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MRI-guided stereotactic ablative radiation therapy for metachronously recurrent pulmonary oligometastases from hepatocellular carcinoma after failure of systemic therapy

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ABSTRACT

Objectives. This article aims to evaluate the feasibility and effectiveness of MRI-guided stereotactic ablative radiotherapy (SABR) for metachronously recurrent pulmonary oligometastases from hepatocellular carcinoma (HCC) when systemic therapies prove ineffective.

Case Presentation. A 47-year-old male with metastatic HCC underwent unsuccessful chemotherapy, targeted therapy, and immunotherapy. The patient had a history of 14 lung metastases, previously treated with respiratory non-gated SABR. However, five new lung metastases emerged, raising concerns about potential pulmonary toxicity. After administering oral capecitabine, tumor growth persisted. To address this, the patient received MRI-guided respiratory-gated SABR using a recently installed system.

Outcome. MRI-guided respiratory-gated SABR was well-tolerated, with no radiation-induced adverse events reported during treatment and a six-month follow-up period. Imaging follow-up demonstrated complete tumor regression, and no new recurrences were observed.

Conclusions. This case report suggests that MRI-guided SABR could be a viable option for managing metachronously recurrent pulmonary oligometastases from HCC, particularly after failed systemic therapies. The precise targeting achieved with minimal toxicity, utilizing a 1 mm margin without an internal target volume, showcases the potential of this approach. However, further scientific investigation is warranted to validate these findings, given the limited scope of this single case report. Nonetheless, MRI-guided SABR holds promise as a safe and effective local treatment modality for lung metastases in HCC patients.

Keywords: oligometastasis, Stereotactic body radiotherapy (SBRT), risk management, intensity-modulated radiotherapy, liver neoplasms

INTRODUCTION

The prognosis of metastatic hepatocellular carcinoma (HCC) after failure of systemic therapy is poor. Radiation therapy may be indicated for oligometastatic HCC [1], however, unlimited repetition of radiation therapy, even for oligometastases, is not possible because of toxicity and unknown efficacy [2]. There are no data on stereotactic ablative radiotherapy (SABR) for metachronously recurrent pulmonary oligometastases from HCC. Here, we report a case of MRI-guided SABR for 5 lung metastases with a history of repeated non-respiratory-gated SABR for 14 pulmonary metastases after failure of systemic therapy. As far as we know, this is the largest number of lung metastases from HCC successfully treated with SABR.

CASE PRESENTATION

A 47-year-old male with metastatic HCC was referred to our hospital after chemotherapy, targeted therapy including sorafenib and lenvatinib, and immunotherapy including nivolumab and pembroli-

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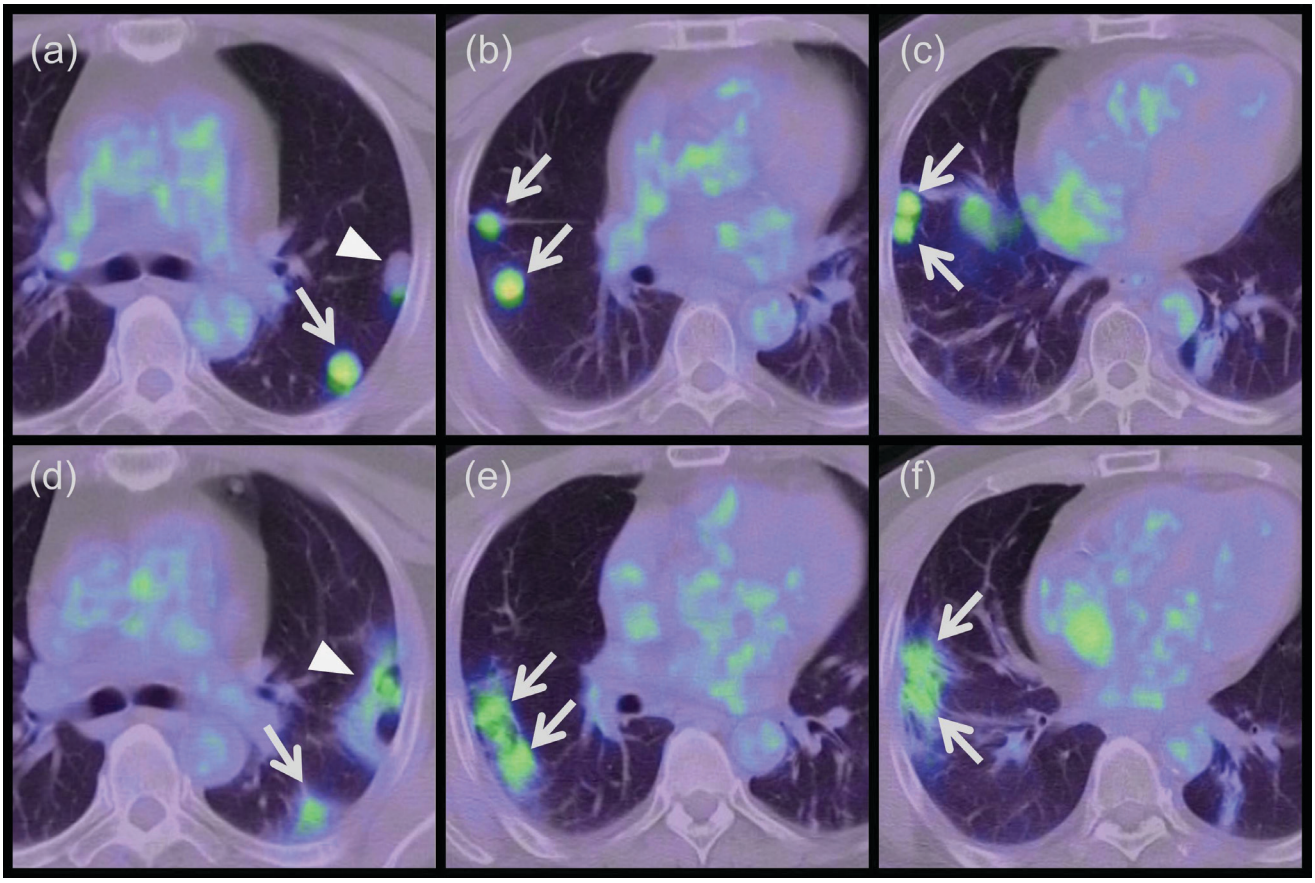

FIGURE 1. 18F-fluorodeoxy glucose (FDG) positron emission tomography (PET)/computed tomography (CT) scan detected five lung metastases.
(a), (b) and **(c)** Before MRI-guided stereotactic ablative radiotherapy (SABR). Hypermetabolic five lung metastases are seen (arrows). Previously irradiated lung metastases are hypometabolic (arrowhead).
(d), (e) and **(f)** Six months after MRI-guided SABR. FDG uptake in pulmonary metastases is reduced and radiation fibrosis is seen (arrows). Necrosis of pulmonary metastases previously irradiated by non-respiratory-gated SABR was progressive (arrowhead).

zumab failed. The patient underwent surgical resection of hepatitis B virus-associated HCC five years ago, and since then, he had a total of 14 lung metastases on four separate occasions, all controlled with respiratory non-gated SABR. Each recurrent lung metastasis was oligometastatic (n = 3, 4, 4, and 3, respectively, from the first time), so a total of 14 lung metastases were sequentially treated. In this time, whole-body 18F-fluorodeoxy glucose (FDG) positron emission tomography/computed tomography (PET/CT) scan detected 5 lung metastases (**Figures 1a, b and c**), the cumulative mean lung dose exceeded 15 Gy, and additional respiratory non-gated SABR could carry the risk of serious pulmonary toxicity, the patient received oral capecitabine. Because the tumor size increased despite capecitabine administration, respiratory-gated SABR was attempted using a newly installed MRI-guided radiotherapy system.

All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Institutional review board approval was waived because every treatment was approved by the national health insurance. Informed consent was obtained from the patient for the use of clinical data.

MRI simulation was performed using transverse true fast imaging with steady precession (FISP) images using 0.35T MRI-guided radiation therapy system (MRIdian® System, ViewRayTM Inc, Oakwood Village, Ohio, USA). Planning target volume (PTV) was defined as the volume containing the tumor or gross tumor volume (GTV) plus 1-mm margins. Internal target volume (ITV) and clinical target volume (CTV) were not set because the patient can be monitored simultaneously with MRI while undergoing SABR. The margin size was calculated from the spatial resolution of the treatment system [3] and set at 1 mm. The prescribed dose to the D95% of the PTV (the dose covering 95% of the PTV) was 40 Gy in 5 fractions. The maximum dose in the PTV was not constrained. In order to lower the total lung V20Gy and mean lung dose, intensity-modulated radiation therapy (IMRT) planning techniques were used. The mean lung dose for treatment of these five lung me-

tastases was 3.2 Gy. Capecitabine was discontinued before SABR. There were no radiation-induced adverse events during treatment and six months of follow-up. On 18F-FDG-PET/CT, all tumors disappeared 6 months after MRI-guided SABR (Figures 1d, e, and f) and no new recurrence was observed.

DISCUSSION

The efficacy and feasibility of radiation therapy for recurrent pulmonary oligometastases from HCC has not yet been studied. This case suggests the possibility of MRI-guided respiratory-gated SABR for lung metastases, even after repeated treatment of lung metastases with respiratory non-gated SABR. If chemotherapy, targeted therapy, and immunotherapy are unsuccessful, local treatment with MRI-guided SABR may be acceptable.

This case report has several strengths. First, it was shown that even without setting an ITV and with only a very small 1 mm margin on the GTV, the lung metastases can be treated precisely and with minimal toxicity to the surrounding normal tissue. These results are consistent with previously reported studies using low-field MRI systems [3,4]. Second, in the case of metachronously repeated pulmonary oligometastases, anti-tumor effects may be expected if local SABR can be safely performed even if the cumulative number of metastases exceeds the category of oligometastases. To the best of our knowledge, there are no reports of a total of 19 metachronously recurrent pulmonary metastases successfully treated with SABR.

This case report has several limitations. First, there is only one case with a short follow-up period of 6 months after MRI-guided SABR. However, the small number of case and short follow-up period are not limitations to suggest proof-of-principle for the feasibility of MRI-guided SABR for metachronously recurrent lung oligometastases. Second, not all lung metastases were treated exclusively with MRI-guided SABR. Before MRI-guided radiation therapy system was installed, the patient was treated with respiratory non-gated SABR and the surrounding normal tissue was also irradiated. Since 14 of the 19 lung metastases could be safely treated with respiratory non-gated SABR, MRI-guided SABR is considered even safer because it reduces radiation exposure to surrounding normal tissue.

CONCLUSIONS

In conclusion, a single case report cannot be generalized to other cases without further scientific verification, however, metachronously recurrent pulmonary oligometastases from HCC might be successfully treated with MRI-guided SABR even if the total number of metastases exceeds the number defined as oligometastases.

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