Advances in Radiation Oncology (2024) 9, 101630

advances in radiation oncology

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Teaching Case

Stereotactic Body Radiation Therapy for Palliative Reirradiation of Acrometastasis in the Hand From Breast Cancer

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Received 25 June 2024; accepted 4 September 2024

Introduction

Metastases distal to the elbow and knee, referred to as acrometastases, are rare, accounting for approximately 0.1% of bony metastases.[1,2] These tumors can present with swelling, erythema, loss of function, and pain, and they generally appear in patients with widespread disease either as part of clinically tracked progression or, in rare instances, as a first presentation of an occult cancer.[3,4] Case reports and literature reviews have described acrometastases stemming from various cancers, including several examples of breast metastases to distal extremities that foreshadowed poor prognosis.[5-9]

Acrometastases are sufficiently uncommon and diverse that no consensus guidance has been described on their management, and hence, treatment remains highly patient-specific.[10] Surgery, specifically amputation and, in rare instances, local excision, is the most common treatment, especially for distal-most tumors. Radiation therapy is also commonly prescribed, with increasing application for proximal tumors where surgery is not feasible. Radiation treatments have predominantly been prescribed as common palliative regimens, including 8 Gy in 1 fraction, 20 Gy in 5 fractions, and 30 Gy in 10 fractions.[11] These treatments usually implement simplistic techniques such as parallel-opposed open fields.

Stereotactic body radiation therapy (SBRT) is becoming increasingly common in palliative treatments for many sites, with well-supported efficacy.[12-14] Many well-established techniques for treating via SBRT can readily be adapted to treating acrometastases. SBRT is a compelling option for increasing the biologic dose to these tumors especially given that multiple case reports have indicated limited or no pain control with conventional regimens,[15-17] Additionally, SBRT may enable safe retreatment of acrometastases for ongoing palliation because of its high precision. In this report, we specifically describe details of localizing and treating a breast cancer acrometastasis with SBRT and compare intensity-modulated RT with alternative modalities for delivering this treatment.

Case Description

Clinical presentation

A 72-year-old woman who had a history of locally advanced left breast cancer treated with neoadjuvant systemic therapy, surgical resection, adjuvant radiation therapy, and hormonal therapy, and who later developed metastatic disease presented to the clinic. At the time of her metastatic disease diagnosis, she was experiencing severe left wrist pain and decreased range of motion. A magnetic resonance imaging (MRI) of the wrist demonstrated disease involvement in

Funding Statement: This work had no specific funding.

Data Availability Statement for this Work: All data generated and analyzed during this study are included in this published article (and its supplementary information files).

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https://doi.org/10.1016/j.adro.2024.101630

the left wrist and hand. Surgical biopsy of this lesion demonstrated disease consistent with her primary left breast cancer. She began systemic therapy and was treated with a single fraction of 7 Gy via parallel-opposed, jaw-defined photon fields with an aperture covering the left hand and wrist (7.6 cm × 12.6 cm). Within 2 months of this treatment, she reported no pain in her left hand and began physical therapy to restore her range of motion. After 1 year, she experienced increased discomfort in her left hand, and a radiograph indicated a new lytic lesion in the third metacarpal. At that time, additional radiation was not recommended because of concern for loss of function in the hand, given observed fibrosis and scarring.

Nearly 5 years later, she presented again with severe left hand pain and swelling because of a progressive acrometastasis in her left hand and no evidence of disease elsewhere in her body. An MRI demonstrated a 4.5-cm marrow-replacing lesion within the third metacarpal shaft with cortical disruption and a soft tissue component also involving the capitate and second metacarpal base. She declined referral to a hand surgeon and presented to radiation oncology again for reconsideration of a second palliative radiation treatment.

Therapeutic intervention

Given the good pain relief provided by her initial radiation course and her oligometastatic disease setting with a single active site of disease in her hand, she was offered SBRT treatment for the recurrent acrometastases, delivering 30 Gy in 5 fractions. For this treatment, she was simulated in the prone position with her left arm extended above her head. Her upper torso position through her left elbow was affixed in a patient-specific mold that was fitted into an immobilization board that in turn was indexed to the treatment table. Her left hand and wrist were pressed into a patient-specific cushion. The hand, wrist, and cushion were then secured to the immobilization board in a thermoplastic mask as shown in Fig. 1B.

Computed tomography (CT) images were acquired with 1-mm slice thickness and 512 × 512 image matrix in a 35-cm field of view. Figure 1A shows a coronal image from this CT acquisition in comparison to a coregistered image from her prior radiation course in 2018. Her treatment setup was replicated on a 1.5 T MRI scanner with an MRI-conditional immobilization board, and images with and without gadolinium contrast were acquired for target delineation as summarized in Fig. 1A. Images were acquired using the body coil for radiofrequency (RF) transmission and the receiver array coil located inside the couch and a large loop coil draped over the hand (with sandbags pressed between coil and hand) for reception. Contrast images were obtained with 2 T_1-weighted pulse sequences, including (1) 2D turbo spin echo to minimize any magnetic susceptibility artifacts that could arise because of the setup and (2) 3D gradient echo acquisitions to enhance gadolinium-tissue contrast. 2D turbo spin

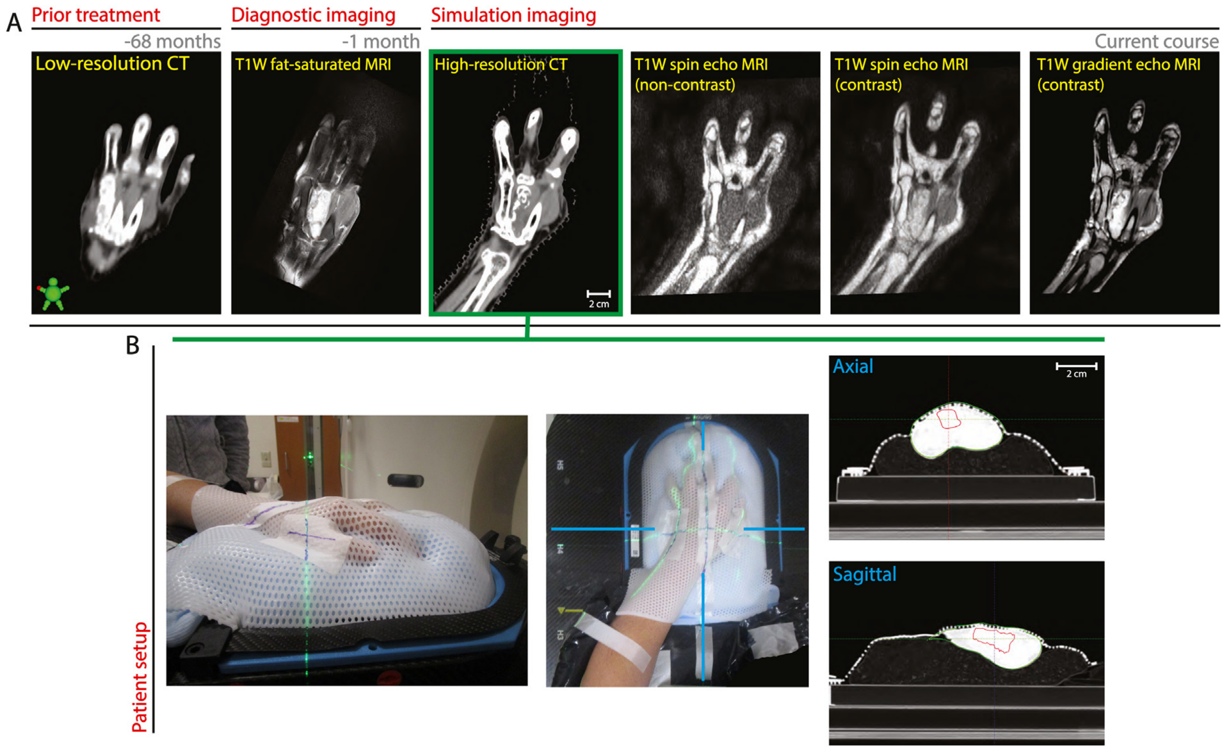

Figure 1 (A) Imaging obtained for the patient, including simulation CT from prior treatment, CT for the current course, and MRI coregistered to the current CT for target delineation. (B) Patient positioning and hand and wrist immobilization for SBRT.

echo images were acquired with repetition (TR) and echo (TE) times of 564 and 10 ms, respectively, with 90° flip angle and 220 phase encoding steps over 3 averages (total acquisition time of 6.5 minutes). 3D gradient echo images were obtained with a TR and a TE of 8.1 and 3.7 ms, respectively, with 10° flip angle and 230 phase encoding steps over 2 averages (total acquisition duration of 5.6 minutes). In reconstruction, images were resampled on a Cartesian grid with 1-mm isotropic resolution.

As shown in Fig. 2A, gross tumor volume (GTV) was defined on simulation CT based on contrast enhancement evident on coregistered MRI. The delineated GTV was 14.8 cm^3 and 4.5 cm (superior-inferior) by 2.2 cm (anterior-posterior) by 1.7 cm (left-right). As supported by high-resolution imaging and localization techniques described below, planning target volume (PTV) was prepared as a 1-mm isotropic expansion of GTV and was 19.8 cm^3.

The treatment plan was prepared with volumetric-modulated arc therapy (VMAT) using 2 full coplanar arcs with complementary collimator angles and 6FFF energy as shown in Fig. 2B. Planning objectives mimicked those from a prior report and the included volume of PTV receiving at least 95% of the prescription to be at least 98% (V95% > 98%) and a maximum plan dose of 108.4% of the prescription dose.[11] Plan optimization was prepared to achieve rapid and isotropic dose fall-off from PTV periphery. Total plan monitor units were 1404 corresponding to a beam-on duration of 120 s. Figure 2C summarizes the dose distribution on the clinical plan. Measurement-based verification of the planned dose was performed according to institutional standards that are similar to recommendations from the American Association of Physicists in Medicine (AAPM).[18] Treatment was delivered on a couch that supports 6 degrees-of-freedom corrections.

Cone-beam CT (CBCT) imaging was acquired for each fraction for daily setup as exemplified in Fig. 3A. The maximum translational and rotational corrections over the 5 fractions were 2.4 mm and 2.5 degrees, respectively. The treatment position was verified after CBCT-derived shifts with perpendicular kV images as shown in Fig. 3B. These images were acquired at oblique and orthogonal views to avoid lateral imaging for which the metacarpal bones may be obscured and support matching in 3 dimensions. No residual error was evident on verification kV imaging that necessitated additional shifts.

Follow-up and outcomes

The patient tolerated treatment without side effects. Within 1 month of treatment, she reported significant improvement in the pain and swelling in her hand. She continued to experience stiffness in the hand. At 3 months following treatment, she reported that pain in her

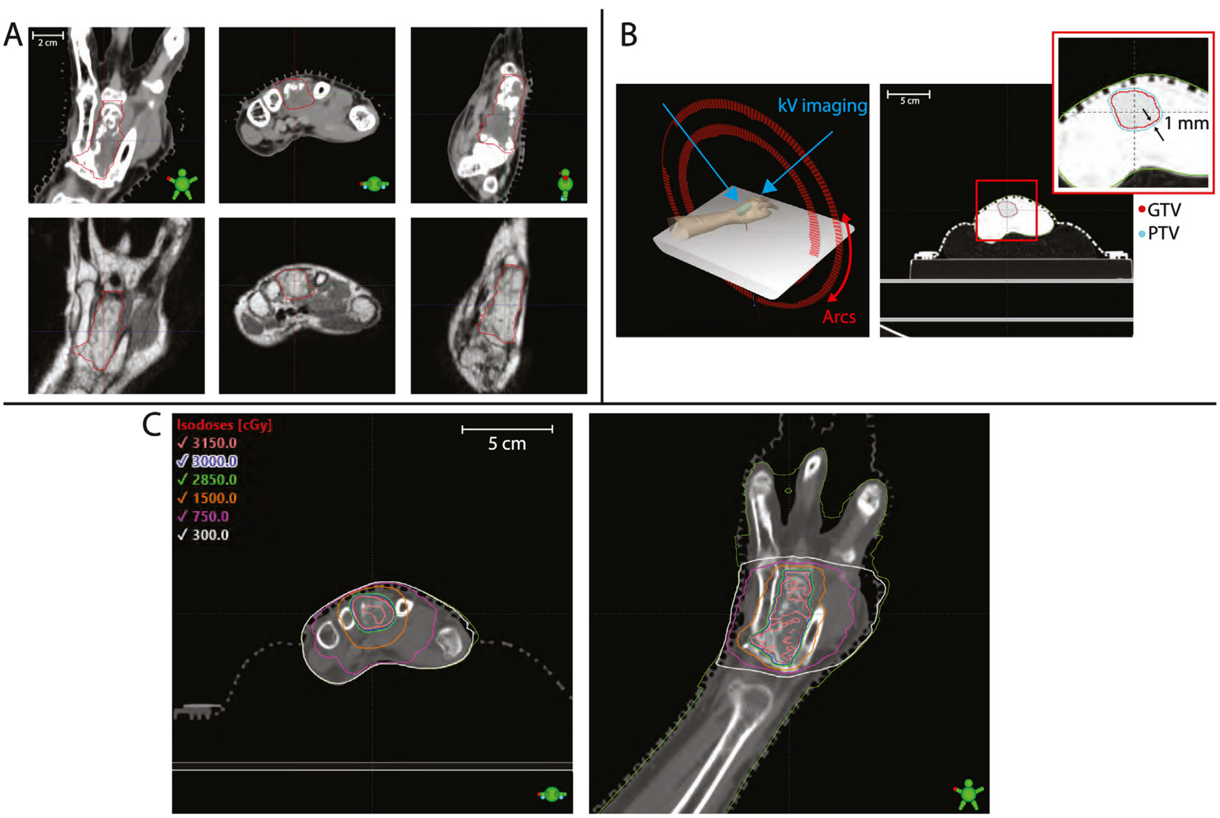

Figure 2 (A) GTV on simulation CT (upper) based on coregistered T1W MRI (lower). (B) VMAT geometry and PTV definition. (C) Dose distribution in axial and coronal views.

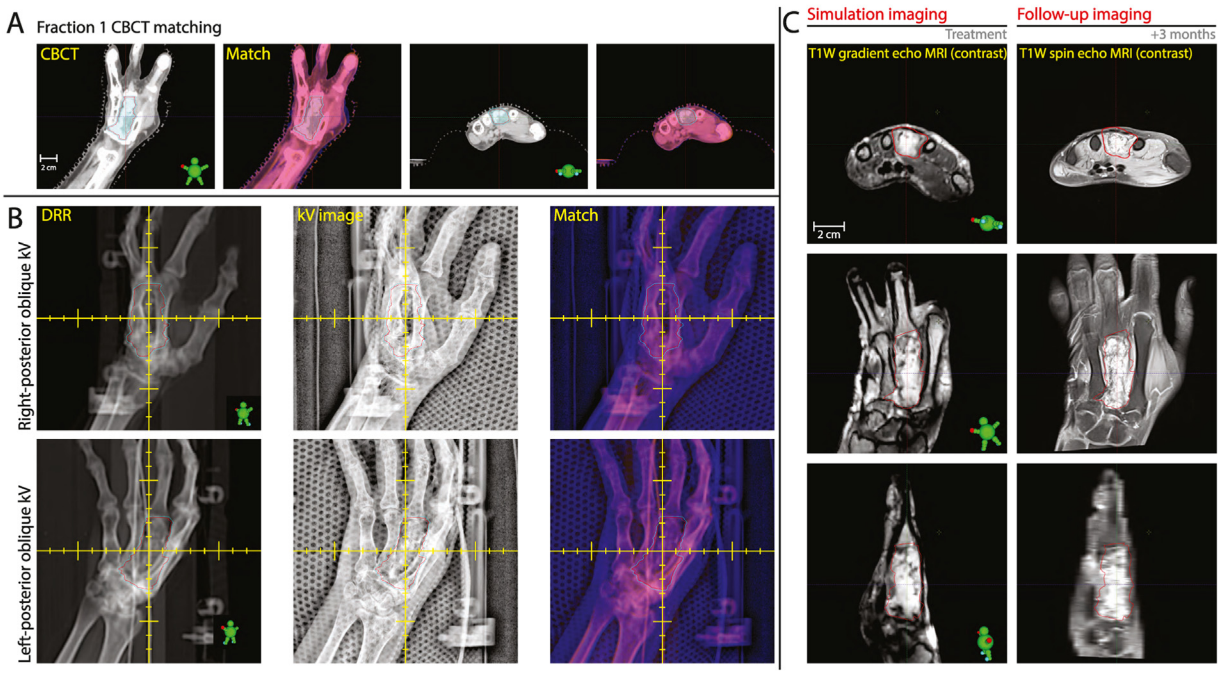

Figure 3 (A) CBCT images from fraction 1, with registration. (B) Oblique and perpendicular kV imaging (middle) that is overlaid without shifts applied (right) to digitally reconstructed radiographs (DRRs) from CT (left). (C) Comparison of target as visualized on T1W MRI on simulation (left column) and 3 months post-treatment (right column).

hand was significantly less and managed with occasional over-the-counter drugs. Left hand numbness remained unchanged since treatment. Follow-up MRI, shown in Fig. 3C, with gadolinium contrast, indicated a reduced size of the lesion to 4.5 cm (superior-inferior) by 1.3 cm (anterior-posterior) by 1.0 cm (left-right). Additionally, previously observed marrow-replacing lesions from 2018 were no longer evident, and pathologic fractures of the fourth and fifth metacarpals had healed. The hamate and capitate appeared slightly collapsed, and a chronic fracture of the fifth metacarapal shaft was unchanged.

Discussion

We successfully treated a well-defined breast acrometastasis via SBRT techniques. Key aspects of this precise treatment included (1) robust and reproducible immobilization that was achieved with patient-specific molds and off-the-shelf equipment, (2) high-resolution CT and contrast-enhanced MRI data sets obtained in the treatment position, (3) VMAT planning technique, and (4) CBCT-based target localization with kV positioning verification. Accurately coregistered CT and MRI enabled precise delineation of GTV, which in turn provided confidence in localization to within 1 mm as prescribed via PTV. With VMAT technique, the PTV conformity index, defined as the ratio of prescription isodose volume to PTV, was 1.0. Additionally, the gradient measure, defined as the difference in radius between spheres of volume equivalent to the 50% and 100% of prescription isodose lines, was just 6.4 mm such that 15 Gy only partially overlapped adjacent metacarpals.

Given the patient's prior radiation treatment, various radiation therapy techniques could be considered to deliver the prescribed dose in the most recent course as highlighted in Fig. 4. Parallel-opposed fields require sufficient block margin to avoid treating PTV periphery in the penumbra, which in turn leads to an unacceptably hot plan with poor conformity. Compensating bolus could be considered to achieve distal target conformity with electron fields. However, electron treatment will produce an unacceptably high dose to the skin and require at least several mm PTV margins for electron-specific setup uncertainties. Intensity-modulated proton therapy is a compelling option for reirradiation because of its distal sparing and sharp lateral penumbra in treating shallow targets. For the proton beamline at our institution, however, intensity-modulated proton therapy yielded poorer conformity, dose fall-off, and hot spot relative to VMAT, and dose fall-off could only be improved at the expense of maximum dose (and vice versa). Finally, a noncoplanar VMAT plan produced marginally better plan quality measured by gradient measure and conformity index, at the expense of the technical complexity of requiring couch rotations. Among these options, coplanar VMAT planning provided an optimal solution in terms of simplicity and quality for delivering the prescribed dose.

In this case report, SBRT enabled aggressive palliation of an acrometastasis for a patient who was first diagnosed

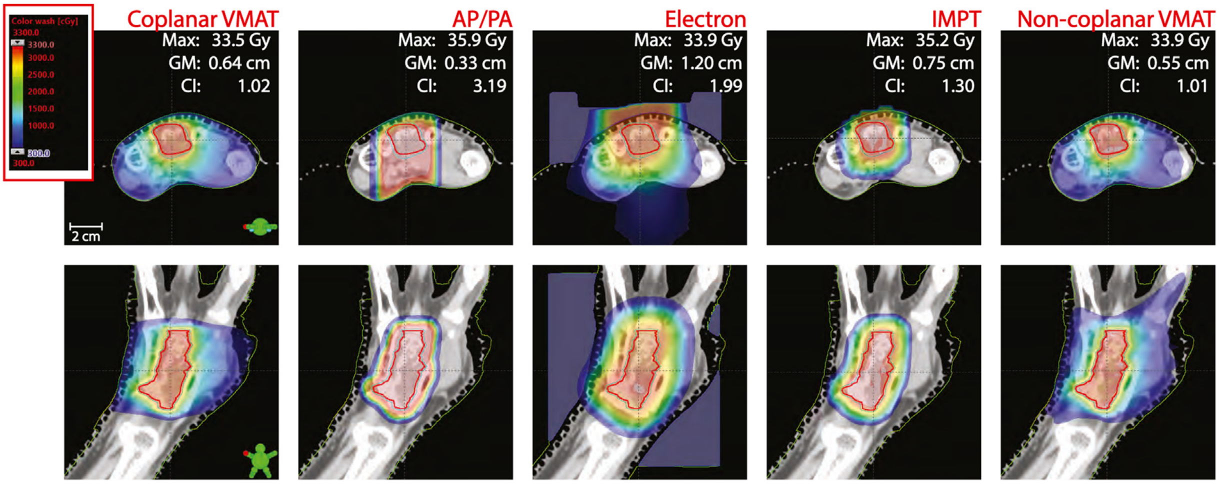

Figure 4 Comparison of various techniques possible for delivering prescribed doses. Coverage is normalized on all plans such that PTV V30 Gy = 98.0%.

with distant metastases from breast cancer over 5 years ago and who at the time of present treatment had a single site of disease. With metastatic disease well-controlled by systemic therapies, the metastasis in the hand meaningfully impacted the patient's daily activities through pain and partial loss of function. Radiation provided effective relief with conventional dosing and technique for several years, and SBRT enabled a second radiation course to a higher biologic doses and a focused target that, at minimum, has provided pain relief immediately after treatment along with intended durable disease control.

Disclosures

None.

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