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Robotic Radiosurgery and the “Fingers of Death”

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Abstract

Background: Stereotactic body radiotherapy is emerging as an effective and efficient method for treating liver tumors, including hepatocellular carcinoma. With the widespread application of this complex treatment modality, new toxicities are encountered.

Case Presentation: We present the case of a patient treated with stereotactic body radiotherapy for a hepatocellular carcinoma who developed unexpected Grade 3 dermatitis in the contralateral axilla.

Discussion: In this paper we examine some of the intricacies of robotic stereotactic body radiotherapy, noting potential sources of unexpected toxicity. We assess the treatment plan and delivery method in our patient to determine potential causes of the dermatitis. We found that the contralateral axilla was not included in the calculation grid, and therefore, the high dose region was not reported.

Conclusions: We present simple practice methods to prevent unexpected “fingers of death” from affecting other patients: calculating the dose to the entire CT volume and limiting the monitor units per node treated.

Categories: Radiation Oncology, Oncology
Keywords: cyberknife, dermatitis, hepatocellular carcinoma, intensity modulated radiotherapy, radiotherapy

Introduction

Inverse-planned intensity modulated radiotherapy (IMRT) has gained widespread acceptance as a means of improving the therapeutic ratio of external beam radiotherapy. This modality traditionally utilizes an increased number of treatment fields with varying degrees of intensity in order to deliver a highly conformal dose to a defined target, while minimizing dose to selected normal structures. In the inverse-planning process, the planner enters a set of parameters into a computer system that utilizes an algorithm to generate a plan that best fits the stated parameters. These parameters include dose constraints for organs at risk and requirements to cover the target volume.

Stereotactic body radiotherapy (SBRT) involves delivering large doses of radiation in a few fractions for selected well-defined tumors outside the central nervous system. There are different methods for delivering SBRT, including conventional isocentric linear accelerator based SBRT, SBRT with modified specialized isocentric linear accelerators and SBRT with a dedicated non-isocentric robotic miniaturized linear accelerators. Delivery using conventional linear accelerators is an attractive option as radiotherapy centres are typically already equipped with such devices and can, with adequate training and relatively small investments in immobilization and motion management devices, deliver SBRT.

One drawback of isocentric SBRT treatment is that much of the dose delivery is limited to the plane of rotation of the accelerator gantry. This can result in higher doses of radiation to normal structure in the same axial plane as the target. Non-isocentric robotic SBRT using the CyberKnife robotic linear acceletor (Accuray, Sunnyvale, Ca.) allows targeting of the tumor from a wider range of directions, spreading out the entrance and exit dose over a wider area. Whereas isocentric SBRT can be delivered with IMRT or with 3D conformal radiation, CyberKnife treatments are by nature inverse-planned.

Since its inception, inverse-planned radiation has faced new challenges. Mohan et al. raised some of these concerns and are credited with coining the term "fingers of death" to described highly fluent beam paths that can deposit large doses of radiation to small volumes of normal tissue removed from the target [1, 2]. As these so-called fingers of death typically occur outside of explicitly specified normal structures, they can be hidden from dosimetric analysis and thus overlooked.

We present a case of Grade 3 dermatitis caused by a highly fluent beam path in a patient treated with robotic SBRT for a hepatocellular carcinoma (HCC).

List of abbreviations:

IMRT - Intesity Modulated RadioTherapy.

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SBRT - Sterotactic Body RadioTherapy.

HCC- HeatoCellular Carcinoma.

MU - Monitor Unit.

PTV-Planning Target Volume.

Case Presentation

The patient is a 71-year-old gentleman who presented for consideration of SBRT for a hepatocellular carcinoma. The patient did not have underlying hepatitis, cirrhosis or other risk factors for development of hepatocellular carcinoma.

He was initially diagnosed with oligometastatic hepatocellular carcinoma in June of 2006 when he presented with worsening low back pain. On investigation he was found to have a liver lesion along with lumbar spine metastases. As he had an unstable L5 vertebra, he underwent excisional biopsy of his metastasis with vertebral reconstruction. Review of the surgical specimen revealed a metastatic carcinoma morphologically and immunohistochemically compatible with hepatocellular carcinoma. Following surgery he received a course of external beam radiotherapy to the lumbosacral spine. He subsequently had repeated transarterial chemoembolizations using cisplatin. These treatments lead to short intervals of tumor stability followed by progression. In February 2009 he began systemic treatment with sorafenib, which he continued until February 2010 when the tumor again progressed. At that time the patient's case was discussed at tumor board, and the consensus was that, in the absence of active metastatic disease, the patient be considered for liver SBRT. At the time he had a solitary 8.3 cm lesion in the right lobe of the liver with an elevated alpha feto protein of 1975 ug/L.

It was decided to proceed with SBRT. Prior to CT planning, the patient had fiducial coils implanted into the liver for tumor tracking purposes. Under CT guidance, two platinum coils were deployed within the normal liver parenchyma surrounding the lesion. A planning CT scan was then performed and co-registered with a diagnostic MRI. The target was outlined as were normal structures (remaining liver, right kidney, small bowel and colon). The gross tumor volume was 242 ml which translated to a Planning Target Volume (PTV) of 405 ml. Because of concerns regarding liver tolerance, a reduced dose of 3000cGy in three fractions was selected. The dose was prescribed to the 77% isodose surface, which covered 97.4% of the planning target volume. The corrected conformity index was 1.21. This was delivered on nonconsecutive days over two weeks. The number of beams was limited to 200, spread over 47 nodes, and the monitor units (MU) per beam were limited to 1000. The entire treatment was planned using a 60 mm fixed cone. The planning software assigned a maximum MU of 697 in at least one beam. The doses to all outlined normal structures were within acceptable limits. The calculation grid encompassed a large area of the body and the medial portion of right upper extremity at the level of the liver. There was a steep dose gradient near the tumor, and the dose throughout the periphery of the calculation grid was low (see figure *1A*).

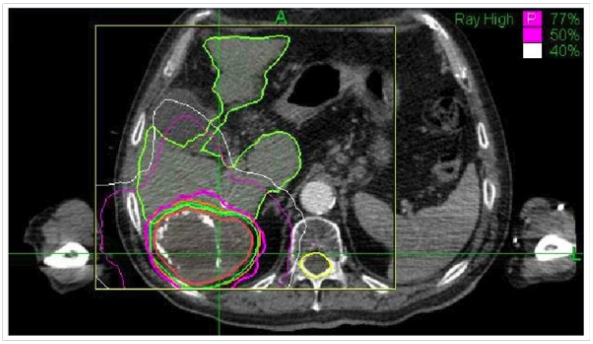

Figure 1A

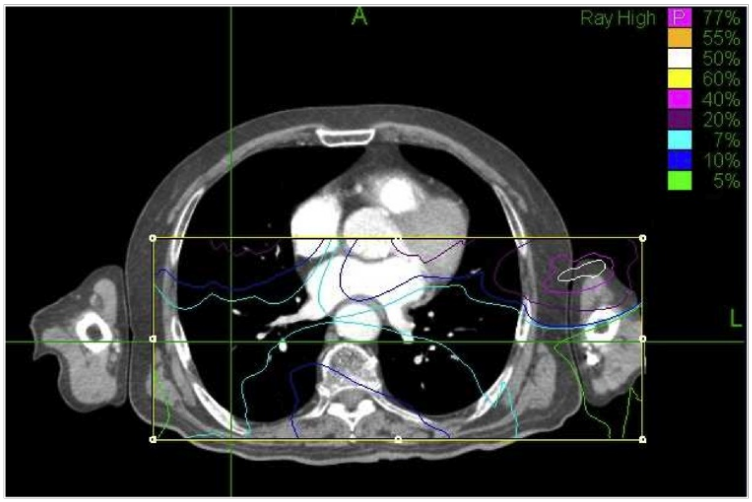

Figure 1B

FIGURE 1: Original calculation grid (1A) and post treatment calculation grid (1B)

In Figure 1A, note the small dose at the contralateral periphery of the calculation grid that does not extend all the way to the contralateral axilla. In Figure 1B the extended calculation grid now clearly demonstrates the area of increased dose in the left axilla (50% of the prescribed dose).

Treatment was delivered on a CyberKnife (Accuray, Sunnyvale, California) in July of 2009 utilizing The Synchrony respiratory tracking system. In August of 2009, the patient presented to the radiation oncology clinic with moist desquamation overlying his liver and right flank and also on his right elbow and left axilla (pictures 1-2).

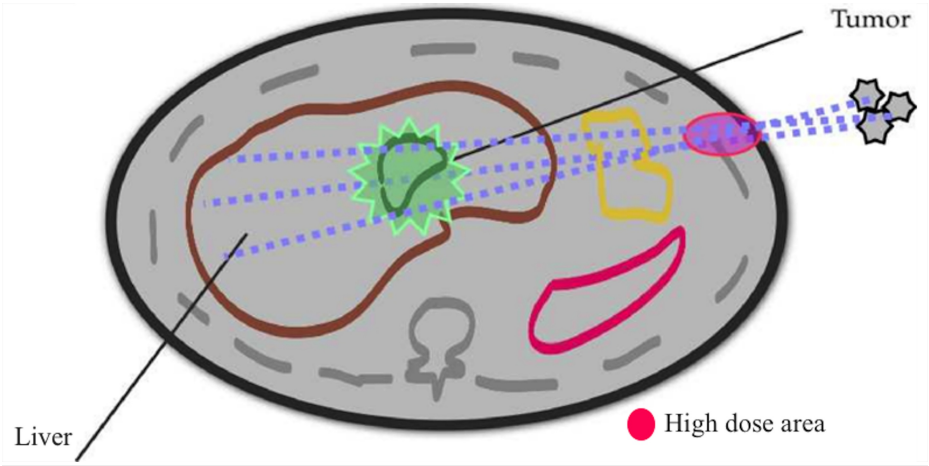

FIGURE 2: Overlapping entrance beamlets in robotic SBRT

Representation of a SBRT treatment plan for a liver tumor. Note the beamleats (blue dashed lines) originating from the same or adjacent nodes and the resulting convergence at the entrance of the beams. The resulting hot spot is an unintended consequence.

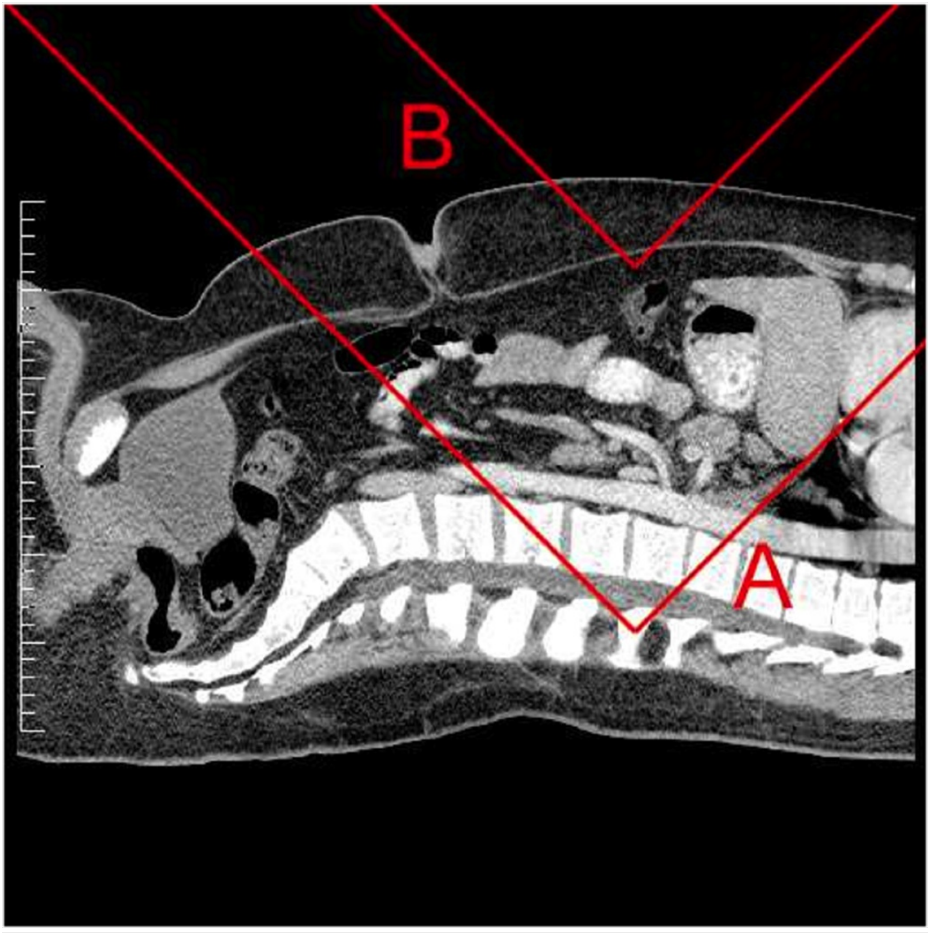

FIGURE 3: Beam entrance vs. target depth in robotic SBRT

Sagittal CT reconstruction showing how a deep target (A) will result in a large area being in the path of possible treatment beams, whereas a shallow (B) target with result in a smaller, more predicable area irradiated.

The left flank, arm and axilla had not initially been included in the calculation grid. Retrospectively, the dose was recalculated over the entire CT scan and, in addition to the expected area of high surface dose on the right flank and medial right arm, an unexpected "finger of death" was noted in the contralateral axilla. A small area in the axilla received a maximum dose of 22.5 Gy (see figure *1B*). This hot spot was located 23-25 cm from the PTV edge. The volume of this hotspot that received greater than 50% of the maximal dose (20 Gy) was 15 cc. The ipsilateral skin received a maximal dose of 27.6 Gy 1.5-6 cm from the PTV edge. The patient was prescribed topical silver sulfadiazene for his dermatitis, and by the next follow-up appointment two months later, the dermatitis had significantly improved (it subsequently completely resolved).

Discussion

Skin toxicity and unexpected areas of high dose have not commonly been the subject of previous reports of robotic radiosurgery [3,4]. In their series of 31 patients treated for HCC, Choi et al. did not describe any skin toxicity [5]. Similarly, Tse et al. did not report any grade 3 or greater dermatitis in their phase I HCC dose escalation study [6]. Grade 3 or greater dermatitis was found to occur in 6% of patients treated with SBRT for lung lesions at MSKCC [7]; however, lung treatments are generally to a higher biological dose (48 Gy in four fractions or 60 Gy in three fractions) than liver treatments. This group found that significant contributors to skin dermatitis were tumors located less than 5 cm from the skin, dose to the skin exceeding 50% of the prescribed dose and using fewer beams (three as opposed to four).

While not often reported, grade 1-2 dermatitis may not be uncommon in liver SBRT. On the other hand, grade 3 or greater dermatitis is probably an uncommon event. The bolus effect of skin folds or that caused by the immobilization device can contribute to the risk of developing dermatitis.

While non-isocentric robotic radiotherapy increases the degrees of freedom in terms of non-coplanar beam paths, it is typically restricted to treating patients supine with arms by their side. Due to the physical limitations of the device, posterior beams cannot be used and all radiation must pass through the anterior or lateral parts of the body. As the user does not directly select the beam paths used, their positioning can be

unpredictable and non-intuitive.

Another intricacy of the CyberKnife system is the utilization of nodes [8]. A node is specific location in the CyberKnife robotic arm path at which the linac will stop to deliver a circular subfield or subfields. The CyberKnife has many node locations but does not utilize them all for every treatment. At a given node, the CyberKnife can deliver multiple subfields by tilting slightly the angle of the beam. At a distance, these different beamlets can hit targets that are fairly well-spaced apart. However, as the beamlets trace back to the origin, they begin to converge and can create higher dose areas quite remote from the target. If, as was the case in our patient, beams enter the left shoulder to treat a target in the right flank, the beams can overlap at the entrance and be a few centimetres apart by the exit (see figure *2*).

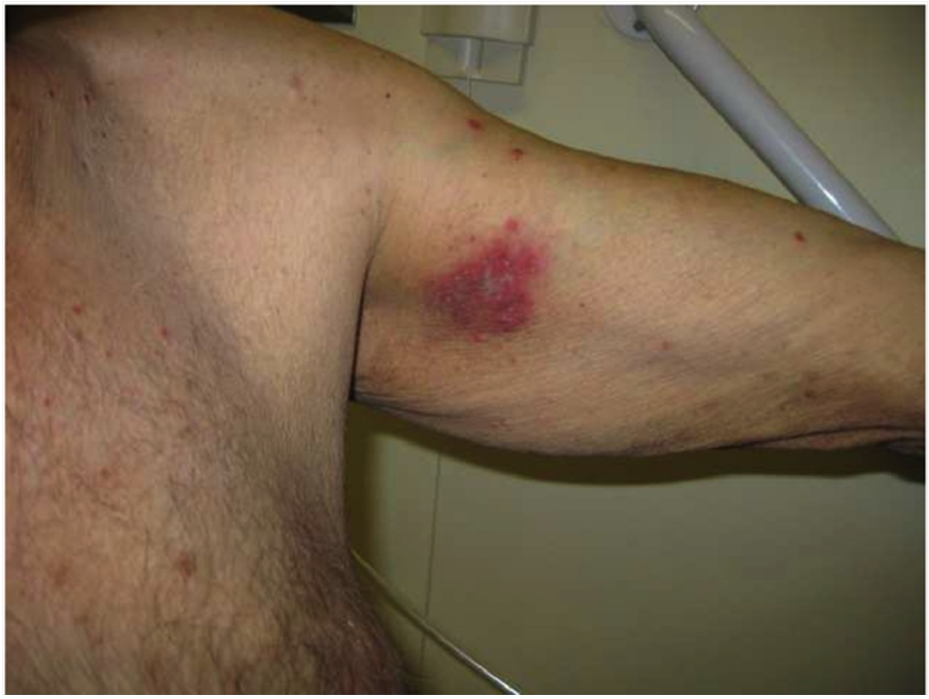

FIGURE 4: Grade 3 dermatitis in contralateral axilla

The distance of the beam entry site to the target relates (figure *3*) to the depth of the tumor (in our case, the target was in the posterior right lobe of the liver). The large number of beams used can be misleading. In conventional radiotherapy, each beam typically treats the entire tumor, whereas the CyberKnife may use small circular collimators to paint a large target. In this way, the dose to any individual section of the target may only come from a small subset of the beams used. A way to avoid issues related to converging entrance beams is to use limits on the number of beams per node or (as has become our preference), limit the total monitor MU may be delivered at each node to 400-500 MU. The use of this constraint for more than 100 subsequent patients has, in our practice, been effective in dealing with this issue.

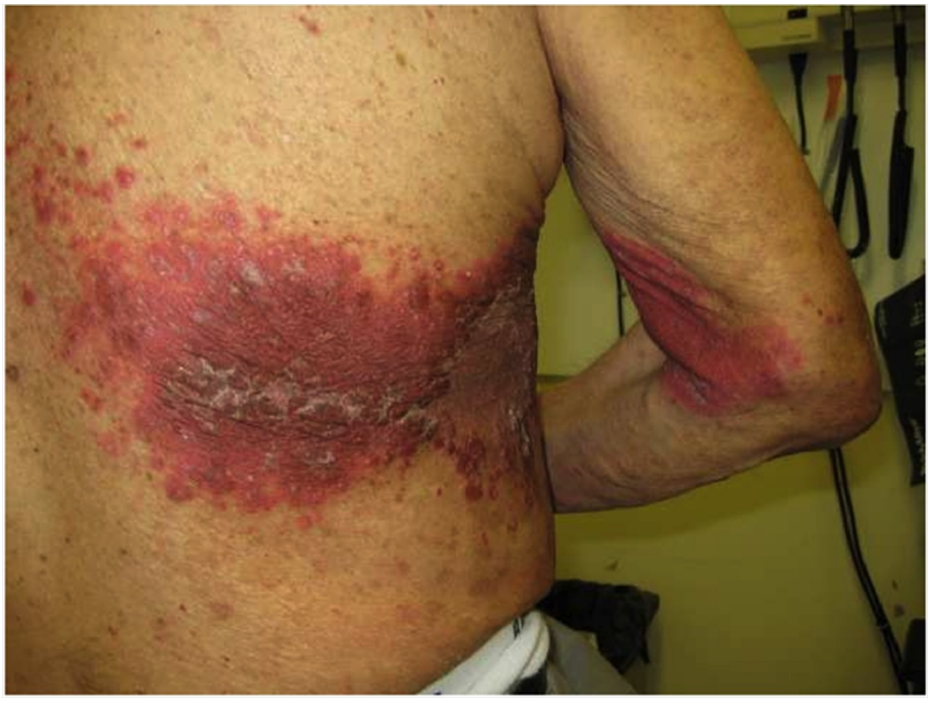

FIGURE 5: Grade 3 dermatitis in the right flank

The lesson learned through this case is that the location of small areas of overdose can be non-intuitive. Thus, it is a safe practice to dedicate extra time to systematically calculate the dose in the entire imaging study before signing off on a CyberKnife treatment plan. This simple safety may already be common practice in other centres but should be considered for a forcing function in the software (i.e. future revisions of the software should not allow plan approval to proceed if the dose has not been calculated over the entire volume).

Conclusions

New technologies, such as robotic radiosurgery, offer exciting treatment opportunities but also new challenges. We have been fortunate that our patient paid a relatively small price (transient dermatitis) for us to better understand how "fingers of death" can occur with CyberKnife radiosurgery. We would recommend to all users to calculate dose over the entire imaged volume before delivering a CyberKnife plan.

Additional Information

Disclosures

Human subjects: All authors have confirmed that this study did not involve human participants or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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