Will partial breast irradiation be a cost-effective alternative to whole breast irradiation in the treatment of early-stage breast cancer?

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Accelerated partial breast irradiation (APBI) is increasingly being used as an alternative to whole breast irradiation (WBI) after lumpectomy in patients with early-stage breast cancers. In this retrospective cost-minimization analysis, APBI with conventional three-dimensional conformal radiation therapy was found to be one third to one half as expensive as other APBI techniques (interstitial brachytherapy and intensity-modulated radiation therapy) and nearly one third less expensive as conventional WBI, assuming that all of these techniques were equally effective in preventing a recurrence of breast cancer. Had indirect treatment costs incurred by patients for travel expenses, meals away from home, and lost work days been included in the calculations, the difference in costs between APBI and WBI would have been even greater.

The standard of care for patients with early-stage breast cancer being treated with breast conservation therapy is whole breast irradiation (WBI) after lumpectomy. However, partial breast irradiation (PBI) is increasingly being used in the management of this disease as an alternative to WBI. The proponents of PBI argue that patients may be undergoing mastectomy or lumpectomy only (ie, without adjunctive radiation therapy) because of the time constraints of 6–7 weeks of standard WBI or the absence of available radiation treatment centers in some geographic areas for patients desiring breast conservation therapy.[1,2] Others, however, point to the relatively short follow-up of patients being treated with PBI and the need for randomized, controlled clinical trials comparing PBI with WBI, similar to the early trials comparing lumpectomy and irradiation with mastectomy.[3,4] The degree of local control and cosmetic outcomes achieved with PBI in breast cancer patients have been published[5,6] and are comparable to the outcomes seen in patients treated with WBI, but with a shorter follow-up and fewer patients than in the WBI series.

This article compares the costs of various PBI treatments and explores other factors that may influence the outcome of an economic analysis comparing WBI with PBI in patients with early-stage breast cancer.

Partial breast irradiation

The term PBI refers to treatment of the lumpectomy cavity with a predetermined margin without irradiating the entire breast. Accelerated partial breast irradiation (APBI) is the term used when treatment is given over a shorter period than the usual 5–6 weeks, using daily radiation fraction sizes larger than the 1.8–2.0 Gy/d associated with standard WBI.

A variety of treatment techniques may be used for the delivery of APBI: interstitial brachytherapy, including use of the MammoSite device (Proxima Therapeutics, Inc., Alpharetta, GA); external beam radiation therapy, using either three-dimensional (3-D) conformal radiation or intensity-modulated radiation therapy (IMRT); and, more rarely, intraoperative radiation therapy with electrons or mini-electron generators capable of delivering orthovoltage treatment. The typical external beam WBI course entails approximately 30–35 treatments delivered over the course of 6–7 weeks. By

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contrast, APBI using either 3-D conformal radiation or IMRT requires 10 treatments given over the course of 2 weeks, and interstitial brachytherapy using, for example, the MammoSite device involves 10 treatments given twice a day over the course of just 1 week. Thus, APBI compresses the duration of treatment from 6–7 weeks to 1–2 weeks and thereby decreases time away from work and travel costs. Most proposed PBI techniques use accelerated schedules based on the assumption that larger daily radiation doses will be tolerated as well as those usually used for WBI because a smaller volume of tissue is irradiated.

Economic analysis

Comparison of a new treatment, drug, or device to a standard treatment, drug, or device is the hallmark of healthcare economic analyses. Costs and outcomes are measured and compared, resulting in an incremental cost-effective ratio. The outcome, or endpoint, will depend on what is being compared and could take the form of years of life gained if a new treatment is being tested or numbers of cancers detected if a new diagnostic test is being evaluated. The cost of the experimental therapy is subtracted from the cost of the standard therapy, which is then divided by the effect of the experimental therapy subtracted from the effect of the standard therapy to arrive at a cost-effectiveness ratio.

Type of analysis

These economic analyses can take the form of a cost-effectiveness, cost-benefit, cost-utility, or cost-minimization analysis. A *cost-effectiveness analysis* results in a ratio of so many dollars for each effect being measured. Such a ratio could be dollars per year of life gained, if one were testing a new chemotherapeutic agent, or it could be dollars per cancer detected, if a new diagnostic test were being evaluated. A *cost-benefit ratio* requires a dollar amount be assigned to the effect being measured and results in a ratio that has no units attached to it. This type of analysis is seldom performed in oncology because of the inherent difficulty in assigning a dollar amount to, for example, a year of life saved or new cancer detected. A *cost-utility analysis* is performed when a preference for a certain health state or utility is assigned to a health state that results in a ratio expressed in units of dollars per quality-adjusted life years (QALY). This analysis is useful in health policy because treatments for different diseases can be compared and ranked based on the resultant ratios. In a *cost-minimization analysis,* the two treatments being compared have equal efficacy, so that the optimal choice is the treatment or drug that is the least expensive.

Perspective

The perspective of the analysis dictates the types of costs collected for an economic analysis of any healthcare technology. All direct medical costs and costs associated with treatment, including travel time, meals, and lost wages or other compensation, would be included if a societal perspective is taken for the analysis. In contrast, only the cost of care reimbursed by Medicare or a third-party payer would be included if the analysis took a payer's perspective.

The analysis perspective is particularly important in this case because patient inconvenience of attending daily radiation sessions and the availability, or lack of availability, of appropriate treatment facilities are reasons patients give for desiring PBI or APBI. Conventional WBI would have a higher assigned cost if travel to and from radiation treatment facilities is factored into the calculations, as well as the cost of lost time from work or paying for child care while receiving daily radiation treatments. A sensitivity analysis would need to be performed to test the impact of assumptions made on the overall outcome of the analysis.

Assumptions

Because this analysis is not framed within the context of a clinical trial, certain assumptions need to be made in calculating the cost and deciding which economic analysis would be the most appropriate to carry out. In performing this analysis, it is assumed that APBI has the same clinical efficacy as WBI in treating patients with early-stage breast cancer, as a rational patient would not choose an inferior treatment based solely on convenience. It is also assumed that patients undergoing PBI or APBI would meet the eligibility criteria of the American Brachytherapy Society and/or the American Society of Breast Surgeons.[1] Using PBI or APBI techniques to treat patients who did not meet these criteria could result in poorer outcomes, biasing the results against APBI. A cost-minimization analysis would be the most appropriate analysis because both treatments are assumed to be equally effective.

Comparison of costs between WBI and APBI

This analysis will take a payer's perspective, based on the assumption that Medicare costs incurred for diagnosis, work-up, and initial lumpectomy and lymph node dissection would not differ between WBI and APBI. Only the cost of administering the radiation treatment will be considered. A comparison of costs between the following techniques will form the basis of this analysis: WBI with conventional irradiation, APBI with 3-D conformal radiation, APBI with IMRT, and APBI performed with the MammoSite device. This analysis will not include intraoperative irradiation as a technique for delivering APBI because the capital costs necessary for providing intraoperative radiation (treatment machinery, shielding of the operating room, etc) may prohibit

a significant number of centers from utilizing this technique. The MammoSite device is being used more frequently in clinical practice and will represent interstitial brachytherapy in this analysis.

A unit costing method will be used based upon treatment in a freestanding outpatient center to combine both the technical and professional components of treatment. A sensitivity analysis will be performed evaluating hospital-based treatment using the professional component and the Ambulatory Payment Classification rates for the technical component. The total radiation dose and fractionation schedules for external beam APBI (both IMRT and 3-D conformal radiation) will follow a recently completed phase I/II clinical trial, protocol RTOG 0319 of the Radiation Therapy Oncology Group (available at www.rtog.org). This phase I/II trial evaluated 3-D conformal radiation confined to the region of the lumpectomy cavity for stage I and II breast carcinoma.

The Current Procedural Terminology (CPT) codes for the procedures used will be matched with the relative value unit (RVU), as provided by the Centers for Medicare & Medicaid Services (www.cms.gov). The frequency of each CPT code will be multiplied by the RVU to arrive at a total RVU that is then multiplied by the national conversion factor, $37.3374/RVU, to arrive at a dollar amount of treatment. The cost of placement of the balloon catheter is estimated to be $2,750, using the Healthcare Common Procedure Coding System (HCPCS) code of C9714. (The cost would be higher if patients had a delayed insertion of the catheter [code C9715].)

Table 1 lists the CPT codes used for each treatment and their frequency of use. The conventional radiation treatment is based upon two tangent fields delivering 4,600 cGy to the entire breast, with a boost of 1,400 cGy with electrons to the lumpectomy site. The interstitial brachytherapy treatment is based upon 10 twice-daily high-dose-rate (HDR) fractions. The 3-D conformal therapy and IMRT APBI are delivered with four fields.[7]

TABLE 1

CPT codes and frequency for breast cancer treatment

Procedure	CPT Code	WBI: conventional radiation	APBI: 3-D conformal radiation	APBI: intensity-modulated radiation therapy	APBI: interstitial brachytherapy (MammoSite)
Treatment planning	77263	1	1	1	1
Complex simulation	77290	1		1	1
3-D simulation	77295		1		1
Simple simulation	77280	1	1	1	1
Isodose distribution	77315	1	1		
Isodose IMRT	77301			1	
Basic calculation	77300	2	4	4	10
Treatment devices	77334	2	4	4	
Portal films	77417	5	2	2	
Treatments conventional	77416	23	10		
Treatments IMRT	77418			10	
Weekly management	77427	5	2	2	
Weekly physics	77336	5	2	2	
Special physics consultation	77370		1	1	1
CT treatment planning	76370	1	1	1	1
Boost					
Weekly physics	77336	1			
Basic calculation	77300	1			
Electrons	77321	1			
Treatment devices	77334	1			
Treatments	77416	7			
Weekly management	77427	1			
Brachytherapy					
HDR 1-4 source	77781				10
Brachy isodose plan	77326				1
Special treatment procedure	77470			1	1

APBI = accelerated partial breast irradiation; WBI = whole breast irradiation

Results

The results of the cost calculations for the three different APBI techniques and conventional radiation are shown in Table 2. Three-dimensional conformal APBI is less costly than conventional WBI because fewer radiation treatments are delivered. The costs associated with IMRT APBI and interstitial brachytherapy are higher than those of conventional WBI because HDR brachytherapy and IMRT are reimbursed at a higher rate than conventional radiation therapy. The number of treatments, 10, is the same for all three APBI treatment techniques. This is a result of the use of IMRT and 10 fractions of HDR brachytherapy.

A sensitivity analysis performed using the RVU for professional bill-

TABLE 2

Calculated cost for conventional whole breast irradiation versus accelerated partial breast irradiation

Treatment	Cost
Conventional whole breast irradiation	$6,542
3-D conformal accelerated partial breast irradiation	$4,533
IMRT accelerated partial breast irradiation	$10,872
Interstitial brachytherapy (MammoSite)	$14,505

IMRT = intensity-modulated radiation therapy

ing and Ambulatory Payment Classifications for the technical billing resulted in 3-D conformal APBI still being less expensive than conventional WBI. IMRT APBI and interstitial brachytherapy remained the two most expensive techniques in this analysis. The analysis did not take patient preference into consideration or include travel costs. Conventional WBI would have higher costs if travel (including housing and meals) to and from the radiation facility was included in the analysis.

Discussion

Three-dimensional conformal APBI was the least expensive treatment modality in this analysis because of the use of conventional 3-D treatment techniques and because only 10 radiation treatments were delivered, compared with typically 30 treatments for conventional WBI. When IMRT was used, the costs escalated due to higher reimbursements for the increased amount of work for IMRT planning.

Intensity-modulated radiation therapy is being investigated in the treatment of early-stage breast cancer because of its ability to spare normal tissues. Sparing of normal tissues is important for breast cancer patients, especially patients with left-sided breast cancers who have received or are being treated with potentially cardiotoxic drugs, such as doxorubicin or trastuzumab (Herceptin). Landau et al[8] evaluated different methods of shielding the heart and found a four-field IMRT treatment technique superior to partial shielding for patients with larger maximum heart depths; however, increased irradiation of the contralateral breast due to scattering was noted with this technique. Because of its lower cost, 3-D conformal APBI would be the preferred treatment for these patients, assuming all treatments had equal efficacy.

The best way to evaluate the cost-effectiveness of different APBI treatment techniques would be for an economic analysis to be incorporated into clinical trials evaluating these treatment modalities. Actual costs of treatment, as well as costs for treatment for recurrences and complications, could be collected. The costs could include treatment as well as non-treatment costs, which can be substantial for the WBI arm if travel and other indirect costs are included. The difference in total cost between WBI and IMRT APBI was $4,330, whereas the difference between interstitial brachytherapy (MammoSite) and WBI was $7,963 per patient. The cost of travel and time off from work would vary with each patient; whether these additional costs would compensate for the higher treatment cost of APBI could only be answered by collecting the data prospectively.

Impact on quality-adjusted life years

Patient utilities or preference for health states could also be measured to determine which treatment resulted in highest QALY. Collection of patient utilities could influence the outcome if patients receiving APBI with IMRT or interstitial brachytherapy had a higher QALY. Yarnold et al[9] compared standard two-dimensional WBI with 3-D IMRT in 306 women with moderate to large breasts who received breast conservation therapy and irradiation. The researchers reported that unwanted dose inhomogeneity associated with two-dimensional WBI impacted negatively on clinically observable late breast changes, such as breast pain, discoloration, and changes in the shape and appearance of the breasts. These late breast changes, in turn, could impact on patients' QALY and change the long-term cost-utility of these treatments if differences became apparent with longer follow-up.

Other considerations

The purpose of this analysis was to compare the costs associated with APBI versus WBI and was not meant to evaluate different APBI treatment techniques in patients with early-stage breast cancers. Conventional 3-D conformal APBI costs less than the other two APBI techniques or conventional WBI. Neither IMRT nor 3-D conformal irradiation requires surgery for placement of a balloon catheter applicator to implant brachytherapy seeds (MammoSite), but daily setup variations and respiratory motion require larger margins around the lumpectomy cavity. These larger margins could affect outcome and cosmesis of the treated breast, with an attendant impact on QALY. Interstitial brachytherapy requires having the applicator in place for at least 5 days, raising the risk of bleeding and infection.

Conclusion

Accelerated partial breast irradiation with conventional 3-D conformal irradiation was found to be a cost-effective alternative to WBI in this cost-minimization analysis, given the stated assumptions of equal efficacy of treatment. The difference in cost between IMRT or interstitial brachytherapy and WBI would be decreased if the greater travel costs and other indirect costs associated with time off from work among patients undergoing WBI were included in the analysis. A prospective randomized trial evaluating efficacy, QALY or utilities, and cost between WBI and APBI is needed to fully answer the question of

whether APBI is a cost-effective alternative to WBI in selected patients with breast cancer.

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