CLINICAL INVESTIGATION

INITIAL CLINICAL EXPERIENCE WITH THE STRUT-ADJUSTED VOLUME IMPLANT (SAVI) BREAST BRACHYTHERAPY DEVICE FOR ACCELERATED PARTIAL-BREAST IRRADIATION (APBI): FIRST 100 PATIENTS WITH MORE THAN 1 YEAR OF FOLLOW-UP

CATHERYN YASHAR, M.D.,* DANIEL SCANDERBEG, PH.D.,* ROBERT KUSKE, M.D.,†
ANNE WALLACE, M.D.,† VICTOR ZANNIS, M.D.,‡ SARAH BLAIR, M.D.,‡ EMILY GRADE,∥
VIRGINIA H. SWENSON,∥ AND CORAL QUIET, M.D.†

Departments of *Radiation Oncology and †Department of Surgery, University of California San Diego, La Jolla, CA; ‡Arizona Breast Cancer Specialists, Phoenix, AZ; ∥Breast Care Center of the Southwest, Phoenix, AZ; and ‖Arizona Oncology Services Foundation, Phoenix, AZ

Purpose: The Strut-Adjusted Volume Implant (SAVI; Cianna Medical, Aliso Viejo, CA) is a multichannel single-entry brachytherapy device designed to allow dose modulation to minimize normal tissue dose while simultaneously maximizing target coverage. This is the first report on the initial 102 patients with nearly 2 years of median follow-up.

Methods and Materials: One hundred two patients were treated at two institutions. Data were collected on eligibility and dosimetry and followed for toxicity and recurrence.

Results: The median follow-up is 21 months. Overall dosimetry is outstanding (median percent of target volume receiving 90% of the prescription dose was 95.9%, volume of target receiving 150% of the prescription dose was 27.8 mL, and volume of target receiving 200% of the prescription dose was 14.0 cm3). No devices were pulled prior to treatment completion. For patients with a skin bridge of less than 7 mm, the maximum median skin dose was 280 cGy (median percent of target volume receiving 90% of the prescription dose was 95.2%, volume of target receiving 150% of the prescription dose was 25.8 cm3 and volume of target receiving 200% of the prescription dose was 12.7 mL). For patients with both chest wall and skin of less than 7 mm, the maximum median lung dose was 205 cGy with simultaneous skin dose of 272 cGy. The rate of telangiectasia was 1.9%. Grade 1 hyperpigmentation developed in 10 patients (9.8%) and Grade 2 fibrosis in 2 patients (1.9%). There were 2 symptomatic seromas and 2 cases of asymptomatic fat necrosis (1.9%). Of the patients, 27% were not eligible for MammoSite balloon brachytherapy (Hologic, Inc., Marlborough, MA) and 5% were not eligible for any balloon brachytherapy. The recurrence rate was 1%. Conclusions: The SAVI appears to safely allow an increase in eligibility for APBI over balloon brachytherapy or three-dimensional conformal radiation, highlighting the outstanding device flexibility to maximize the target dose and minimize the normal tissue dose. The device was well tolerated by patients. © 2010 Elsevier Inc.

Accelerated partial-breast irradiation, Breast cancer, Brachytherapy, SAVI, Strut-Adjusted Volume Implant.

INTRODUCTION

Breast conservation was a radical improvement and paradigm shift over mastectomy when it was proven to afford similar local control and equivalent survival in randomized prospective studies with greater than 20 years of follow-up (1, 2). Adjunct whole-breast irradiation (WBI) given over 5 to 6 weeks to increase local control became the standard of care. Efforts to increase the efficiency of adjuvant therapy and decrease unnecessary normal tissue effects led to the development of partial-breast irradiation. The ability to limit the amount of breast tissue irradiated was predicated on the observation that most breast cancer recurrences occur near the original tumor bed, and recurrent cancers remote from the original tumor were not decreased by WBI (3–5).
Originally given as low–dose rate interstitial multicatheter brachytherapy, the availability of high–dose rate machines transitioned most patients to irradiation twice daily for 5 days, termed accelerated partial-breast irradiation (APBI) (6–10). Several studies have published results showing that in a properly selected patient population treated with APBI, local control is similar to WBI with greater than 5 years of follow-up (11–13). The first randomized prospective trial with greater than 5 years of follow-up has been published, reporting equivalent breast cancer local control between APBI and WBI, as well as superior cosmetic outcome in the APBI arm (14). The National Cancer Institute, the National Surgical Adjuvant Breast and Bowel Project (NSABP B-39), and the Radiation Therapy Oncology Group (RTOG 0413) have an ongoing prospective randomized trial randomizing eligible women between WBI and APBI. In addition, there are at least five other randomized prospective trials evaluating APBI ongoing worldwide: the GEC-ESTRO (Groupe Européen de Curiethérapie–European Society for Therapeutic Radiology and Oncology) trial using interstitial brachytherapy, the Italian ELIOT (intraoperative radiotherapy with electrons) study of intraoperative electrons, the TARGIT (targeted intraoperative radiation therapy) trial of targeted intraoperative radiotherapy of the Clinical Trials Group of the University College London, the RAPID trial (randomized trial of accelerated partial breast irradiation) with three-dimensional (3D) conformal therapy of the Canadian Ontario Clinical Oncology Group, and the U.K. IMPORT LOW (intensity modulated and partial organ radiotherapy for breast cancer patients at low risk, early stage) trial using intensity-modulated radiation therapy for APBI.

Three methods of APBI are available in the NSABP trial: interstitial brachytherapy, MammoSite balloon brachytherapy (Hologic, Inc., Marlborough, MA), and 3D conformal therapy. Recommendations for women interested in APBI off-protocol vary, leaving uncertainty about eligibility criteria rampant, and the necessity for thorough informed consent essential.

The majority of the data on APBI used interstitial brachytherapy, but use of APBI accelerated with the introduction of a single-entry balloon device, MammoSite, and 3D conformal therapy (15–20).

Despite the increasing popularity of APBI, the initial methods of delivery have limitations. Interstitial brachytherapy was the first method described, but despite the preponderance of data and experience, many North American radiation oncologists are inadequately trained and lack the equipment to perform this specialized technique. The MammoSite balloon increased the ease and popularity of APBI, but early experience showed that because of the inability to dosimetrically modulate dose, inadequate skin and chest wall (CW) spacing led to unacceptable toxicity (15, 21, 22). In addition, although 3D conformal therapy is available in virtually all radiation centers, small-breasted women were often excluded because of recommended limitations on the allowable percentage of ipsilateral breast tissue irradiated or limitations on the allowable normal organs traversed by exit dose. Moreover, there have been recent reports of increased unacceptable toxicity using this method (23–25).

Several new devices have been introduced into the market to overcome these limitations. Each of these devices seeks to combine the flexibility of interstitial brachytherapy by introducing multiple catheters with the ease of placement of the single-entry balloon device. The Contura balloon (SenoRx, Irvine, CA) incorporates a central catheter and 4 fixed peripheral struts to allow normal and target tissue dose modulation by varying dwell times in the various catheters. Early published experience has been favorable, but patient numbers are small and follow-up has been short (26). The Strut-Adjusted Volume Implant (SAVI; Cianna Medical, Aliso Viejo, CA) combines a central catheter with 6, 8, or 10 peripheral catheters to allow maximal flexibility in tumor cavity size conformance and dose modulation (Fig. 1). Published reports on the SAVI are also preliminary, but both devices appear to increase dose modulation and allow a greater proportion of women to undergo APBI (27, 28). This study reports on the clinical and dosimetric outcome of the first 102 patients treated with the SAVI breast brachytherapy device with nearly 2 years of follow-up.

METHODS AND MATERIALS

From November 2006 through March 2009, a total of 102 patients completed treatment with the SAVI breast brachytherapy device at Arizona Oncology Services (Phoenix, AZ) or the University of California San Diego (UCSD) (La Jolla, CA). All patients underwent a lumpectomy and axillary lymph node evaluation with either sentinel lymph node biopsy or full axillary dissection. This study is a retrospective review of the combined subjects from both institutions, and institutional review board approval was obtained from

![Fig. 1. Strut-Adjusted Volume Implant (SAVI). This photo shows the 4 sizes available, from left: 10-1, 8-1, 6-1, and 6-1Mini.](image-url)
each institution for this project. Criteria for treatment included invasive breast cancer or ductal carcinoma in situ, tumor size of 3 cm or less, age of 40 years or greater, and node negative and final margins negative per NSABP definition. Exclusion criteria included multicentricity or positive margins. There were no exclusions on skin, rib, CW, lung, or heart distance. Patient characteristics are presented in Table 1.

Placement of the brachytherapy device was performed by a closed-cavity technique by either the treating radiation oncologist or the oncologic surgeon after the lumpectomy and final review of the pathology for eligibility criteria. The appropriate-sized device was inserted either through the original lumpectomy scar or through a separate incision as an outpatient procedure. The procedure was performed with patients under local anesthesia and, in some, with anxiolytic agents. The decision regarding the entry site was made to orient the SAVI device along the longest axis of the lumpectomy cavity to maximize coverage, and this was generally done under ultrasound guidance. Antibiotics were used at the physician’s discretion in 50% of the patients for either prophylaxis or suspected infection. After placement, a planning computed tomography scan (CT) was performed. Computed tomography images were imported in the PLATO planning system (Nucletron B.V., Veenendaal, the Netherlands). The tumor bed was outlined by the treating radiation oncologist, and the device was digitized into the software by the treating radiation physicist. A full technical description of device usage is available in previously published guidelines (27). The planning target volume was defined by a 1-cm expansion on the edge of the tumor bed minus CW musculature, ribs, and skin. Dose was prescribed to deliver 34 Gy to the planning target volume, 3.4 Gy twice daily, with a separation of at least 6 hours between fractions. Before each fraction, the device and surrounding tissue were evaluated by either orthogonal films or CT. Immediately after the final treatment, the device was collapsed and removed without either anxiolytic agents or local anesthesia. The wound was reap proximated with Steri-Strips (3M, St Paul, MN) and dressed to remain dry for a minimum of 48 hours.

Patients were followed up every 3 to 4 months for the first year. An ipsilateral mammogram was performed 6 months after surgery. Follow-up examinations included a history and physical examination. Both patient symptoms and examination findings were graded by use of the Common Toxicity Criteria, version 2.0 (29). Patients were treated with hormonal therapy, chemotherapy, or both at the discretion of the treating oncologist (Table 1).

**RESULTS**

The patients’ ages ranged from 41 to 87 years, with a median of 60.5 years. Most patients were postmenopausal (78%). The median follow-up has been 21.1 months (range, 9.4–31.7 months).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median</th>
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<tr>
<td>Age (y)</td>
<td>60.5 (41–87)</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>78%</td>
</tr>
<tr>
<td>Tumor size (cm)</td>
<td>1.1 (0.1–3.5)</td>
</tr>
<tr>
<td>Estrogen receptors</td>
<td>88.2% positive</td>
</tr>
<tr>
<td>Progesterone receptors</td>
<td>77.4% positive</td>
</tr>
<tr>
<td>Her2neu</td>
<td>68.6% negative</td>
</tr>
<tr>
<td>Unknown estrogen,</td>
<td>1%, 2%, and 24.6%, respectively</td>
</tr>
<tr>
<td>progesterone, and Her2neu</td>
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</table>

The median tumor size was 1.1 cm (range, 0.1–3.5 cm). The tumors were positive for estrogen receptors in 88.2% of patients, progesterone receptor positive in 77.4% of patients, and Her2neu negative in 68.6% of patients. Of the patients, 1%, 2%, and 24.6% had unknown values for estrogen, progesterone, and Her2neu, respectively. Ductal carcinoma in situ was present in 30 patients (29.4%), and in the remainder it was invasive (Table 2).

No devices were pulled for inadequate coverage, normal tissue proximity, or poor conformity. In 1 patient an ulcer developed at the insertion site, and it was considered to have unrecognized outward displacement of the device with resultant increased skin dose. Subsequently, daily fractional measurements of the protrusion of the device were added to the quality-assurance check to monitor for “in-and-out” device movement.

Dosimetry was outstanding with a median percent of target volume receiving 90% of the prescription dose (V90) of 95.9% (range, 82–100%), volume of target receiving 150% of the prescription dose (V150) of 27.8 cm3 (range, 7.6–61.4 mL), and volume of target receiving 200% of the prescription dose (V200) of 14.0 cm3 (range, 3.7–42.8 mL). The maximum median skin dose was 255 cGy per fraction. Skin to tumor bed edge ranged from 0.1 mm to 4.4 cm, with a median distance of 1.0 cm. For those patients with skin spacing of less than 7 mm (median, 4.75 mm; range, 1–6 mm), the maximum median skin dose was 280 cGy per fraction (80% of prescription dose), with a median V90 of 95.2% (range, 90–99%), V150 of 25.8 cm3 (range, 7.6–45 cm3), and V200 of 12.7 cm3 (range, 3.7–20 cm3). The maximum median CW dose in the patients treated at UCSD with less than 7 mm from the CW as defined by the pectoralis was 445 cGy per fraction, with a rib maximum median dose of 293.5 cGy per fraction and lung maximum median dose of 226 cGy per fraction (66.4% of prescription dose). The corresponding dosimetry for this population of patients was a median V90 of 93.8% (range, 82–99%), V150 of 21.6 cm3 (range, 8.2–38.5 cm3), and V200 of 10.4 cm3 (range, 3.7–17.4 cm3). For those patients treated at UCSD with a simultaneous skin and CW distance of less than 7 mm (7 patients), the median maximum skin and CW doses (median pectoralis, rib, and lung, respectively) were 272 cGy per fraction (80% of prescription dose) and 411 cGy, 264 cGy, and 205 cGy per fraction (120%, 77%, and 60% of the prescription dose, respectively) with a median V90 of 93%, V150 of 19.9 cm3, and V200 of 10.6 cm3.

During follow-up, there has been 1 in-field recurrence. Cosmesis was excellent, with telangiectasia developing in 2 patients, for a rate of 1.9%. Grade 1 hyperpigmentation

<table>
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<tr>
<th>Histology</th>
<th>No. (%)</th>
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<tr>
<td>Infiltrating ductal carcinoma</td>
<td>66 (64.7)</td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>32 (31.3)</td>
</tr>
<tr>
<td>Tubular carcinoma</td>
<td>4 (3.9)</td>
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developed in 10 patients (9.8%), and fibrosis developed in 16 patients (15.5%), but only 2 of those patients had Grade 2 fibrosis (1.9%). There have been 2 symptomatic seromas, for an incidence of 1.9%. There have been 2 cases of asymptomatic fat necrosis at 1 year or greater, seen on routine imaging, for an incidence of 1.9%. Of the patients, 5% were not eligible for any sort of balloon brachytherapy (skin bridge ≥3 mm) and 27% were not eligible for MammoSite brachytherapy (skin bridge <7 mm).

DISCUSSION

This is the first report on the SAVI device, with nearly 2 years of follow-up, that shows that the SAVI safely allows an increase in patients eligible for single-entry APBI over balloon brachytherapy or 3D conformal radiation, highlighting the outstanding flexibility of the device to maximize the dose to the target tissue and minimize the dose to tissues at risk, including sparing skin and CW simultaneously. The device was well tolerated by patients with minimal short-term toxicity and likely decreased long-term toxicity giving the ability to modulate dose to patient constraints. Breast cancer control is outstanding, although follow-up is limited. However, given that dosimetry coverage is equivalent to MammoSite, we anticipate that the control rate should be similar and the long-term normal tissue consequences minimized. Although the study is retrospective in nature, the data show that the introduction of the SAVI device offers more women the opportunity to undergo APBI.

APBI is becoming increasing popular despite the pending randomized prospective trials. The randomized Hungarian trial has shown equivalent breast cancer control with superior cosmetic outcome when comparing interstitial brachytherapy with WBI (14). Interstitial breast brachytherapy is not commonly taught in North American residency programs and is therefore not commonly available, nor is intraoperative electron therapy.

The MammoSite device, because of its ease of placement and straightforward dosimetry, greatly increased the popularity of APBI in North America, both from a physician’s perspective and from a patient’s perspective. Unfortunately, in a parallel fashion, the ease of planning of the MammoSite also reflects its relative lack of dosing flexibility. As a consequence, close proximity of skin, ribs, and CW limit its use because of increased normal tissue dose and subsequent toxicity. Recommendations to minimize normal tissue toxicity eliminated from eligibility small-breasted women (A or B cup) or patients with tumor beds with less than 7 mm of tissue between the balloon edge and skin surface. The skin distance limitation was intended to keep the skin dose at 145% of the prescription dose or less and to prevent skin toxicity. In addition, concerns regarding the CW and heart dose are emerging (30, 31).

Three-dimensional conformal therapy, though the most readily available, still excludes some women from undergoing APBI. Per guidelines, dose should not exit through the lung, heart, or contralateral breast. In addition, the treated breast tissue should represent less than 30% of the ipsilateral whole-breast volume. These safety guidelines, again, exclude small-breasted women and often those with inner quadrant lesions. In larger-breasted women, without permanent markers such as clips, tumor bed localization is difficult. The breast is a mobile structure, especially in large-breasted women, complicating quality assurance. Finally, some early reports of increased, unexpected normal tissue toxicity make this option less attractive, as well as concerning, until more safety data are accumulated and published (24, 25).

Patients, even when counseled about the lack of prospective randomized trials showing equivalency, are attracted to both the accelerated schedule and the decrease in normal tissue exposure to irradiation, and many are choosing APBI. It is offered widely off-protocol with careful patient selection and proper informed consent.

This is the initial report on the first 102 patients treated with the SAVI breast brachytherapy device, with a median
follow-up of over 21 months. Dosimetry has been outstanding, with the median V90 covering 95.9% of the target for the entire patient population, and a V90 of 95.2% in patients with less than 7 mm of skin spacing. Even those with simultaneous limitations on skin and CW have low rib and lung dose (median, 264 cGy per fraction and 205 cGy per fraction, respectively) while maintaining low skin dose (median, 272 cGy per fraction) and excellent dosimetry (median V90, V150, and V200 of 93%, 19.9 cm³, and 10.6 cm³, respectively) (Fig. 2). Evaluation of CW dose is difficult because the breadth of the CW musculature can alone vary the subsequent dose to rib and lung as evidenced by the variability of distance and dose to rib and lung when the device was quite close to the CW musculature.

Cosmetic outcome has been excellent, with no incidence of telangiectasia, fibrosis, or hyperpigmentation, because of the unique ability to conform to patient anatomy, although follow-up remains modest. Local recurrence is low, at less than 1%, and similar to early reports of other trials on APBI.

REFERENCES


