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MINIREVIEWS

Use of stereotactic radiosurgery in the treatment of gynecologic malignancies: A review

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Abstract

Recent retrospective studies have reported the use of stereotactic radiosurgery (SRS) in the treatment of gynecologic cancers. SRS uses real-time imaging and high dose radiation beams attached to precise robotic arms to target malignant lesions while sparing normal tissue. The purpose of this review is to examine the indications for SRS in gynecologic oncology, review the current literature regarding the use of SRS in gynecologic cancers, and identify future directions for research in this area. Literature on stereotactic radiosurgery was reviewed using the PubMed search engine. Articles written in English from 1993-2013 were reviewed, and 20 case series and clinical trials were included. The safety and efficacy SRS has been demonstrated in all gynecologic disease sites including cervical, endometrial, vulvar, vaginal, and ovarian cancers. Indications for its use include non-central pelvic recurrences in previously irradiated patients, complex or non-resectable disease recurrence, and solitary brain metastases. Toxicities are usually mild, though grade 3-4 toxicities have been reported. SRS is a promising second line treatment modality for patients with primary or recurrent disease who cannot undergo standard surgical or radiation therapy. Further research is required to determine optimal dosing and fractionation schedules, delineate appropriate patient populations, and assess longterm morbidity and survival.

Key words: Stereotactic radiosurgery; Stereotactic body radiotherapy; Gynecologic oncology

Core tip: Stereotactic radiosurgery is a novel treatment modality in gynecologic oncology. Its use has been reported for inoperable primary tumors, recurrent tumors in or near irradiated fields, and isolated pelvic nodal metastases. Associated toxicities are usually mild. Though further research is needed to establish the role of SRS in gynecologic oncology, it represents an important second line therapy in appropriately selected patients.

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INTRODUCTION

Stereotactic radiosurgery (SRS) is an emerging technology in the treatment of gynecologic cancers. It targets malignant lesions using real-time imaging in combination with high dose radiation beams attached to precise robotic arms. First used in the treatment of intracranial lesions, technological advancements in radiation and

image-guidance have allowed for its use in a variety of extracranial locations. Because SRS can focus on targets with sub-millimeter accuracy, it has been used for inoperable primary tumors near radiosensitive tissues, recurrent tumors in or near irradiated fields, and isolated pelvic nodal metastases. Its precise beams spare normal tissues and result in decreased toxicity when compared to conventional radiotherapy.

SRS is of particular interest in women with gynecologic malignancies, since many of these patients will recur in or near previously irradiated tissues, inoperable anatomic regions, or sites inaccessible to traditional radiation therapy[1]. Recent retrospective studies have reported on the safety and efficacy of SRS in the treatment of gynecologic cancers. The purpose of this review is to examine the indications for SRS in gynecologic oncology, review the current literature regarding the use of SRS in gynecologic cancers, and identify future directions for research in this area.

STEREOTACTIC RADIOSURGERY

Stereotactic radiosurgery combines the complex dose distributions of intensity modulated radiation therapy (IMRT), the accuracy, reproducibility, and high doses of radiosurgery, and the fractionation of external beam radiation therapy to build a technique capable of treating complex abdominal-pelvic tumors. In this method, linear accelerators generate multiple X-ray beams, which can precisely target malignant tissues using advanced treatment planning, real-time imaging, and/or fiducial marker localization. The precision of these X-ray beams allows delivery of high doses to the tumor while sparing normal tissues. Doses are usually divided into 1-5 fractions given over 1-2 wk. Body immobilizers may be used to maintain spatial relationships during treatment sessions. Real-time image guidance ensures accurate tumor location, as abdominal and pelvic structures can exhibit substantial inter- and intra-fraction movement.

SRS has been utilized for lung, liver, pancreatic, renal, prostate, spinal, and pelvic tumors. It was first described for use in liver and lung lesions in the 1980s and has been used for gynecologic cancers since 2006. Twelve, small retrospective case series and one phase II clinical trial have described single institution experiences with SRS in the treatment of uterine, cervical, vaginal, vulvar, and ovarian cancers (Table 1). These series include a combined 291 patients who have undergone SRS for distant, local, lateral pelvic, or isolated pelvic node recurrences or as a substitute for brachytherapy in primary disease. One study specifically reported hematologic toxicities associated with SRS. Populations in these studies were heterogeneous, and varying doses and fractionation schedules have been described. Differences in reporting these results make it difficult to calculate a composite rate of survival, loco-regional control, or disease response.

The largest population was described by Kunos *et al*[1], in a phase II clinical trial evaluating the safety and efficacy of SRS in 50 patients with recurrent cervical, endometrial, ovarian, and vulvar cancer. SRS was used to deliver 24 Gy in 3 fractions to a clinical target volume (CTV) that included the gross tumor volume (GTV) as well as surrounding fluorodeoxyglucose (FDG)-avid areas. The positron emission tomography (PET) images were overlaid and co-registered with computed tomography (CT) scans in order to accurately target the entire tumor site. One patient had a complete response, and the overall response rate (defined as complete response, partial response, or stable disease without progression) was 96%. Sixty-two percent of patients showed clinical benefit at 6 mo. Most toxicity was mild, though one patient did experience grade 4 hyperbilirubinemia and another developed an enterovaginal fistula. The study authors concluded that SRS was safe and efficacious for patients with recurrent gynecologic malignancies[1]. All other data are derived from case series, and no controlled trials have been published. While studies mostly describe patients with endometrial or cervical primaries, SRS has been utilized for all gynecologic disease sites.

CERVICAL CANCER

Since radiation therapy is commonly used in cervical cancer, SRS is an attractive option for inoperable patients with primary or recurrent disease. Overall, 76 cases describing the use of SRS in cervical cancer have been published in 9 series. Four papers describe its use in the primary setting (usually as a substitute for brachytherapy), while others report its use for loco-regional, para-aortic node, or pelvic side-wall recurrences. All series included only patients who were unsuitable or unwilling to undergo other treatment modalities such as brachytherapy or surgical resection.

The largest series of patients treated with SRS for primary disease was published by Hsieh *et al*[2] in 2013. They described 9 patients with locally advanced cervical cancer who were treated with SRS (*via* helical tomotherapy) as a replacement for brachytherapy boost after the standard dose of EBRT and concurrent cisplatin. These patients were unable to undergo the recommended brachytherapy due to anatomic factors or medical comorbidities. Though three-year actuarial loco-regional control was 77.8%, three-year disease free survival was only 28.6%. Distant metastases were the most common pattern of failure, suggesting efficacy of SRS in controlling central pelvic disease[2]. Mollà *et al*[3] reported similar results when treating primary disease. Their population included seven cervical cancer patients who underwent EBRT with SRS boost due to high-risk disease after initial surgical management. Only one patient recurred within the 12-month follow up period; however, actuarial values were not calculated. Toxicities were low in both series, consisting mostly of grade 1 or 2 sexual and GI symptoms. However, one patient did have grade 3 diarrhea, and another had grade 3 thrombocytopenia. One patient with stage 4A disease developed a rectovaginal fistula. Four patients

Table 1 Summary of case series of stereotactic radiosurgery

Ref.	*n*	Cancer types	Disease setting	Dose	Response/ control rate	Survival	Grade 3/4 toxicities	Patterns of failure
Molla *et al*[3]	16	Cervical (7) Uterine (9)	Primary (stage 1-3) and recurrence	EBRT 45 GyT SRS 14-20 Gy/2-5 fractions +/- para-aortic boost (2 pts)	15 pts NED at 12.6 mo (1 recurrence)	Not reported	Rectal bleeding (1)	Not reported
Deodato *et al*[13]	11	Ovarian (4) Cervical (4) Uterine (3)	Recurrence	SRS 20-30 Gy/4-6 fractions	83.3% overall response rate 63% recurrence at 19 mo	Not reported	None	Systemic/distant progression (*n* = 4) Local progression (*n* = 1) Local and systemic progression (*n* = 1)
Guckenburger *et al*[7]	19	Cervical (12) Uterine (7)	Recurrence	EBRT 50 Gy SRS 15 Gy/3 fractions +/- vaginal BT (3 pts)	3 yr local control rate 81%	Median OS 25 mo, PFS 16 mo	Intestino-vaginal fistula (2) Small bowel ileus (1)	Systemic progression (*n* = 7) Local tumor progression (*n* = 1) Comorbid illness (*n* = 1) Unknown (*n* = 1)
Choi *et al*[10]	30	Cervical (28) Uterine (2)	Recurrence	EBRT 27-45 Gy SRS 13-45 Gy/1-3 fractions	4 yr local control rate 67.4%	Median PFS 32 mo	Various (5)	Locoregional failure (13.8%) Distant mets (10.3%) Local and distant failure (6.9%)
Dewas *et al*[9]	16	Cervical (4) Uterine (1) Rectal (4) Anal (6) Bladder (1)	Recurrence	EBRT 36-66 Gy (3 pts) SRS 36 Gy/6 fractions	1 yr local control rate 51.4%	Median OS 11.5 mo (DFS 8.3 mo)	None	Not reported
Haas *et al*[6]	6	Cervical (6)	Primary (stage 3B-4)	EBRT 45 Gy SRS 19.5-20 Gy/ 3-5 fractions +/- 50.4-61.2 Gy IMRT boost (5 pts)	100% local control at 14 mo	100% at 14 mo	None	Not reported
Hsieh *et al*[2]	9	Cervical (9)	Primary (stage 3B-4A)	EBRT 50.4 Gy SRS 15-27 Gy/ 5-9 fractions	3 yr local control rate 77.8%	Median OS 13 mo	Diarrhea (1) Thrombocytopenia (1) Rectal bleeding (3) Rectovaginal fistula (1)	Distant metastases (44%)
Hsieh *et al*[2]	31	Uterine (31)	Primary (stage 1B-3C)	IMRT or SRS *via* HT 45-50.4 Gy/25-28 fractions ICBT 4.5-5 Gy x 2-6 fractions	Not reported	Median OS 21 mo	None	Distant metastases
Kubicek *et al*[19]	11	Cervical 7) Uterine (2) Vaginal (2)	Primary (stage 2-3C) and recurrence	EBRT or IMRT 45-50.4 Gy SRS 5-27.5 Gy/1-5 fractions	Not reported	73% overall survival at follow-up	Rectal bleeding (1)	Not reported
Kunos *et al*[20]	3	Vulvar (3)	Recurrence	SRS 24 Gy/3 fractions	Not reported	1-3 mo PFS	None	Out of field recurrence
Kunos *et al*[15]	5	Endometrial (1) 0varian (3) Cervical (1)	Recurrence	SRS 5-8 Gy x 3-5 fractions	Not reported	Not reported	Fatigue (1)	Distant metastases
Kunos *et al*[1] Phase Ⅱ trial	50	Cervix (9) Endometrial (14) Ovarian (25) Vulvar (2)	Recurrence	SRS 24 Gy/3 fractions	6 mo clinical benefit 68%	Median OS 20.2 mo	Hyperbilirubinemia (1) Enterovaginal fistula (1)	Out of field recurrence (62%)

EBRT: External beam radiation therapy; SRS: Stereotactic radiosurgery; NED: No evidence of disease; BT: Brachytherapy; OS: Overall survival: HT: Helical tomotherapy; IMRT: Intensity modulated radiation therapy; PFS: Progression free survival.

had rectal bleeding following treatment[3]. Two other papers by Hsieh *et al*[4,5] report similar findings in this patient population, and Haas *et al*[6] described 100% disease free survival at 14 mo in a series of six patients treated with SRS boost for primary disease.

These rates of local control exceed that of brachytherapy in many studies; however, the small sample sizes, short duration of follow-up, and lack of a brachytherapy control group make it impossible to compare the two treatments. Still, the authors of these papers suggest that SRS could be considered as an alternative to brachytherapy boost, especially in patients unsuited for brachytherapy.

SRS has been more frequently described for recur-

Figure 1 CyberKnife (left) and GammaKnife (right). The CyberKnife device employs a mobile frame to radiate tumors in complex locations. The GammaKnife provides head immobilization for more accurate radiation delivery.

rent disease. Guckenberger *et al*[7] describe its use in 12 patients with local recurrences of cervical cancer. Six patients in this study (which included patients with endometrial and cervical cancer) had undergone previous radiation, though most had received only vaginal brachytherapy. The majority of patients had been surgically treated for their primary disease. Those who had not had previous EBRT underwent standard external radiation at a dose of 45 Gy followed by a SRS boost using 14-20 Gy in 3 fractions. Patients previously treated with external beam radiation underwent only SRS. Loco-regional control was again excellent, with 81% loco-regional control at 3 years. Overall 3-year survival was 34%, and systemic disease progression remained the most common pattern of failure[7]. This survival rate is similar to that of patients who undergo brachytherapy boost after EBRT for recurrent disease.

Interestingly, while pelvic sidewall recurrences carry a poor prognosis in patients treated with brachytherapy boost, location was not found to be a prognostic factor for patients treated with SRS[8]. Dewas *et al*[9] included four cervical cancer patients in their series describing SRS for lateral pelvic recurrences of cervical, uterine, anal, rectal, and bladder cancers. In this study, previously irradiated patients were treated with CyberKnife SRS (36 Gy in 6 fractions) for lateral pelvic masses (Figure 1). While disease free survival remained relatively low (8.3 mo), the authors argued that this treatment delayed local progression, as these recurrences would usually progress much more rapidly, improving quality of life. No grade 3 or higher toxicities were noted, and self-reported pain scores were improved after treatment. However, results should be interpreted with caution, as none of these patients exhibited unequivocal response. Favorable response was reported based on decreased uptake of contrast material on follow up PET studies[9]. Further research is needed to determine whether SRS is superior to alternate radiation modalities in patients with lateral pelvic recurrences.

Another clinical challenge in recurrent cervical cancer occurs in patients with isolated, unresectable, para-aortic nodal recurrence. Though this type of recurrence is rare, it is associated with a poor prognosis and high post-treatment morbidity due to the radiosensitivity of surrounding organs, particularly the small bowel. Because of the precision of its radiation beams, SRS could be an excellent treatment modality for this type of recurrence. Choi *et al*[10] described their experience in 28 patients with cervical cancer recurrence confined to para-aortic nodes. These patients received EBRT followed by SRS boost with 33-45 Gy in 3 daily fractions. Twenty-five patients received cisplatin before, during, or immediately after their radiation courses. Four year overall survival was 50.1%, and 96.5% of patients had at least partial response. Median time to disease progression was 32 mo. Though this population is small, SRS appears to be associated with improved overall survival, fewer toxicities, and shorter treatment times when compared for EBRT for nodal para-aortic recurrence[11,12].

In combination, these reports indicate that SRS may be a promising therapeutic modality for primary and recurrent cervical cancer, especially in patients who have undergone previous radiation and/or are not candidates for surgical resection. Further studies are needed to clarify patient populations most likely to benefit from SRS. The role of concurrent chemotherapy with SRS is also an important area of research, as distant metastases are the most common sites of failure.

ENDOMETRIAL CANCER

SRS has been similarly studied in endometrial cancer. Seventy cases of SRS use for primary or recurrent endometrial cancer have been described in nine unique series. However, dosing regimens are not uniform, and study populations are heterogeneous. SRS has been used as a substitute for both EBRT and brachytherapy boost after

surgical therapy for high-risk disease, as well as in the treatment of recurrent endometrial cancer. It has also been used as a substitute for IMRT, due to it's improved accuracy and ability to target higher doses of radiation to precise areas of tissue.

The largest series of SRS in the primary setting was published by Hsieh *et al*[2]. They reported 31 cases of FIGO stage I B to ⅢC uterine cancer, in which either SRS or IMRT was used as a substitute for EBRT after surgical staging for primary disease. IMRT or SRS was followed by vaginal brachytherapy in all patients. Two patients received concurrent cisplatin. This study is unique in that it is the only study that has compared SRS to another treatment modality. However, the study was not powered to detect statistical differences between the groups. While the study found no differences in overall survival or toxicity in SRS when compared to IMRT, SRS did provide significantly better critical organ sparing for the rectum, bladder, femoral heads, and intestines when compared to IMRT using dose-volume histograms. One cervical stump failure occurred in each group, and no grade 3 or 4 toxicities were noted[2].

SRS has also been studied as a substitute for brachytherapy in patients with primary endometrial cancer. Mollà *et al*[3] included nine patients with FIGO stage Ⅰ-Ⅲ uterine cancer in their series describing SRS boost after primary or post-operative EBRT. As described above, patients received 45 Gy EBRT or IMRT followed by 14-20 Gy SRS, usually following surgical treatment for either endometrial or cervical cancer. While most subjects had primary disease, two patients were enrolled due to local relapse. Patients underwent therapy at varying doses and fractionations. At 12-month median follow up, no recurrences were reported for the endometrial cancer group. Mostly grade 1 or 2 toxicities were noted, though one of the patients with recurrent endometrial cancer experienced persistent (grade 3) rectal bleeding 18 mo after re-irradiation at the vaginal vault[3].

SRS is more commonly used in the setting of recurrent endometrial cancer, especially in previously irradiated patients. Both Guckenberger *et al*[7] and Deodato *et al*[13] have published separate series describing the use of SRS for distant or local recurrences of endometrial and cervical cancers. Favorable rates of local control were demonstrated, though statistics for cervical vs. uterine cancers were not separately reported. Both series were small, including only seven and three endometrial cancer patients, respectively[7,13]. Two patients with isolated para-aortic nodal recurrences of endometrial cancer were also included in the above-mentioned study by Choi *et al*[10] with results as described above. While it is likely that results from cervical cancer patients could be extrapolated to those with endometrial cancers, it is difficult to draw conclusions with these small patient populations. Study authors have suggested that SRS could benefit patients with pelvic or para-aortic node recurrences who are not candidates for exenteration or salvage radiotherapy; however, further studies are needed to confirm these results and delineate optimal SRS dosing and fractionation.

OVARIAN CANCER

While the use of radiation therapy is much more common in endometrial and cervical cancers, SRS has also been used in the treatment of recurrent or non-operative ovarian cancers. Higginson *et al*[14] describe the use of SRS for patients with isolated lung metastasis, para-aortic nodes, or vaginal cuff recurrences after primary surgery and adjuvant therapy.

Kunos *et al*[15] included three cases of ovarian cancer in a 2009 report of their single-institution experience with SRS. These cases involved patients with multiple local and distant recurrences treated with multiple courses of chemotherapy, prior radiation, and/or surgeries. One patient with FIGO stage ⅢC papillary serous cancer received primary surgery followed by two differing chemotherapy courses, as well as a repeat operation with intra-operative radiation before opting for SRS in the place of pelvic exenteration for a third relapse of her cancer. Stable disease remained after radiotherapy and the patient was without evidence of progression for 9 mo, treated with concurrent bevacizumab and cyclophosphamide. Another patient was free of disease at 10 mo after SRS was used to treat a persistent vaginal lesion following primary debulking, several chemotherapy courses, and external pelvic radiation. A third patient who underwent SRS after multiple surgeries, one dose of intra-operative radiation, and 3 mo of single-agent chemotherapy had stable disease at six month follow up with no more than grade 2 acute toxicities[15].

Deodato *et al*[13] described four other cases of SRS use in ovarian cancer. Three patients were without evidence of disease at 37, 31, and 19 mo after undergoing SRS to presacral lymph nodes, hepatic lesions, and supraclavicular nodes, respectively. One patient was alive with disease at 18 mo after SRS dosing to anterior mediastinal and left internal mammary nodes[13]. Further studies are needed to define the appropriate patient population for SRS use in ovarian cancer. Currently, SRS is only used as a palliative measure for patients with localized, recurrent disease.

TOXICITIES

Most toxicities associated with SRS are mild and self-limiting. They include grade 1-2 fatigue, diarrhea, dysuria, nausea, and sexual side effects. However, rare grade 3 toxicities have been reported in almost every series. Rectal bleeding was reported in 4 patients in two different series of patients receiving EBRT followed by SRS boost. One of these events occurred in a patient with a history of prior radiation; however, the other patients with rectal bleeding had not undergone previous radiation therapy. Four patients in three series reported enterovaginal fistulas; all of these occurred in the recurrent setting[1,2,7].

The largest study of toxicities associated with SRS was published by Kunos *et al*[16] in 2012. This retrospec-

tive series analyzed hematologic toxicity in 61 women treated with SRS for stage 4 gynecologic malignancies. Ninety-three percent of these patients had received chemotherapy prior to SRS. Twenty-five percent had grade 2 fatigue, but the incidence of grade 3 fatigue was only 3%. All symptoms resolved by 30 d post-radiation. No neutropenia was reported; however, 5% of women had grade 1 anemia (Hb < 10.0 g/dL), and there were single incidences of grade 1, 2, and 3 thrombocytopenia. Further studies are required to better estimate the rates of non-hematologic toxicities, though it is difficult to isolate SRS as the cause of morbidity, since many patients receive surgery, chemotherapy, and other methods of radiation prior to receiving SRS[16].

SRS IN GYNECOLOGIC CANCER

For now, the indications for SRS in gynecologic oncology remain undefined. Our review found three clinical scenarios for which SRS could provide benefit. These include non-central pelvic recurrences in previously irradiated patients, complex or unresectable disease recurrence, and solitary brain metastases (Table 2). This is an especially promising area of research, as few treatment options are available for these patients.

RECURRENT CERVICAL CANCER

Patients with locally advanced primary cervical cancer are usually treated with curative chemoradiation. Others may undergo primary surgery but require adjuvant chemoradiation due to high-risk pathologic features, positive margins, positive parametria or positive pelvic lymph nodes. In this population, utilization of traditional radiotherapy in a previously radiated field is associated with prohibitive toxicity, and thus, SRS may represent a suitable alternative. While central pelvic recurrences can be treated with surgical exenteration, many patients have non-central recurrences or comorbid conditions that make them unsuitable for aggressive surgical resection with significant quality of life implications. Currently, the majority of these patients are treated with systemic chemotherapy using cisplatin, paclitaxel, and bevacizumab (following presentation of GOG 240)[17] or are enrolled in clinical trials. Cyberknife SRS represents another therapeutic alternative and has decreased morbidity compared to exenteration. Series by Guckenberger, Dewas, and Deodata report mostly grade 1-2 toxicity, even in previously irradiated patients[7,9,13]. In one series, two out of the three patients with grade 3-4 toxicities had received prior radiation; however, most previously irradiated patients did not suffer significant morbidity[7].

COMPLEX OLIGOMETASTASES

Although the location of gynecologic cancer recurrence is unpredictable, patients with cervical and endometrial cancer commonly recur in the pelvis. A proportion, however, will have distant disease recurrence in complex locations involving the abdominal retro-peritoneum. Clinical options in this setting are limited, as access for adequate surgical resection is difficult to achieve. Treatment using chemotherapeutics or biologic agents is encouraged, and a combined approach utilizing systemic chemotherapy in conjunction with SRS is promising. Research regarding the above is limited, and given the unmet clinical need, warrants further investigation. There are well-defined selection criteria for utilization of SRS in the treatment of oligometastases for other primary disease sites such as lung, prostate and liver, and this data can may be extrapolated to gynecologic cancer patients.

Table 2 Indications for SRS in recurrent and metastatic gynecologic malignancy

Recurrent cervical cancer	Recurrence in a previously radiated fields Recurrence in patients who are not candidates for pelvic exenteration
Complex oligometastases	Unresectable oligometastases Oligometastases in abdominal retroperitoneum
Central nervous system and brain metastases	Intracranial lesions not accessible to Gamma Knife

CENTRAL NERVOUS SYSTEM AND BRAIN METASTASES

Central nervous system (CNS) and brain metastases are rare in gynecologic malignancies. Between 0.4%-1.2% of cervical cancers involve intracranial metastases, and percentages are similar for other pelvic disease sites. These lesions are usually treated with whole brain radiation or Gamma Knife stereotactic radiosurgery (Figure 1). A series by Menedez *et al*[18] included 14 patients with brain metastases from primary endometrial, ovarian, or cervical cancer. Patients received 16-20 Gy and experienced median survival of 5-13 mo. While the CyberKnife system is not well studied in gynecologic malignancies, its use is described for brain metastases in primary lung, breast, colon, and other cancers. CyberKnife eliminates the need for target fixation and allows for expanded treatment freedom for large or complex lesions.

The preference for Gamma Knife in the treatment of brain and spinal cord metastasis stems from the theoretical improvement in accuracy, 0.5 mm or less, over Cyber Knife (1 mm or less), although these measurements have been disputed (Figure 1). Additionally, the smaller size of the Gamma Knife collimators reduce the potential injury to neighboring normal brain tissue, improving long term morbidity. The Gamma Knife also improves precision using a rigid immobilization device to prevent head movement during treatment. Conversely, utilization of CyberKnife SRS, allows for improved therapeutic versatility given the dynamic nature of the robotic arms, compensating for target organ motion, and allowing access to portions of the CNS that are difficult to treat using

Gamma Knife therapy.

FUTURE RESEARCH

While SRS is a promising treatment modality for inoperable or recurrent gynecologic cancers, many aspects of treatment remain uncertain. The available series describing SRS use heterogeneous dosing and fractionation schedules, and the optimal regimen has not been delineated. Controlled trials comparing SRS to brachytherapy or IMRT are also needed. Studies of SRS use for adjuvant therapy in high risk disease could further define the role of SRS in gynecologic malignancies. Today, SRS remains a second line treatment, reserved for patients with primary disease who are unsuitable for standard surgical or radiation therapy or for recurrent disease in a previously irradiated field.

Because most patients in the above-mentioned series suffered disease recurrence or progression outside the treatment area, many researchers have proposed concurrent chemotherapy with SRS to prevent progression of occult disease. Twenty five patients reported in the literature have received concurrent cisplatin during SRS, and four patients have received other chemotherapy regimens within 4 mo of SRS[1,2,3,7,10]. However, this patient population is too small for any comparisons to be made regarding the benefits of concurrent chemotherapy. A phase I clinical trial of palliative SRS with gemcitabine and carboplatin is currently enrolling patients with recurrent or persistent cervical, endometrial, ovarian, vulvar, and vaginal cancers (NCT01652794).

CONCLUSION

SRS is an emerging area of radiation oncology, which has been successfully used in high risk gynecologic malignancies. Because of its unique ability to precisely target malignant lesions while sparing surrounding normal tissues, SRS can safely radiate tumors that may be difficult or impossible to treat with surgery or conventional radiotherapy. SRS has been described for all gynecologic malignancies and appears to have an excellent safety profile. Further research is necessary to determine optimal dosing and fractionation schedules, delineate appropriate patient populations, and evaluate long term survival and morbidity.

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