

Real-time MRI-guided radiation therapy for choroidal metastases after hippocampal avoiding whole brain radiotherapy

MR-řízená radioterapie v reálném čase u choroidálních metastáz po hipokampus šetřícím celomozkovém ozáření

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Summary

Background: Eye tumors are moving targets, but there have been no reports of radiation therapy with real-time monitoring. **Case:** A 54-year-old woman with metastatic breast cancer was referred for treatment of diplopia due to choroidal metastasis after hippocampal avoiding whole brain radiotherapy. Since visual acuity was preserved and long-term survival was expected, real-time MRI-guided intensity-modulated radiation therapy (36 Gy in 20 fractions) was performed. No adverse events occurred during treatment or during the subsequent one-year follow-up period. The patient's diplopia resolved and no choroidal recurrence was observed during the follow-up period. **Conclusion:** MRI-guided radiation therapy may be a safe and effective treatment for choroidal metastases after hippocampal avoiding whole brain radiotherapy.

Key words

image-guided radiotherapy – choroidal tumor – retinal neoplasms – intensity-modulated radiation therapy

Souhrn

Východiska: Oční nádory jsou pohyblivým cílem léčby, ale v literatuře není žádná zmínka o radioterapii s monitorováním v reálném čase. **Případ:** Žena ve věku 54 let s metastazujícím karcinomem prsu byla odeslána k léčbě diplopie v důsledku choroidální metastázy po hipokampus šetřícím celomozkovém ozáření. Vzhledem k tomu, že zraková ostrost byla zachována a očekávalo se dlouhodobé přežití, byla provedena MR-řízená radioterapie s modulovanou intenzitou v reálném čase (36 Gy ve 20 frakcích). Během léčby ani během následného ročního sledování se nevyskytly žádné nežádoucí příhody. Pacientčina diplopie ustoupila a během sledovacího období nebyla pozorována žádná recidiva nádoru choroidey. **Závěr:** MRI-řízená radioterapie může být bezpečnou a účinnou léčbou choroidálních metastáz po hipokampus šetřícím celomozkovém ozáření.

Klíčová slova

obrazem řízená radioterapie – nádor choroidey – novotvary sítnice – radioterapie s modulovanou intenzitou

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Autoři deklarují, že v souvislosti s předmětem studie nemají žádné komerční zájmy.

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Introduction

There is no standard treatment for choroidal metastases, but external beam radiation therapy is recommended because of its low toxicity and greater efficacy compared to systemic therapies [1–3]. Although doses of 35.5 Gy or more have been reported to be necessary to achieve adequate therapeutic effects [3], radiation exposure to the optic nerve and lens must be minimized after hippocampal avoiding whole brain radiotherapy (HA-WBRT) to preserve visual acuity. MRI-guided radiation therapy (MRIgRT) can monitor both the planning target volumes (PTV) and the surrounding normal tissues at the same time, instantly avoiding irradiation to organs at risk (OAR). Here, we report a case of breast cancer with choroidal metastases treated with MRIgRT, avoiding irradiation to the optic nerve and the lens after HA-WBR.

Case report

A 54-year-old woman with cerebellar metastatic luminal A-subtype breast cancer (cT4aN3M1, Stage IV, AJCC, 8th ed.) was referred to our department for treatment of diplopia due to choroidal metastasis in the right eye. Aromatase inhibitors and CDK4/6 inhibitors were administered and all metastatic lesions (lymph nodes and lungs) as well as the primary tumor were controlled for the past 3 years. However, 6 months prior to the referral, multiple metastases

in the cerebellum developed, and HA-WBRT was performed. The intraorbital proximal 5 mm of both optic nerves were irradiated with 40 Gy in 20 fractions using helical tomotherapy (Hi-ART system, Accuray, Madison, Wisconsin, United States) (Fig. 1a).

At the time of referral, bilateral visual acuity was normal and no metastases were found on MRI (Fig. 1b). Optical coherence tomography (OCT) of the right eye demonstrated the hyporeflective choroidal nodules of approximately 500–600 μm and subretinal fluid (Fig. 1c). OCT of the left eye was normal. Based on the findings of OCT, a diagnosis of choroidal metastasis was made. MRIgRT was performed to prevent the PTV from overlapping the right optic nerve and also to reduce radiation exposure to the lens. 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. Written informed consent was obtained from the patient for the treatment and publication of this case report.

The patient was immobilized using the individually formed mask and underwent MRI simulation on 0.35T MRIgRT system (MRIdian[®] System, ViewRay Inc, Oakwood Village, Ohio, USA). Transverse true fast imaging with steady-state free precession (true FISP) images were used for

the target delineation. The clinical target volume (CTV) was defined as the right whole zona optica retinae, and the PTV was defined as a 5-mm margin expansion from the CTV. A 5-mm brush was not used. The prescribed dose to the D95% of PTV (the dose covering 95% of PTV) was 36 Gy in 20 fractions with a maximum of 40 Gy (Fig. 2). The treatment plan was carried out using intensity-modulated radiation therapy (IMRT). Dose constraints were set so that the radiation dose to the area within 10 mm of the proximal optic nerves was less than 12 Gy in 20 fractions. The mean lens dose was set to be below 7 Gy, since the mean lens dose of 7 Gy was estimated to have a 5-year cataract incidence of 20% and 25% with the logistic and Cox regression models [4]. The patient was treated with real-time MRIgRT system (MRIdian[®] System, ViewRay Inc, Oakwood Village, Ohio, USA) via beam control in the sagittal plane including the right lens at four frames per second. Each MRIgRT session takes approximately 40 min from set-up to completion. Three weeks after the start of MRIgRT, the patient's diplopia resolved and the tumor disappeared on OCT. No adverse events occurred during treatment or during the subsequent one-year follow-up period. No choroidal recurrence was observed during the follow-up period.

Discussion

Choroidal metastasis is an important factor that reduces the quality of life of pa-

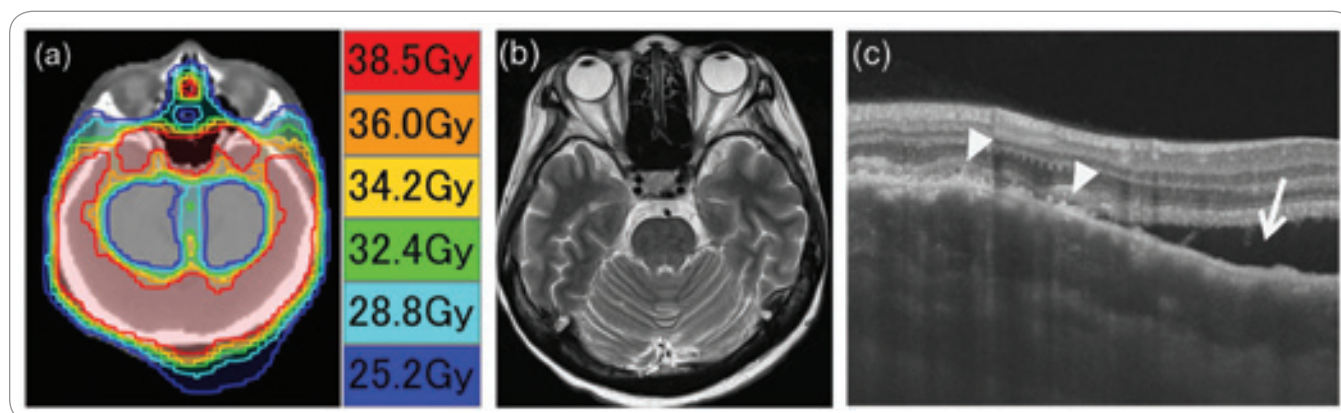


Fig. 1. A 54-year-old female with choroidal metastasis of breast cancer in the right eye. (a) Isodose lines of hippocampal avoiding whole brain radiotherapy with corresponding actual radiation dose. The intraorbital proximal 5 mm of both optic nerves were irradiated with a mean dose of 40 Gy in 20 fractions using helical tomotherapy. (b) T2-weighted turbo spin-echo MRI showed no metastatic tumors in the brain or eyes. (c) Optical coherence tomography demonstrated the irregular and undulating anterior surface (arrowheads) with subretinal fluid (arrow).

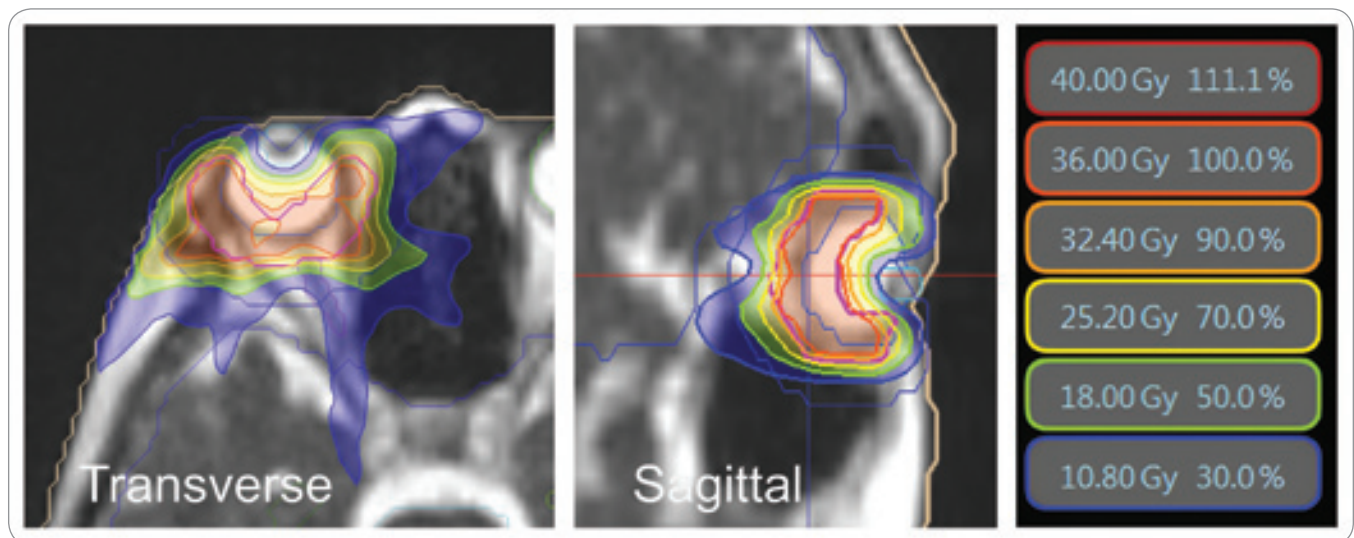


Fig. 2. MRI-guided radiation therapy isodose lines with corresponding actual radiation dose.

tients with metastatic cancer. Radiation therapy is an effective treatment, but real-time monitoring has been difficult with CT-guided radiation therapy due to low tissue contrast, limited temporal resolution, and an increased risk of cataracts due to radiation exposure. MRIgRT has the potential to be an effective treatment, because it allows real-time monitoring of the target and surrounding normal tissue without the use of X-rays and provides higher tissue contrast than CT. To the best of our knowledge, this is the first report of choroidal tumor successfully treated with MRIgRT [5].

This report has several strengths. First, radiation therapy was initiated before vision loss. MRI did not detect choroidal metastases, but OCT clearly identified metastatic foci, suggesting the importance of collaboration with an ophthalmologist. Second, this is the first proof-of-principle for MRIgRT in which eye movements are monitored in real time. If eye movements can be monitored accurately in real time, higher doses of radiation may be delivered to the retinal tumors without increasing adverse events [5–7].

There are several limitations in this study. First, MRI sequence parameters are not optimized for treatment of retinal or choroidal tumors. In our coun-

try, only true FISP sequences are available for radiation treatment planning and real-time MRI monitoring. In addition, only sagittal images are available for real-time monitoring of eye movements during MRIgRT. Since the eyes tend to move laterally, monitoring with two images, a transverse and a sagittal image, is more accurate than monitoring with a sagittal image alone. Second, the treatment period of 4 weeks is a bit long. However, as all lesions except choroidal metastases were controlled and long-term survival was expected, the 4-week treatment period is not a major limitation. Third, if eye movements can be accurately monitored in real time, the CTV and PTV definitions should also be modified and optimized for MRIgRT. However, at present, the CTV and PTV settings for MRIgRT for ocular tumors have not been established and will be the subject of future research. The reason for a 5-mm PTV margin in this case was that the slice thickness for MRIgRT treatment planning was 2.5 mm, and the lesion should have been detected in multiple slices.

Conclusion

In conclusion, a single case report cannot be generalized to others without further scientific verification, however,

real-time MRIgRT may be a safe and effective treatment for choroidal metastasis after hippocampal avoiding whole brain radiotherapy.

Author contributions

Yukihiro Hama, Etsuko Tate: patient management, conceptualization of case study, collection of study material, manuscript drafting, and manuscript revision & editing. All authors approved the final version of the manuscript.

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