CASE REPORT

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MRI-GUIDED HYPOFRACTIONATED INTENSITY-MODULATED RADIATION THERAPY AFTER WHOLE-BREAST SIMULTANEOUS INTEGRATED BOOST RADIATION IN EARLY BREAST CANCER: A NON-SURGICAL APPROACH

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Summary

Radical radiotherapy is a novel non-surgical approach to the treatment of early breast cancer. In order to administer a sufficient dose of radiation to the tumor while minimizing the side effects, the exposure to the surrounding normal tissues must be minimized. A 46-year-old woman with early-stage triple-negative breast cancer was treated curatively with MRI-guided hypofractionated intensity-modulated radiation therapy after a whole-breast integrated boost radiation, because the patient refused surgery and chemotherapy. Six months after treatment, the tumor disappeared completely without adjuvant chemotherapy, and there were no recurrences or adverse events two years after treatment. In conclusion, MRI-guided hypofractionated intensity-modulated radiation therapy following simultaneous whole-breast integrated boost radiotherapy may be a feasible alternative treatment for early breast cancer.

KEYWORDS: *breast neoplasm; image-guided radiotherapy; intensity-modulated radiotherapy; radiation dose hypofractionation*

INTRODUCTION

Early-stage triple-negative breast cancer (TNBC) is commonly treated with a combination of neoadjuvant chemotherapy, breast-conserving surgery, radiation therapy, and adjuvant chemotherapy(1). Surgery and chemotherapy can be physically and emotionally distressing, leading some patients to refuse one or both treatment options. On the other hand, radiation therapy has recently gained attention as an alternative to standard radical treatment(2), but its use is limited due to the toxicities caused by higher doses of radiation such as induration, rib fractures, and pneumonitis(3). MRI-guided radiation therapy provides excellent tissue contrast and can monitor the movement of the target during radiation therapy, allowing real-time imaging of the respiratory movement of the breast cancer and precise delivery of high doses of radiation(4,5). Here, we report a case of early-stage TNBC that was successfully treated with MRI-guided intensity-modulated radiation therapy (IMRT) following simultaneous whole-breast integrated boost radiation therapy.

CASE REPORT

A 46-year-old woman with an unremarkable medical and family history was referred to our hospital for treatment of localized TNBC. She had already undergone biopsy and whole-body fludeoxyglucose positron emission tomography (FDG-PET)/CT, and was diagnosed with stage IIA breast cancer (cT2 N0 M0, grade 3, human epidermal

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growth factor receptor 2-negative, estrogen receptor-negative, progesterone receptor-negative, Ki-67 50%, Clinical Prognostic Stage Group IIB). Contrast-enhanced MRI of the breast showed an oval lesion with marked enhancement and irregular margins in the right breast (Figure 1a). She was initially recommended for standard treatment; however, after refusing chemotherapy and surgery, she was referred for radical radiation therapy.

All procedures adhered to the ethical guidelines of the 1975 Declaration of Helsinki. Institutional review board of the Edogawa Hospital (RO2018112) approved the study protocol, and the patient signed informed consent before treatment.

Radiation therapy was administered in two sessions. In the first session, simultaneous integrated boost (SIB) radiation therapy was performed to treat the whole breast, with a higher dose delivered to the tumor visualized by contrast-enhanced MRI using helical tomotherapy. The clinical target volume (CTV) for the entire right breast was defined using CT imaging. This includes the entire breast, the skin, glandular tissue, and the underlying pectoralis muscle. The planning target volume (PTV) for the entire right breast (PTV1a) was defined by CTV with variable three-dimensional margins to account for respiratory motion and setup error. The gross tumor volume (GTV) for breast cancer was defined using contrast-enhanced MRI. A fusion image combining CT and MRI was generated, and breast cancer PTV was calculated by adding a 3 mm three-dimensional margin to the GTV, excluding the skin and pectoralis muscle (PTV1b). The doses delivered to the 95% of PTV1a and PTV1b were 45 Gy and 50 Gy in 25 fractions, respectively.

After the first session, CT and contrast-enhanced MRI were performed, and a plan for the second session was made. Contrast-enhanced MRI immediately after the first session showed that the tumor had shrunk and contrast enhancement had decreased (Figure 1b). The GTV for the boost radiation therapy plan was defined by contrast-enhanced MRI. The PTV2 was then generated by adding a 3 mm three-dimensional margin to the GTV, excluding the skin and pectoralis muscle, without accounting for respiratory motion or setup errors. Contrast-enhanced MRI was fused with 0.35T MRI images from the MRI-guided radiation therapy system (MRIdian, ViewRay Inc., Mountain View, CA, USA), and PTV2 was treated with MRI-guided hypofractionated IMRT. The dose received by 95% of the PTV2 was 30 Gy in 8 fractions.

To summarize: in the first session, the whole breast was irradiated with 45 Gy, and the GTV with 50 Gy in 25 fractions over 5 weeks, and in the second session, the residual tumor was irradiated with 30 Gy in 8 fractions over 1.5 weeks (Figure 2).

Grade 1 dermatitis was observed during radiation therapy, but there was no grade 2 or higher adverse events during or after radiation therapy. Six months after receiving radical radiation therapy, the tumor had completely disappeared (Figure 1c), and there were no recurrences or adverse events two years post-treatment (Figure 1d). The patient refused systemic chemotherapy, so no additional adjuvant treatment was administered following the radiation therapy.

Discussion

To our knowledge, this is the first report of early-stage breast cancer successfully treated with whole-breast SIB radiation therapy followed by MRI-guided hypofractionated IMRT. If radiation therapy can safely and effectively control early breast cancer, surgery can potentially be avoided. Whether local control of early breast cancer can be achieved with radiation therapy alone is an important issue for further research.

There are several strengths to this case report. First, whole-breast radiation therapy can reduce the size of the primary tumor, ultimately reducing the PTV in the boost radiation therapy plan. Additionally, employing the use of the SIB technique for whole breast, radiation therapy has increased the dose delivered to the primary site, enhancing further its antitumor effect. Second, because MRI-guided radiation therapy allows for real-time monitoring of the breast during radiation treatment, there is no need to account for respiratory motion or setup errors when creating the PTV, allowing for a reduction the size of the PTV.

There are several limitations to this case report. The treatment duration for whole-breast radiation therapy was 5 weeks for 25 sessions, as conventional fractionated doses were used. Given that hypofractionated and conventionally fractionated whole-breast radiation therapy are comparable in terms of efficacy and safety(6), treat-

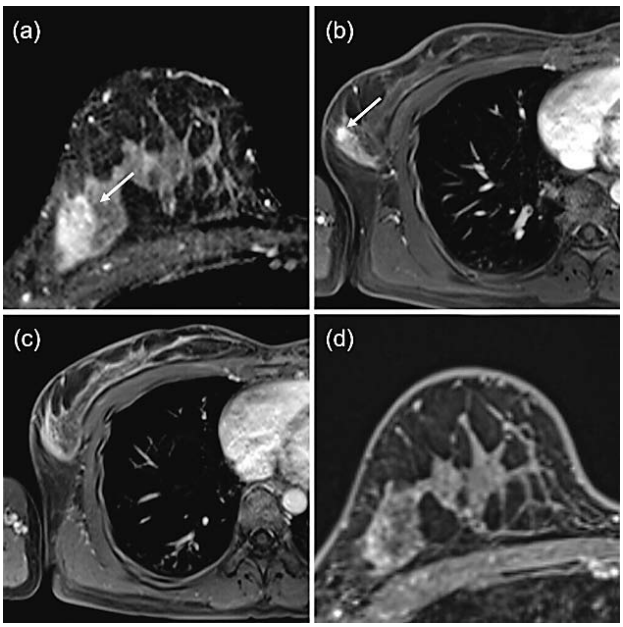

Figure 1. Contrast-enhanced MRI of the right breast.
(a) A small lesion with marked enhancement and irregular margins is seen in the right breast (arrow).
(b) A small residual lesion (arrow) can be seen after simultaneous integrated boost radiotherapy of the whole breast.
(c) Six months after radiotherapy, the breast cancer had completely disappeared.
(d) Two years after radiotherapy, no locoregional recurrence was observed.

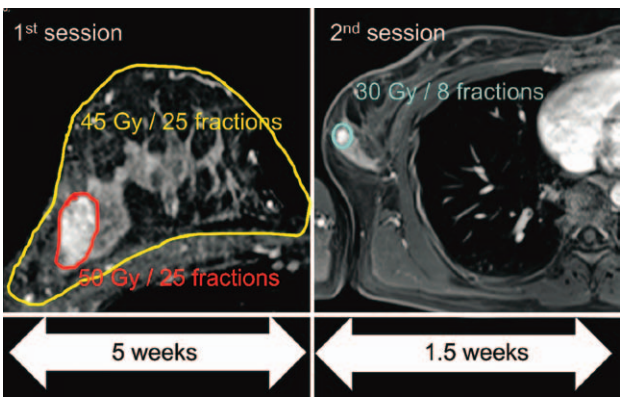

Figure 2. Treatment plan diagram.
In the first session, 50 Gy was delivered to the gross tumor volume and 45 Gy to the whole breast in 25 fractions over 5 weeks. In the second session, 30 Gy was delivered to the residual gross tumor volume in 8 fractions over 1.5 weeks.

ment time could be further reduced when hypofractionated whole-breast radiation therapy is used. Second, the optimal dose and fractionation schedule for MRI-guided boost radiation therapy is not known. MRI-guided radiation therapy allows real-time monitoring of the breast and surrounding normal tissue, reducing PTV margins and delivering high doses of radiation to the tumor. MRI-guided radiation therapy may play an important role in the radical treatment of early breast cancer in the near future. In MRI-guided radiation therapy, ultra-hypofractionation(7) can be used to further benefit from the reduced total treatment time. However, tumor shrinkage during one week of treatment is unknown. On the other hand, tumor shrinkage during conventional fractionated radiotherapy, as presented in this case, may reduce PTV in subsequent boost radiotherapy. In the non-surgical setting, the tissue contrast of MRI is superior to that of CT, allowing precise irradiation of the tumor without marking. This case report demonstrates the proof of principle of MRI-guided radiation therapy in the non-surgical setting, but indications, total dose, and fractionation methods are issues for further research.

Conclusion

In conclusion, a single case report cannot be generalized to others without further scientific validation, but MRI-guided hypofractionated IMRT after whole-breast SIB radiation therapy may be a feasible alternative local treatment for early breast cancer.

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Sažetak

HIPOFRAKCIONIRANA TERAPIJA ZRAČENJEM MODULIRANOG INTENZITETA VOĐENA MRI-OM NAKON SIMULTANE INTEGRIRANE POJAČANE RADIOTERAPIJE CIJELE DOJKE U RANOM RAKU DOJKE: NEKIRURŠKI PRISTUP

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Radikalna radioterapija je novi nekirurški pristup liječenja ranog raka dojke. Kako bi se primijenila dovoljna doza zračenja na tumor a smanjile nuspojave, izloženost okolnih normalnih tkiva mora biti minimalizirana. Prikazujemo slučaj 46-godišnje žene s trostruko-negativnim rakom dojke u ranom stadiju koja je liječena kurativno magnetskom rezonancijom vođenom terapijom zračenja hipofrakcijskog intenziteta, i integriranom pojačanom radioterapijom cijele dojke, nakon što je bolesnica odbila kirurški zahvat i kemoterapiju. Šest mjeseci nakon liječenja tumor je potpuno nestao bez adjuvantne kemoterapije, a dvije godine nakon liječenja nema znakova recidiva niti nuspojava. Zaključno, MRI-om vođena hipofrakcionirana terapija zračenjem moduliranog intenziteta nakon simultane integrirane pojačane radioterapije cijele dojke može biti izvedivo alternativno liječenje ranog raka dojke.

KLJUČNE RIJEČI: *Neoplazma dojke; radioterapija vođena magnetskom rezonancom; radioterapija modulirana intenzitetom; hipofrakcionirana radioterapija*