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CASE REPORT

What if a tumor is significantly enlarged just before stereotactic body radiation therapy? A case report and review of the literature

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Abstract

Stereotactic body radiation therapy (SBRT) plays an important role in early stage non-small cell lung cancer. Tumor growth before radiotherapy planning (RTP) or during SBRT has been reported in lung cancer patients; however, little is known of growth during the period in-between (i.e. after RTP but before SBRT). An 83-year-old man referred to our hospital and diagnosed with medically inoperable non-small cell lung cancer was noted to have significant tumor progression on day 1 of cone beam computed tomography just before the planned SBRT delivery. Because of uncertainty of the underlying etiology and unfamiliarity with this phenomenon, we made a clinical decision to arrange re-simulation and revise our treatment to conventional fractionated radiotherapy (CFRT). After an initial response, distant metastases occurred eight months after CFRT. The patient received best supportive care and was under hospice care at the last follow-up (27 months after CFRT). We report a case with significant tumor growth just before planned SBRT. Optimal management in this scenario requires further investigation.

Introduction

Stereotactic body radiation therapy (SBRT) plays an important role in early stage non-small cell lung cancer (NSCLC), in which image guidance plays a crucial role.[1–4] But what if the tumor is significantly enlarged just before SBRT and image guidance is no longer feasible? Herein we report our experience of a such a case. The research ethics committee of our institution approved this study (CMUH105-REC2-070).

Case report

An 83-year-old man was diagnosed with medically inoperable clinical stage T2N0M0 right upper lobe NSCLC by bronchoscopic exam (patent airway, but endobronchial ultrasound-guided biopsy revealed large cell carcinoma), followed by positron emission tomography-computed tomography (PET-CT) after a chest X-ray revealed abnormal results during routine surveillance for chronic obstructive pulmonary disease. He was referred for SBRT on July 15, 2013. Radiotherapy simulation was arranged on July 17, 2013 using abdominal compression with free breathing CT, complemented with inhale/exhale CT. We used a clinical target volume of at least 5 mm around the gross tumor and a 5 mm planned target volume margin, and planned for 62Gy/10Fx (for a biological equivalent dose of around 100 Gy10) (Fig 1a). The tumor shape was relatively spherical, with a volume of 11.4 cc. Although the patient was well and did not experience any discomfort, such as fever or cough, during the period between RTP to planned SBRT, the tumor was found to be significantly enlarged after verification using cone-beam computed tomography (CBCT) on day 1 (August 1, 2013) of the planned SBRT (Fig 1b). The

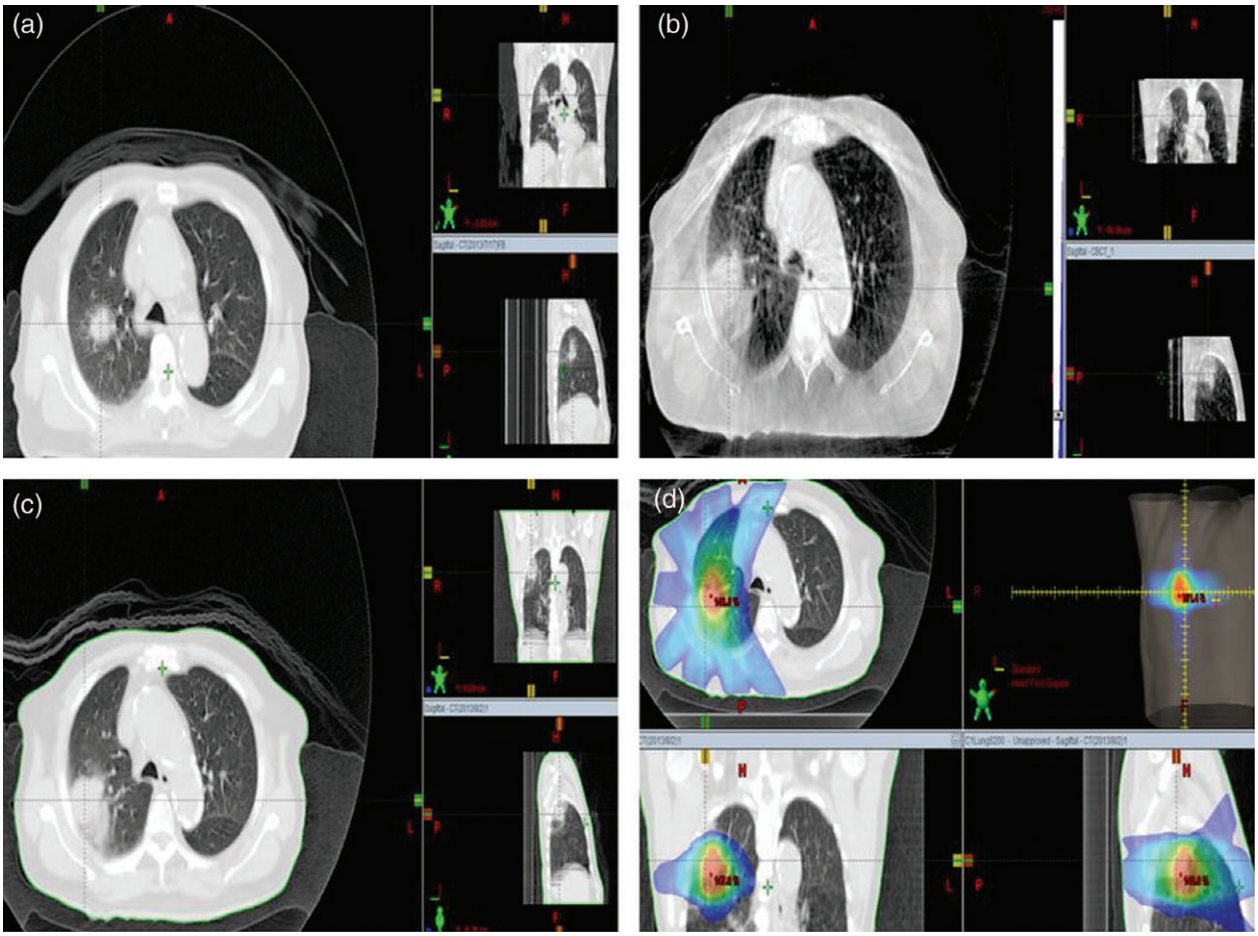

Figure 1 Tumor image on (**a**) initial simulation (gross tumor volume, GTV = 11.4 cc), (**b**) cone-beam computed tomography, (**c**) re-simulation (GTV = 30 cc), and (**d**) re-simulation and isodose distribution, if treated using the original plan. Please note, axial images were not presented at the same level but at the level with the greatest diameter; therefore, the orthogonal image was also displaced.

center of the tumor mass had changed significantly. Because of the uncertainty regarding his underlying disease status, we ceased plans for SBRT and arranged alternate simulation treatment for August 2, 2014 (Fig 1c). At that time, the tumor was larger (volume 29.9 cc) with an altered shape, elongating toward the cranial/lateral side. As we expected, the original SBRT plan could not fully cover the current tumor, especially at the cranial/lateral part (Fig 1d). Although there was a bronchus located within the initial tumor mass and we could not exclude the possibility of atelectasis, we were still uncomfortable regarding the true etiology. We decided that it was impractical to consider repeating a pathological exam and PET-CT. We changed our plan to conventional fractionated radiotherapy (CFRT) of 74 Gy in 37 fractions (74 Gy but not 60Gy for radiotherapy only) after discussion with referring physicians. The patient completed the treatment without incident and showed an initial response on follow-up computed tomography (CT) on November 21, 2013. However, during a subsequent CT on April 2, 2014, new lung metastasis was detected. The patient received best supportive care thereafter and was under hospice care at last follow-up (November 26, 2015).

Discussion

We searched PubMed using (lung cancer) AND ((stereotactic body radiotherapy) OR (stereotactic ablative radiotherapy)) AND ((volume*) OR (enlarged) OR (growth) OR (progressed) OR (progression)) as keywords to find relevant studies. Among 1083 studies, we found that tumor growth before radiotherapy planning (RTP) in lung cancer patients treated with SBRT had been reported.[5] There were also studies reporting potential tumor growth during SBRT.[6] However, less is known of the period in-between (i.e. after RTP but before SBRT), as seen in this case. Murai *et al.*

investigated potential tumor growth from "CT to before referral" to "CT for treatment planning or positioning before SBRT" in 201 patients. In the time period from diagnostic CT to simulation or positional CT (i.e. start of RTP or CBCT, respectively), no T stage progression was found in 41 of the patients. However, this study did not differentiate "from diagnosis to simulation" and "from simulation to treatment" (the in-between period in our study).[7] Salamekh *et al.* evaluated the trend of tumor growth of 18 lung tumors from 15 cases. They found no obvious tumor enlargement in the first CBCT when compared with tumor contouring on the planning CT. However, the interval from simulation to CBCT was not reported in this study.[8] Although a wait time of up to four weeks has been reported to be acceptable,[7] it is still possible that a tumor might be significantly enlarged between RTP and SBRT, as shown in this case. Optimal management in this scenario requires further investigation. A recent textbook considered the concept of re-examination using CBCT and re-simulation for adaptive SBRT to tailor technical aspects of treatment, as up to 32% of patients experienced significant changes in their tumor during SBRT.[9–11] Significant dosimetric improvement could be achieved by tailoring SBRT to each patient after reassessing tumor growth before proceeding with SBRT.

In conclusion, to our knowledge, we report the first case to show significant tumor progression specifically just before planned SBRT (not before RTP or during SBRT). Volumetric image guidance is crucial to identify this potential clinical scenario, although optimal management requires further investigation.

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Disclosure

No authors report any conflict of interest.

References

1 Timmerman R, Paulus R, Galvin J *et al.* Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA* 2010; **303**: 1070–6.
2 Chang JY, Senan S, Paul MA *et al.* Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: A pooled analysis of two randomised trials. *Lancet Oncol* 2015; **16**: 630–7.
3 Guo Y, Zhuang H, Zhao L, Yuan Z, Wang P. Influence of different image-guided tracking methods upon the local efficacy of CyberKnife treatment in lung tumors. *Thorac Cancer* 2015; **6**: 255–9.
4 Chang JY, Dong L, Liu H *et al.* Image-guided radiation therapy for non-small cell lung cancer. *J Thorac Oncol* 2008; **3**: 177–86.
5 Atallah S, Cho BC, Allibhai Z *et al.* Impact of pretreatment tumor growth rate on outcome of early-stage lung cancer treated with stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys* 2014; **89**: 532–8.
6 Gunter T, Ali I, Matthiesen C, Machiorlatti M, Thompson D, Algan O. Gross tumour volume variations in primary non-small-cell lung cancer during the course of treatment with stereotactic body radiation therapy. *J Med Imaging Radiat Oncol* 2014; **58**: 384–91.
7 Murai T, Shibamoto Y, Baba F *et al.* Progression of non-small-cell lung cancer during the interval before stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys* 2012; **82**: 463–7.
8 Salamekh S, Rong Y, Ayan AS *et al.* Inter-fraction tumor volume response during lung stereotactic body radiation therapy correlated to patient variables. *PLoS One* 2016; **11** (4): e0153245.
9 Wagner H. Non-small cell lung cancer. In: Gunderson LL, Tepper JE (eds). *Clinical Radiation Oncology*, 3rd edn. Elsevier, Philadelphia, PA 2012; 805–38.
10 Bhatt AD, El-Ghamry MN, Dunlap NE *et al.* Tumor volume change with stereotactic body radiotherapy (SBRT) for early-stage lung cancer: Evaluating the potential for adaptive SBRT. *Am J Clin Oncol* 2015; **38**: 41–6.
11 Qin Y, Zhang F, Yoo DS, Kelsey CR, Yin FF, Cai J. Adaptive stereotactic body radiation therapy planning for lung cancer. *Int J Radiat Oncol Biol Phys* 2013; **87**: 209–15.

