Early Experience With Balloon Brachytherapy for Breast Cancer

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Hypothesis: Partial-breast irradiation for carcinoma by a single source of radiation placed in the center of a balloon inserted in the lumpectomy cavity is an effective method of treating breast cancer. Previous interstitial radiation therapy using iridium seeds placed within multiple catheters has been shown to be effective but impractical and cosmetically unacceptable to women.

Design: Prospective registry study.

Setting: Three university and community hospitals.

Patients: Women 40 years and older with histologically diagnosed in situ and invasive T1 through T2 and N0 or N1 breast cancer treated with lumpectomy and axillary node sampling were invited to enter this institutional review board–approved study.

Main Outcome Measures: Evaluation of immediate and short-term complications, patients’ acceptance of the treatment, and cosmesis are reported.

Results: Of the 129 eligible patients enrolled, 112 completed the treatment. Of these, transient skin erythema was noted in 28, localized edema in 3, and skin blisters adjacent to the balloon in 9. Infection developed in 7, necessitating drainage and antibiotic administration. In 10 patients, sonographically demonstrated seromas that developed after removal of the device were aspirated percutaneously. In 4 patients, punctured or ruptured balloons had to be replaced before the treatment could be completed. Patients quickly adjusted to the breast distension caused by the balloon, and their acceptance of the procedure was good. The cosmetic outcome was rated high. There were no recurrences during this very short follow-up.

Conclusions: Our early short-term experience indicates balloon brachytherapy to be an acceptable alternative to external beam radiation for selected operable breast cancers. The 1-week treatment time allows working women and those who live at a distance from radiation centers to choose breast conservation rather than mastectomy.

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Breast conservation therapy (BCT), defined as surgical removal of the tumor and sampling of the regional nodes followed by whole-breast irradiation, is generally considered an option for patients with operable breast cancer. Long-term follow-up reports indicate equally good results in terms of disease-free and overall survival compared with mastectomy.1,2 The major advantages of BCT compared with mastectomy are the cosmetic outcome and reduced psychological trauma to the patient. Its main disadvantages are the treatment time of 6 weeks and inconvenience of traveling, especially for older patients living in parts of the country with difficult access to a radiation therapy center. Brachytherapy, a limited irradiation of the tissue adjacent to the primary cancer, is an alternative to external beam radiation in BCT. The rationale for this approach is that 80% of breast recurrences appear at the site of the primary tumor.3,7 Conventional brachytherapy requires the insertion of up to 20 catheters with indwelling needles into the breast around the lumpectomy site. At each treatment, the needles are removed and replaced with iridium Ir 192 radioisotope seeds for approximately 15 minutes. Brachytherapy performed with the MammoSite applicator (Proxima Therapeutics, Inc, Alpharetta, Ga) allows an easier implantation for radiation delivery to the breast tissue around the lumpectomy cavity. The applicator consists of a double-lumen catheter with a balloon similar to that of a Foley catheter, which is inflated once the catheter is inserted into the lumpectomy cavity (Figure 1).

The overall objective of this study was to evaluate the safety and efficacy of the...
MammoSite catheter was inserted into the lumpectomy cavity because of persistent positive margin findings. Two of the 3 participating institutions excluded patients with pathological stages I and II breast cancer. The practice of irradiating the entire breast has been an integral part of breast-conserving therapy (BCT) and has yielded results equivalent to mastectomy for operable breast cancers. The practice of irradiating the entire breast was based on results of the detailed histological examination of patients with T1 through T2 breast cancers revealing residual in situ and invasive carcinoma after simulated partial mastectomy. This concept of multifocality and the implied need for whole-breast irradiation was subsequently emphasized by Holland et al. The National Surgical Adjuvant Breast Project B-06 randomized prospective trial confirmed that at 10 years, the recurrence rate of 53% in nonirradiated breasts was significantly higher than that of 12% in irradiated breasts (P < .001).

A closer look at the in-breast failure pattern reveals that most (67%-100%) of the recurrences appear in the...
immediate vicinity of the primary tumor. In addition, more recent publications on the pathological examination of lumpectomy and mastectomy specimens reveal that the microscopic foci of malignancy are within 1 cm of the primary tumor.

Based on these observations and reports, several investigators began to treat patients with brachytherapy alone after lumpectomy. King et al from the Oschner Clinic, New Orleans, La, described 50 patients treated with segmental mastectomy and interstitial brachytherapy for Tis, T1, and T2 breast cancer and compared the outcome with that of a matched group of patients treated with external beam radiation. At a median follow-up of 75 months, the 2 groups were similar for grade III toxic effects, locoregional recurrence rates, and cosmesis scores. Vicini et al reported 174 cases of early breast cancer managed with lumpectomy followed by radiotherapy restricted to the tumor bed using an interstitial implant. They compared the results with those of a matched series of cases from the same institution treated with external beam radiation and found no difference in terms of local recurrence, distant metastasis, and disease-free survival at 5 years.

Edmundson et al were first to report on the partial irradiation of the breast for carcinoma using the MammoSite device. The investigators achieved satisfactory irradiation to 1 cm of the breast tissue immediately adjacent to the balloon surface and noted that the device was easy to use. They also reported that at a minimum distance of 5 mm between the balloon surface and the skin, the latter received less than 150% of the calculated dose, which was deemed to be safe. Subsequently, Keisch et al used the MammoSite balloon device for brachytherapy in women with early-stage (T1 N0 M0) breast cancer who had undergone partial mastectomy. Of the 70 patients enrolled in the study, 43 (61%) completed the treatment. The main factors limiting the initial use of the device were skin-to-balloon surface distance and balloon-cavity conformance. In the present series, the completion rate was higher (87%), probably due to gained experience, but we still encountered similar complications, some of which may be resolved in the future.

COMPLICATIONS AND SUGGESTED SOLUTIONS

Balloon Puncture and/or Rupture

Early in our experience, we encountered fluid leakage from the balloon and its deflation in 4 cases. On 1 occasion, the balloon had been punctured by metallic clips inserted in the breast parenchyma at the time of lumpectomy. The operative field was reexplored, the clips were removed, and a new balloon was inserted. Clip placement practice was discontinued afterward. In another case, the inflated balloon was inadvertently punctured by a needle during closure of the incision. Since then, the balloon has been inflated to its predetermined volume after the incision is closed. Two of the balloon ruptures were spontaneous with no identifiable causes.

Balloon-to-Skin Distance

Close proximity of the iridium seed to the breast skin has been reported to cause skin necrosis. The minimum acceptable distance between the balloon surface and the skin as determined by CT images during prebrachytherapy simulation is generally considered to be 5 mm. In 6 cases in this series, the device was removed and the patients were treated with external beam radiation because of unacceptable skin distance. This problem is encountered when the tumor is too close to the skin or the breast is small with little subcutaneous tissue. To overcome this problem, we suggest the following solutions.

First, with tumors close to the surface, an ellipse of skin 1 to 2 cm wide immediately above the palpable anterior surface of the tumor should be removed. The subcutaneous layer is approximated with interrupted sutures while the balloon remains deflated.

Second, in most cases the maneuver described in the previous paragraph provides the minimum 5-mm distance between the outer surface of the balloon and the skin. However, in slim women when the tumor is located in the inner half of the breast (16% in this series), the goal might not be attained. In 2 cases, 1 of us (K.D.) used ultrasound guidance to temporarily increase the distance from 2 to 3 mm to 5 mm by injecting 20 mL of isotonic sodium chloride solution subcutaneously before each treatment. This process may be further facilitated by leaving a 20-gauge angiocather in the subcutaneous space for the duration of the treatment. Clearly the whole process has to be performed with strict attention to sterility. The patients cited herein completed their brachytherapy without infection but with a moderate degree of overlying erythema lasting 2 to 3 weeks.

Infection

Seven cases of wound infection involving the lumpectomy cavity (6%) were recorded in 112 patients treated with brachytherapy using the MammoSite device. Perioperative intravenous antibiotics were given to most but not all patients. In 1 patient, the indolent wound was eventually operatively debrided and did not completely heal until 11 months after balloon insertion, leaving an unsightly indentation in the breast. It is likely that the combination of the infection and the close balloon-to-skin distance acting in concert made the complication far more severe than it would have been with only 1 of the factors alone. Our infection rate, however, is in line with the incidence reported by other investigators.

Close observation of the entry point of the catheter into the breast during 10 sessions of treatment in the radiation therapy department revealed that adequate sterility was not maintained during insertion of the iridium seed into the balloon. An externally located part of the catheter measuring 2 to 3 cm in length moved in and out of the breast when the patient changed from supine to upright positions. One of us (K.D.) has begun anchoring the catheter to the skin with 2 nonconstricting sutures in an attempt to avoid this movement. Topical antibiotics should be applied to the catheter entry point, and attention should be paid to good catheter care during the treatment week.

OTHER ADVERSE EFFECTS

Skin Reactions

With some exceptions, the following minor to moderate degrees of skin reactions lasting up to 3 months were
noted: erythema in 28 patients, edema in 3, and blisters in 9. Minimal degree of telangiectasia of the skin overlying the balloon was noted in 10% of patients. One patient who had a 5-mm balloon-to-skin distance and in whom an abscess also developed has had a chronic, slowly healing skin ulceration during a period of 10 months.

Seroma

Results of postbrachytherapy ultrasound examination in 10 patients revealed variable amounts of fluid collection (seromas) after the balloon was removed. In symptomatic cases, the fluid was aspirated in the office with ultrasound guidance.

PATIENT ACCEPTANCE AND COSMETIC EVALUATION

During the early phase of our experience, the MammoSite device was placed in the breast at the time of lumpectomy (26% in the series). This policy was changed after realizing that several patients required reexcision for positive margin findings. It was then decided to insert the device at the time of reexcision, or if the margins were reported to be clear, at a separate session (74% of cases). The procedure was performed with ultrasound guidance through a small skin incision under local anesthesia and/or sedation.

During the initial 24 hours after insertion, all patients experienced a variable degree of discomfort due to the breast distension by the balloon. However, they adjusted to this temporary discomfort and completed the 5-day course of radiation treatment.

The cosmetic result was judged primarily by the patients with input from the medical personnel during the follow-up visit 1 to 6 months after the completion of brachytherapy. Although photographs were taken to objectively compare the treated with the untreated breast, this comparison was not uniformly performed. Based on a modified Harvard Scale,16 the cosmesis was rated excellent/good in 80%, fair in 15%, and poor in 5%.

We concede that not all patients with operable breast cancer who may choose BCT are candidates for brachytherapy. In our series of 129 patients from 3 medical centers, 112 (87%) completed the prescribed 1 week of treatment within an average interval of 10 days after the initial lumpectomy. Compared with 6 weeks of conventional external beam radiation, the difference is a significant saving of time. However, there are still some unresolved problems. Seventeen (13%) of 129 patients who enrolled in the study were not treated (Figure 2). Four patients with axillary node metastases were excluded by 2 investigators. The rationale for this policy was based on the recommendation of the American Brachytherapy Society that such patients should be treated with whole-breast irradiation due to possible increased risk of local recurrence.17 In the present study, 1 investigator (K.D.) included 6 patients with positive node findings and small metastases in 1 to 3 axillary lymph nodes. All 6 patients were treated with chemotherapy after their course of brachytherapy was completed. To date, none have shown local recurrence.

In addition, 6 of 129 patients were not treated because the balloon-to-skin distance was less than 5 mm. We have suggested maneuvers that can circumvent this problem.

Of 112 patients who completed brachytherapy, the major complication was infection in 7 patients. We believe that this morbidity can be avoided by meticulous attention to catheter care in addition to the steps suggested herein.

CONCLUSIONS

We have presented the initial encouraging experience of 3 groups of surgeons and radiation therapists at 3 medical centers treating operable breast cancers with lumpectomy and brachytherapy using the MammoSite device. Based on available data, we believe that the suitable candidate for this treatment is a perimenopausal or postmenopausal patient with a moderate to large breast and less than 3 cm of invasive or in situ tumor located in the midlateral part of the breast. Brachytherapy with the MammoSite catheter has distinct advantages compared with whole-breast irradiation, including a much shorter treatment time that enables working women and those at a distance from radiation centers to consider breast conservation. The single catheter placement is technically easier to learn and apply than the multiple catheters. The long-term results, including the incidence of local recurrence, will be the subject of future reports.

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REFERENCES


DISCUSSION

John H. Donohue, MD, Rochester, Minn: Whole-breast teletherapy radiation administration over 5 1/2 to 6 weeks is the standard of care for women undergoing BCT. Because most in-breast tumor recurrences occur in the vicinity of the primary tumor, recent attention has focused on the efficacy of limited field radiation therapy in breast cancer patients. Several small, mostly single-institution publications have reported 5-year results with this technique. These studies have included external beam, intraoperative, implant, and balloon catheter radiation therapy techniques. The data reveal high local control rates with these treatments, all of which were completed in less than a week. The patient acceptance and cosmetic results have generally been excellent.

In the current patient series, 112 (87%) of women chosen for a high-dose-rate brachytherapy using a double-lumen balloon catheter and an iridium Ir 192 source completed the treatment. Ten 340-cGy doses were given using a 3-day, twice-a-day schedule. Skin changes consisting of erythema, edema, and blisters were noted in almost a third of women. Whereas the incidence of these side effects in line with standard BCT results, the 6% infection rate with the balloon catheter seems higher than usual. This treatment was completed on average within 10 days of the operation. Few patient complaints were noted, and the cosmesis was uniformly rated as good or excellent with short-term follow-up. The authors correctly state the need for long-term results with this technique.

My first question is when should this treatment be utilized at the present time? Is its use outside of a research protocol reasonable, or are long-term results of sufficiently powered phase 3 studies comparing limited-field and whole-breast radiation therapy needed first? This is an important question because with the time savings inherent to limited-field radiation therapy, many breast cancer patients will demand this treatment before sufficient data mature to rule out unanticipated long-term problems. Also, what is the cost of your limited-field treatment, and how does it compare to your standard breast radiation therapy?

Your patient selection criteria were broader than other reported experiences with balloon brachytherapy catheters since you included ductal carcinomas in situ, infiltrating lobular carcinomas, and some T2 cancers. There must be a maximum tissue volume adequately treated, especially because breast compression by inflation of the outer balloon increases the volume of surrounding tissue receiving the desired radiation dose. What is the largest tumor that should be treated with this technique?

Similarly, was the cause for nonconformity of the balloon to the tissue cavity in 3 patients a function of the volume of breast parenchyma excised, or was the shape of the biopsy cavity too dissimilar to a sphere? If the latter reason was the cause, is a poor balloon fit more likely in women with dense breast parenchyma? And do these women with dense breasts experience more discomfort during this therapy?

Was the reason for some investigators excluding patients with nodal metastasis a concern about Adriamycin recall complications or because they believe all node-positive patients require axillary radiation therapy? And do you believe that women with limited axillary nodal metastases are good candidates for limited-field radiation therapy?

For women with in-breast failures after this treatment, I presume second primary cancers distinct from the first tumor will be treated in the same fashion without excessive injury to normal tissues. However, how should local failures adjacent to the initial carcinoma be managed?

Finally, can you provide more data on your measurement of cosmetic outcomes? Prior studies in this field have shown that patients rate their cosmesis after lumpectomy most leniently. Surgeons give the lowest grades, and third-party observers deem the results somewhere between the other 2 judges. What scale was utilized for the measurement of cosmesis, and who did the grading?

Dr Dowlatshahi, I appreciate your bringing this report of a new and promising technique in breast cancer care to our attention. This therapy could especially benefit women living far from a radiation oncology center who at the present time opt for mastectomy because of logistic problems with standard radiation therapy. Given its advantages over current whole-breast treatment, hopefully the long-term results of limited field radiation therapy are excellent, and this treatment becomes the standard of care for most breast cancer patients.

Dr Dowlatshahi: I do not think that this technique is ready for general use. I think there are still some problems regarding its application, as well as the complications that I outlined. Therefore, this should still be performed under institutional review board regulations.

The cost of the treatment is no less than the external beam radiation. The device is pretty expensive. I guess it is going to be about the same as that for conventional treatment. We treated tumors up to 4 cm. The invasive masses were about 2 to 2.5, but the ones with the ductal carcinoma in situ were up to 4 cm.

For cosmetic outcome, I think the best judge is the patient herself. In our series we judged them by our own surgeons and the nurse practitioners, but probably in the future the Harvard Scale evaluation of the cosmesis should be employed.

Edward H. Phillips, MD, Los Angeles, Calif: I have several technical questions. First, you mentioned using saline to increase the gap between the skin and the balloon. How long does this effect last? That leads to my second question. Do you study the catheter placement with CT scan or ultrasound before each treatment, or each day of the treatment, or not at all? And third, since the brachytherapy adds a centimeter, some-
The alternative treatment techniques are the subject for a future clinical trial. I think National Surgical Adjuvant Breast Project is considering doing a large-scale clinical trial on this method of therapy.

James E. Goodnight, Jr, MD, PhD, Sacramento, Calif: I have 2 questions. If you placed a balloon at the time of lumpectomy and your pathologist returns a positive margin on permanent sections, how do you handle that? Secondly, there is a theoretical risk of seeding of the balloon tract. Has that been borne out in practice? That is, the catheter comes out through a tract. Is that tract actually radiated by the brachytherapy? In other words, presumably that is a risk that there would be seeding of that tract as the catheter comes out of the breast.

Dr Dowlatshahi: The answer to your first question is every time we had to get negative margins. If there were positive margins, the patient had to be reexcised, and that was the reason why we went from the immediate to delayed insertion of the device to make sure that we had clear margins. As for removal of the catheter, if there is no cancer in the cavity, we don't expect any seeding, and we have not given any radiation treatment to the breast subsequent to the removal of the catheter.

Norman C. Estes, MD, Peoria, Ill: Were the wound infections that you had with the intraoperative balloon placement, or were a number of those when you actually reopened the site and placed the catheter postoperatively?

Dr Dowlatshahi: No, the wound infection was noted after the radiation therapy was completed. In fact, 2 to 3 days after the completion of radiation therapy, and I don't think it had to do with the breakage of the sterile field during the time of placement.

Dr Estes: But I thought you said that you would do an excision, and then at another setting the wound was reopened and the catheter placed which is a modification of the initial technique.

Dr Dowlatshahi: The catheters were placed into the wound subsequent to the pathology report, and the infection occurred after the completion of radiation therapy.

Dr Estes: I have a long experience with brachytherapy and there is a very high infection rate, but the difference is that you don't reenter the wound. The wound infections in brachytherapy done traditionally are mainly after the radiation has been done or if you have to reenter the wound. At all costs I would try not to reenter the wound, and I wondered if that was a factor here.

Dr Dowlatshahi: Well, you do reenter the wound either by not opening it or you may go through a stab incision and place the catheter into the space.

Nora M. Hansen, MD, Santa Monica, Calif: If the catheter is placed in a delayed fashion, is it the radiologist or the surgeon who places the catheter? Can you describe the technical aspects of placing the catheter? Do you have to take the patient back to the operating room or do you use ultrasound or CT guidance to assist you with the placement of the catheter?

Dr Dowlatshahi: Surgeons insert the catheter. Ultrasound-guided catheter placement is practiced if the margins are clean. In several cases where we had positive margin, we reexcised and placed the catheter under direct vision.

Correction

Error in Text. In the article titled “Image of the Month,” published in the March issue of the Archives (2004; 139:341), the breast mass is on the left side, not the right.