function effectively as a two-dimensional compensator. These plans should not be billed as IMRT, because there is no true inverse planning used in this technique. Smith et al. (1) were unable to distinguish these two forms of IMRT from their dataset. The use of segmented tangents may be comparable to more complex inverse-planned IMRT for the large-breasted patient in reduction of moist desquamation and maintenance of good cosmesis by improving radiation dose homogeneity.

In conclusion, the use of IMRT in breast cancer is still to be decided. The current level of evidence to support this growing practice is weak, and the benefit of IMRT observed in the randomized trials (4–6) could likely be achieved with simple segmentation using two tangential fields that have been three-dimensionally planned. This report by Smith et al. (1) suggests that radiation oncology practice is driven by what pays and not by what improves patient care—a dangerous path to undertake. The true value of inverse-planned IMRT in breast cancer will most likely be for patients with complex anatomy, such as severe pectorus excavatum, or for patients who need comprehensive nodal targeting. As such, we must focus our efforts on identifying the most appropriate group of patients in whom we can demonstrate a clinical benefit with this approach.

References


Affiliations of authors: Department of Radiation Oncology, Boston Medical Center, Boston University School of Medicine, Boston, MA (LAK); and Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY (SNP).