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Technical Note

Considerations regarding carotid artery dose in radiotherapy of the cervical spine

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A R T I C L E I N F O

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A B S T R A C T

Radiation to the carotid arteries, e.g. in the context of head and neck cancer treatment, is one of several risk factors for artery stenosis. In principle, this fact may also have implications for stereotactic cervical spine radiotherapy, because long-term survival can be achieved in patients with oligometastatic disease and favorable prognostic features. Here, we suggest that radiation dose distributions with reduced dose to the carotid artery are achievable when planning stereotactic cervical spine radiotherapy. Patients with high likelihood of long-term survival may benefit from such vessel-sparing approaches.

Introduction

Spinal metastases have long been treated with palliative radiotherapy, for indications such as pain relief, recalcification of bone defects and consolidative treatment after surgery [1]. More recently, high-dose radiotherapy, mostly stereotactic body radiotherapy (SBRT), has been utilized in selected cases [2,3], in particular patients with oligometastatic cancer [4]. This development was due to the fact that better local control can be obtained, and that patients who survive for several years after radiotherapy may benefit from durable local control. Spinal SBRT may also result in adverse effects if the radiation dose to normal tissues exceeds their tolerance. In this context, considerable efforts were made to define acceptable dose constraints for the spinal cord, and also the risk of bone fracture, esophagitis or bowel toxicity has been addressed [5,6].

When treating parts of the cervical spine, the carotid artery(ies) may be located very close to the planning target volume (PTV). Previous research has shown that reduced blood perfusion due to vessel stenosis after several years may occur in different settings, e.g. radiotherapy for head and neck cancer or skull base tumors [7–10]. As discussed by these authors, radiation-induced vessel stenosis is believed to be caused by a combination of direct vessel wall damage leading to intimal proliferation, necrosis of the media, periadventitial fibrosis and accelerated atherosclerosis, and indirect effects resulting from radiation-induced obliteration of the adventitial vasa vasorum. Long-term morbidity may be aggravated by vascular adverse events.

Dosimetric studies have demonstrated that doses close to the prescription dose (or even higher in case of hot spots in the relevant organ at risk) are difficult to avoid in challenging anatomic sites [11,12]. This effect is often more pronounced if the target volume is large and irregularly shaped. Here, we present considerations for treatment planning that are relevant to patients with expected long-term survival despite presence of distant metastases in the cervical spine.

Methods

This technical note originates from our institution's recent implementation of linac-based spine SBRT during which several published guidelines and dose constraints were reviewed. While planning our first patient with a cervical spine metastasis according to our standard workflow (treatment planning computed tomography without intravenous contrast), we realized that the carotid arteries, which were not routinely contoured, may receive high doses of radiation and we wondered whether or not dose reductions could be achieved. Re-planning after contouring of the relevant part of the carotid artery was performed (Varian Eclipse® and TrueBeam®). The results are discussed in the context of other indications for radiotherapy in the same region of the body.

Results

As illustrated in Table 1, severely hypofractionated spine SBRT may

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Table 1
Equi-effective dose calculation according to the linear-quadratic (LQ) model for late-responding tissue with α/β value 2 Gy. Both equivalent dose in 2-Gy fractions (EQD2) and biologically effective dose (BED) were calculated.

Fractionation	Corresponding EQD2	BED
30 fractions of 2 Gy	60	120
25 fractions of 2 Gy	50	100
3 fractions of 9 Gy	74	148.5
80 % of 3 fractions of 9 Gy	50	99.4
2 fractions of 12 Gy	84	168
80 % of 2 fractions of 12 Gy	56	111.4

result in considerable equi-effective doses in tissues located close to the target volume. As displayed in Fig. 1a-c, large interindividual differences exist regarding shape and size of the clinical target volume (CTV), which often is located close to the carotid artery(ies). In addition, comorbidity can cause impaired blood perfusion already before radiotherapy. Fig. 2a shows a clinical example of a well-lateralized metastasis, where the original treatment plan was developed according to standard operating procedures without contouring of the carotid artery. Later on, the ipsilateral carotid artery was contoured, followed by carotid-sparing re-planning. As shown in Fig. 2b and Table 2, comparable CTV coverage was obtained while maintaining maximum doses to the spinal canal, spinal cord and pharyngeal mucosa. Both maximum and mean carotid artery dose could be reduced successfully.

Discussion

The carotid artery(ies) may be exposed to high doses of radiation not only when treating head and neck or skull base cancers, but also in the context of spine SBRT. The amount of exposure varies with paraspinal tumor infiltration and also margin width that is needed to ensure adequate dose to the CTV. In the present example, high maximum and mean doses to the artery were observed. Dose reduction was feasible. For most patients with metastatic cancer, carotid-sparing dose distributions will not translate into clinical benefit, due to the discrepancy between remaining life span and time to development of late toxicity. In these cases, priority should be given to target volume coverage and safe spinal cord and pharynx/esophagus doses. Balancing the established planning objectives is often challenging, however, as illustrated in Fig. 2, additional consideration of the carotid artery dose may be feasible in the minority of patients with good prognosis. According to data from the head and neck cancer setting, patients with expected survival of >5 years and those aged <60 years may benefit most from lowering the risk of carotid artery injury [13]. Contouring consensus guidelines have been published by Brouwer et al. [14], which cover the common and internal carotid arteries, both of which may be relevant depending on the metastasis location. Regarding dose constraints, specific recommendations cannot be made in view of the lack of supporting data, however the dose to the carotid arteries should be kept as low as reasonably achievable [15,16].

Modifying factors such as pre-existing vascular damage (Fig. 1c) would strengthen the case for carotid-sparing techniques, as well as regular post-treatment assessment of vessel patency and early intervention, if needed. We have not systematically assessed carotid-sparing treatment plans in a series of patients. Other authors have done so, e.g. Vitolo et al. in patients with nasopharyngeal cancer [17]. The median mean dose to the carotid arteries was 65.7 Gy with intensity-modulated radiotherapy (IMRT) versus 58.4 Gy with simpler 3-field technique ($p < 0.001$). After application of dose constraints to the carotid arteries, they were able to reduce the mean carotid dose to 54 Gy in the IMRT re-plans. Other groups have evaluated carotid-sparing techniques in patients with glottis or breast cancer [18,19]. According to studies of radiotherapy in patients with nasopharynx cancer, the vertebral artery is also at risk of developing identical radiation-induced late damage [20]. No clear dose recommendations exist for this artery either. As indicated in Fig. 2,

Fig. 1. A. Treatment planning axial computed tomography (CT): 51-year-old male patient with spinal metastasis (C6, large soft tissue component, osseous extension not limited to vertebral corpus (yellow arrow)) from hepatocellular carcinoma (red arrow indicates carotid artery, no calcification present). B. Treatment planning axial computed tomography (CT): 71-year-old male patient with osteoblastic spinal metastasis (C6) from prostate cancer (red arrow indicates carotid artery, no calcification present). C. Treatment planning axial computed tomography (CT): 84-year-old male patient with osteoblastic spinal metastases from prostate cancer (red arrow indicates carotid artery, major calcification present). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

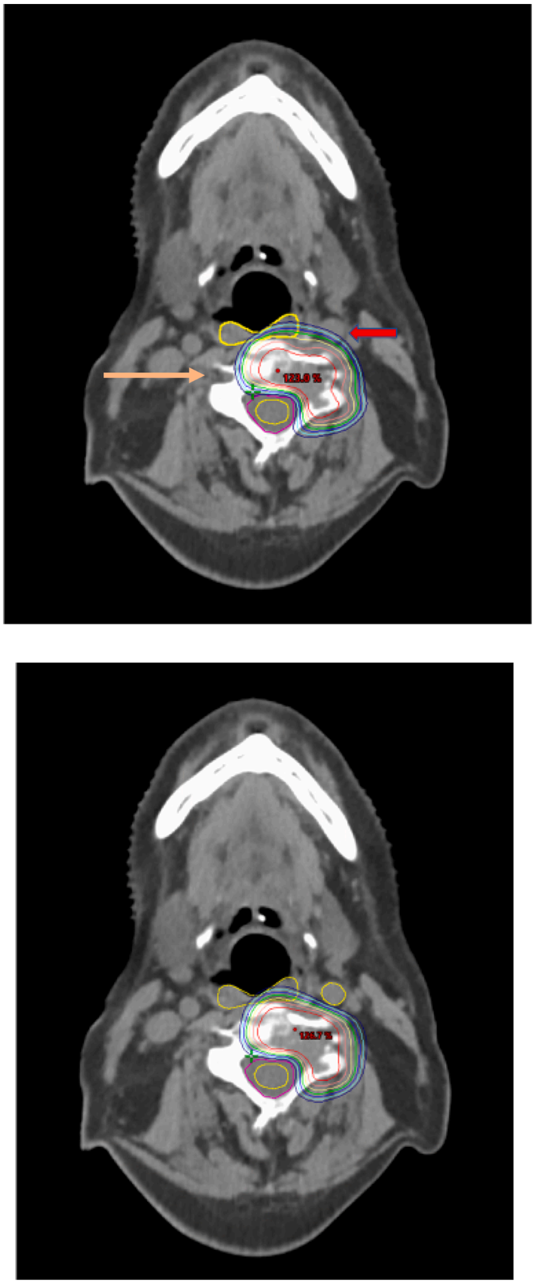

Fig. 2. A. Treatment planning axial computed tomography (CT): 74-year-old male patient with osteolytic spinal metastasis from clear cell kidney cancer (orange line: clinical target volume; red arrow indicates carotid artery; orange arrow indicates contralateral vertebral artery); volumetric modulated arc treatment plan: 100% isodose in yellow; lowest displayed isodose: 80% (dark blue); calculated in Varian Eclipse®. B. After re-planning: reduced dose to the carotid artery. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Standard treatment plan and optimized plan.

Parameter	Standard	After re-planning
Clinical target volume, minimum	82 %	81 %
Clinical target volume, D98	95 %	95 %
Clinical target volume, mean	112 %	114 %
Carotid artery, maximum	99 %	86 %
Carotid artery, mean	70 %	41 %

depending on the extent of metastatic involvement, the ipsilateral vertebral artery is often located inside the PTV, while the contralateral vertebral artery can be spared. It appears prudent to ensure that carotid-sparing planning avoids an unintentional dose increase to the vertebral artery.

High SBRT doses to the mediastinum or lung hilum and high cumulative doses to the carotid artery administered when re-irradiating head and neck cancer have been linked to serious bleeding events, e.g. carotid blow-out [21]. However, in the context of cervical spine SBRT artery stenosis appears more relevant, unless such treatment is performed as re-irradiation. The present results are limited by the lack of clinical data demonstrating the benefits of lower carotid artery doses in this particular setting and the fact that only one patient was re-planned and only one planning system and SBRT platform was utilized.

Conclusion

Radiation dose distributions with reduced dose to the carotid artery are achievable when planning cervical spine SBRT. Patients with high likelihood of long-term survival may benefit from such vessel-sparing approaches that lower the risk of artery stenosis.

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Ethics approval

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Consent to participate

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Consent for publication

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Declaration of Competing Interest

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

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