Conference Scene
Future Oncology

Best of International Stereotactic Radiosurgery Society Congress 2013: stereotactic body radiation therapy. Part I: spinal tumors

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11th International Stereotactic Radiosurgery Society Congress

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The 11th biennial International Stereotactic Radiosurgery Society Congress represented another historical gathering of professionals in the field of stereotactic radiosurgery. This congress was held on 16–20 June 2013 in Toronto (ON, Canada), and the chairman was Arjun Sahgal, the co-chair was Michael Schwartz and president of the society was Jean Regis. The congress attracted 550 attendants from all over the world and over 300 abstracts were presented. Among the abstracts presented, 62 (36 oral) were pertaining to stereotactic body radiation therapy (SBRT). Exciting new findings were presented by colleagues from North America, Europe and Asia. This short conference scene (part I) provides a summary of the best abstracts on SBRT for spinal tumors presented in the congress. A separate conference scene on SBRT for nonspinal tumors (part II) also appears in this issue of *Future Oncology*.

Spinal tumors

The Radiation Therapy Oncology Group is conducting a Phase II/III trial of stereotactic body radiation therapy (SBRT) for spinal metastasis (RTOG 0631) and preliminary results demonstrating the feasibility and safety of the Phase II component were presented in the plenary session of the International Stereotactic Radiosurgery Society congress by Ryu [1]. Forty-one patients each with one to three spinal metastases were enrolled in the study and each lesion was treated to a dose of 16 Gy in one fraction. Among them, 36 (30 with one lesion and six with two lesions) had on-study information. All the patients were successfully treated with SBRT according to protocol guidelines, with spinal cord constraints met in all patients. All the patients had optimal (91%) or acceptable image-guided radiotherapy compliance. Grade 1–2 and grade 3–5 SBRT-related adverse events were observed in seven and zero patients, respectively. Grade 3–4 non-SBRT-related adverse events were observed in four patients [1]. Clinical outcomes with respect to local control (LC) and pain control will follow as data mature, and the Phase III portion of the trial comparing conventional radiotherapy to a dose of 8 Gy in one fraction and SBRT to a dose of 16–18 Gy is ongoing.

Colleagues from University of Toronto (ON, Canada) reported several important studies in spinal SBRT. In one study, Sahgal's group assessed spinal cord motion in spinal SBRT with the use of dynamic axial and sagittal MRI in 33 patients [2]. They found that the median physiologic oscillatory spinal cord motion in the anteroposterior, lateral and superoinferior directions were 0.17, 0.20 and 0.24 mm, respectively. The corresponding maximum values were 0.92, 0.93 and 0.83 mm, respectively. Corresponding bulk displacements from gross patient motion were 0.44 mm (median)/1.77 mm (maximum), 0.52 mm (median)/2.87 mm (maximum) and 0.59 mm (median)/3.90 mm (maximum), respectively [2]. Bulk displacements were more

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Future Medicine part of fsg

than 1.5 mm in 5.6, 11.1 and 16.7% of vertebral levels in the anteroposterior, lateral and superoinferior directions, respectively [2]. The findings of this study underscore the importance of robust immobilization and the use of planning organ at risk volume for spinal cord during treatment planning of spinal SBRT. In another study, Becker N *et al.* from the University of Toronto found that with the addition of flattening-filter-free beams for volumetric modulated arc therapy, the treatment delivery times could be reduced by 57 and 75% for 6 and 10 MV, respectively [3]. Hyde *et al.,* also from the University of Toronto, examined the impact of treating multiple consecutive vertebrae as a single volume with spinal SBRT on positional accuracy based on 415 verification cone-beam computed tomography images. A total of 25, 16, 20 and six treatments were given for single thoracic vertebrae, multiple thoracic vertebrae, single lumbar vertebrae and multiple lumbar vertebrae, respectively [4]. The absolute intrafraction translational motion averaged over all directions for single thoracic vertebrae, multiple thoracic vertebrae, single lumbar vertebrae, and multiple lumbar vertebrae were 0.54, 0.54, 0.36 and 0.47 mm, respectively. The corresponding absolute intrafraction rotational motion averaged over all directions were 0.31°, 0.26°, 0.23° and 0.27°, respectively [4]. The percentage of cases that were not covered by the 1.5-mm planning target volume margin were 3.8, 4.0, 1.0 and 0.85%, respectively. A statistically significant difference between single and multiple spinal segments was only observed for lumbar and not thoracic vertebrae, although there were more treatments that went beyond tolerance for thoracic vertebrae [4]. This study underscores the importance of planning a target volume margin expansion for spinal SBRT and very close monitoring of intrafraction motion, especially when multiple lumbar vertebrae are included in a single volume.

The outcomes for patients with renal cell carcinoma (RCC) spinal metastases and postoperative spinal metastasis patients treated with SBRT at the University of Toronto were also presented [5,6]. In the first study, outcomes from 37 patients with 71 RCC spinal metastases treated with SBRT to a dose of 18–30 Gy in one to five fractions (median: 24 Gy in two fractions) were presented. The 1-year overall survival (OS) and LC rates were 64 and 83%, respectively [5]. The most common site of failure was epidural space, with two out of three of the lesions that failed occurring there. Oligometastatic status was the only factor predicting OS [5]. In the second study, 80 patients with spinal metastases were treated with postoperative SBRT. The 1-year LC and OS rates were 84% and 63%, respectively [6]. Failure in the epidural space occurred in 71% of the lesions that failed. Treatment with one or two fractions and postoperative grade 0 or 1 epidural disease predicted LC [6]. The findings of these studies were in keeping with the observations from other series where one of the most common places for failure was the epidural space, and this was most likely due to underdosing of the epidural disease caused by aggressive attempts to spare the spinal cord or poor tumor biology. The postoperative series was of high importance as it showed for the first time the value of aggressive debulking of epidural disease to maximize LC outcomes following SBRT. [7]. Since both studies had median follow-up intervals of ≤12 months, a much longer follow-up is required to determine the long-term LC and confirm results.

Pain flare and vertebral compression fractures (VCFs) are commonly encountered complications of spinal SBRT and colleagues from the University of Toronto who have a large body of experience with this technique presented three papers pertaining to these issues. In the first paper, Thibault *et al.* presented data on VCFs after SBRT for spinal metastases from RCC [8]. The observed incidence was 16%, which is similar to a prior study that included all histologies from the same group [9]. The only predictive factor was baseline VCFs [8]. It does not appear that spinal metastases from RCC are significantly different from other histologies in terms of risk of VCF after SBRT. In the second paper, Chiang *et al.* prospectively evaluated pain flare associated with SBRT for spinal metastasis, and the incidence was striking at 68.3% [10]. This paper has since been published in *International Journal of Radiation Oncology, Biology and Physics* after abstract submission [11]. In the third study [12], which has since been published in *Journal of Neurosurgery Spine* after abstract submission [13], the clinical, radiologic and pathologic findings of two patients with radiographic evidence of late VCF after SBRT for spinal metastasis were presented. Radiation necrosis and radiation fibrosis were observed in those two patients after 20 Gy in one fraction and 24 Gy in two fractions, respectively [13]. Biopsy is recommended by the group if it is uncertain whether the marrow signal changes represent radiation-induced effect or tumor progression. Colleagues from University of Pittsburgh (PA, USA) also presented the findings of histologic examination of spinal metastases after SBRT, although in a much larger series. Among the 222 patients treated with single fraction SBRT to a dose of 14–20 Gy, 15 required subsequent surgery. Ten out of the 15 had surgery for suspected

progressive disease causing compression of spinal cord or cauda equina and five out of the 15 for symptomatic VCF and/or mechanical instability [14]. Thirteen cases showed varying degrees of inflammation. Among the ten cases with suspected progression, under the light microscope, nine showed a tumor within the specimen, two showed ectatic vessels, nine had fibrotic marrow and nine had necrosis [14]. The two latter studies help spinal SBRT practitioners to better understand the pathophysiologic changes in spinal metastases treated with ablative radiotherapy.

Chang *et al.* from the Korea Institute of Radiological and Medical Science (Seoul, South Korea), presented their outcomes on SBRT for spinal metastases from hepatocellular carcinoma. Twenty seven patients with 39 spinal metastases were treated with CyberKnife® (Accuray, CA, USA) SBRT to a single equivalent dose of 20 Gy (range: 12–28.5 Gy). The local recurrence rate was 23.1% [15]. Pain control was achieved in 84.6% of the lesions and 21.2% had recurrent pain. The median OS and progression-free survival (PFS) rates were 8 (19 for age ≤52 years and 7 for >52 years) and 7 months, respectively [15]. Patients who had prior radiotherapy had poorer PFS. No neurologic complications were observed. Given the short mean follow-up of 11.1 months, continued follow-up is necessary to determine long-term PFS. This is the largest series on hepatocellular carcinoma spine SBRT known to date.

Sohn *et al.* from Inje University Ilsan Paik Hospital (Goyang, South Korea) presented their experience with SBRT for benign intradural extramedullary spinal tumors. Sixty-two patients with neurogenic tumors (41 schwannomas and 11 neurofibromas) and meningiomas (ten) were treated with SBRT using mostly a single-fraction regimen, delivering 13 and 15 Gy to neurogenic tumors and meningiomas, respectively [16]. Eight patients with giant presacral and intraosseous schwannomas, or en-plaque type or atypical meningiomas were treated with 2–5 Gy. Two patients with neurofibromas developed malignant transformation of their SBRT-treated tumors, and one patient with atypical meningioma developed neurologic toxicity [16]. Four patients required repeat SBRT for either newly developed neurogenic tumors or recurrent meningiomas. Pain relief was achieved in the three patients with giant intraosseous schwannomas. Marchetti *et al.* from Fondazione IRCCS Istituto Neurologico C Besta (Milan, Italy), presented their results on the use of SBRT for intradural benign spinal tumors in 20 patients with 24 tumors (14 meningiomas, nine schwannomas and one neurofibroma). Eleven lesions were treated with single fraction SBRT to a dose of 10–15 Gy and the rest were treated with multisession SBRT to a dose of 16.8–30 Gy in 4–6 Gy fractions [17]. At a median follow-up of 43 months, the freedom-from-progression rate was 100%. Neurologic status was either preserved or improved and there were no permanent treatment-induced sequelae. Significant and durable pain relief was achieved in all lesions with pain [17]. While the results of the above two studies were promising, given the fact that benign spinal tumors typically grow slowly, a much longer follow-up is required to better define the role of SBRT in this group of tumors. The malignant transformation of neurofibroma induced by radiotherapy is a real risk and this was once again demonstrated in the study by Sohn *et al.* study [16].

Conclusion

The spine SBRT sessions at the International Stereotactic Radiosurgery Society were a major success with high scientific quality abstracts presented.

Financial & competing interests disclosure

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