Cancer of the cervix is one of the most frequently diagnosed cancers among women. Every year, 575,000 women are diagnosed with invasive cervical cancer globally, with 13,800 in the United States, 54,500 in Europe and 96,922 in India with 65-75 per cent presenting in locally advanced stage 1,2.

The incidence of metastatic disease at the time of diagnosis ranges from five to eight per cent 3-4. The 10 yr actuarial incidence of distant metastases ranges from 26, 39 and 75 per cent in International Federation of Gynaecology and Obstetrics (FIGO) stage IIB, IIIB and IVA, respectively 5,6. Further, the most frequent sites of distant metastases are lung (21-39.3%), para-aortic lymph nodes (PALN) (11%), bone (16.3%), liver (12.2%), abdominal cavity (8%), brain (1.4%) and supraclavicular node (SCLN) (7%) 7,8. Patients treated with concurrent chemoradiation (CCRT) and brachytherapy (BT) constitute a vast majority of patients who develop disease relapse at distant sites. The disease-free survival (DFS) in FIGO stage IIB-IV is 61-76 per cent, suggesting that close to 25-35 per cent of patients will present with...
progression\(^9\). Post-treatment failure is observed at distant sites in 16-25 per cent of patients\(^{10-13}\).

Chemotherapy (CTh) administered with palliative intent constitutes the mainstay of treatment in metastatic or recurrent setting with dismal survival of 2-18 months\(^{14-21}\). Recently, metastatic disease or recurrent disease has been classified based on number of lesions, sites of involvement; with limited number (usually <3) and involvement as oligometastatic disease (OMD)\(^{22}\). Niibe and Hayakawa\(^{23}\) have suggested that if OMD is eliminated, a patient may be cured, as occurs in loco-regional tumours. A phase II trial by Palma et al\(^{24}\) utilizing stereotactic body radiation therapy (SBRT) in addition to systemic CTh in OMD reported overall survival (OS) benefit in the SBRT arm with grade 2 or higher toxicity 29 per cent with 4.5 per cent mortality in the SBRT arm versus nine per cent and no mortality in the standard of care arm. In addition, the updated analysis has shown durable response and no detrimental effect on the quality of life (QOL) of the patients\(^{25}\). Although the study had multiple primary cancer subtypes with OMDs, only a limited number of patients had gynaecological cancer and no patients with cervical cancer were included.

An international coordinated effort (ESTRO-ASTRO consensus) is in the process to better define this patient population that may benefit from intensified treatment approaches\(^{26}\). OMD presently includes patients who present with ≤3 metastasis and >3-5 metastases which is largely independent of the primary tumour and metastases location\(^{26}\). ESTRO-EORTC group has further classified OMD considering the timing of presentation of metastases, receipt of any systemic therapy before appearance of lesion and response of metastases to the systemic therapy\(^{22}\).

This review summarizes the existing evidence for the use of RT in the treatment of OMD and ORD in cervical cancer.

**Role of systemic therapy agents**

Currently, the recommended standard first-line regimen for the treatment of metastatic cervical cancer is the combination of cisplatin and paclitaxel, which has shown mild to modest improvement\(^{18}\). In addition, other chemotherapeutic agents including topotecan\(^{15,19}\) and gemcitabine\(^{17}\) have been investigated and have shown slight improvement. Further, addition of immunotherapy and targeted therapies such as bevacizumab, pembrolizumab and cediranib has shown promising results, with bevacizumab combined with standard CTh recommended as a first-line therapy in metastatic or recurrent cervical cancer\(^{16,20,27}\).

Though the results of these therapies are encouraging, their cost, availability and storage in developing countries have been a challenge and a limiting step for access. A cost-effective analysis done by Klag et al\(^{28}\) suggested that the combination of cisplatin and paclitaxel was the most cost-effective regimen and the addition of bevacizumab, although providing survival benefit, was not sustainable. Phippen et al\(^{29}\) suggested that the addition of bevacizumab to CTh was not affordable.

**Combining radiation with targeted agents and immunotherapy**

Various trials are underway combining SBRT or hypofractionated high-dose RT therapy and immunotherapy (NCT03452332, NCT03277482, NCT03614949, NCT03312114, NCT03192059) in recurrent or metastatic cervical cancer as shown in Table I. The accrual of these trials is ongoing, and the results are awaited which will help to further define the management and the optimal dose and fractionation schedules of RT.

**Role of pelvic radiation in patients with de novo metastatic disease**

In patients with limited metastatic disease at the time of first clinical presentation, integration of local therapy with systemic therapy has been used by various investigators which has shown to provide progression-free survival (PFS) and OS benefits. The primary goal of delivering local therapies is to eradicate the local disease which could translate into clinical and survival benefits. Stenger et al\(^{30}\) analyzed 3169 patients of upfront metastatic cervical cancer treated with CTh alone versus CTh and pelvic RT; the addition of pelvic RT demonstrated significant survival benefit (23.2 vs. 10.1 months). Further, the median survival was longer in patients receiving RT dose >45 Gy and those receiving brachytherapy along with external beam RT with benefit seen even in patients with distant and nodal metastasis. A retrospective analysis of 2838 patients confirmed survival benefit (19.2 months vs. 10.1 months) with local definitive RT with CTh as compared to systemic CTh and palliative RT\(^{31}\). Another retrospective analysis by Yin et al\(^{32}\) confirmed the benefit of definitive RT with CTh over palliative RT and CTh and observed that mortality was due to distant progression rather
than local progression after definitive RT. European Society for Medical Oncology (ESMO), European Society of Gynaecological Oncology (ESGO) and European Society for Radiotherapy and Oncology (ESTRO) guidelines also recommend treating pelvis (gross disease with elective irradiation of immediate nodal level) with CTh in localized metastatic disease. Local RT also helps to alleviate the symptoms and pain associated with the disease. In a survey conducted within the EMBRACE group, it was revealed that all the participants agreed on delivering local RT in OMD with 68.2 per cent preferring CCRT and BT while 31.8 per cent preferred adding systemic therapy. There is evidence that local RT improves survival in metastatic cervical cancer at presentation as shown in above studies; though most of the data are retrospective and prospective studies are needed. Further, no robust evidence exists about the benefit of elective irradiation of nodal targets while delivering local RT in such settings.

### Role of radiation therapy in patients with metastasis to distant nodal sites

The spread of cervical cancer is stepwise with involvement of pelvic lymph nodes first followed by PALN and then systemic organs. Supraventricular nodal (SCLN) metastasis: The incidence of SCLN metastasis is approximately 1.5-8.6 per cent with or without PALN metastasis at presentation with a five-year OS rate of 16.5 per cent. In a study of 24 patients who had distant nodal metastases at presentation, patients receiving CCRT followed by BT had better PFS and OS and complete response (CR) rates as compared to those receiving CTh alone. In a retrospective analysis, 25 patients with both para-aortic nodes (PALN) and SCLN metastases received RT to the PALN and left SCLN (59.4 Gy) and 50.4 Gy to the pelvis with platinum-based CTh concurrently followed by BT. The median OS of the patients was 32 months.

---

| Clinical trial identifier | Diseases | Immunotherapy | Radiation therapy | Endpoint | Secondary endpoint |
|--------------------------|----------|---------------|-------------------|----------|--------------------|
| NCT03452332 Phase I     | Recurrent or metastatic cervical, vaginal or vulvar cancers | Tremelimumab + durvalumab | SABR with 3 fractions separated by 48 h | AE | Response to treatment; PFS; OS; TTNT |
| NCT03277482 Phase I     | Metastatic or unresectable endometrial, ovarian (ovarian epithelial, fallopian tube, primary peritoneal), cervical, vaginal or vulvar cancer | Tremelimumab and durvalumab | Hypofractionated short course (either 1 or 5 days) | MTD | ORR; LRR, LCR, ARR, RD, PFS, OS |
| NCT03614949 Phase II    | Recurrent or metastatic cervical cancer | Atezolizumab q3w 1 week | SBRT with 24 Gy in 3 fractions | ORR | PFS; OS |
| NCT03312114 Phase II    | Metastatic fallopian tube cancer, primary peritoneal carcinoma, recurrent epithelial cancer of ovary | Avelumab Stereotactic treatment (e.g. SABR/SBRT) | ORR | OS; CR; TTP; median response duration |
| NCT03192059 Phase II    | Advanced or refractory cervical cancer, endometrial carcinoma, or uterine sarcoma | Immunomodulators Vitamin D, aspirin, cyclophosphamide, and lansoprazole plus curcumin with pembrolizumab | EBRT 24 Gy in 3 fractions, a fraction every 28 h | ORR | Incidence of AE; best OR; PFS; OS |

AE, adverse event; ARR, abscopal response rate; CR, complete response; LCR, local control rate; LRR, local-regional recurrence; MTD, maximum tolerated dose; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RD, response duration; SABR, stereotactic ablative radiation therapy; SBRT, stereotactic body radiation therapy; TTNT, time to next treatment; TTP, time to progression; EBRT, external beam radiation therapy.
with 64 per cent experiencing grade 3 or more acute haematologic toxicity. Another study done in seven patients reported five year OS of 57 per cent when RT was delivered to SCLN along with pelvic RT and CTh, although the rate of acute haematologic toxicity was 67 per cent with no chronic toxicities. In another study of 38 patients treated with definitive RT to OMD sites of cervical cancer including SCLN, mediastinum, lung and PALN, the median OS was 50.7 months and PFS was 21.7 months with <3 per cent grade ≥3 toxicity. In such patients, CCRT followed by CTh was feasible with acceptable late toxicity, although the acute haematologic toxicity was reported to be higher. However, given uncommon presentation and differences concerning treatment, no consensus exists about the RT dose to SCLN. In addition, whether the target volume should include the entire nodal chain or only the involved node is unclear, and more studies focussing on these aspects are needed.

**Inguinal nodal metastasis:** The incidence of inguinal nodal metastasis at diagnosis is <2 per cent. There are no robust guidelines for the management of inguinal node metastases; most of the evidence is based on case reports and individual practices. Being close to pelvic RT fields, the majority of RT oncologists extend the RT fields to include the inguinal nodes with concurrent CTh, with RT doses up to 45 Gy to the pelvis with an additional 9-15 Gy boost are recommended for the involved inguinal nodes and the preferred CTh agent is cisplatin 40 mg/m² weekly. The role of neoadjuvant or adjuvant CTh or node dissection is not defined in such a setting.

**Mediastinal nodes metastasis:** The incidence of mediastinal nodes at diagnosis is rare and is under-reported. Positron emission tomography computed tomography (PET-CT) is useful in the diagnosis of mediastinal nodes along with thoracotomy or video-assisted thoracic surgery. SBRT is becoming an attractive modality of treatment in recent times and a retrospective analysis of 52 patients with 84 mediastinal and hilar nodes treated with SBRT median dose of 35 Gy (range 30-50) in five fractions improved OS to 31.7 months. A total of nine per cent local failures were observed at two years and 11.5 per cent of patients experienced grade 3 or more toxicity; however, a vast majority of toxicities were transient with 1.9 per cent developing grade 5 toxicity (radiation pneumonitis). The authors concluded that SBRT to mediastinal and hilar lymph node metastases was feasible with acceptable toxicity.

**Cervical cancer with visceral metastases**

Cervical cancer with lung metastasis: Approximately 4.1-7.7 per cent of patients with cervical cancer develop lung metastasis. The number of nodules, possibility of surgical resection (SR), time interval between the appearance of metastases and initial treatment and receipt of CTh affect the outcomes.

In selected patients who present with limited metastatic disease, SR or RT targeting metastatic sites with systemic therapy should be offered. In a retrospective review of 529 patients with 776 lesions, after lung metastasectomy, the ninety month survival rate was 30 per cent, however very few patients with good general condition and adequate pulmonary reserve could undergo surgery. SBRT is a feasible approach to resection. There are limited studies on SBRT in pulmonary oligometastatic setting, and most of the evidence of SBRT in the lung was derived from stage I non-small cell lung cancer who were medically inoperable. Studies utilizing SBRT in lung metastases from various primary cancers in de novo metastatic or recurrent setting are shown in Table II. In dose-escalation studies, patients treated with 8 Gy ×5 fractions showed CR in 51 per cent and partial response in 33 per cent with only one patient experiencing grade 3 or more toxicity. In another dose-escalation study, SBRT was delivered 20 Gy ×3 fractions in 38 patients with 63 lesions, the actuarial local control (LC) was 96 per cent at two years with a median OS of 19 months with only eight per cent experiencing grade 3 or more toxicity. Hou et al treated 19 patients with cervical cancer with 29 lung metastases with 56-64 Gy in 7-8 fractions and the one-year LC and OS were 75.6 and 76.8 per cent with only one patient developing grade 3 pneumonitis. They concluded that SBRT was safe and efficacious and could be an alternative to surgery. Patients with a good general condition, limited pulmonary metastases (three or fewer), adequate pulmonary function and potentially treatable extra-thoracic disease can be considered as suitable candidates for SBRT. Total dose, fractionation depends upon the location of the tumour and proximity to critical structures. Based on two studies, dose constraints for SBRT in lung primaries are shown in Table III.

Cervical cancer with liver metastases: The incidence of cervical cancer with liver metastases is 1.2-2.2 per cent, with poor survival with CTh alone. In limited liver metastases, resection of metastases is traditionally the choice of treatment with the majority of evidence...
comes from colorectal cancer and has shown excellent outcomes\textsuperscript{66–74} as shown in Table IV. LC of liver metastases by use of SBRT is promising, providing 60–90 per cent at two years; however, tumour volume, receipt of prior CTh and RT dose have a definite role to play\textsuperscript{68–71}. In spite of good local LC in treated site, distant progression is the cause of mortality; hence, combining systemic therapy with SBRT is justified; however, the sequencing of these therapies is crucial for adequate tumour control and survival. Severe toxicity related to SBRT is uncommon with the risk of RT-induced liver disease reported in SBRT is low\textsuperscript{75}.

In a study evaluating the role of SBRT in various OMD sites (lung, liver and nodes) in 45 patients (9 patients with cervix primaries) with 70 lesions, the CR was 64 per cent with no patients progressing after achieving CR at a median follow up of survivors of 40 months with 13 per cent grade 1–2 acute toxicity and no grade 3 or more acute or long-term toxicity; no progression was seen in patients who achieved CR\textsuperscript{76}. A similar study of treating oligometastatic sites with definitive RT has shown improved survival 42 (95% confidence interval: 21–63) months with no local or in-field recurrence\textsuperscript{77}. Studies using high dose per fractions schedule with the aim to deliver ablative doses have shown improved survival in OMD at presentation\textsuperscript{78–80} and including recurrent disease post-curative therapy as well\textsuperscript{81,82}. Administration of CTh before SBRT has shown poor tumour control likely due to the killing of sensitive clones and remains of CTh-resistant clones\textsuperscript{83}. This study predicted that in patients receiving no CTh before SBRT, biological effective dose (BED) of 209±67 Gy, but in those receiving CTh prior to SBRT, BED of 286±78 Gy needed for 90 per cent control probability at two years. In addition, BED >100 Gy, tumour volume <40 cm\textsuperscript{3} and metastasis with the head neck (median 37 months) and breast (32 months) primary tumours have better survival than arising from colorectal (30 months) and lung primaries (26 months)\textsuperscript{84}. In a study by Hong \textit{et al}\textsuperscript{85} in 89 patients treated with SBRT to liver metastases,
the mutation in KRAS oncogene was the strongest predictor of poor LC and tumours with both KRAS and p53 mutation were radioresistant with one-year LC 20 per cent versus 69.2 per cent in the non-mutated cohort. This study highlights the importance of tumour genotyping before SBRT and treatment intensification in such a subset of patients. Ideal candidates for liver metastasis SBRT should have a good performance status, sufficient hepatic reserve, no metastatic disease outside liver and an uninvolved liver volume of 700 ml or greater. Table V shows dose constraints from different studies for liver SBRT.

Cervical cancer with bone metastasis: Bone metastases incidence varies from 0.8 to 23 per cent in cervical cancer. Vertebral column, mainly the lumbar and thoracic spine (48%) followed by pelvis, is the most common site of involvement, with the majority of them (67%) detected within the first year of the radical treatment. Vertebral metastases, if left untreated or delayed, can cause spinal cord compression and irreversible neurological deficit. RT can provide pain relief and can stabilize fractures; however, the majority of patients can relapse. In a study of 105 patients treated with an RT dose of 30 Gy in 10 fractions, the median survival was 10 months with 60 per cent of patients responding to pain. In addition, the use of local treatment was associated with improved survival than the survival of seven months observed in patients receiving CTh alone ($P=0.011$). In spine metastases, the traditional dose fractionation regimen used was 8 Gy single fraction, 20 Gy in five fractions and 30 Gy in 10 fractions providing good symptomatic relief but poor LC. With high-dose SBRT ranging from 15 to 45 Gy in 1-5 fractions, LC improves along with PFS and delay in CTh switchover. In other histologies, bone SBRT has increased LC up to 85-90 per cent using 15-30 Gy in 1-3 fractions. In a retrospective analysis of 1400 patients, LC was 90 per cent at 15 months post-SBRT with <1 per cent risk of myelopathy.

| Parameters                      | RTOG 0236 protocol | RTOG 0915 protocol |
|---------------------------------|--------------------|--------------------|
| Dose prescription               | 60 Gy/3#           | 34 Gy/1#           | 48 Gy/4#           |
| PTV                             | 95 per cent PD to 95 per cent volume | 95 per cent PD to 95 per cent volume | 95 per cent PD to 95 per cent volume |
|                                 | 99 per cent PD to 90 per cent volume | 99 per cent PD to 90 per cent volume | 99 per cent PD to 90 per cent volume |
| CTV                             | 100 per cent PD to 100 per cent volume | 100 per cent PD to 100 per cent volume | 100 per cent PD to 100 per cent volume |
| Spinal cord                     | Max $<$18 Gy       | Max $<$14 Gy $<$0.35 cm$^3$-10 Gy $<$1.2 cm$^3$-7 Gy | Max 26 Gy $<$0.35 cm$^3$-20.8 Gy $<$1.2 cm$^3$-13.6 Gy |
| Lungs                           | V20 $<$10-15 per cent | $<$1500 cm$^3$-7 Gy $<$1000 cm$^3$-7.4 Gy | $<$1500 cm$^3$-11.6 Gy $<$1000 cm$^3$-12.4 Gy |
| Heart                           | Max $<$30 Gy       | Max $<$22 Gy $<$15 cm$^3$-$<$16 Gy | Max $<$34 Gy $<$15 cm$^3$-28 Gy |
| Oesophagus                      | Max $<$27 Gy       | Max $<$15.4 Gy $<$5 cm$^3$-$<$11.9 Gy | Max $<$30 Gy |
| Proximal bronchial tree         | Max $<$30 Gy       | Max $<$20.2 Gy $<$4 cm$^3$-$<$10.5 Gy | Max $<$34.8 Gy $<$4 cm$^3$-15.6 Gy |
| Skin                            | Max $<$24 Gy $<$10 cm$^3$-$<$40 Gy | Max $<$26 Gy $<$10 cm$^3$-23 Gy | Max $<$36 Gy $<$10 cm$^3$-33.2 Gy |
| Brachial plexus                 | Max $<$24 Gy       | Max $<$17.5 Gy $<$3 cm$^3$-$<$14 Gy | Max $<$27.2 Gy $<$3 cm$^3$-23.6 Gy |

Superscript numerals denote reference numbers. PD, prescription dose; Gy, gray; PTV, planning target volume; CTV, clinical target volume; RTOG, Radiation Therapy Oncology Group.
patients post-laminectomy, spine SBRT is feasible with one-year LC ranging from 85 to 95 per cent with no grade three or higher acute or late toxicities. In non-spine metastases, SBRT 30-35 Gy in five fractions showed

| Study                  | Lesions | Patients | Primary | Dose         | LC          | Survival | Toxicity            |
|------------------------|---------|----------|---------|--------------|-------------|----------|---------------------|
| Blomgren et al., 1995  | Variable| 31       | Mixed   | 8-66 Gy/1-4# | 80 per cent | NR       | Haemorrhagic gastritis in 2 patients |
| Hoyer et al., 2006     | 1-6 cm  | 44       | Majority CRC | 45 Gy/3#   | Two years 86 per cent | Two years 62 per cent | Liver failure 1 Gastritis 2 |
| Rusthoven et al., 2009 | 1-3     | 47       | Majority CRC | 60 Gy/3#   | Two years 92 per cent | Median 17 months | Grade 3 <2 per cent |
| Lee et al., 2009       | Variable| 68       | Majority CRC | 28-60 Gy/3# | One year 71 per cent | Median 18 months | Grade 3-8 patients Grade 4-1 patients |
| Goodman et al., 2010   | 1-5     | 26       | Majority CRC | 18-30 Gy/1# | One year 77 per cent | OS       | Grade 2-4 patients |
| Rule et al., 2011      | 1-5     | 27       | Majority CRC | 30 Gy/3#   | One year    | Two years OS | Two years 49 per cent |
| Mahadeva et al., 2018  | Variable| 427      | Majority CRC | 45 Gy/3# (range 12-60 Gy) | One year 84 per cent | One year 74 per cent | NR |

Table IV. Studies evaluating stereotactic body radiation therapy in liver metastases

Superscript numerals denote reference numbers. CRC, colorectal cancer; Gy, gray; OS, overall survival; LC, local control; NR, not reported; #: fractions

| Structures              | Wulf et al.75 | Rusthoven et al.67 | Hoyer et al.70 | QUANTEC86 |
|-------------------------|----------------|--------------------|----------------|-----------|
| Prescription dose       | Low dose group-3×10 Gy or 4×7 Gy prescribed to the PTV-encl 65 per cent isodose | High dose group-3×12-12.5 Gy or 1×26 Gy/PTV enclosing 80 per cent isodose | 12-20 Gy×3 fractions prescribed to isodose line covering PTV | 15 Gy×3 fractions | NA |
| Liver-CTV               | 30 per cent <21 Gy 50 per cent <15 Gy | 700 ml <15 Gy | 700 ml <15 Gy | 700 ml <15 Gy | Dmean <15 Gy |
| Stomach                 | D5 ml <21 Gy | Dmax <30 Gy | D1 ml <21 Gy | Dmax <30 Gy |
| Bowel                   | D5 ml <21 Gy | Dmax <30 Gy | D1 ml <21 Gy | Dmax <30 Gy |
| Oesophagus              | D5 ml <21 Gy | NA | D1 ml <21 Gy | NA |
| Bilateral kidney        | NA | Dmax <18 Gy | Dmax <18 Gy | NA |
| Spinal cord             | NA | D35 <15 Gy | D35 <15 Gy | NA |
| Heart                   | D5 ml <21 Gy | Dmax <18 Gy | Dmax <18 Gy | Dmax <20 Gy |

Gy, gray; PTV, planning target volume; NA, not applicable; CTV, clinical target volume; QUANTEC, quantitative analyses of normal tissue effects in the clinic; Dmax, maximum density
excellent LC of 87 per cent at two years with 8.5 per cent fracture rates in the treated sites and the man time to fracture was 8.4 months. Similarly, post 24 Gy single fraction, the LC was 91.4 per cent at one year with no late grade three or higher toxicities and pain resolution in 88 per cent of the patients with non-spine bone oligometastasis. Two patients developed pathological fractures, but both were asymptomatic. Various studies, meta-analysis, and ASTRO statement have confirmed that single-fraction RT therapy is as efficacious and safe as fractionated RT; however, the retreatments rates are higher with single-fraction RT. The addition of bisphosphonates and denosumab with RT has shown benefit in reducing skeletal-related events and combining them is prudent. Sprave et al. assessed QOL in patients with spine metastases post-conventional RT and SBRT, and there was no difference between the two regimens across all domains and pain-related scores.

Cervical cancer with brain metastases: Brain metastasis in cervical cancer is rare ranging from 0.5 to 1.2 per cent. Brain metastases cause not only morbidity and mortality but also neurocognitive decline, leading to poorer QOL. Good prognostic factors are age less than 50 at diagnosis, good performance status, single or less than three lesions and absence of extra-cranial lesions.

With palliative whole-brain RT (WBRT), the survival ranges from 3 to 7 months. In single or limited metastasis, SR followed by WBRT has shown significantly better outcomes as compared to WBRT alone, 10-11.5 months versus six months. Further, the LC rates and OS for patients with a single metastasis treated either with SR followed by WBRT or with stereotactic radiosurgery (SRS) alone are similar. WBRT followed by SR was beneficial to decrease local and distant recurrence, although there was no benefit in OS.

SRS plus WBRT has shown benefit in OS (10.6 vs. 5.3 months, P=0.001), LC (88.9 vs. 55.6%) and time to progression (8.1 vs. 4 months) as compared to WBRT alone in brain metastasis in lung cancer. Two studies have confirmed that SRS boost has local, survival benefit over WBRT alone in limited brain metastases and should be considered in patients with good performance status and controlled extra-cranial disease.

Studies evaluating the role of SRS in cervical cancer with brain metastases are limited; however, all three studies have shown survival and LC benefit.

There is an evidence to suggest that SR when done before WBRT in a single metastasis versus upfront WBRT alone leads to improved OS and functional status in the patients. At present, there is no level I evidence justifying WBRT or SRS after surgery and the decision of adjuvant treatment should be made judiciously.

While LC and OS continue to be the prime end points, neurocognitive deterioration should be considered while planning treatment and emphasis must be given to improve the QOL of the patients. The role of SRS is evolving and currently limited to boost after WBRT, as monotherapy in <5 metastases, as salvage therapy after the previous WBRT, post-operative RT and in radio-resistant brain metastases.

Cervical cancer with peritoneal deposits: Peritoneal deposits in squamous cell carcinoma of the cervix at diagnosis are extremely rare and comparatively more in adenocarcinoma than in squamous histology. Conventionally, CTh with palliative intent used to be the treatment modality. One case report has shown that excision of limited deposits followed by CCRT (including the deposit and track site of excision) can be curative and provides long-term disease control and survival. However, no definitive guidelines exist for the treatment of peritoneal deposits and decisions should be made on an individual basis depending upon the patient’s conditions and extent of disease.

de Vin et al. proposed an algorithm based on four risk factors affecting OS in OMD: presence of non-adenocarcinoma histology, presence of intracranial metastases, synchronous OMD and male gender. Based on this, the OS ranges from 40 to 4 months in the presence of 0 and all four risk factors, respectively.

Locoregional recurrence after curative therapy

The incidence of nodal recurrence post-curative therapy in locally advanced cervical cancer ranges from 4.7 to 18.9 per cent while the central recurrence (local and regional) rate ranges from 7.6 to 25 per cent and isolated para-aortic ranges from 1.7 to 12 per cent. Patients presenting with only local relapse with no distant metastasis can be offered treatments with curative intent with the choice of treatment depending upon the receipt of the prior treatment. Women who are likely to benefit from surgical management include those who present with a central pelvic recurrence without sidewall fixation or associated hydronephrosis, and small tumour size.
Patients who present with loco-regional relapse post-hysterectomy can be offered RT with or without CTh. Vaginal vault or parametrial relapse can be considered for external beam RT with BT or BT alone with five-year survival ranging from six to 55 per cent\textsuperscript{120,121}. Mahantshetty et al\textsuperscript{122} analyzed 30 patients treated with brachytherapy to a median dose of 42 Gy (range 37 to 46 Gy) and reported two-year LC 44 per cent, PFS 42 per cent and OS 52 per cent with grade three proctitis and cystitis and grade two small bowel toxicity in three (10\%) patients. In addition, long intervals between two RT schedules and high brachytherapy dose favoured better outcomes\textsuperscript{122}. In a phase III randomized study comparing neoadjuvant CTh followed by surgery versus RT and CTh in FIGO stage IB2, IIA and IIB, 12.3 per cent of patients developed local recurrence only and 6.3 per cent received local and distant post-surgery; around 30 per cent of them received salvage RT\textsuperscript{123}. Although the primary analysis showed difference in DFS between the two arms, no difference was seen in OS. Effective salvage of recurrence using RT with or without CTh may be one of the reasons\textsuperscript{22}. NCCN 2020\textsuperscript{124} and ESMO-ESGO-ESTRO\textsuperscript{33} guidelines state that patients with central recurrence, who have not received RT or failed outside the treatment fields, should undergo surgical resection if feasible followed by adjuvant RT (including brachytherapy) if feasible, and systemic therapy. In patients who have received prior RT and have a central recurrence, pelvic exenteration is advised, while in non-central disease, pelvic re-irradiation can be offered or systemic CTh\textsuperscript{33,124}.

In patients presenting with nodal relapse, surgical debulking, RT with CTh, or best supportive care can be offered; however, the prognosis is variable; with three-year OS rate of patients who underwent RT and CT being 85.7 per cent; surgery 66.7 per cent; CTh only 48.8 per cent; RT only 41.3 per cent and best supportive care 0 per cent (\(P=0.014\))\textsuperscript{125}. Re-irradiation with or without CTh is feasible without much side toxicity. In a study, 22 cervical cancer patients with LN recurrence post-surgery were treated with salvage RT (median dose 60 Gy) with (n=18) or without (n=4) CTh\textsuperscript{126}. Patients treated with CTh and RT achieved a longer five-year PFS 72.9 per cent and OS rate 60 per cent with less than 20 per cent recurrence occurring inside the RT field\textsuperscript{126}. In a retrospective analysis of 28 patients with recurrent genitourinary malignancies after a median disease-free interval of 9.5 years, RT to a median dose of 50 Gy using hypofractionated schedule showed good symptomatic relief and no grade 2-4 toxicity\textsuperscript{127}. The authors suggested that a median cumulative dose of 100 Gy could achieve successful palliation without much toxicity in a patient previously treated with RT\textsuperscript{127}. A clinical trial exploring the role of IMRT in the re-radiation of the pelvis in recurrent cervical cancer is ongoing (NCT03170570). SBRT is an attractive option; it can deliver higher doses using highly conformal RT and in a shorter overall treatment time. SBRT has been tried in para-aortic nodal recurrences from gastric, prostate and gynaecological primaries\textsuperscript{128-133} as shown in Table VI. In a study on 91 patients (13\% patients had cervical cancer primary) Loi et al\textsuperscript{134} treated pelvic and para-aortic nodal relapse with SBRT 48 Gy in six fractions (biological equivalent dose of 86 Gy), and showed a median OS of 36 months and PFS of 79 per cent at four years with no late grade three or more toxicity. Park et al\textsuperscript{132} treated 100 patients of recurrent oligometastatic cervical cancer using SBRT and reported two-year PFS of 82 per cent and OS of 57 per cent. Choi et al\textsuperscript{132} treated 30 patients using SBRT 33-45 Gy in three fractions with four-year LC and PFS of 67.4 and 45 per cent, respectively, with grade three toxicity occurring in one patient only after 20 months of treatment. Although the evidence in pelvic re-irradiation using hypofractionated SBRT in cervical cancer is emerging, data from other pelvic malignancies have shown promising results\textsuperscript{135}. A survey within the EMBRACE network showed that for out-of-RT field nodal recurrences, 63.7 per cent preferred treating with the intent of curing the disease with RT and CTh, while for in RT field recurrences, palliation was the aim of the treatment\textsuperscript{34}. Thus, re-irradiation of the pelvis in recurrent cervical cancer is an area of significant uncertainty and further trials are warranted.

**Future considerations**

The ESTRO-EORTC expert groups have classified OMD based on different characteristics of the patients who underwent treatment with curative intent and sub classified into oligorecurrence, oligoprogression and oligopersistence, which is being prospectively evaluated\textsuperscript{22}. These authors have started OLIGOCARE project, a prospective project which is currently accruing patients with OMD, where the researcher can follow up their work which will establish further
which treatment is best suited to individual patients (available from: https://project.eortc.org/e2-radiate/platform/). A nomogram is also available to stratify oligometastatic patients based on the sex of the patient, timing of presentation of the disease, presence of intracranial metastases, histology and KPS score and to plan individualized care. A recent survey highlighted the need of joint approach and clinical trials to decide the optimal management of OMD and ORD in cervical cancer.

**Conclusion**

Metastatic cervical cancer possesses a challenge in diagnosis and treatment, and with conventional CTh, the survival remains poor. Treatment intensification using RT in local and metastatic sites, especially SBRT, has shown promising results with improved OS and PFS. As the role of SBRT continues to grow, the utility of this approach in cervical cancer needs to be explored.

| Author (year) | Number of patients | Re-irradiation | Primary cancer | SBRT dose | Outcomes | Toxicity |
|---------------|-------------------|----------------|----------------|-----------|----------|----------|
| Bonomo et al\(^{138}\), 2013 | 26 (32 nodes) | Not reported | Gynaecological and prostate | 36 Gy/3# in majority | LC-100 per cent | No acute or severe toxicity |
| Corvò et al\(^{139}\), 2013 | 33 | 3 ReRT (median previous RT dose-30 Gy) | Pancreas and colon | 35 Gy/5# weekly | LC-83 per cent at 2 years | No acute or late grade 3 or more toxicity |
| Jereczek-Fossa et al\(^{140}\), 2012 | 69, (94 nodes) | 20 lesions | Gastro-intestinal, prostate | 24 Gy in 3# | Three years | Late grade 3 or more in 3 patients |
| Kim et al\(^{141}\), 2010 | 7 | No | Gastric | 48 Gy/3# | Three years OS-43 per cent, local relapse in 1 patient | No late toxicity |
| Choi et al\(^{142}\), 2009 | 30 | 4 patients | Cervix, endometrial, gastric | 33-45 Gy/3# | Four years | Late grade 3 in one patient |
| Bignardi et al\(^{143}\), 2011 | 19 | No | Miscellaneous | 45 Gy/6# | Two years LC-77.8 per cent PFS-19.7 per cent OS-93.3 per cent | Late grade 3 in one patient |

OS, overall survival; PFS, progression-free survival; LC, local control; RT, radiation therapy; SBRT, stereotactic body radiation therapy; Gy, gray

**Financial support & sponsorship:** None.

**Conflicts of Interest:** None.

**References**

1. Reichheld A, Mukherjee PK, Rahman SM, David KV, Pricilla RA. Prevalence of cervical cancer screening and awareness among women in an urban community in South India – A cross sectional study. *Ann Glob Health* 2020; 86: 30.
2. Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: A worldwide analysis. *Lancet Glob Health* 2020; 8: e191-203.
3. Friedlander M, Grogan M; U.S. Preventative Services Task Force. Guidelines for the treatment of recurrent and metastatic cervical cancer. *Oncologist* 2002; 7: 342-7.
4. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. *CA Cancer J Clin* 2017; 67: 7-30.
5. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynaecol Obstet* 2009; 105: 103-4.
6. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer 2019; 144 : 1941-53.

7. Zhang Y, Guo Y, Zhou X, Wang X, Wang X. Prognosis for different patterns of distant metastases in patients with uterine cervical cancer: A population-based analysis. J Cancer 2020; 11 : 1532-41.

8. Perez CA, Grigsby PW, Camel HM, Galakatos AE, Mutch D, Lockett MA. Irradiation alone or combined with surgery in stage IB, IIA, and IIB carcinoma of the uterine cervix: Update of a nonrandomized comparison. Int J Radiat Oncol Biol Phys 1995; 31 : 703-16.

9. Raut A, Chopra S, Mittal P, Patil G, Mahanshetty U, Gurram L, et al. FIGO classification 2018: Validation study in patients with locally advanced cervix cancer treated with chemoradiation. Int J Radiat Oncol Biol Phys 2020; 108 : 1248-56.

10. Tan LT, Pötter R, Sturdza A, Fokdal L, Haie-Meder C, Schmid M, et al. Change in patterns of failure after image-guided brachytherapy for cervical cancer: Analysis from the RetroEMBRACE Study. Int J Radiat Oncol Biol Phys 2019; 104 : 895-902.

11. Sturdza A, Pötter R, Fokdal LU, Haie-Meder C, Tan LT, Mazeron R, et al. Image guided brachytherapy in locally advanced cervical cancer: Improved pelvic control and survival in RetroEMBRACE, a multicenter cohort study. Radiother Oncol 2016; 120 : 428-33.

12. Fortin I, Jürgenliemk-Schulz I, Mahanshetty UM, Haie-Meder C, Hoskin P, Segedin B, et al. Distant metastases in locally advanced cervical cancer pattern of relapse and prognostic factors: Early results from the EMBRACE study. Int J Radiat Oncol Biol Phys 2015; 93 : S8-9.

13. Sasidharan A, Mahanshetty UM, Gurram L, Chopra S, Engineer R, Maheshwari A, et al. Patterns of first relapse and outcome in patients with locally advanced cervical cancer after radiochemotherapy: A single institutional experience. Indian J Gynecol Oncol 2020; 18 : 3-8.

14. Fiorica JV, Blessing JA, Puneky LV, Secord AA, Hoffman JS, Yamada SD, et al. A Phase II evaluation of weekly topotecan as a single agent second line therapy in persistent or recurrent carcinoma of the cervix: A Gynecologic Oncology Group study. Gynecol Oncol 2009; 115 : 285-9.

15. Monk BJ, Huang HQ, Cella D, Long HJ 3rd; Gynecologic Oncology Group Study. Quality of life outcomes from a randomized phase III trial of cisplatin with or without topotecan in advanced carcinoma of the cervix: A Gynecologic Oncology Group Study. J Clin Oncol 2005; 23 : 4617-25.

16. Monk BJ, Mas Lopez L, Zarba JJ, Oaknin A, Tarpin C, Termnruanglert W, et al. Phase II, open-label study of pazopanib or lapatinib monotherapy compared with pazopanib plus lapatinib combination therapy in patients with advanced and recurrent cervical cancer. J Clin Oncol 2010; 28 : 3562-9.

17. Monk BJ, Sill MW, McMeekin DS, Cohn DE, Ramondetta LM, Boardman CH, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: A Gynecologic Oncology Group study. J Clin Oncol 2009; 27 : 4649-55.

18. Moore DH, Blessing JA, McQuellon RP, Thaler HT, Cella D, Benda J, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: A gynecologic oncology group study. J Clin Oncol 2004; 22 : 3113-9.

19. Long HJ 3rd, Bundy BN, Grendys EC Jr., Benda JA, McMeekin DS, Sorosky J, et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: A Gynecologic Oncology Group Study. J Clin Oncol 2005; 23 : 4626-33.

20. Tewari KS, Sill MW, Penson RT, Huang H, Ramondetta LM, Landrum LM, et al. Bevacizumab for advanced cervical cancer: Final overall survival and adverse event analysis of a randomised, controlled, open-label, phase 3 trial (Gynecologic Oncology Group 240). Lancet 2017; 390 : 1654-63.

21. Kitagawa R, Katsumata N, Shibata T, Kamura T, Kasamatsu T, Nakanishi T, et al. Paclitaxel plus carboplatin versus paclitaxel plus cisplatin in metastatic or recurrent cervical cancer: The Open-Label Randomized Phase III Trial JCOG0505. J Clin Oncol 2015; 33 : 2129-35.

22. Guckenberger M, Lievens Y, Bouma AB, Collette L, Dekker A, deSouza NM, et al. Characterisation and classification of oligometastatic disease: A European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus recommendation. Lancet Oncol 2020; 21 : e18-28.

23. Niibe Y, Hayakawa K. Oligometastases and oligo-recurrence: The new era of cancer therapy. Jpn J Clin Oncol 2010; 40 : 107-11.

24. Palma DA, Olson R, Harrow S, Gaede S, Louie AV, Haasbeek C, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): A randomised, phase 2, open-label trial. Lancet 2019; 393 : 2051-8.

25. Olson R, Senan S, Harrow S, Gaede S, Louie A, Haasbeek C, et al. Quality of life outcomes after stereotactic ablative radiation therapy (SABR) versus standard of care treatments in the oligometastatic setting: A Secondary Analysis of the SABR-COMET Randomized Trial. Int J Radiat Oncol Biol Phys 2019; 105 : 943-7.

26. Lievens Y, Guckenberger M, Gomez D, Hoyer M, Romero AM, Scorsetti M, et al. Definition of Oligometastatic Disease from a Radiation Oncology perspective: an ESTRO-ASTRO Consensus Document. : 1–17.

27. Symonds RP, Gourley C, Davidson S, Carty K, McCartney E, et al. Consensus Document. : 1–17.
28. Klag N, Walter AC, Sheely KM, Manahan KJ, Geisler JP. Is the routine use of bevacizumab in the treatment of women with advanced or recurrent cancer of the cervix sustainable? *Clinicoecon Outcomes Res* 2016; 8 : 287-91.

29. Phippen NT, Leath CA 3rd, Havrilesky LJ, Barnett JC. Bevacizumab in recurrent, persistent, or advanced stage carcinoma of the cervix: Is it cost-effective? *Gynecol Oncol* 2015; 136 : 43-7.

30. Stenger M. Definitive Pelvic Radiation Therapy Plus Chemotherapy and Survival in Newly Diagnosed Metastatic Cervical Cancer 2018; 2018. Available from: https://ascopost.com/News/59164, accessed on August 31, 2020.

31. Venigalla S, Guttmann DM, Horne ZD, Carmona R, Shabason JE, Beriwal S. Definitive local therapy is associated with improved overall survival in metastatic cervical cancer. *Pract Radiat Oncol* 2018; 8 : e377-85.

32. Yin Z, Lou H, Tang H, Ni J, Zhou Q, Chen M. Efficacy of radical doses of pelvic radiotherapy for primary tumor treatment in patients with newly diagnosed organ metastatic cervical cancer. *Radiat Oncol* 2019; 14 : 82.

33. Cibula D, Pötter R, Planchamp F, Avall-Lundqvist E, Fischerova D, Haie Meder C, *et al.* The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer. *Int J Gynecol Cancer* 2018; 28 : 641-55.

34. Chopra S, Mangaj A, Sharma A, Tan LT, Sturdza A, Jürgenliemk-Schulz I, *et al.* Management of oligo-metastatic and oligo-recurrent cervical cancer: A pattern of care survey within the EMBRACE research network. *Radiother Oncol* 2021; 155 : 151-9.

35. Frumovitz M, Querleu D, Gil-Moreno A, Morice P, Jhingran A, Munsell MF, *et al.* Lymphadenectomy in locally advanced cervical cancer study (LiLACS): Phase III clinical trial comparing surgical with radiologic staging in patients with stages IB2-IVA cervical cancer. *J Minim Invasive Gynecol* 2014; 21 : 3-8.

36. Hong JH, Tsai CS, Lai CH, Chang TC, Wang CC, Chou HH, *et al.* Recurrent squamous cell carcinoma of cervix after definitive radiotherapy. *Int J Radiat Oncol Biol Phys* 2004; 60 : 249-57.

37. Henriksen E. The lymphatic spread of carcinoma of the cervix and of the body of the uterus; a study of 420 necropsies. *Am J Obstet Gynecol* 1949; 58 : 924-42.

38. Kim HS, Kim T, Lee ES, Kim HJ, Chung HH, Kim JW, *et al.* Impact of chemoradiation on prognosis in stage IBV cervical cancer with distant lymphatic metastasis. *Cancer Res Treat* 2013; 45 : 193-201.

39. Kim JY, Kim JY, Kim JH, Yoon MS, Kim J, Kim YS. Curative chemoradiotherapy in patients with stage IBV cervical cancer presenting with paraortic and left supraclavicular lymph node metastases. *Int J Radiat Oncol Biol Phys* 2012; 84 : 741-7.

40. Lee SH, Lee SH, Lee KC, Lee KB, Shin JW, Park CY, *et al.* Radiation therapy with chemotherapy for patients with cervical cancer and supraclavicular lymph node involvement. *J Gynecol Oncol* 2012; 23 : 159-67.

41. Ning MS, Ahobila V, Jhingran A, Stecklein SR, Frumovitz M, Schmeler KM, *et al.* Outcomes and patterns of relapse after definitive radiation therapy for oligometastatic cervical cancer. *Gynecol Oncol* 2018; 148 : 132-8.

42. Ouldamer L, Marret H, Acker O, Barillot I, Body G. Unusual localizations of sentinel lymph nodes in early stage cervical cancer: A review. *Surg Oncol* 2012; 21 : e153-7.

43. Yavas G, Ata O, Celik C. An Unusual Case of Cervical Cancer with Inguinal Lymph Node Metastasis: A Case Report and Review of the Literature. *Arch Clin Med Case Reports* 2017; 01 : 11-8.

44. Shahi J, Poon I, Ung YC, Tsao M, Bjarnason GA, Malik NH, *et al.* Stereotactic body radiation therapy for mediastinal and hilar lymph node metastases. *Int J Radiat Oncol Biol Phys* 2021; 109 : 764-74.

45. Carlson V, Delclos L, Fletcher GH. Distant metastases in squamous-cell carcinoma of the uterine cervix. *Radiology* 1967; 88 : 961-6.

46. Clavero JM, Deschamps C, Cassivi SD, Allen MS, Nichols FC 3rd, Barrette BA, *et al.* Gynecologic cancers: Factors affecting survival after pulmonary metastasectomy. *Ann Thorac Surg* 2006; 81 : 2004-7.

47. Ki EY, Lee KH, Park JS, Hur SY. A clinicopathological review of pulmonary metastasis from uterine cervical cancer. *Cancer Treat Rev* 2016; 48 : 266-72.

48. Younes RN, Gross JL, Taira AM, Martins AAC, Neves GS. Surgical resection of lung metastases: results from 529 patients. *Clinics (Sao Paulo)* 2009; 64 : 535-41.

49. Lo SS, Fakiris AJ, Chang EL, Mayr NA, Wang JZ, Papiez L, *et al.* Stereotactic body radiation therapy: A novel treatment modality. *Nat Rev Clin Oncol* 2010; 7 : 44-54.

50. Okunieff P, Petersen AL, Philip A, Milano MT, Katz AW, Boros L, *et al.* Stereotactic Body Radiation Therapy (SBRT) for lung metastases. *Acta Oncol* 2006; 45 : 808-17.

51. Wulf J, Haedinger U, Oppitz U, Thiele W, Mueller G, Flentje M. Stereotactic radiotherapy for primary lung cancer and pulmonary metastases: A noninvasive treatment approach in medically inoperable patients. *Int J Radiat Oncol Biol Phys* 2004; 60 : 186-96.

52. Hof H, Hoess A, Oetzel D, Debus J, Herfarth K. Stereotactic single-dose radiotherapy of lung metastases. *Strahlenther Onkol* 2007; 183 : 673-8.

53. Ricardi U, Filippi AR, Guarnieri A, Ragona R, Mantovani C, Giglioli F, *et al.* Stereotactic body radiation therapy for lung metastases. *Lung Cancer* 2012; 75 : 77-81.

54. Ossi MF, Carnevale A, Valerianni M, De Sanctis V, Minniti G, Cortesi E, *et al.* Clinical outcomes of single dose stereotactic radiotherapy for lung metastases. *Clin Lung Cancer* 2013; 14 : 699-703.

55. Filippi AR, Franco P, Ricardi U. Is stereotactic ablative radiotherapy an alternative to surgery in operable stage I non-
small cell lung cancer? Rep Pract Oncol Radiother 2014; 19 : 275-9.

56. Wersäll PJ, Blomgren H, Lax I, Källkner KM, Linder C, Lundell G, et al. Extracranial stereotactic radiotherapy for primary and metastatic renal cell carcinoma. Radiother Oncol 2005; 77 : 88-95.

57. Milano MT, Katz AW, Zhang H, Okunieff P. Oligometastases treated with stereotactic body radiotherapy: Long-term follow-up of prospective study. Int J Radiat Oncol Biol Phys 2012; 83 : 878-86.

58. Kang JK, Kim MS, Kim JH, Yoo SY, Cho CK, Yang KM, et al. Oligometastases confined one organ from colorectal cancer treated by SBRT. Clin Exp Metastasis 2010; 27 : 273-8.

59. Salama JK, Hasselle MD, Chmura SJ, Malik R, Mehta N, Yenice KM, et al. Stereotactic body radiotherapy for multisite extracranial oligometastases: Final report of a dose escalation trial in patients with 1 to 5 sites of metastatic disease. Cancer 2012; 118 : 2962-70.

60. Ernst-Steeken A, Lambrecht U, Mueller R, Sauer R, Grabenbauer G. Hypofractionated stereotactic radiotherapy for primary and secondary intrapulmonary tumors: First results of a phase I/I study. Strahlenther Onkol 2006; 182 : 696-702.

61. Rusthoven KE, Kavanagh BD, Burri SH, Chen C, Cardenes H, Chidel MA, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for lung metastases. J Clin Oncol 2009; 27 : 1579-84.

62. Hou X, Wang W, Zhang F, Hu K. Stereotactic body radiation therapy for oligometastatic pulmonary tumors from cervical cancer. Asia Pac J Clin Oncol 2019; 15 : e175-80.

63. Timmerman RD, Hu C, Michalski J, Straube W, Galvin J, Johnstone D, et al. Long-term results of RTOG 0236: A Phase II Trial of Stereotactic Body Radiation Therapy (SBRT) in the treatment of patients with medically inoperable stage I non-small cell lung cancer. Int J Radiat Oncol Biol Phys 2014; 84 : S30.

64. Videtic GM, Paulus R, Singh AK, Chang JY, Parker W, Olivier KR, et al. Long-term follow-up on NRG oncology RTOG 0915 (NCCTG N0927): A randomized phase 2 study comparing 2 stereotactic body radiation therapy schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer. Int J Radiat Oncol Biol Phys 2019; 103 : 1077-84.

65. Kim GE, Lee SW, Suh CO, Park TK, Kim JW, Park JT, et al. Hepatic metastases from carcinoma of the uterine cervix. Gynecol Oncol 1998; 70 : 56-60.

66. Høyer M, Swaminath A, Bydder S, Lock M, Méndez Romero A, Kavanagh B, et al. Radiotherapy for liver metastases: A review of evidence. Int J Radiat Oncol Biol Phys 2012; 82 : 1047-57.

67. Rusthoven KE, Kavanagh BD, Cardenes H, Stieber VW, Burri SH, Feigenberg SJ, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for liver metastases. J Clin Oncol 2009; 27 : 1572-8.

68. Andratschke N, Alheid H, Allgäuer M, Becker G, Blanck O, Boda-Heggemann J, et al. The SBRT database initiative of the German Society for Radiation Oncology (DEGRO): Patterns of care and outcome analysis of stereotactic body radiotherapy (SBRT) for liver oligometastases in 474 patients with 623 metastases. BMC Cancer 2018; 18 : 283.

69. Blomgren H, Lax I, Näslund I, Svanström R. Stereotactic high dose fraction radiation therapy of extracranial tumors using an accelerator. Clinical experience of the first thirty-one patients. Acta Oncol 1995; 34 : 861-70.

70. Høyer M, Roed H, Traber Hansen A, Ohlhuis L, Petersen J, Nelleman H, et al. Phase II study on stereotactic body radiotherapy of colorectal metastases. Acta Oncol 2006; 45 : 823-30.

71. Lee MT, Kim JJ, Dinniwell R, Brierley J, Lockwood G, Wong R, et al. Phase I study of individualized stereotactic body radiotherapy of liver metastases. J Clin Oncol 2009; 27 : 1585-91.

72. Goodman KA, Wiegener EA, Maturen KE, Zhang Z, Mo Q, Yang G, et al. Dose-escalation study of single-fraction stereotactic body radiotherapy for liver malignancies. Int J Radiat Oncol Biol Phys 2010; 78 : 486-93.

73. Rule W, Timmerman R, Tong L, Abdulrahman R, Meyer J, Boike T, et al. Phase I dose-escalation study of stereotactic body radiotherapy in patients with hepatic metastases. Ann Surg Oncol 2011; 18 : 1081-7.

74. Mahadevan A, Blanck O, Lanciano R, Peddada A, Sundararaman S, D’Ambrosio D, et al. Stereotactic Body Radiotherapy (SBRT) for liver metastasis – Clinical outcomes from the international multi-institutional RSSearch® Patient Registry. Radiat Oncol 2018; 13 : 26.

75. Wulf J, Guckenberger M, Haedinger U, Oppitz U, Mueller G, Baier K, et al. Stereotactic radiotherapy of primary liver cancer and hepatic metastases. Acta Oncol 2006; 45 : 838-47.

76. Laliscia C, Fabrini MG, Delishaj D, Morganti R, Greco C, Cantarella M, et al. Clinical outcomes of stereotactic body radiotherapy in oligometastatic gynecological cancer. Int J Gynecol Cancer 2017; 27 : 396-402.

77. Ahobila V, Ning MS, Jhingran A, Frumovitz M, Schmeler K, Eifel PJ, et al. Outcomes and patterns of relapse following definitive radiation therapy for treatment of oligometastatic cervical cancer. Int J Radiat Oncol 2017; 99 : S26-7.

78. Huang K, Jia M, Li P, Han J, Zhang R, Li Q, et al. Radiotherapy improves the survival of patients with metastatic cervical cancer: A propensity-matched analysis of SEER database. Int J Gynecol Cancer 2018; 28 : 1360-8.

79. Seo YS, Kim MS, Cho CK, Yoo HJ, Jang WI, Kim KB, et al. Stereotactic body radiotherapy for oligometastases confined to the para-aortic region: Clinical outcomes and the significance of radiotherapy field and dose. Cancer Invest 2015; 33 : 180-7.

80. Tree AC, Khoo VS, Eeles RA, Ahmed M, Dearaley DP, Hawkins MA, et al. Stereotactic body radiotherapy for oligometastases. Lancet Oncol 2013; 14 : e28-37.
Stereotactic body radiotherapy for recurrent or oligometastatic uterine cervix cancer: A cooperative study of the Korean Radiation Oncology Group (KROG 14-11). *Anticancer Res* 2015; 35 : 5103-10.

Mesko S, Sandler K, Cohen J, Konecný G, Steinberg M, Kamrava M. Clinical outcomes for stereotactic ablative radiotherapy in oligometastatic and oligoprogressive gynecological malignancies. *Int J Gynecol Cancer* 2017; 27 : 403-8.

Klement RJ, Guckenberger M, Alheid H, Allgäuer M, Becker G, Blanck O, et al. Stereotactic body radiotherapy for oligo-metastatic liver disease – Influence of pre-treatment chemotherapy and histology on local tumor control. *Radiother Oncol* 2017; 123 : 227-33.

Ricco A, Davis J, Rate W, Yang J, Perry D, Pablo J, et al. Lung metastases treated with stereotactic body radiotherapy: The RSSearch® patient Registry’s experience. *Radiat Oncol* 2017; 12 : 35.

Hong TS, Wo JY, Borger DR, Yeap BY, McDonnell EL, Willers H, et al. Phase II study of proton-based stereotactic body radiation therapy for liver metastases: Importance of tumor genotype. *J Natl Cancer Inst* 2017; 109 : 1-8.

Bentzen SM, Constine LS, Deasy JO, Eisbruch A, Jackson A, Marks LB, et al. Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC): An introduction to the scientific issues. *Int J Radiat Oncol Biol Phys* 2010; 76 : S3-9.

Thanaprapasr D, Narththanarung A, Likittanasombut P, Na Ayudhya NI, Charakorn C, Udomsupayakul U, et al. Bone metastasis in cervical cancer patients over a 10-year period. *Int J Gynecol Cancer* 2010; 20 : 373-8.

Disibio G, French SW. Metastatic patterns of cancers: Results from a large autopsy study. *Arch Pathol Lab Med* 2008; 132 : 931-9.

Yoon A, Choi CH, Kim HJ, Park JY, Lee YY, Kim TJ, et al. Contributing factors for bone metastasis in uterine cervical cancer. *Int J Gynecol Cancer* 2013; 23 : 1311-7.

Ost P, Jereczek-Fossa BA, As NV, Zilli T, Mueacevic A, Olivier K, et al. Progression-free survival following stereotactic body radiotherapy for oligometastatic prostate cancer treatment-naive recurrence: A multi-institutional analysis. *Eur Urol* 2016; 69 : 9-12.

Wang XS, Rhines LD, Shiou AS, Yang JN, Selek U, Gning I, et al. Stereotactic body radiation therapy for management of spinal metastases in patients without spinal cord compression: A phase 1-2 trial. *Lancet Oncol* 2012; 13 : 395-402.

Garg AK, Shiou AS, Yang J, Wang XS, Allen P, Brown BW, et al. Phase Ⅲ trial of single-session stereotactic body radiotherapy for previously unirradiated spinal metastases. *Cancer* 2012; 118 : 5069-77.

Hall WA, Stapleford LJ, Hadijapanayis CG, Curran WJ, Crocker I, Shu HK. Stereotactic body radiosurgery for spinal metastatic disease: An evidence-based review. *Int J Surg Oncol* 2011; 2011 : 979214.
107. Patchell RA, Tibbs PA, Walsh JW, Dempsey RJ, Maruyama Y, Kryscio RJ, et al. A randomized trial of surgery in the treatment of single metastases to the brain. N Engl J Med 1990; 322 : 494-500.

108. Mintz AH, Kestle J, Rathbone MP, Gaspar L, Hugenholtz H, Fisher B, et al. A randomized trial to assess the efficacy of surgery in addition to radiotherapy in patients with a single cerebral metastasis. Cancer 1996; 78 : 1470-6.

109. Mehta MP, Rozental JM, Levin AB, Mackie TR, Kubsad SS, Gehring MA, et al. Defining the role of radiosurgery in the management of brain metastases. Int J Radiat Oncol Biol Phys 1992; 24 : 619-25.

110. Flickinger JC, Kondziolka D, Lunsford LD, Coffey RJ, Goodman ML, Shaw EG, et al. A multi-institutional experience with stereotactic radiosurgery for solitary brain metastasis. Int J Radiat Oncol Biol Phys 1994; 28 : 797-802.

111. Patchell RA, Tibbs PA, Regine WF, Dempsey RJ, Mohiuddin M, Kryscio RJ, et al. Postoperative radiotherapy in the treatment of single metastases to the brain: A randomized trial. JAMA 1998; 280 : 1485-9.

112. Li B, Yu J, Suntharalingam M, Kennedy AS, Amin PP, Chen Z, et al. Comparison of three treatment options for single brain metastasis from lung cancer. Int J Cancer 2000; 90 : 37-45.

113. Andrews DW, Scott CB, Sperduto PW, Flanders AE, Gaspar LE, Schell MC, et al. Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: Phase III results of the RTOG 9508 randomised trial. Lancet 2004; 363 : 1665-72.

114. Mahmoud-Ahmed AS, Suh JH, Barnett GH, Webster KD, Kennedy AW. Tumor distribution and survival in six patients with brain metastases from cervical carcinoma. Gynecol Oncol 2001; 81 : 196-200.

115. Chung SB, Jo KI, Seol HJ, Nam DH, Lee JI. Radiosurgery to palliate symptoms in brain metastases from uterine cervix cancer. Acta Neurochir (Wien) 2013; 155 : 399-405.

116. Niibe Y, Karasawa K, Nakamura O, Shinoura N, Okamoto K, Yamada R, et al. Survival benefit of stereotactic radiosurgery for metastatic brain tumors in patients with controlled primary lesions and no other distant metastases. Anticancer Res 2003; 23 : 4157-9.

117. de Vin T, Engels B, Gevaert T, Storme G, De Ridder M. Stereotactic radiotherapy for oligometastatic cancer: A prognostic model for survival. Ann Oncol 2014; 25 : 467-71.

118. Bandyopadhyay A, Mukherjee U, Ghosh S, Ghosh S, Sarkar SK. Pattern of failure with locally advanced cervical cancer – A retrospective audit and analysis of contributory factors. Asian Pac J Cancer Prev 2018; 19 : 73-9.

119. Nomden CN, Pötter R, de Leeuw AA, Tanderup K, Lindegaard JC, Schmid MP, et al. Nodal failure after chemo-radiation and MRI guided brachytherapy in cervical cancer: Patterns of failure in the EMBRACE study cohort. Radiother Oncol 2019; 134 : 185-90.

120. Jain P, Hunter RD, Livsey JE, Coyle C, Swindell R, Davidson SE. Salvaging locoregional recurrence with radiotherapy after surgery in early cervical cancer. Clin Oncol (R Coll Radiol) 2007; 19 : 763-8.

121. Ijaz T, Eifel PJ, Burke T, Oswald MJ. Radiation therapy of pelvic recurrence after radical hysterectomy for cervical carcinoma. Gynecol Oncol 1998; 70 : 241-6.

122. Mahantshetty U, Kalyani N, Engineer R, Chopra S, Jamema S, Ghadi Y, et al. Reirradiation using high-dose-rate brachytherapy in recurrent carcinoma of uterine cervix. Brachytherapy 2014; 13 : 548-53.

123. Gupta S, Maheshwari A, Parah P, Mahantshetty U, Hawaldar R, Sastri Chopra S, et al. Neoadjuvant chemotherapy followed by radical surgery versus concomitant chemotherapy and radiotherapy in patients with stage IB2, IIA, or IIB squamous cervical cancer: A randomized controlled trial. J Clin Oncol 2018; 36 : 1548-55.

124. NCCN Guidelines Cervical Cancer v1 2020; 2020. Available from: HYPERLINK "https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf" https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf, accessed on March 13, 2020.

125. Kubota H, Tsujino K, Sulaiman NS, Sekii S, Matsumoto Y, Ota Y, et al. Comparison of salvage therapies for isolated para-aortic lymph node recurrence in patients with uterine cervical cancer after definitive treatment. Radiat Oncol 2019; 14 : 236.

126. Jeon W, Koh HK, Kim HJ, Wu HG, Kim JH, Chung HH. Salvage radiotherapy for lymph node recurrence after radical surgery in cervical cancer. J Gynecol Oncol 2012; 23 : 168-74.

127. Kamran SC, Curreri SA, Muralidhar V, Nguyen PL, Martin NE, Boyajian R, et al. Re-irradiation of the pelvis for a genitourinary second malignant neoplasm or a local recurrence after full-dose pelvic radiotherapy for a pelvic cancer: Experience in a high-volume cancer center. J Clin Oncol 2016; 34 (Suppl) : 494.

128. Bonomo P, Cipressi S, Saieva C, Greto D, Masì L, Piair F, et al. Clinical outcome of stereotactic body radiotherapy for abdominal lymph node metastases. Tumori 2013; 99 : 611-6.

129. Corvò R, Lamanna G, Vegge S, Belgioia L, Bosetti D, Alo D, et al. Once-weekly stereotactic radiotherapy for patients with oligometastases: Compliance and preliminary efficacy. Tumori 2013; 99 : 159-63.

130. Jereczek-Fossa BA, Piperno G, Ronchi S, Catalano G, Fodor C, Cambria R, et al. Linac-based stereotactic body radiotherapy for oligometastatic patients with single abdominal lymph node recurrent cancer. Am J Clin Oncol 2014; 37 : 227-33.

131. Kim MS, Cho CK, Yang KM, Lee DH, Moon SM, Shin YJ. Stereotactic body radiotherapy for isolated paraaortic lymph node recurrence from colorectal cancer. World J Gastroenterol 2009; 15 : 6091-5.

132. Choi CW, Cho CK, Yoo SY, Kim MS, Yang KM, Yoo HJ, et al. Image-guided stereotactic body radiation therapy in patients with isolated para-aortic lymph node metastases from uterine cervical and corpus cancer. Int J Radiat Oncol Biol Phys 2009; 74 : 147-53.
133. Bignardi M, Navarria P, Mancosu P, Cozzi L, Fogliata A, Tozzi A, et al. Clinical outcome of hypofractionated stereotactic radiotherapy for abdominal lymph node metastases. *Int J Radiat Oncol Biol Phys* 2011; 81: 831-8.

134. Loi M, Frelinghuysen M, Klass ND, Oomen-De Hoop E, Granton PV, Aerts J, et al. Locoregional control and survival after lymph node SBRT in oligometastatic disease. *Clin Exp Metastasis* 2018; 35: 625-33.

135. Murray LJ, Lilley J, Hawkins MA, Henry AM, Dickinson P, Sebag-Montefiore D. Pelvic re-irradiation using stereotactic ablative radiotherapy (SABR): A systematic review. *Radiother Oncol* 2017; 125: 213-22.

136. Van den Begin R, Engels B, Collen C, de Vin T, Defauw A, Dubaere E, et al. The METABANK score: A clinical tool to predict survival after stereotactic radiotherapy for oligometastatic disease. *Radiother Oncol* 2019; 133: 113-9.

*For correspondence:* Dr Supriya Chopra, Department of Radiation Oncology, Advanced Centre for Treatment, Research & Education in Cancer, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai 400 012, Maharashtra, India.

e-mail: supriyasastri@gmail.com