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Uncovering the armpit of SBRT: An institutional experience with stereotactic radiation of axillary metastases

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ABSTRACT

Purpose/objective(s): The growing use of stereotactic body radiotherapy (SBRT) in metastatic cancer has led to its use in varying anatomic locations. The objective of this study was to review our institutional SBRT experience for axillary metastases (AM), focusing on outcomes and process.

Materials/methods: Patients treated with SBRT to AM from 2014 to 2022 were reviewed. Cumulative incidence functions were used to estimate the incidence of local failure (LF), with death as competing risk. Kaplan-Meier method was used to estimate progression-free (PFS) and overall survival (OS). Univariate regression analysis examined predictors of LF.

Results: We analyzed 37 patients with 39 AM who received SBRT. Patients were predominantly female (60 %) and elderly (median age: 72). Median follow-up was 14.6 months. Common primary cancers included breast (43 %), skin (19 %), and lung (14 %). Treatment indication included oligoprogression (46 %), oligometastases (35 %) and symptomatic progression (19 %). A minority had prior overlapping radiation (18 %) or surgery (11 %). Most had prior systemic therapy (70 %).

Significant heterogeneity in planning technique was identified; a minority of patient received 4-D CT scans (46 %), MR-simulation (21 %), or contrast (10 %). Median dose was 40 Gy (interquartile range (IQR): 35–40) in 5 fractions, ($BED_{10} = 72$ Gy). Seventeen cases (44 %) utilized a low-dose elective volume to cover remaining axilla. At first assessment, 87 % had partial or complete response, with a single progression. Of symptomatic patients (n = 14), 57 % had complete resolution and 21 % had improvement. One and 2-year LF rate were 16 % and 20 %, respectively. Univariable analysis showed increasing BED reduced risk of LF. Median OS was 21.0 months (95 % [Confidence Interval (CI)] 17.3-not reached) and median PFS was 7.0 months (95 % [CI] 4.3–11.3). Two grade 3 events were identified, and no grade 4/5.

Conclusion: Using SBRT for AM demonstrated low rates of toxicity and LF, and respectable symptom improvement. Variation in treatment delivery has prompted development of an institutional protocol to standardize technique and increase efficiency. Limited followup may limit detection of local failure and late toxicity.

Introduction

Use of highly conformal, high-dose-per-fraction stereotactic body radiotherapy (SBRT), (also known as stereotactic ablative radiotherapy: SABR) has grown over the past two decades for both primary [1] and metastatic cancers [2], facilitated by incremental technological advancements [3]. This has led to adoption in less common anatomic sites, including lymph nodes [4]. SBRT offers benefits over conventionally fractionated radiation (CFRT), including a higher biologic effective dose (BED) believed to improve tumour control [5], fewer treatments improving convenience for patients, reducing system costs [6] and reducing time of systemic therapy breaks. However, SBRT may come with higher risks when treating targets close to critical and sensitive OARs [7]. Indications for SBRT are rapidly expanding, with promising randomized data in the setting of oligometastatic [8] and oligoprogressive settings [9], and high conformity to spare structures in re-treatment scenarios [10].

Regional metastatic disease to the axilla (AM) is common in breast

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cancers however, distant metastasis from other solid malignancies are much more rare, though can develop from lung [11], skin [12], gynecologic and others [13]. Historically, conventionally fractionated radiation (CFRT), moderately hypofractionated palliative radiation regimens, surgery or systemic therapies have been used to manage axillary disease, depending on histology, extent of disease, and patient factors [14–16]. Side effects following radiation to this region include lymphedema, fibrosis, and rarely, brachial plexopathy.

Use of SBRT for AM can be challenging: respiratory motion, proximity to important organs at risk (OARs) and prior radiation to the surrounding area such as the breast or lung, can further complicate the equation of maximizing control while limiting toxicity. Further, indications for SBRT, dose, fractionation, OAR constraints, prescription parameters and diagnostic procedures vary widely across institutions and practitioners, with no randomized evidence to guide clinicians. In our institution, both the Radiation Oncologists (RO) and therapy teams are organized as disease-site-based specialists to leverage specialization. AM reside at the intersection of several disease sites, including the breast, lung, head and neck and skin teams. As such, axillary SBRT has been practiced with different protocols depending upon physician, resource availability, and patient factors (mobility, fitness, prior treatment, imaging contraindications, etc).

While some series [17,18] have included a small number of axillary targets in their SBRT analyses, there are very limited published data on outcomes, toxicities and techniques for specifically treating this region of the body. We conducted a retrospective review of our institutional SBRT experience for AM, focusing on outcomes, safety, and process.

Methods

Patient selection

A single-institution retrospective review was performed including adult patients treated with SBRT (defined here as 5 fractions of radiation or less to a biologically effective dose of (BED_{10}) 48.0 Gy or higher (30 Gy in 5 fractions minimum), delivered using volume-modulated arc therapy (VMAT) or intensity modulated radiation therapy (IMRT)) to AM from January 2014 to September 2022. Institutional ethics approval was obtained.

Patients with metastatic or non-operable recurrent disease in the axilla (including lymph node(s) or subcutaneous deposits) of any histology from all primary sites were included. Patients were excluded if undergoing concurrent hypofractionated treatment to breast primary and axillary metastases (treated on trial at our institution). Treatment indications were grouped into three categories: 1) oligometastases (OM: $\leq$5 total metastases; includes breast cancer patients with isolated, non-operable axillary lymph node recurrence), 2) oligoprogression (OP: $\leq$5 progressive metastases in the setting of otherwise stable disease), 3) Dominant area of progression (DAP: polymetastatic patients with growing lesion(s) treated to provide local control to manage or prevent symptoms) [19].

Baseline patient demographics, tumour characteristics, radiation planning and radiation dosimetry were retrospectively abstracted.

Treatment overview

Simulation, planning and treatment parameters, including setup and immobilization, prescription dose, fractionation, schedule, volumes, and margins varied across patients, and are reported as an outcome of interest in results. For simulation, no standard protocol or institutional guidelines were implemented. The use of contrast-enhanced CT simulation, or addition of MR simulation was at the discretion of the treating physician. Various immobilization techniques were available, including use of a 5-point thermoplastic head and shoulder mask, a customized indexed rigid Blue-BAG vacuum cushion (Elekta AB, Stockholm, Sweden) referred to as “thorax bag”, and a customized rigid Vac-Lok vacuum cushion (CIVCO Medical Solutions, Kalona, IA, USA). All patients were treated with either step-and-shoot intensity modulated radiation therapy (IMRT) or volumetric modulated arc therapy (VMAT) on Elekta Synergy or Agility (Elekta AB, Stockholm, Sweden) linear accelerators. Treatment was planned on Pinnacle treatment planning system (Phillips Medical Systems, Madison, WI, USA). Kilavoltage cone-beam CT (CBCT) was performed daily, pre-treatment.

Endpoints and statistical analysis

Patients underwent CT imaging surveillance at 3 months post treatment. Thereafter, CT scans were generally performed at 3–4 month intervals, depending on treatment indication and treating oncologist.

The primary endpoint was per-lesion local failure (LF), defined as any growth in treated lesion or nodal mass (within high dose PTV) on two or more consecutive post-treatment CT scans. As adjuncts, pathology demonstrating recurrent disease, or indisputable evidence of clinical recurrence with imaging or clinical exam were evaluated. When identified, failure was backdated to initial time point indicating growth. Date of failure was calculated from start of SBRT to date of LF. Secondary endpoints included regional failure, per-patient progression-free survival (PFS), overall survival (OS), symptom response, toxicity, planning and treatment parameters.

Descriptive statistics were generated to summarize baseline clinical characteristics, treatment characteristics, and toxicities. Competing risks analysis was used to estimate the incidence of local failure (LF), with death from any cause as a competing risk. Patients lost to follow-up without event of interest were censored. As an exploratory analysis for potential factors predictive of LF, univariable competing risks regression based on the Fine and Gray method was performed. No multivariable regression was done due to the low number of events. No analysis for predictors of toxicity was performed due to the low number of events. The Kaplan-Meier method was used to estimate PFS and OS.

Regional failure was defined similarly to LF: growing adenopathy in the ipsilateral axilla, but outside of previously radiated high dose PTV. Progression free survival (PFS) was defined as start of treatment date to the date of local, regional, or distant progression, or death from any cause. OS was defined as start of treatment to the date of death from any cause. Patients were censored at last follow-up if without event of interest. Toxicity was assessed per Common Terminology for Adverse Events (CTCAE) version 5.0. Symptom and initial tumour response were classified as complete response (CR), partial response (PR), stable disease (SD) or progressive disease (PD). Symptom response was evaluated subjectively from clinician notes, while tumour response was classified as per radiographic assessment within 6 months following completion of SBRT.

Simulation and planning parameters were obtained from institutional treatment planning system. Dosimetry data and treatment volumes were abstracted from archived plans in the institutional treatment planning system. Metrics of interest included gross tumour volume (GTV), internal target volume (ITV), clinical target volume (CTV- high and low dose if used), planning target volume (PTV- high and low dose if used), PTV and CTV expansion margins, target volume coverage (V95%), maximum dose to PTV, conformity index (CI – defined as prescription isodose line volume divided by PTV volume), and dose constraints for organs at risk (OARs, e.g. lung, brachial plexus and skin).

All analyses were performed in Microsoft Excel (Redmond, Washington, USA).

Results

Demographics

In total, 37 patients with 39 AM who received SBRT were available for analysis. Baseline tumour and patient demographics are summarized in Table 1. Patients were predominantly female (62.2 %), Eastern

Table 1
Patient demographics and tumour characteristics.

Variable	n	Characteristics
Per patient	**37**	
Median Follow-Up Time in Months (interquartile range)	37	14.6 (9.5—23.6)
Mean Age in Years (standard deviation)	37	72.0 (±14.1)
Sex		
Male	14	37.8 %
Female	23	62.2 %
ECOG		
0	4	10.8 %
1	19	51.4 %
2	13	35.1 %
3	1	2.7 %
Treatment indication	37	
Oligometastatis	13	35.1 %
Oligoprogression	17	45.9 %
Symptomatic Progression	7	18.9 %
Per Lesion	**39**	
Cancer Primary		
Breast	16	41.0 %
Skin	7	17.9 %
Lung	5	12.8 %
Kidney	4	10.3 %
Gynecologic	2	5.1 %
Gastrointestinal	2	5.1 %
Other*	3	7.7 %
Histology		
Invasive Ductal Carcinoma	16	41.0 %
Adenocarcinoma	8	20.5 %
Melanoma	3	7.7 %
Renal Cell Carcinoma	3	7.7 %
Squamous Cell Carcinoma	3	7.7 %
Other**	6	15.4 %
Axillary Nodal Level***		
1	39	100 %
2	7	17.9 %
3	2	5.1 %
Prior Axillary Surgery		
No	35	89.7 %
Yes	4	10.3 %
Prior Radiation Therapy		
Never/No overlap	32	82.1 %
Yes (with dose overlap)	7	17.9 %
Prior Chemotherapy		
None	12	30.8 %
Yes (but not directly before SBRT)	10	25.6 %
Yes (directly before SBRT)	17	43.6 %
Systemic Management		
Concurrent with SBRT	4	10.3 %
Paused and restarted after SBRT	8	20.5 %
Systemic therapy changed after SBRT	5	12.8 %
Systemic therapy initiated after SBRT	5	12.8 %
No systemic immediately following SBRT	17	43.6 %

Definitions: ECOG: Eastern Cooperative Oncology Group; SBRT = Stereotactic body radiation therapy.
*Head and neck, primary of unknown origin, prostate.
**Merkel cell, serous, apocrine, clear cell carcinomas.
***Lesions included nodal conglomerates which could span more than 1 axillary level.

Cooperative Oncology Group (ECOG) performance status 0–1 (62.2 %), and elderly (median age: 72). Common primary cancers included breast (n = 16, 41.0 %), skin (n = 7, 17.9 %), and lung (n = 5, 12.8 %). All treated targets involved level I of the axilla, while 7 involved level II (17.9 %) and 2 involved level III (5.1 %). Treatment indication included oligoprogression (n = 18, 46.2 %), oligometastases (n = 14, 35.9 %), and symptomatic progression (n = 7, 17.9 %). A minority had prior overlapping radiation (n = 7, 17.9 %) or regional surgery (n = 4, 10.3 %), while most had prior systemic therapy (n = 26, 66.7 %). Only a minority of patients (n = 4, 10.3 %), received concurrent systemic therapy, which included pertuzumab/trastuzamab (n = 1), capecitabine (n = 1), pembrolizumab (n = 1), and trastuzamab alone (n = 1).

Treatment technique

Significant heterogeneity in simulation, planning and treatment was identified, with full details summarized in Table 2. Immobilization included 5-point thermoplastic mask (n = 12, 32 %), Vacloc (n = 12, 32 %) and arms-up thorax bag (n = 11, 30 %). 4-D CT scans were obtained in 46 %, a concurrent MR simulation fused to the planning CT for volume definition in 21 %, and intravenous contrast in 10 %. One case utilized fused PET/CT imaging. The majority (90 %) utilized a Hexapod (Elekta AB) robotic couch to correct for treatment setup errors in 6 degrees of freedom.

Median dose was 40 Gy (interquartile range (IQR): 35–40) in 5 fractions, (BED_{10} = 72 Gy), over a median of 12 days (IQR: 9–14). Seventeen cases (44 %) utilized a low-dose elective (all 25 Gy in 5 fractions) volume to cover remaining axilla. Five (14 %) cases used a high dose clinical target volume expansion.

Median planning target volume margin was 5 mm (range: 3–10 mm), and plans were generated with 5 different dose constraint protocols. Patients underwent daily image-guidance with cone beam CT. Fig. 1 displays two AM treatments using different technique.

Treatment response

Treatment response was available for 37 cases of AM. At first radiographic assessment (~3 months post SBRT), 88 % (n = 34) had

Table 2
Simulation, Planning and Treatment Variables.

Variable	n	Characteristics
Immobilization		
5 Point Mask	12	30.8 %
Thorax Bag	11	28.2 %
Vacloc + Wing Board	9	23.1 %
SBRT Board	4	10.3 %
Vacloc	3	7.7 %
4D CT Simulation		
No	21	53.8 %
Yes	18	46.2 %
IV Contrast During Simulation		
No	35	89.7 %
Yes	4	10.3 %
MR Simulation		
No	31	79.5 %
Yes	8	20.5 %
Diagnostic PET/CT Fused		
No	38	97.4 %
Yes	1	2.6 %
Prescription		
30 Gy/5fx	5	12.8 %
35 Gy/5fx	12	30.8 %
40 Gy/5fx	19	48.7 %
45 Gy/5fx	2	5.1 %
24 Gy/2fx	1	2.6 %
Prescription BED10	39	72.0 (59.5, 72.0)
Prescription BED3	39	146.7 (116.7, 146.7)
Prescription Target Volume		
GTV	5	12.8 %
CTV	3	7.7 %
ITV	13	33.3 %
PTV	18	46.2 %
Target Dosimetry		**Median (Intraquartile range)**
GTV diameter (mm)	39	25.0 (7.0 – 75.0)
PTV Dmax (Gy)	39	41.6 (37.4, 43.1)
PTV Mean Dose (Gy)	39	38.9 (35.5, 41.0)
OAR dosimetry		
Brachial Plexus Dmax (Gy)	34*	27.8 (21.7, 31.1)

SBRT = stereotactic body radiotherapy; Fx = fraction; GTV = gross tumour volume; CTV = clinical target volume; PET/CT = positron emission tomography and computed tomography scan. PTV = Planning target volume; Dmax = maximum point dose within volume; Gy = Gray.
*Total not equal to 39 as contour missing on 5 plans.

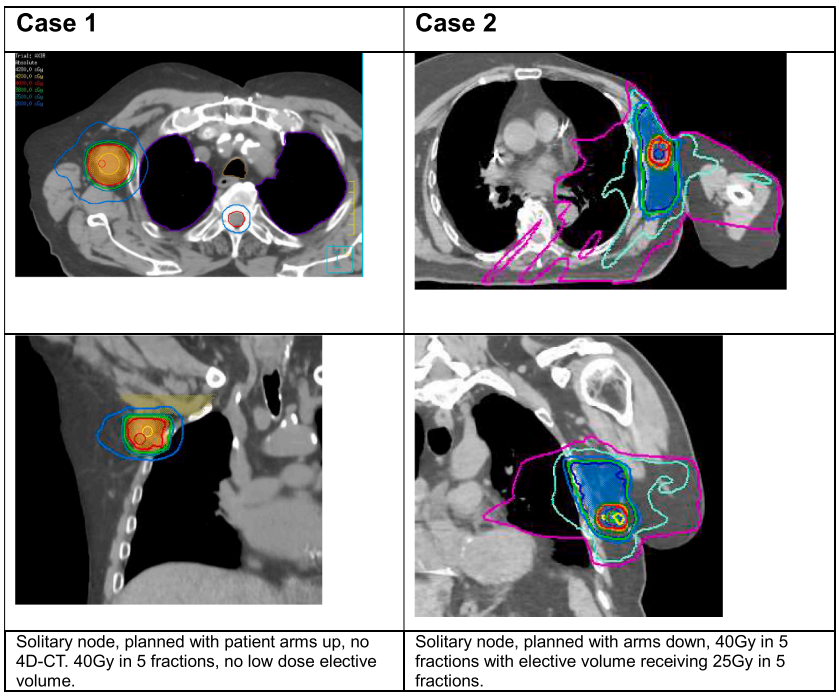

Fig. 1. Illustrative Axillary SBRT Cases

objective response (n = 7, 19 % complete; n = 27, 73 % partial), 5 % (n = 2) had stable disease, with a single progression. Of symptomatic patients (n = 14), 57 % (n = 8) had complete symptom resolution at first post-treatment clinical assessment, while 21 % (n = 3) had partial relief. A single patient had progressive symptoms.

Local failure (LF)

Median follow-up time was 14.6 months. Six-month, 1, 2 and 3-year LF rate were 2.6 %, 16 %, 20 % and 25 %, respectively. Fig. 2 displays the cumulative incidence function curve of local failures.

Of 9 total lesions with LF, 4 received salvage local therapy including 3 treated with re-irradiation (20 Gy in 5 fractions), and 1 with salvage lymph node dissection.

On univariable analysis (Table 3), only higher prescription dose (BED_{10}) was associated with reduced LF (HR: 0.92 [0.86–0.99]; p = 0.02).

Regional control

Of 7 regional failures identified, only 2 occurred without prior or concurrent failure locally and or distantly. Three occurred in cases utilizing a lower dose elective axillary coverage (3/17, 17.6 %) and 4 occurring in those without (4/17, 18.2 %). Regional failures were uniformly asymptomatic, and managed with change in systemic therapy, or observation.

Progression-free survival and overall survival

Median PFS was 7.0 months (95 % [Confidence Interval (CI)] 4.1–11.4), Fig. 3a. One-2 and 3-year PFS rates were 30 %, 19 % and 8 %, respectively.

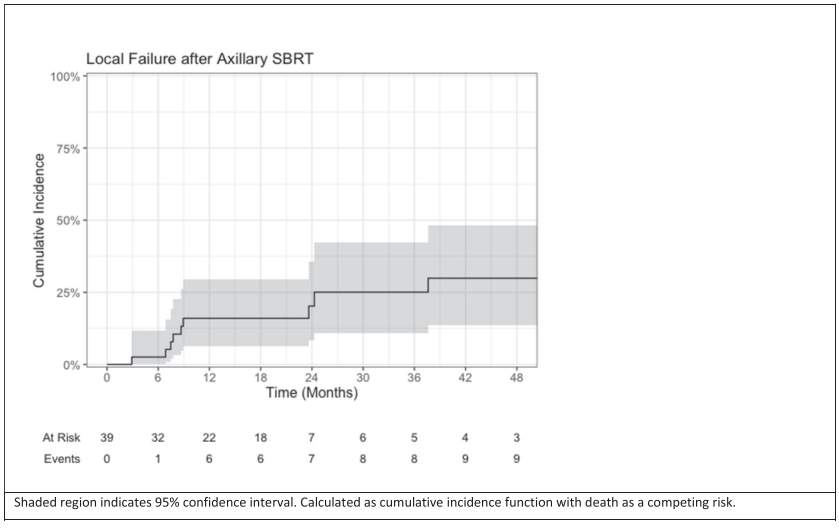

Fig. 2. Cumulative incidence function of local failure after axillary SBRT.

Table 3
Univariable Fine Gray Regression for Local Failure (9 events).

Risk factors	n	Hazard ratio (95% C. I.)	P value
Sex (male vs. female)	39	0.51 (0.10, 2.50)	0.41
Age (every 1 year increase)	39	1.00 (0.96, 1.05)	0.96
ECOG (2-3 vs. 0-1)	39	0.19 (0.02, 1.58)	0.13
Primary (breast vs. not breast)	39	1.03 (0.29, 3.63)	0.96
Axillary Target Number (1 vs. <1)	39	0.68 (0.17, 2.60)	0.57
Prescription Volume (PTV vs. other)	39	0.67 (0.18, 2.53)	0.55
ITV Use (yes vs. no)	39	1.70 (0.49, 5.87)	0.40
Elective Volume Use (yes vs. no)	39	0.59 (0.16, 2.21)	0.44
PTV Volume (per cc increase)	39	1.00 (1.00, 1.01)	0.09
PTV Dmax (per Gy increase)	39	0.93 (0.83, 1.03)	0.17
PTV V95% (per % increase)	39	1.02 (0.92, 1.13)	0.73
Overlap with Prior RT (yes vs. no)	39	1.46 (0.32, 6.72)	0.63
Prescription BED10 (every 1 Gy increase)	39	0.92 (0.86, 0.99)	0.02

ECOG: Eastern Cooperative Oncology Group; PTV= planning target volume; ITV= Internal target volume; DMAX= maximum dose; V95%= volume of target receiving 95% of prescription dose; cc= cubic centimeter; RT= radiation therapy; BED10= Biologically effective dose to tumour assuming alpha/beta ratio of 10Gy.

Median OS was 21.0 months (95 % [CI)] 19.1 – not reached), Fig. 3b. One-, 2 and 3-year OS rates were 74 %, 44 % and 29 %, respectively.

Toxicity

Acute grade 1 or 2 toxicities were identified in 43 % (n = 16) of patients, predominantly dermatitis. There were 2 cases of grade 3 late toxicity. The first was a case of brachial plexopathy was identified in a patient who had arm paresthesia and weakness related to tumour involvement prior to treatment. This patient previously received 50 Gy in 25 fractions to the ipsilateral breast and regional lymph nodes 16 years prior to receiving axillary SBRT. A dose of 35 Gy in 5 fractions was prescribed on retreatment, and the brachial plexus received a maximum of 36 Gy due to gross tumour involvement. This treated lesion demonstrated partial response over subsequent scans. The second was a case of skin ulceration where the tumour had initial skin involvement, and which subsequently showed evidence of local recurrence. There were no grade $\geq$ 4 toxicities.

Discussion

This series represents, to our knowledge, the first report specifically on technical factors and outcomes for patients with AM treated with SBRT. Our study provides anatomic-site specific technique and outcome data to a growing body of literature on lymph-node targeting SBRT in the metastatic setting. To date, nodal SBRT series have focused primarily on abdominopelvic [23,24] and mediastinal/hilar lymph nodes [25].

Aggressive management of metastatic disease in the axilla is becoming increasingly important with accumulating randomized evidence demonstrating the oncologic benefit of ablative treatments in oligometastatic [8,20] (and to a lesser extent, oligoprogessive [9]) lesions. In the palliative setting, SBRT offers the ability to deliver high BED treatment in an effort to maximize tumour control, which in turn, may lead to improved symptom control symptoms, while offering condensed schedules improving patient convenience and cost-effectiveness [21,22].

With nodal metastasis, debate persists regarding treating an isolated nodal mass ('involved node radiation'), or a nodal chain to reduce risk of regional failure. In our cohort, elective treatment of the axillary nodal region was left to the discretion of the treating radiation oncologist. Retrospective analyses comparing focal and elective nodal treatments in oligorecurrent prostate cancer have favoured whole pelvis radiation in terms of overall disease control [30]. Two prospective studies investigating involved node radiation in OM prostate cancer showed the majority (>60 %) who had treatment to a lymph node initially had subsequent failures occurring further along the nodal chain, rather than distantly [31,32]. While subsequent nodal treatments may be feasible, impact on outcomes is unclear [30,31], and tumour biology and systemic therapy options for likely impact subsequent failure pattern. The randomized Phase-II PEACE V-STORM trial is investigating LN SBRT compared to whole pelvis CFRT (with focal boost) in prostate cancers [33]. In prospective cohort of metastatic LNs treated with SBRT from heterogeneous primaries, Franzese et al did not use elective nodal coverage, and found excellent rates of LC, but high rates of out-of-field nodal failures of 50.4 % at 2 years [34]. Rates of regional failure were very low in our series (n = 7), although nearly half (42 %) of these patients received elective dose to adjacent axillary nodal volume. Further, this was the site of first failure in only 2 patients, both of whom had elective nodal treatment. In the absence of high-level data, several factors can help guide decision-making. Treatment indication is

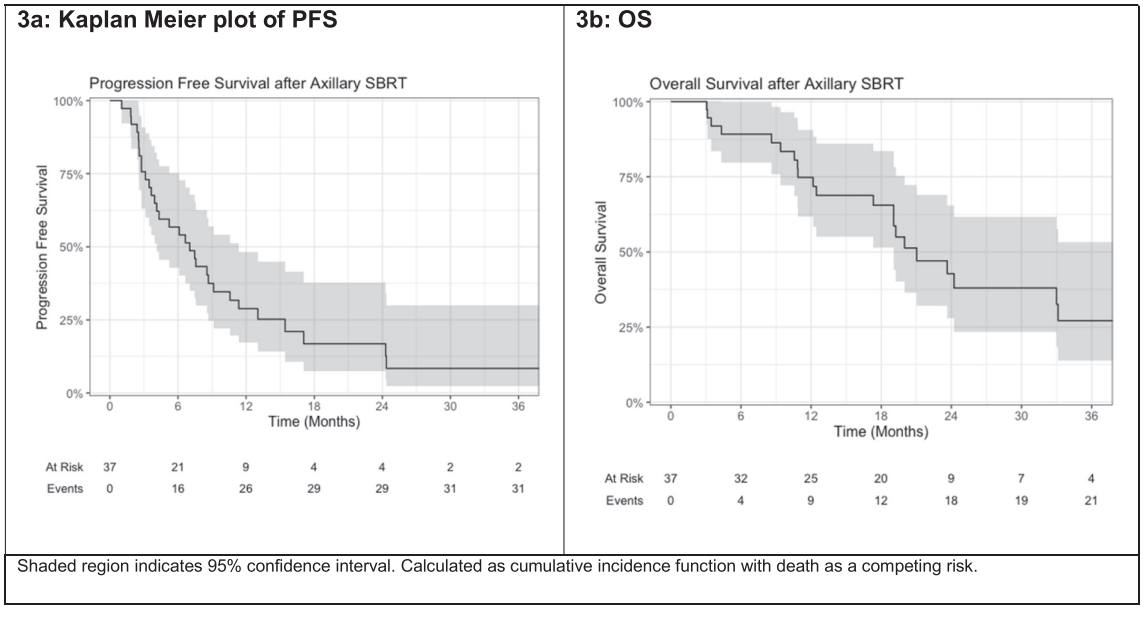

Fig. 3. Kaplan Meier plot of PFS (A) and overall survival (B).

important: a growing conglomerate causing pain in a diffusely metastatic patient may warrant targeted therapy in order to control disease while avoiding undue toxicity. Conversely, in an oligorecurrent breast cancer patient ineligible for surgical resection, elective treatment volume to known at-risk axillary levels seems reasonable. Additionally, prior treatments and subsequent risk of toxicity including chronic lymphedema or plexopathy may reasonably lead to reduced treatment volumes.

In contrast to other extra-cranial applications of SBRT, we report fair rates of oncologic control, which is likely due to the lower BED_{10} doses utilized. While challenging to interpret given the small number of total events, the incidence of local failure in our series did not appear to plateau. This may have been due to several factors including dose delivered, primary histology, and interactions with systemic therapies. The relatively conservative doses prescribed relate to risk of nearby OARs (e.g. brachial plexus if treating upper axilla), and the LF rates observed are in keeping with dose-escalation data [35], and are in range of many nodal SBRT series [25–27]. Our analysis did not demonstrate significant patient, or tumour factors associated with LF. Given associations with tumour size [28] and histology [26,29] in other series, our small sample size and heterogeneous population limit interpretation from this finding. Tolerance of the brachial plexus to hypofractionated radiation is debated: a review of ongoing clinical trials demonstrated a maximum dose of 26–32.5 Gy in 5 fractions (BED_3 = 71–103) [36], while a modeling study [37] suggested lower than expected inferior brachial plexus toxicity with doses of 40 Gy in 5 fractions (BED_3 = 146.7) [37]. Understanding plexopathy risk and impact of BED on LF may guide dose escalation efforts moving forward. In our cohort, mixed histologies, tumour sizes, treatment and simulation techniques, and small numbers make it difficult to distinguish each variable's impact on LF. Data on nodal control after SBRT compared with non-nodal targets is mixed: LN SBRT was associated with less LF than parenchymal or bony targets in a recursive partitioning analysis [27], while other prospective series have not shown significant differences [38], and still others nodal involvement as a negative prognostic factor [39]. While other oncologic benefits (PFS, OS) of local treatment remain unclear from our series, dose escalation may offer improved local control over conventional palliative radiotherapy, which in itself can be meaningful to patients, in a sensitive location where disease progression can often cause significant morbidity.

Variance in across planning and treatment of AM with SBRT at our center has prompted a quality improvement initiative to harmonize the process, through the multidisciplinary creation of a standardized protocol. Within radiation therapy, undue variance has been shown to create issues in departmental efficiency, and patient outcomes [40–44]. A standardized protocol has the potential to reduce risk of error [45], improve evaluability of plans [46], cross-institutional collaboration [47], and improve the ability to generate cohesive research data [48]. A working group including radiation therapy, medical physics and radiation oncology representatives conducted a process mapping exercise was performed to identify differences in the site-specific approaches. An iterative process of protocol revision led to development of a standardized protocol. Key elements of the new protocol include use of MRI and 4D-CT simulation, patients positioned arms-up on MR-compatible indexed equipment, a homogenous and thorough set of dose constraints, standardized process for daily image-guided radiation therapy (IGRT). Draft protocol elements are included in the Supplementary files.

In addition to the above-stated trials to define appropriate LN volume, use of MR-linac may help to accurately define and track LN or OARs during treatment [49]. Combining or sequencing radiation with immunotherapy or targeted therapies to manage metastases is of interest [50]. Further we await reporting of accruing Phase III trials on oligometastatic disease [51,52].

Limitations

Despite the novelty, presented findings must be considered in the context of study limitations, including the small number of patients and lesions, lack of comparator group, heterogeneity, and inherent biases of retrospective cohort studies. The short followup period may limit identification of failures and late toxicities.

Conclusions

In this first, dedicated series of AM SBRT, low rates of toxicity, and good rates of response, LF and symptom improvement were observed across a heterogeneous group of patients and treatment indications. As treatment was delivered with a variety of individual treatment differences, an institutional protocol is under development to standardize technique, optimize efficiency, and improve evaluability.

Patient consent statement

Patients did not explicitly provide consent given the retrospective nature of the study. Ethics approval was obtained from the Institutional Research Ethics Board (*Sunnybrook – ID: 5107*) based on the limited risk of harm to participants, and adequate anonymization.

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None.

CRediT authorship contribution statement

A. Mutsaers: Project administration, Investigation, Methodology, Writing – original draft. **G.J. Li:** Formal analysis. **J.S. Fernandes:** Validation, Writing – review & editing. **S. Ali:** Investigation, Writing – review & editing. **E.A. Barnes:** Writing – review & editing, Investigation. **H. Chen:** Writing – review & editing, Investigation. **G.J. Czarnota:** Writing – review & editing, Investigation. **I. Karam:** Writing – review & editing, Investigation. **D. Moore-Palhares:** Writing – review & editing, Investigation. **I. Poon:** Writing – review & editing, Investigation. **H. Soliman:** Writing – review & editing, Investigation. **D. Vesprini:** Writing – review & editing, Investigation. **P. Cheung:** Writing – review & editing, Methodology, Investigation. **A.V. Louie:** Supervision, Methodology, Investigation, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctro.2024.100730.

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