Radical chest wall resection and hyperfractionated accelerated radiotherapy for radiation-associated angiosarcoma of the breast: A safe and effective treatment strategy

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Abstract
Radiation-associated angiosarcomas (RAS) of the breast are vascular tumors arising in a previous radiation field for primary breast cancer. They occur rarely but confer a high probability of local recurrence (LR) and poor prognosis. A wide range of treatment strategies exists due to limited evidence, and although resection is the definitive treatment, LR rates remain high. It has been suggested hyperfractionated accelerated radiotherapy (HART) has the potential to prevent LR. The sarcoma group at the Juravinski Cancer Centre (JCC) reports our experience of nine patients treated with radical resection and adjuvant HART. This is one of the largest reported cohorts we are aware of to receive this treatment. The JCC pathologic data base was reviewed between the year 2006-2015 for patients with RAS. Patients who received radical surgery and immediate HART were eligible. Patients underwent radical chest wall resection and en bloc mastectomy. Radiotherapy was then delivered to 4500 cGy in 45 fractions three times daily using parallel opposed photon beams and electron patching, or volumetric modulated arc therapy. Primary outcome was recurrence-free survival in months, and records were reviewed for descriptive reports of toxicity. We compared our results to other institutions experience with surgery alone or other adjuvant therapies. Median follow-up was 19 months (range 3-41 months). One of nine patients developed LR and developed metastasis, one died of other causes, and seven are alive with no recurrent disease. There were seven reports of mild skin toxicity during treatment. One patient developed chronic wound healing complications which eventually resolved and one patient developed asymptomatic radiation osteitis of a rib. On the basis of our experience at the JCC, we recommend treatment with radical chest wall resection and adjuvant HART to prevent recurrence in RAS patients. As demonstrated in our patients, the large normal tissue volume irradiated is tolerable with in combination with small fraction sizes, and no major toxicities were seen. Further investigation into adjuvant therapy regimens and prospective studies are required to reach consensus on optimal treatment for this disease.

Keywords
hyper fractionated, local control, radiation-associated breast angiosarcoma, reirradiation, toxicity
BACKGROUND

Radiation-associated angiosarcomas of the breast (RAS) are vascular tumors arising in a previous radiation field for primary breast cancer. RAS is defined by a sarcoma in the previous field of irradiation, a latency period of at least 3 years and histologic difference from the primary tumor. They occur rarely but confer a high probability of local recurrence (LR) and poor prognosis.

Radiation-associated angiosarcomas is rare (incidence of 0.9 in 1000 patients) however, with the increasing number of long term breast cancer survivors this risk may continue to increase. There is little evidence to guide treatment so most centers have adopted regimens from the limited reports in the literature or radiation-associated sarcoma treatment in other sites. Surgical removal is the definitive treatment however the type and extent of surgery required is controversial. Most patients undergo wide local excision or mastectomy, however it has also been suggested that the entire previous radiation field be removed.

Despite surgical resection of gross disease local recurrence is high. The French series reported on nine patients who underwent salvage mastectomy, and only one was alive at 32 months. This necessitates consideration of adjuvant therapy, and chemotherapy, radiotherapy and hyperthermia (HT) have been used inconsistently in the literature. In many cases, there is reluctance to consider radiation as part of a multi-modality treatment approach given the prior exposure to radiation therapy; consequently, the role for radiotherapy has been as a salvage treatment or palliation. It is often delivered at suboptimal doses and fractionation schemes even when used adjuvantly.

Previous irradiation to the field poses challenges in balancing toxicity with dose needed to control aggressiveness of the tumor.

A regimen of hyperfractionated accelerated radiotherapy (HART), however, has been reported in the literature, the rationale being threefold: smaller fraction sizes are better tolerated by normal tissue; shorter treatment time may improve disease control; and multiple fractions per day may help prevent repopulation by tumor cells which can occur in rapidly dividing angiosarcoma cells. One institution reports outcomes between patients treated with neo-adjuvant vs adjuvant HART were similar (n = 14), however, investigators recommended the use of preoperative HART to prevent tumor seeding at surgery, downsize gross disease before surgery, and to reduce doses of radiotherapy required.

On the other hand, upfront surgery and adjuvant radiotherapy may facilitate primary wound closure, decreases risk of wound complications, and allow a uniform chest wall shape for a more conformal radiotherapy dose distribution. The sarcoma group at the Juravinski Cancer Centre (JCC) therefore has implemented an approach of upfront radical chest wall resection and en bloc mastectomy with adjuvant HART. We report on one of the largest groups, to our knowledge, to receive radical chest wall resection and postoperative HART at our center for RAS of the breast. We compare our results to the literature to determine whether this regimen achieves local control with an acceptable toxicity profile.

MATERIALS/METHODS

A pathology data-base search was performed at our center, Hamilton Health Sciences, to identify all resection specimens of RAS of the breast between 2006 and 2015. Cases of atypical vascular lesions, Stuart–Treeves syndrome and primary angiosarcoma were excluded.

To be included patients must have had a previous ipsilateral breast cancer diagnosis and received breast conserving therapy (BCT), or lumpectomy plus adjuvant radiotherapy, with a recurrence in the radiotherapy field. Patients must have been evaluated by the JCC sarcoma group including a surgical, radiation and medical oncologist, and sarcoma pathologist, and deemed candidates for radical treatment. Patients were allowed to have previous surgery for RAS prior to referral to the sarcoma group for recurrence.

Patients were excluded if they refused HART in the immediate postoperative period, were non-compliant with treatment, or were deemed not to be candidates for HART by the group. Patients were excluded if they did not receive radical surgery; however in cases of recurrent or very limited disease standard surgery may have been modified based on individual patient and clinical judgment and patients were still included.

Pathology reports had been reviewed by a sarcoma pathologist (IK, SP) at time of diagnosis, and operative notes were reviewed for surgical details. Radiotherapy records, plans, and patient charts were reviewed for treatment details and outcome information.

Given the undersizing of these tumors on imaging (both size of lesions and extent of distribution) and the extensive stippling effect or multifocality of these lesions, a soft tissue sarcoma approach, rather than a mastectomy approach was used in the surgical resection of these patients. This permitted resection of a large majority of the tissue at risk removing the primary focus of the prior planned radiation field, specifically the entire breast tissue with its overlying skin. The entire thorax, neck, and abdomen down to the level of the umbilicus was prepped and draped. Any ulcerated tumors were contained with isolated adhesive dressings to control tumor cell shed. A wide elliptical incision is drawn including the skin up to 3-4 cm inferior to the clavicle, and skin 2 cm inferior to the inframammary crease, with extension of the ends of this wide belly ellipse well into the axilla and onto the sternum or more commonly extending just under the contralateral inframammary fold. The entire breast tissue en bloc with all overlying and surrounding skin and the pectoralis major fascia was resected. In the cases where preoperative MRI raised any concern of the violation of the pectoralis facia or muscle, the pectoralis muscle was also taken en bloc. The raising of skin flaps during resection was limited to the minimal flap at the superior aspect of the wound up to the level of the clavicle. Postresection wounds were irrigated with water. Wound closure employed extensive local advancement flaps to provide immediate soft tissue closure allowing for short time interval to adjuvant radiation therapy. Superior flaps were raised into the lower neck; inferior flaps were raised from the abdomen and extended as far down as to the level of the...
umbilicus. Flaps were raised from underlying fascia, advanced and closed with interrupted sutures. The deep layer of the subcutaneous tissue which is fibrous in nature is closed medially and laterally, then the deep dermis, followed by the subcuticular layer. In younger patients, a wound closure may necessitate a split thickness skin graft and negative wound pressure therapy was employed. Jackson Pratt drains were used to avoid seroma formation.

Radiation therapy was initiated within 12 weeks of sarcoma surgery in all cases. Radiation dose was 4500 cGy three times daily (TID) in 100 cGy fractions, with additional 1500 cGy in 100 cGy TID fraction boost for positive or close margins. Treatments were separated by at least four hours. The clinical target volume (CTV) included the entire chest wall defined by the mid-sternum medially; mid-axillary line laterally; inferior border of the clavicle superiorly; 3 cm below the contralateral inframammary fold inferiorly; to the fascia of the chest wall at the deep margin and the skin anteriorly. A 1 cm vaseline gauze was used in most cases to bolus the skin on the chest wall. If the surgical incision site extends outside the CTV it is included with a 1 cm expansion. The entire volume was expanded 1 cm to create a planning target volume (PTV) used for set up variation, except for the deep CTV margin which is extended 0.5 cm to avoid increased radiotherapy dose the lung.

Initially, patients receiving HART were treated with parallel opposed photon (POP) beams for the lateral chest wall with medial electron patches. This combination of techniques minimizes the volume of lung treated in comparison to the large lung fields encompassed by lateral POP beams alone. More recently volumetric modulated arc therapy (VMAT) planning was adopted, which achieves a more conformal distribution along the chest wall and further minimizes both lung volume and high-dose delivery to the lungs to avoid pulmonary toxicity. Treatment planning with POP fields for lateral segments extended to the mid-axilla and intraclavicular regions, and medially covering 1.5 cm of lung. These photon beams were angled away from the midline and non-divergent, and matched with the divergence of the electron field, which covered the anterior chest wall. Energies included between 6 megavolt (MV) and 18 MV beams for photo fields and 6 to 9 MeV for electron fields depending on the thickness of the chest wall.

More recently, a VMAT technique has been employed to achieve higher dose conformity along the chest wall. The prescription and maximum dose were directed into the PTV volume with the use of PTV optimization rings. Maximum dose objectives were created for heart and lung contours, and optimization rings were used to minimize dose to areas of these organs within the PTV. Radiotherapy was delivered in two arcs using 6 MV energy beams.

Primary endpoint was recurrence-free survival in months. Time to recurrence was calculated from date of sarcoma surgery to last follow-up or death. Secondary end points included overall survival (OS) in months, site of recurrence (local or distant) and toxicity. Follow-up time and OS months were censored at the last visit to clinic. Descriptive reports of toxicity were collected for both acute and chronic toxicity. This study has been approved by the Hamilton Integrated Research Ethics Board.

3 | RESULTS

Eleven patients with radiation-associated angiosarcoma were identified between 2006 and 2015. Two patients refused adjuvant radiotherapy and were excluded, with nine patients total who completed their entire radiotherapy course. The median time to development of angiosarcoma after diagnosis of breast cancer was 9.1 years (range 5.3-12.1). All patients had T1-2N0 breast cancer or ductal carcinoma in situ and received BCT (Table 1).

Two patients had previous surgery and had developed recurrence prior to referral to the sarcoma group. Six patients received radical chest wall resection and en bloc mastectomy or pectoralis major resection. This is our standard surgical resection practice. Two patients (patient 8, 9) were felt to have disease which could be adequately excised with simple mastectomy, and one (patient 6) had previous radical chest wall resection and developed a small isolated recurrence and was then referred to the sarcoma group. Surgery type and pathologic data are summarized in Table 1 for each patient.

Four patients were treated with a combination of medial electron patches and lateral chest wall photon beams (three with lateral parallel opposed pairs and one with intensity modulated radiotherapy to the lateral chest wall). Five patients were treated with volumetric arc therapy (VMAT) plans. All patients completed HART without serious complications. Only one patient required a 1500 cGy in 15 fraction boost for a close 0.2 cm negative margin. One patient (patient 3) received adjuvant doxorubicin and ifosfamide chemotherapy for four cycles for that felt to be rapidly progressive disease.

Median follow-up was 19 months (range 3-41 months) and average follow-up was 20.3 months (Table 1). One patient developed recurrence (patient 3), which was both local and distant, in the form of diffuse subcutaneous nodules. She unfortunately succumbed to her disease after several cycles of palliative chemotherapy. Patient 1 died of unrelated cerebrovascular causes with no evidence of disease, and the remaining seven patients are alive with no evidence of disease. Crude recurrence rate was therefore 11.1%.

Of the nine patients who received radiotherapy, seven had mild acute toxicity documented in on-treatment review notes. Descriptions included erythema, edema, hyperpigmentation and desquamation, and one patient developed chest wall pain. One patient had no documented skin reaction.

Three patients had no documented chronic toxicity following radiotherapy. One patient developed asymptomatic radiation osteitis noted on a chest x-ray. One patient developed mild chronic wound healing complications postradiotherapy, which resolved after several months of follow-up. This patient also had two previous surgeries prior to her final surgery and HART. The remaining four patients had mild fibrosis, edema, or telangiectasia documented on physical exam.

4 | DISCUSSION

Radiation-associated angiosarcomas of the breast are rare, but aggressive tumors with a high risk of local recurrence and poor
TABLE 1  Summary of RAS of the breast patient treatment and outcome data

| Pt no. | BC adjuvant treatment | Latency to RAS | Clinical size (cm) | Previous surgery prior to JCC sarcoma group referral | Surgery | Pathologic size (cm) | Pathologic margin vs Unifocal | HART technique | HART dose | Recurrence (mo) and site | Follow-up (mo) | Status |
|--------|-----------------------|----------------|-------------------|-----------------------------------------------------|---------|---------------------|-----------------------------|----------------|----------|-------------------------|---------------|--------|
| 1      | 4256 cGy/16f + 1000 cGy/4f boost | 146 | 10 | No | R chest wall resection + en bloc mastectomy | NR | 1.5 cm NM | Unifocal | Lateral CW IMRT + medial electron patch | 4500 cGy/45f TID | None | 24 | DND |
| 2      | 4256 cGy/16f + HRT | 105 | 0 | Yes—bilateral simple mastectomy | R chest wall resection + en block pectoralis major resection | 2 | 2 cm NM | Unifocal | VMAT | 4500 cGy/45f TID | None | 8 | ANED |
| 3      | 4256 cGy/16f + HRT | 68 | 10 | No | R chest wall resection + en bloc mastectomy | 10 | NM, distance not reported | Unifocal | Lateral CW + axilla POP + medial electron patch | 4500 cGy/45f TID | 9 mo LR-CW and DR-arms and back | 25 | DOD |
| 4      | 4256 cGy/16f + HRT | 104 | NR | No | R chest wall resection + en bloc mastectomy | 5.2 | 2.6 cm NM | Unifocal | VMAT | 4500 cGy/45f TID | None | 3 | ANED |
| 5      | 5000 cGy/25f + CT | 109 | 11 | No | L simple mastectomy + pectoralis major resection | 12 | 0.2 cm NM | Unifocal | Lateral CW POP + medial electron patch + electron boost | 4500 cGy/45f TID | 1900 cGy/15 TID boost | None | 41 | ANED |
| 6      | 5000 cGy/25f | 120 | 4 | Yes—right simple mastectomy and right chest wall excision | R chest wall resection and wide local excision for residual disease | 0.6 | 0.5 cm NM | Unifocal | VMAT | 4500 cGy/45f TID | None | 19 | ANED |
| 7      | 4256 cGy/16f + HRT | 144 | 18 | No | L chest wall resection + en bloc mastectomy | 9.7 | 3.3 cm NM | Unifocal | VMAT | 4500 cGy/45f TID | None | 23 | ANED |
| 8      | 4256 cGy/16f | 127 | NR | No | L simple mastectomy | 0.6 | 1 cm NM | Unifocal | Lateral CW POP and electron patch | 4500 cGy/45f TID | None | 13 | ANED |
| 9      | 4256 cGy/16f + HRT | 64 | 7 | No | R simple mastectomy | 7 | 3 cm NM | Unifocal | VMAT | 4500 cGy/45f TID | None | 6 | ANED |

RAS, radiation-associated angiosarcoma; BC, breast cancer; f, fraction; R, right; L, left; HART, hyperfractionated accelerated radiotherapy; CT, chemotherapy; HRT, hormone therapy; NM, negative margin; CM, close margin (<1 cm); PM, positive margin; NR, not reported; VMAT, volumetric modulated arc therapy; POP, parallel opposed pair; DND, died with no disease; DOD, died of disease; AWD, alive with disease; ANED, alive with no evidence of disease.
They are often difficult to differentiate from benign vascular lesions and postradiation changes and are generally not seen on follow-up mammograms. Generally, they occur a median of 6–7 years after lumpectomy and radiotherapy or BCT. Biopsy is gold standard for diagnosis, however, sampling error can misdiagnose lesions as vascular atypia and for this reason should be followed closely and repeated. Genomic amplification of MYC also differentiate RAS from vascular atypia. Both the radiation treatment characteristics and patient factors which may predispose women to RAS development are unknown, however, it has been suggested that post-treatment edema or fibrosis of the breast tissue may contribute to development of secondary AS.

The rarity of this disease has prevented the feasibility of randomized trials and the majority of experience is in the form of retrospective series (Table 2). The variation in aggressiveness of treatments and outcomes reported further complicates identifying an optimal regimen. As a result, consensus in optimal adjuvant therapy regimen has not been reached among centers.

As with most radiation-associated sarcomas in other sites, surgery is generally the primary therapy however the extent of resection required is controversial. Local excision with wide margins of 3.5 cm and deep resection to the pectoralis fascia, completion mastectomy, and excision of all tissue in the previous radiotherapy field have all been considered. Morgan et al found a trend toward superior local recurrence-free survival of 80.0% vs 10.0 months (P = .065) in 33 RAS patients who had excision of the entire radiotherapy field as a primary treatment. Other series have suggested complete chest wall resection is required to prevent local recurrence.

At the JCC, we have adopted a radical approach of radical chest wall resection and en bloc mastectomy to remove any previously irradiated tissue with wide margins. We feel this approach is most effective at obtaining negative margins given RAS can be multifocal, and clinical assessment of disease extent is not always reliable.

As previously suggested, obtaining negative margins is essential in preventing local recurrence and may potentially impact survival. Jalali et al reviewed 14 patients and found both time to local recurrence (3 vs 23 months) and average survival (6 vs 42 months) improved with greater than 10 mm pathologic margins. The presence of more extensive disease at baseline in the incomplete group may however have biased these results. Li et al also reported retrospectively that of RAS patients (n = 76) who received radical excision of all previously irradiated skin, vs wide excision or mastectomy alone, local recurrence was 23% vs 76%, and distant metastasis was 18% vs 76%. Disease specific survival at 5 years was also statistically lower at 86% vs 46% (P < .01).

Despite aggressive surgery, recurrence risk remains high, and a rapid time to recurrence between 6 and 13 months on average has been suggested by several studies. A review of 75 cases of surgically resected RAS found 73% LR, the majority within a year of surgery, and 96% were located within the tumor bed or mastectomy scar. Billings et al reported of 27 patients with RAS, local recurrence after surgery was 29% and 2 year OS was 32%. Another retrospective study (n = 31) found 14 of 19 patients with recurrence (6 month average) had initial R0 resection. Although re-excision may lead to improved local control and survival, not all patients are suitable candidates.

This high local recurrence rate with surgery alone suggests the need to consider adjuvant therapies. Chemotherapies including paclitaxel have been used adjuvantly to prolong or prevent recurrence with variable results. Torres et al reviewed 95 cases of RAS, and found a statistically significant advantage in local recurrence-free survival in those patients treated with chemotherapy at 81.4% and 62.8% vs surgery alone at 56.2% and 36.9% 1 and 5 years, respectively (P = .0003). Most of these patients were treated with mastectomy.

Hyperthermia in combination with radiotherapy with or without surgery has been used in RAS patients as well. Investigators found local control rates were higher with surgery at 91%, 46% and 41% vs without surgery 54%, 32%, and 22% for 1 month, 3 months, and 3 years, respectively. In this study, HT was delivered once weekly following irradiation or twice per week for six sessions. Radiotherapy, however, was delivered in either standard or hypofractionated courses (2-5 Gy fractions) for a total dose of 32-54 Gy. The effectiveness of this dose regimen has been questioned in comparison to other hyperfractionated accelerated treatments.

A systematic review of RAS patients in 2014 identified 222 patients, 142 from retrospective series and 80 from case reports. The majority of patients (68%) received surgery alone, 17% surgery and re-irradiation and 6% surgery with chemotherapy. The remaining 9% received primary treatments without surgery. Despite its limited use, surgery combined with radiotherapy had a better 5-year local-recurrence free interval of 57% compared to 34% for surgery alone (P = .008). The overall 5-year OS for all patients was 43%.

The review suggests a potential benefit with adjuvant radiotherapy. Given RAS itself is caused by radiotherapy physicians may be reluctant to administered re-irradiation, and patients are potentially at higher risk for normal tissue toxicity. The University of Florida series is one of the largest documented cohorts treated with HART following mastectomy. Radiation was given generally to 45 Gy in 100 cGy fractions TID with or without a boost (median 59.7 Gy). The rationale for using accelerated, hyperfractionated (more fractions of smaller dose) therapy for this aggressive cancer is to prevent repopulation of tumor cells with multiple treatments per day, allow re-assortment of tumor cells into sensitive cell cycle phases and avoid progression with a shorter treatment time. This regimen also theoretically decreases toxicity to the normal and previously irradiated surrounding tissue in the (eg, chest wall, lung, and heart) with small fraction sizes.

Outcomes were similar between those treated preoperatively and postoperatively in terms of local recurrence in the Florida study. Five patients recurred, either distantly or at the HART field margin. Investigators recommended preoperative HART to prevent tumor seeding at surgery and improve chance of negative margins at resection by downsizing the tumor. Lower doses of radiotherapy may also be required neo-adjuvantly, with 45-50 Gy being standard dose vs potentially 60-70 Gy for positive margins following surgery.
TABLE 2  Treatment and outcome data for studies reporting RAS of the breast

| Study            | Type                  | Treatment                                                                 | Radiation                              | Recurrence                      | Time to recurrence | OS               |
|------------------|-----------------------|---------------------------------------------------------------------------|----------------------------------------|----------------------------------|--------------------|------------------|
| Smith (2014)     | N = 14 RAS breast patients Retrospective 6/14 recurrent disease after previous surgery for RAS at median 2 mo | Mastectomy → HART (n = 5) HART → mastectomy (n = 8) HART alone (n = 1) | 45 Gy in 1 Gy fractions three times per day 70 Gy boost to macroscopic disease and 60 Gy to surrounding 2 cm margin | N = 1 chest wall margin of HART N = 4 lung mediastinum, contralateral axilla | NR | OS and CSS at 2 yr and 5 yr 86% |
| Palta (2010)     |                       | Mastectomy alone (n = 6) Mastectomy + RT (n = 1) Mastectomy + CT + RT (n = 1) Mastectomy + RT + brachytherapy (n = 1) | 30 Gy in 10 Gy fractions (n=1) 45 Gy + brachytherapy (dose NR) | Median 7.5 mo | NR | Median survival 15.5 mo |
| Marchal (1999)   | N = 9 RAS breast patients Retrospective | Radical mastectomy (n = 4) Simple mastectomy (n = 2) Wide local excision (n = 2) Palliative excision (n = 1) | None | 2/9 local recurrence 1/9 distant skin recurrence | Median LR 2 mo post-mastectomy | OS 67% at 81 mo median follow up |
| Lindford (2011)  | N = 9 RAS breast patients Retrospective | Complete mastectomy or wide local excision R0 (n = 7) or R1 (n = 6) | None | LR 86% in R0 vs 100% in R1 | Median LR 3 mo R0 vs 23 mo R0 | 2 yr OS 42% in R0 group vs 10% R1 group |
| Jallali (2012)   | N = 13 RAS breast patients Retrospective | Mastectomy (n = 22) wide local excision (n = 7) Mastectomy→radiotherapy (n = 1) Mastectomy→chemotherapy (n = 1) | 50.4 Gy postoperative RT | 19/31 LR 14/19 initial R0 resection 4/31 LRR 9/31 DR | Median 6 mo to LR | Median DFS 16 mo Median DSS 37 mo |
| Linthorst, 2013  | N = 23 RAS breast, patients + 1 axillary melanoma patient Retrospective | RT + HT (n = 13) preop RT→mastectomy (n = 3) Mastectomy→RT (n = 8) | RT 32-54 Gy (mean 35 Gy) in 2-5 Gy fractions weekly HT once weekly × 4 or bi-weekly × 6 | N = 11 local recurrence N = 5 distant N = 3 combination | LR in 4/11 RT + HT group range 6-51 mo LR in 4/11 surgery group range 7-8 mo | Median OS 13 mo surgery + RT 5 mo HT + RT |
| Senien et al. 2012 | N = 31 RAS breast patients Retrospective | Mastectomy (n = 22) wide local excision (n = 7) Mastectomy→radiotherapy (n = 1) Mastectomy→chemotherapy (n = 1) | 50.4 Gy postoperative RT | 19/31 LR 14/19 initial R0 resection 4/31 LRR 9/31 DR | Median 6 mo to LR | Median DFS 16 mo Median DSS 37 mo |
| Uryvaev (2015)   | N = 6                  | Simple mastectomy (n = 6) | 54 Gy (n = 2) Doxorubicin chemotherapy (n = 2) | 2/6 LR 1/6 DR | Median 13 mo | 4/6 patients alive no disease. Median follow up 41.8 mo |
| Fodor (2006)     | N = 8 RAS breast patients Retrospective | Radical mastectomy (n = 9) | None | 6/8 LR 5/8 DM | Median 5 mo to LR | Median survival 19.5 mo 2 yr angiosarcoma specific survival 18% |

(Continues)
On the other hand, preoperative radiotherapy can potentially make previously irradiated tissue even more difficult to resect and close with primary intention. It may also result in chronic wound complications. Following surgery, gross disease has been resected and the chest wall shape is therefore likely to be more homogenous. This allows adequate target volume coverage without large dose inhomogeneities.

Our series is one of the largest to date to our knowledge reporting on the use of postoperative HART. Despite variations in the literature in treatment volume for these patients, at our center, the CTV includes the entire chest wall. This ideally prevents recurrences in any residual previously treated tissue with BCT not removed at surgery. In our study only one of nine patients developed a recurrence with postoperative HART. Our patients were followed up for a median of 19 months, while many studies reported average recurrences between 6 months to 1 year.2

One patient with wound healing issues over a period of several months postradiotherapy which eventually healed. No other significant toxicities were reported. Our results suggest HART and radical chest wall resection used in combination is a safe and effective treatment for these patients.

It is evident based on institutional reports of patients with RAS and literature reviews27,28 that further investigation into adjuvant therapy for RAS is required. In the meantime, based on our experience at the JCC we recommend treatment with radical chest wall resection and adjuvant HART to prevent recurrence in RAS patients. As demonstrated in our patients, the large normal tissue volume irradiated is tolerable with in combination with small fraction sizes, and no major toxicities were seen. There may also be a role for other therapies including chemotherapy or HT and further exploration is required. Future investigation into adjuvant therapy regimens is warranted and prospective studies are required to reach consensus on optimal treatment for this disease.

5 | CONCLUSION

Adjuvant HART for localized RAS of the breast has shown promising results in achieving local control. Despite concerns of using HART in previously irradiated and resected tissue, the tolerability of this treatment appears promising. Further experience and follow-up time is required to reach a consensus on the most effective treatment approach for patients with RAS of the breast.

CONFLICT OF INTEREST

No conflicts of interest to disclose.

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