Role of stereotactic body radiotherapy in gynecologic radiation oncology

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ABSTRACT

Stereotactic body radiotherapy (SBRT, also referred to as stereotactic ablative radiotherapy (SABR)) has been used in the treatment of primary and metastatic solid tumors, and increasingly so in gynecologic oncology. This review article aims to summarize the current literature describing the utility of SBRT in the primary, recurrent, and limited metastatic settings for gynecologic malignancies. The use of SBRT in both retrospective and prospective reports has been associated with adequate control of the treated site, particularly in the setting of oligometastatic disease. It is not, however, recommended as an alternative to brachytherapy for intact disease unless all efforts to use brachytherapy are exhausted. While phase I and II trials have established the relative safety and potential toxicities of SBRT, there remains a dearth of phase III randomized evidence, including the use of immunotherapy, in order to better establish the role of this technique as a method of improving more global outcomes for our patients with gynecologic cancers.

FUNDAMENTAL BASIS FOR STEREOTACTIC BODY RADIOTHERAPY (SBRT)

Radiation therapy is commonly integrated into combined modality treatment for many gynecologic cancers. In the modern era, the use of stereotactic body radiotherapy (SBRT, also referred to as stereotactic ablative radiotherapy (SABR)) has been used in a variety of solid tumors, and increasingly so in gynecologic oncology. By definition, SBRT consists of precisely delivered radiation in large dose fractions in 1–5 treatments, with limited dose delivered to the surrounding normal tissue. The first common use of stereotactic irradiation was in the context of intracranial disease (stereotactic radiosurgery), and the use of this technique was adapted extracranially as SBRT.[1] The first uses of SBRT in the extracranial setting occurred in Japan in the late 1990s, gaining traction in the USA and Europe in the early 2000s.[2] Since then, this technique has been adapted for the use of a wide array of clinical scenarios for both primary and metastatic tumors.

The basic principles of SBRT lie within radiobiology and physics. In order to achieve sufficient cellular injury to targets and spare normal tissue, there must be a fine balance of dose distribution and amount of radiation per treatment. Classically, radiation therapy is given in smaller fractions (1.8–2 Gy per fraction) over the course of 20–35 daily treatments, in order to maximize the differential ability of normal tissue to repair sub-lethal damage while still causing malignant cell death. SBRT, in contrast, reduces this to 1–5 total treatments, ranging from 24 Gy in a single fraction to 60 Gy in 3–5 fractions. These fractionation schemes vary depending on the goals of treatment, neighboring normal tissues, and provider/institutional protocols; however, all of these schedules aim to achieve biologic effective doses (BED) sufficient to control targets and remain below the threshold for normal tissue injury. Malignant and fast-growing tissues are less sensitive to fraction size, while most normal tissues are more sensitive. This is the historical rationale for why larger fraction sizes have been avoided, particularly when treating in close proximity to sensitive tissues.

This paradigm can be circumvented by more accurate radiation delivery techniques, both in the precision of how the treatment volume may be shaped to fit a given target (such as with the use of techniques such as intensity-modulated radiotherapy and volumetric-modulated arc therapy techniques), but also in the precision of imaging at the time of treatment delivery and patient immobilization. Many modern linear accelerators include 'on-board' imaging capabilities, which can confirm that the targets of treatment are encompassed by the irradiated volume while simultaneously ensuring that normal tissues are excluded (Figure 1). This imaging can be performed on a per-fraction basis, such that day-to-day variations in patient set-up and organ motion can be accounted for (Figure 2). When planning for SBRT, patient set-up includes an immobilization device that minimizes potential set-up errors during treatment delivery. This is coupled with evaluation of whether the patient can lie still during treatment, a crucial component when assessing patients in clinic for potential SBRT. There are also means of tracking and/or limiting respiratory motion, such that targets within mobile structures such as the lung and liver can be treated with much smaller margins. The combination of these two technical advancements—more conformal treatment plans and more accurate delivery—allows for increased sparing of normal tissues compared with that typically seen with standard fractionation (Figure 3).

In this review article we discuss the current and future directions of the use of SBRT in primary, recurrent, and oligometastatic gynecologic malignancies.

Figure 1 A modern linear accelerator with on-board imaging arms deployed. Opposite the treatment head, conventional 'portal' imaging of the treatment beam can be obtained with a mega-voltage detector panel (†). On the sides of the accelerator, a paired kilo-voltage X-ray source and detector panel (*) are oriented orthogonal to the treatment head. These can obtain plain films, fluoroscopic images and, when rotated 360°, a cone-beam computed tomography (CBCT) image for volumetric imaging of the patient in the treatment position. A ceiling mounted infrared camera (‡) can track respiratory motions of the chest wall to account for internal movement of targets and normal tissues.

SBRT IN THE MANAGEMENT OF PRIMARY AND LOCALLY RECURRENT DISEASE

Initial localized treatment of cervical cancers generally includes the use of brachytherapy boost after external beam. The role of SBRT in lieu of brachytherapy for those who have relative contraindications or lack of access to the procedure is an important topic of investigation.[3]

There have been few studies that have reviewed outcomes of patients who received SBRT boost in lieu of brachytherapy boost for a primary gynecologic malignancy (Table 1). A retrospective study including 25 patients with newly diagnosed cervical cancer treated with external beam radiotherapy followed by SBRT boost reported a 3-year local control rate of 80.9% with 20% of patients experiencing grade 3 toxicity including hematuria and hematochezia.[4] Patients included in this analysis were unable to undergo brachytherapy boost due to either anatomic issues (ie, narrow vagina or cervical stenosis), tumor size felt to be too large for adequate brachytherapy dose distribution, morbid obesity, or other medical co-morbidities precluding brachytherapy. The authors of this study conclude that although SBRT may not replace brachytherapy, SBRT may be a reasonable alternative if a patient is unsuitable for brachytherapy or if the procedure is not available. However, it is notable that there have been recent advances in the techniques in brachytherapy as well. Image-guided brachytherapy using three-dimensional imaging such as magnetic resonance imaging (MRI) for planning allows for highly precise and individualized treatment. A recent report from the multi-institutional prospective EMBRACE study of 1426 women using these techniques found a local control of 92%
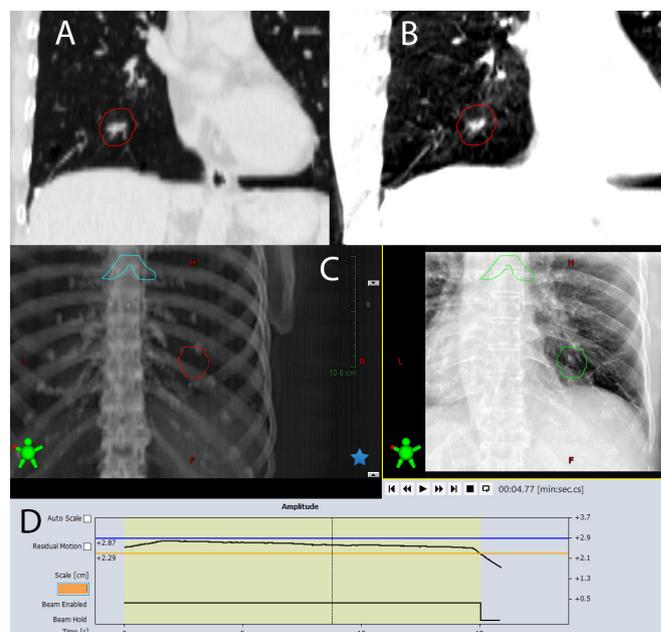

Figure 2 Images obtained during the treatment of an isolated lung metastasis from uterine cancer with no other sites of active disease. A computed tomographic (CT) image from the treatment plan with a planning treatment volume overlaid in red (A) is compared directly to a cone-beam CT (CBCT) image obtained at the time of treatment delivery (B) by a radiation oncologist at the time of each fraction. Live postero-anterior fluoroscopic images (C) can then be examined while the patient is instructed to hold their breath to limit motion of the target and nearby normal tissues. (D) A tracing of chest wall motion during both immediate pre-treatment imaging and treatment delivery to ensure that the motion is within the expected excursion (black line of tracing within the lower limit (orange line) and upper limit (blue line) during 15 s of treatment delivery).

at 5 years and 6.8% genitourinary, 8.5% gastrointestinal, and 5.7% vaginal toxicity, comparing favorably with SBRT studies.[5]

The role of SBRT as a boost to a primary tumor has also been studied in a few prospective trials. A phase I dose escalation trial from Japan including patients with stage IB1–IIIB cervical cancer ineligible for intracavitary brachytherapy treated with SBRT boost suggested 22.5 Gy in three fractions to be a safe regimen, although this dose is significantly lower than that routinely achieved with brachytherapy.[6] A phase II trial involving SBRT boost as an alternative to brachytherapy for patients with locally advanced cervical cancer demonstrated sub-optimal outcomes with a high rate of toxicity.[7] In this trial published by Albuquerque et al, patients were enrolled if they had declined brachytherapy, were deemed medically unfit to undergo the procedure, or would have required interstitial brachytherapy due to tumor extent but instead elected to forego this and enroll on trial. The 2-year local control was 70% and 2-year overall survival was 53%, with rates of grade 3 or higher late gastrointestinal toxicity of 27% at 2 years. The study closed early (15/21 patients received treatment) due to poorer than expected toxicity outcomes for patients with large tumor volume (>95 mL). The authors further concluded that SBRT may be useful in patients with small cervical tumors (approximately <95 mL). In general, the use of SBRT for primary gynecologic tumors in lieu of
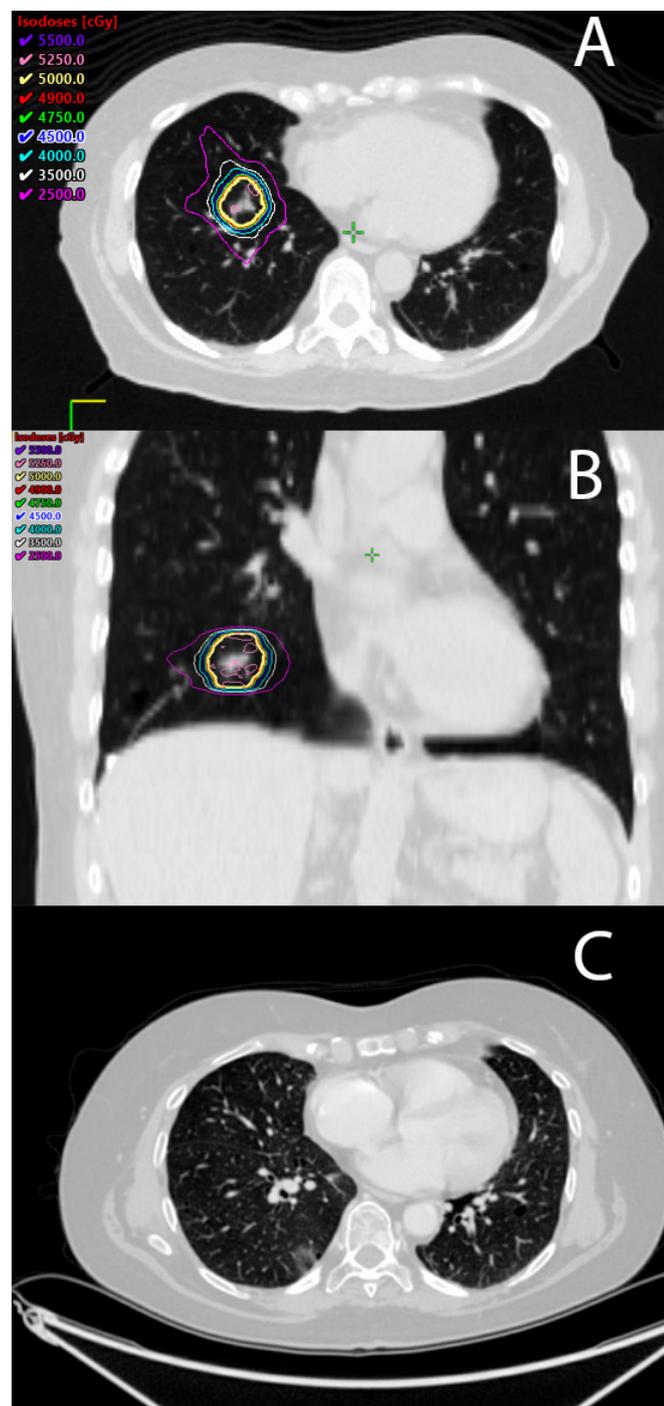
Figure 3 Clinical example of stereotactic body radiotherapy (SBRT) used to treat a solitary lung metastasis from recurrent and metastatic uterine cancer. At the time of treatment the patient had undergone systemic therapy and a single lung nodule was the only site of disease on imaging, which had demonstrated progression on multiple prior chest computed tomographic (CT) images. A treatment plan was developed to deliver 50 Gy in five fractions over 2 weeks (axial image (A) and coronal image (B) of the SBRT plan). The patient tolerated this course with no symptoms. (C) On the follow-up CT at 6 months, the pulmonary nodule was no longer visible and no new sites of disease were seen. She remained asymptomatic at last follow-up 1 year after SBRT.

brachytherapy (when available) is not recommended due to these sub-optimal results unless all efforts to use brachytherapy have been exhausted.[8]

There is limited information on the use of SBRT in the setting of recurrent tumors that have previously been irradiated. In a study that reported five cases of locally recurrent gynecologic cancers who received SBRT following definitive radiation therapy, there were no grade 3 toxicities reported and at least temporary local control was achieved (6 months at shortest and 19 months at longest).[9] There is, however, a lack of data, both retrospectively and prospectively, that specifically investigates the role of SBRT at the primary site for locally recurrent gynecologic cancers following definitive radiotherapy, likely due to the heterogenous nature of these scenarios. As optimal external beam and brachytherapy are designed to deliver a high dose of radiation directly to the cervix, treating a recurrence with additional (and often less) radiation is not likely to result in a better outcome. Thus, primary surgical resection with consideration of intra-operative radiation therapy is a preferred approach for these cases. However, given the improvement of pelvic control with modern upfront radiotherapy techniques, including image-guided brachytherapy, these cases may become more infrequent.

However, in a parallel RetroEMBRACE observational study of image-guided brachytherapy, 222 of 731 patients developed treatment failure, with 57% being distant failure alone and 23% having both pelvic and distant failure.[10] The authors conclude that, while excellent outcomes for primary disease control are achievable, there is a need for improved management of distant disease in order to optimize patient survival.

SBRT AND THE OLIGOMETASTATIC STATE

Oligometastatic disease is a term that was coined in the 1990s by Weichselbaum and Hellmann, referring to a limited number (generally <5 sites) of metastatic disease.[11] They posit that there is a favorable sub-group of patients with metastatic disease that may benefit from localized metastases-directed ablative therapy, including surgical resection[12 13] and SBRT.[14–16]

The use of radiation therapy directed to all sites of metastatic disease has been explored in colorectal,[17] lung,[18] and breast cancers,[19] with long-term survival rates ranging between 15% and 30%. In 2014, the phase I NRG-BR001 clinical trial began enrolling patients with breast, prostate, or non-small cell lung cancer and ≤4 metastases. In the 35 patients included in the results of the trial, there was no dose-limiting toxicity.[20] The safety of SBRT in lung[21] and liver metastases[22] has also been established in multi-center phase I/II trials, with 2-year local control of 96% and 92% of the treated lung and liver metastatic lesions, respectively. A randomized phase II/III trial of the use of ablative radiotherapy and/or surgical resection in breast cancer metastases, NRG BR002, opened in 2014 and data reporting is still in process. The SABR-COMET trial randomized 99 patients across multiple solid tumor sites with 1–4 metastases to ablative radiotherapy versus no radiotherapy. Of note, only two patients with primary gynecologic primaries were included. In this trial, systemic therapy was acceptable at the discretion of the prescribing medical oncologist and/or multi-disciplinary tumor board's recommendation in both arms of the randomization. The results of this trial revealed a trend

Table 1 Studies using stereotactic body radiotherapy (SBRT) for primary or centrally recurrent disease in the pelvis

Study	Year of publication	Primary sites	Primary vs recurrent	Type of study	Patients included (n)	Notable outcomes
Albuquerque et al[7]	2019	Cervix	Primary	Phase II prospective	15	The study closed early (with 15/21 patients having received treatment) due to poorer than expected outcomes. 2-year LC 70%; 2-year OS 53%. Grade 3 or higher late GI of 27% at 2 years
Haas et al[48]	2012	Cervix	Primary	Retrospective	5	1 year LC 100%. No grade 3 or higher toxicities
Hsieh et al[49]	2013	Cervix	Primary	Retrospective	9	2 grade 3 toxicities (thrombocytopenia and diarrhea). 3-year LC 77.8%
Ito et al[6]	2019	Cervix	Primary	Phase I prospective	6	22.5 Gy in three fractions determined to be tolerable fractionation with no dose-limiting toxicities
Kubicek et al[50]	2013	Cervix (n=7), uterine (n=2), vaginal (n=2)	Primary	Retrospective	11	Median follow-up for surviving patients was 420 days. 8/11 patients alive at last follow-up, 1/11 with local recurrence. Two patients had acute toxicity (grade 2 dysuria and grade 2 GI); one patient with late toxicity (grade 3 GI bleed)
Lee et al[4]	2021	Cervix	Primary	Retrospective	25	3-year LC 80.9%, PFS 40.9%, OS 77.1%. Five (20%) grade 3 toxicity (3 genitourinary, 3 GI)
Marnitz et al[51]	2013	Cervix	Primary	Prospective	11	Five grade 3 hematologic toxicities, one grade 4 toxicity (leukopenia). No local recurrence at median follow-up of 6 months
Kunos et al[9]	2009	Cervix (n=1), uterine (n=1), ovarian (n=3)	Recurrence	Retrospective	5	Five case reports of locally recurrent gynecologic cancers treated with SBRT. No grade 3 toxicities reported

BED, biologic effective dose; GI, gastrointestinal; LC, local control; OS, overall survival; PFS, progression-free survival; SBRT, stereotactic body radiotherapy.

towards improved overall survival (HR 0.57 (95% CI 0.30 to 1.10), p=0.09) and disease-free survival (HR 0.47 (95% CI 0.30 to 0.76), p=0.0012).[15] In the long-term results of this trial, the difference in overall survival was more pronounced than the initial analysis at 42.3% (95% CI 6% to 34%) in the SABR arm and 17.7% (95% CI 28% to 56%) in the control arm (stratified log-rank p=0.006).[23] The phase II ORIOLE randomized trial of SABR versus observation in oligometastatic prostate cancer found similar results of improved progression-free survival (PFS) (HR 0.30 (95% CI 0.11 to 0.81), p=0.002) in the ablative therapy arm.[24] An example of a

treatment plan for lung metastases treated with SBRT is shown in Figure 2.

The use of systemic therapy with consolidative or adjuvant local therapy has also been investigated in randomized trials. The EORTC 40004 phase II trial randomized patients with liver metastases to systemic therapy with radiofrequency ablation to the metastatic lesions versus systemic therapy alone. The results of this study showed improved PFS (HR 0.57 (95% CI 0.38 to 0.85), p=0.005) and overall survival (HR 0.58 (95% CI 0.38 to 0.88), p=0.01) in the systemic therapy and radiofrequency ablation group.[25] In another phase II study investigating the use of consolidative radiotherapy therapy in non-small cell lung cancer with ≤3 metastatic lesions, long-term data showed improved PFS (14.2 months with consolidative therapy vs 4.4 months with maintenance therapy or observation, p=0.022) and overall survival (37.6 months with consolidative therapy vs 9.4 months, p=0.034), compared with patients on maintenance systemic therapy alone.[26]

SBRT IN GYNECOLOGIC OLIGOMETASTASES

The role of SBRT in treating gynecologic oligometastatic disease has not yet been clearly defined. There are minimal published prospective studies investigating the role of SBRT in oligometastatic gynecologic malignancies (Table 2). Despite this lack of data, a recent survey published in 2020 of an international group of radiation oncologists regarding the use of SBRT in gynecologic malignancies indicated that clinicians would consider SBRT for nodal (81%) or primary recurrent disease (91%).[27] An important consideration when reviewing this literature is acknowledging variations in tumor biology and patterns of disease among gynecologic cancers. For example, primary ovarian cancers typically spread via intra-peritoneal shedding while cervical cancer tends to spread by direct extension.[28] However, following treatment of a localized cervical cancer, patterns of failure tend to favor distant metastases (approximately 50% following standard treatment).[29] In a Korean retrospective study including over 1300 patients with primary cervical cancer investigating patterns of treatment failure, of those with recurrence 59.5% were distant while 21.5% recurred both locally and distantly.[30] The recently reported RetroEMBRACE observational study found a similar pattern in the 222 recurrences among 731 women treated; 57% experienced distant recurrences and 23% had both pelvic and distant components.[9] The authors conclude that, while excellent outcomes for primary disease control are achievable, there is a need for improved management of distant disease in order to optimize patient survival.

There is also a potentially curable sub-set of patients with metastatic cervical cancer to the supraclavicular lymph node region. Retrospective studies have analyzed survival outcomes for this specific patient population. In two Korean studies including women with metastatic cervical cancer to the supraclavicular nodes, 3-year survival was reported to be between 49% and 67%.[31] [32] A study from Washington University in St Louis in 24 women with supraclavicular disease treated with definitive chemoradiation found 5-year survival of 22%.[33] In these studies, patients received definitive doses of radiotherapy to the pelvis and involved supraclavicular nodes with concurrent chemotherapy. However, these series used

conventionally fractionated radiation and the role for SBRT in this clinical scenario is not well defined.

There are a few retrospective studies that investigated outcomes of ovarian oligometastatic disease. In one study reporting 82 patients diagnosed with ovarian cancer with 156 metastatic lesions treated with SBRT, control of the treated lesions at 2 years was found to be 68% and the median systemic treatment-free interval after SBRT was 7.4 months.[34] Another retrospective study including 35 patients with oligometastatic ovarian cancer treated with SBRT yielded a 2-year lesional control of 80%, with a higher dose (BED >35 Gy) associated with improved control.[35] A retrospective study including 20 patients (10 ovarian and 10 uterine) with a single metastatic site treated with SBRT revealed that patients with smaller tumors (<50 mL) had improved local control (5-year local control <50 mL 100% vs >50 mL 65%; p<0.02).[36]

In a prospective phase II trial evaluating the efficacy of SBRT in 49 patients with metastatic gynecologic tumors, there was a 96% response rate in the treated lesions with a median PFS of 7.8 months and overall survival of 20.2 months.[37] This was followed by the phase I trial by Kunos et al in which carboplatin and gemcitabine were delivered concurrently with SBRT to 12 patients, demonstrating that the combination therapy was tolerable but with notable grade 3 (n=10) and 4 (n=2) toxicities including neutropenia and hypokalemia, although this is likely more attributable to chemotherapy than to SBRT.[38] There are a number of ongoing studies exploring the safety and efficacy of SBRT in oligometastatic gynecologic cancer including a phase I trial (NCT03325634) of patients with recurrent ovarian or uterine cancer with ≤3 active sites of disease and a recently closed phase I trial (NCT0258293) reporting feasibility of MRI-guided SBRT to ≤3 sites of metastatic ovarian cancer.

A 2017 systematic review by Mendez et al outlined the data regarding the role of radiotherapy for gynecologic malignancies and concluded that local control and toxicity seemed to be acceptable with SBRT to both primary and metastatic tumors.[39] A total of 189 patients in six studies had pelvic and para-aortic lymph nodes treated with SABR with a combined local control of 83% and grade 3–4 gastrointestinal toxicity in 3.8% of patients.[40–45] In a recent systematic review article by Yegya-Raman et al, the authors compiled and analyzed 16 unique studies, either retrospective or prospective, that included SBRT for oligometastases from gynecologic origin.[28] Six hundred and sixty-seven patients and more than 1000 metastatic lesions were identified, with the most common primary site being ovarian (57.6%). Overall, the authors noted that local control ranged from 70% to 100% in studies that reported outcomes, and that disease progression often occurred outside the SBRT field. Of the studies included, 12 allowed for regional nodal metastases to be included as a site of oligometastatic disease and, of the sites treated, 64% were nodal metastases. There appeared to be a range (2–83%) of grade 3 toxicities in seven of the 16 included studies,[37 38 40 41 46 47] as well as four grade 4 toxicities (ranging from 2% to 8%) in three of the reported studies.[37 38 40] Grade 3 toxicities included gastrointestinal (duodenal ulcer, esophagitis, and diarrhea), hematologic (neutropenia, thrombocytopenia, and leukopenia), and genitourinary (hemorrhagic cystitis), and grade 4 toxicities included neutropenia, hypokalemia, and hyperbilirubinemia. The use of concurrent chemotherapy in several of these studies is

Table 2 Studies using stereotactic body radiotherapy (SBRT) for limited distant metastatic disease

Study	Year of publication	Primary sites	Type of study	Patients included (n)	Notable outcomes
Ovarian					
Aghdam et al[36]	2020	Ovarian and uterine	Retrospective	20	Smaller tumors (<50 cm^3) had improved LC (5-year LC for small vs large volume 100% (p<0.01) and 65% (p<0.02))
Lazzari et al[34]	2018	Ovarian	Retrospective	82	156 metastatic lesions treated with SBRT had 2-year LC of 68% and median systemic treatment-free interval after SBRT of 7.4 months
Kowalchuk et al[35]	2020	Ovarian	Retrospective	35	2-year LC of 80% with a BED >35 Gy to be predictive of improved LC
Macchia et al[45]	2020	Ovarian	Retrospective	261	Age ≤60, lymph node lesion ≤18 cm^3 treated to BED >70 Gy had the greatest complete response
Cervix					
Hou et al[52]	2019	Cervix	Retrospective	19	2-year PFS 37%, 2-year OS 77%
Ning et al[46]	2018	Cervix	Retrospective	38	2-year PFS 48%, 2-year OS 74%. One grade 3 toxicity (esophagitis)
Park et al[40]	2015	Cervix	Retrospective	85	2-year PFS 43%, 2-year OS 58%. Two late grade 4 toxicities (rectovaginal fistula)
Mixed					
Kunos et al[37]	2012	Ovarian (n=25), uterine (n=14), cervix (n=9), vulvar (n=2)	Phase II	50	Response rate of 96%; median PFS 7.8 months and OS 20.2 months. One grade 4 toxicity (hyperbilirubinemia)
Kunos et al[38]	2015	Ovarian (n=7), uterine (n=4), primary peritoneal (n=1)	Phase I	12	Safety of concurrent chemotherapy (carboplatin/gemcitabine) with concurrent SBRT. Grade 4 neutropenia (n=1), hyperkalemia (n=1)
Mesko et al[47]	2017	Ovarian (n=15), uterine carcinoma (n=8), carcinosarcoma (n=1), cervix (n=2), vagina (n=2)	Retrospective	28	Favorable vs unfavorable response associated with tumor size (17.2 vs 57.6 mm, p=0.0044) and BED (79.0 vs 59.6 Gy, p=0.027). One grade 3 toxicity
Onal et al[53]	2020	Ovarian (n=8), cervix (n=21)	Retrospective	29	1- and 2-year local control rates for all patients were 84% and 84%, respectively. Complete response after SBRT were prognostic for survival

Continued

Table 2 Continued

Study	Year of publication	Primary sites	Type of study	Patients included (n)	Notable outcomes
Seo et al[41]	2015	Mixed population with PA nodal oligometastases (52/88 of gynecologic origin)	Retrospective	88	5-year LC 92%; 5-year OS 52%

BED, biologic effective dose; LC, local control; OS, overall survival; PA, para-aortic; PFS, progression-free survival; SBRT, stereotactic body radiotherapy.

likely responsible for the hematologic and hypokalemia toxicities seen, given the small irradiated volumes characteristic of SBRT.[37 38]

SBRT, SYSTEMIC THERAPY, AND IMMUNOTHERAPY

A major shift in the treatment paradigm within oncology is the use of immunotherapy in addition to other systemic therapy and radiation therapy. A synergistic effect between SBRT and immunotherapy may be possible, although it is not yet proven clinically. It is hypothesized that release of antigens due to SBRT may enhance the efficacy of immunotherapy. Additionally, typical radiation plans for pelvic treatment may include a large volume of bone marrow within the pelvis and lumbar spine, leading to acute and late hematologic toxicities. Since SBRT uses much smaller irradiated volumes, these techniques may be less immune suppressive and allow for better immune system activation when combined with these agents.

There are now a number of ongoing clinical trials that are aiming to investigate the safety and response rate of targeted agents and immunotherapy in combination with SBRT. A phase I trial (NCT03452332) will assess the safety of SBRT in addition to tremelimumab and durvalumab in the treatment of ≤2 oligometastases from cervical, vaginal, or vulvar cancer. A phase II trial (NCT03614949) is assessing the response rate of SBRT followed by atezolizumab in ≤2 oligometastases in recurrent, persistent, or metastatic cervical, vaginal, or vulvar cancer. Finally, another phase II trial (NCT03192059) is assessing the response rate of an index lesion from advanced or refractory cervical cancer, endometrial carcinoma, or uterine sarcoma plus at least one oliogmetastasis treated with an immunomodularity cocktail followed by pembrolizumab and SBRT.

CONCLUSION AND FUTURE DIRECTIONS

The utility of SBRT in the treatment of local and distant gynecologic malignancies remains an active area of investigation. It is evident that there is a body of literature that supports the use of SBRT in both the retrospective and prospective setting to achieve control of the treated site, particularly in the setting of limited metastatic disease. However, it is not recommended as an alternative to brachytherapy for intact disease unless all efforts to use brachytherapy are exhausted. While phase I and II trials have established the relative safety and potential toxicities of SBRT, there remains a dearth of phase III randomized evidence, including the use of immunotherapy, in order to better establish the role of this technique as a method of improving more global outcomes for our patients with gynecologic cancers.

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