Elekta

Case study

Single fraction, pre-operative MR-guided partial breast irradiation for early-stage right breast carcinoma

Case

Early-stage right breast carcinoma

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Overview

Up to 80% of breast cancer patients receive radiation therapy as part of their treatment[1]. Traditionally, this has been administered to the whole breast postoperatively and fractionated over 5–6 weeks[1]. While effective, such lengthy treatment schedules are difficult for patients, particularly the elderly and those living in rural or underserved areas.

More recently hypofractionated regimens have been shown to be equally efficacious, while reducing the burden on patients[1]. For example, in the FAST-Forward trial, delivery of 26 Gy in five fractions over one week produced similar local control and safety to 40 Gy in 15 fractions over three weeks for patients with early-stage breast cancer[1].

In addition to this shift towards hypofractionation, and given that up to 90% of recurrences are located close (within 10 mm) to the lumpectomy site, we have also seen a trend towards accelerated partial breast irradiation (APBI), where the radiation dose is restricted to high-risk tissue. This technique has demonstrated similar results compared to whole breast irradiation, with reduced toxicity, patient convenience and cosmetic outcomes[2].

Building on these findings, there has been growing interest in further reducing fractionation to a single post-operative treatment[3]. A single fraction partial breast dose of up to 30 Gy has been investigated[3], with no evidence of disease recurrence at time of publishing.

MR-guided radiation therapy (MRgRT) provides the opportunity to further improve the accuracy of radiation therapy to small tumors that are less visible by CT, increasing confidence to locate the tumor and deliver an ablative dose in a single fraction. With the availability of this advanced technology, the Olivia Newton John Cancer Wellness and Research Centre is conducting a prospective, single-arm study (the RICE study[5]) to evaluate single fraction preoperative APBI for the treatment of early-stage breast cancer using the Elekta Unity MR-Linac.

Rationale for pre-operative single fraction radiation therapy (RT)

The rationale for treating the tumor and margin using a single, pre-operative fraction (rather than postoperatively) is the ability of MRgRT to better-target the intact tumor in situ and to reduce normal tissue irradiation. Pre-operative RT also eliminates uncertainty that could be caused by post-surgical breast distortion and the presence of seroma. By providing exceptional soft tissue contrast, MR guidance allows greater distinction between the tumor and surrounding healthy tissue, which reduces contouring variability, enhances definition of the tumor volume, and enables delivery of a single high dose fraction.

Following MRgRT, the treated tissue is surgically removed by wide local excision with no further irradiation of healthy tissue.

Minimizing RT to normal tissue should help to reduce toxicity and, by decreasing the number of required visits, the overall burden on the patient is greatly reduced. The RICE study aims to assess the feasibility and efficacy of MR-guided, single-dose pre-operative radiation therapy for early-stage breast cancer.

RICE study details

Funded by the National Breast Cancer Foundation (NBCF) the RICE study will treat 30 patients with single fraction radiation therapy prior to surgery, according to the treatment protocol (figure 1).

This is a dramatic decrease from the number of treatments required for standard radiation therapy (figure 2). Patients enrolled on the RICE study must fulfil the specified inclusion/exclusion criteria (table 1), with hormone receptor and HER2 status confirmed by core biopsy.

RICE Protocol

- Biopsy, FDG PET/CT, FES PET/CT, MR DWI
- MR simulation and planning CT
- MRgRT planning
- F0: End-to-end testing
- F1: 21 Gy single fraction MR-guided PBI (within ten days of sim)
- Five weeks post-RT: MR DWI to assess tumor response
- Six weeks post-RT: WLE with SLNB
- Surgical tissue samples correlated with pre-op imaging
- Follow up two weeks, six months and 12 months post-surgery

Figure 1.
RICE study protocol.

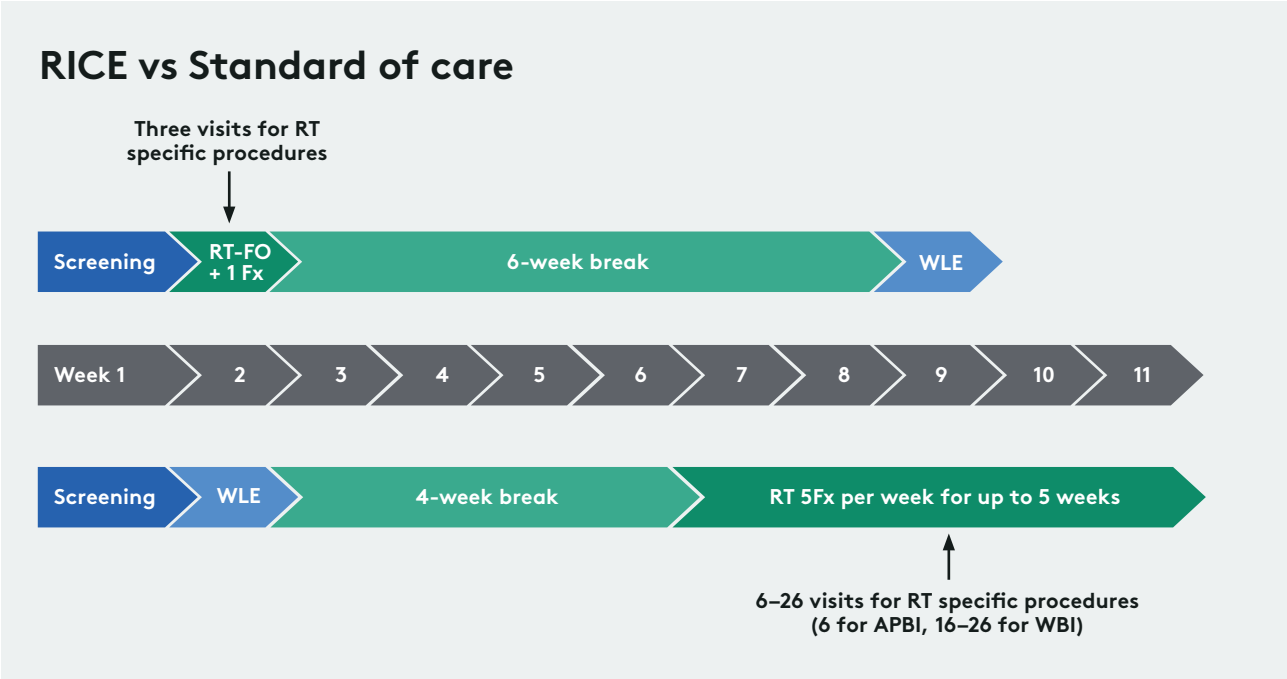

Figure 2.
RICE study treatment schedule compared to current standard of care.

Inclusion criteria	
Age	**≥60 years**
Tumor subtype	Unifocal
Tumor size	≤2 cm (visible on pretreatment imaging)
Tumor grade	<3 (1 or 2)
Lymphovascular space invasion	Absent
Hormone receptors (ER&PR)	Positive
HER2	Negative
Nodal status	Negative
Exclusion criteria	
Previous radiation therapy to same breast	
Skin or chest wall involvement	
Absolute contraindication to MRI or PET	

Table 1.
RICE study inclusion/exclusion criteria.

The following case study describes the single fraction, pre-operative MR-guided partial breast radiation therapy delivered to one patient enrolled in the RICE study.

Case overview

Routine screening detected a right breast lesion (measuring 14 mm on imaging) in this 73-year-old female patient. Biopsy confirmed a grade 1 invasive ductal carcinoma (IDC), which was estrogen receptor (ER) positive, progesterone receptor (PR) positive and HER2 negative.

Since the patient met the criteria for inclusion in the HREC approved RICE study (table 1), and for the reasons described above, consent was obtained for her to receive single fraction MRI-guided partial breast radiation therapy using the Elekta Unity MR-Linac.

According to the RICE protocol, pre-treatment imaging for diagnostic workup included [18F] FDG PET/CT and [18F] FES PET/CT. In addition, diffusion-weighted magnetic resonance imaging (DWI) was performed in order to compare and assess the tumor response post-treatment.

MR simulation and planning CT scans were obtained with the patient in supine position and arms raised (figure 3). These images were acquired on the same day for radiation therapy planning purposes, and to provide expected visibility by MRI on Unity. MR simulation was performed on a 1.5 T Philips Ingenia MR scanner (matching the strength of the Unity MR scanner). A T2 3D transverse MRI scan was used for planning and treatment verification.

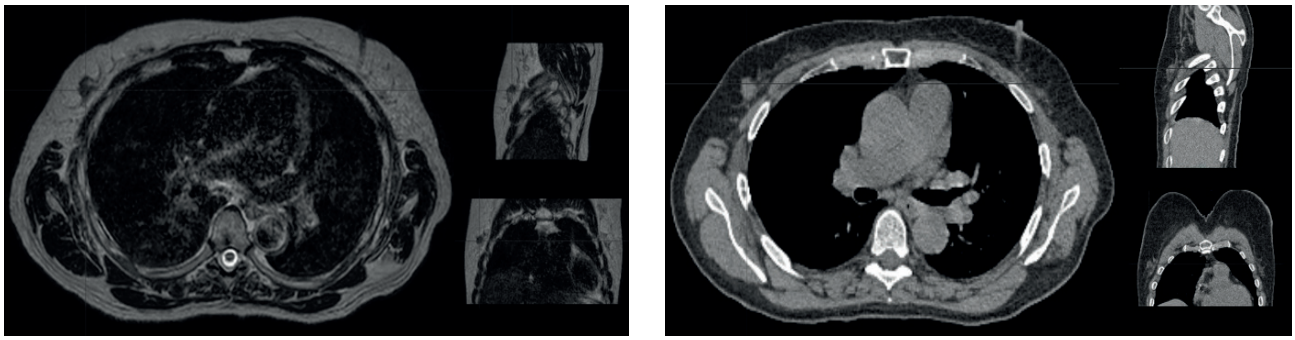

Figure 3.
MR simulation (left) and planning CT (right) images of right breast carcinoma.

The planning images were co-registered and an IMRT treatment plan was generated using Monaco version 5.51 to deliver 21 Gy in a single fraction to the tumor plus margin (figure 4). The GTV to CTV margin was 15 mm, with an additional 3 mm for the PTV.

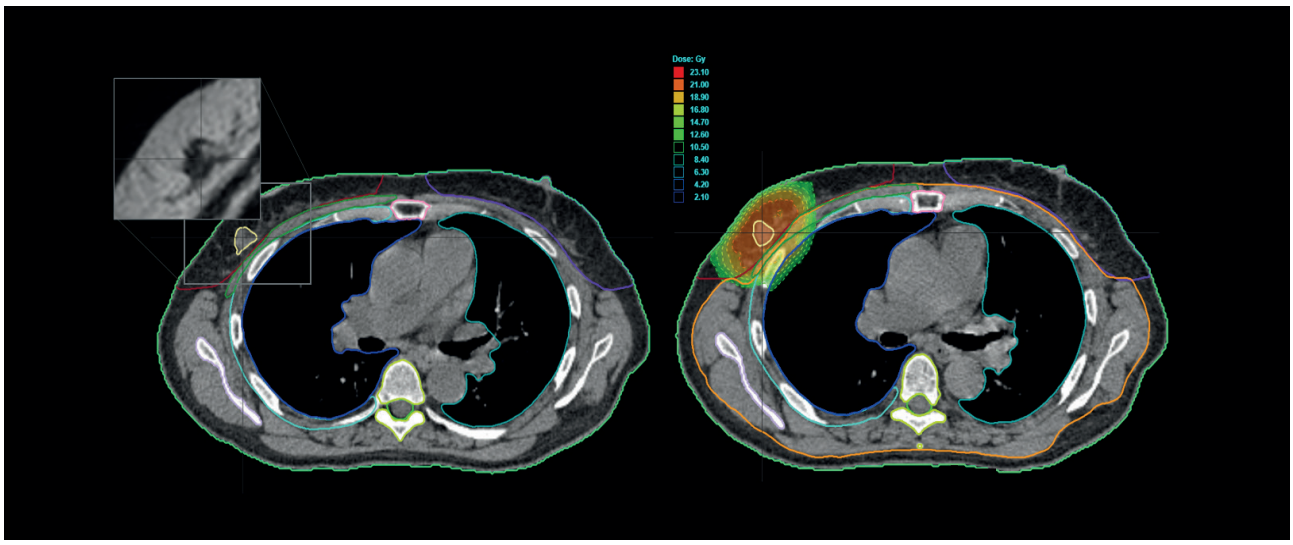

Figure 4.

Single fraction pre-operative MRgRT treatment plan with reference MR images.

Treatment delivery

An F0 session was performed two days prior to treatment delivery for end-to-end testing of imaging visibility and workflow, and to assess patient tolerance to the treatment timeframe. In addition to allowing the patient to become familiar with the treatment environment, this session was also a good opportunity to ensure there were no major changes in the tumor since the time of simulation.

On the day of treatment (ten days following simulation), the patient was set up in the supine position with both arms raised and supported by a vacuum bag. A T2 3D transverse MR scan was obtained on Unity for plan adaptation. The Adapt to Shape lite (ATS lite) workflow was used in order to maintain rigid contours, except for skin as this is a dose limiting structure. Shapes and setup were consistent, with no changes to the GTV or OARs between simulation and treatment verification scans. BFFE cine MR imaging was performed during treatment for motion monitoring. The treatment session lasted for 50 minutes with a beam on time of ten minutes.

Patient tolerance

The patient tolerated both the F0 and treatment well. Completing F0 prior to treatment provided them with the confidence that they were able to lie still for the required time to deliver treatment, as well as providing further opportunities for questions and familiarity with the environment.

The option to complete a single preoperative treatment over three weeks post-op was a significant motivation to get through the expected treatment duration. The patient was prescribed prophylactic dexamethasone and had no acute erythema, pain or swelling.

Post-radiation therapy

The patient reported no treatment related toxicity–pain, swelling or erythema—post treatment. Five weeks after radiation therapy, DWI was repeated on the Philips 1.5 T Ingenia scanner to assess treatment response.

One week later, the patient underwent breast-conserving surgery, using a wide local excision, and sentinel lymph node biopsy. The surgery was completed with clear margins and no sentinel node involvement. The patient did experience a minor infection following surgery, but this was resolved with a course of antibiotics. The surgical tissue was collected for a pathological evaluation to assess treatment response.

At six months follow up, the patient is well with occasional breast pain and mild fibrosis and minor skin changes around the treatment site.

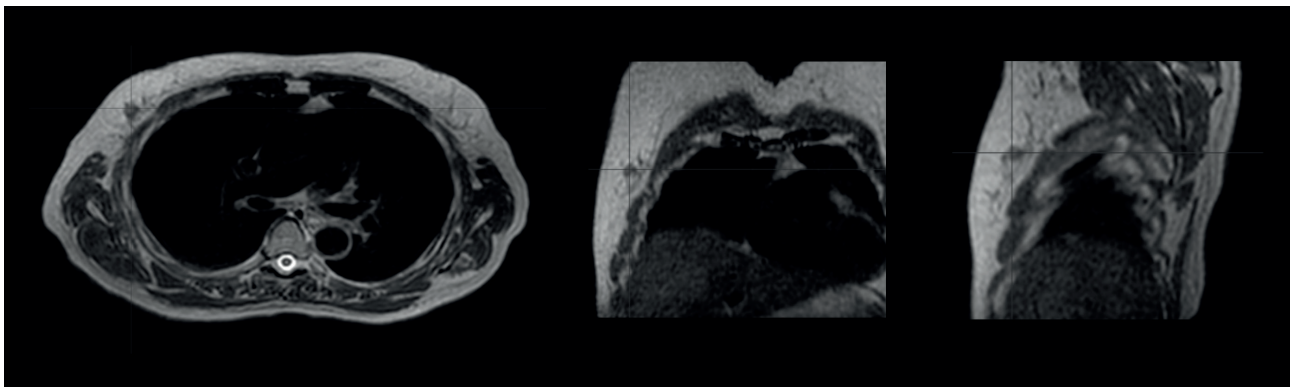

Figure 5.
Elekta Unity MR imaging offers superior soft tissue visualization compared to CT imaging.

Why Elekta Unity?

This case demonstrates that single fraction, 21 Gy APBI can be safely delivered in the pre-operative setting. The MR-Linac's ability to integrate real-time MRI during radiation therapy treatment offers superior tumor-targeting precision (and the ability to adapt if required) over traditional CT-Linac external beam methods (figure 5). This precise targeting allows accurate tumor irradiation, potentially reducing the treatment field while protecting surrounding healthy tissue. The pre-operative approach also provides the opportunity to assess the tumor response to radiation by functional MRI. Although evidence on pre-operative RT treatment response assessment by MRI is still accruing, if a pathologic complete response can be more accurately predicted after pre-operative APBI, surgery could potentially be omitted in such low-risk patients.

Additionally, the use of a single fraction is expected to enhance patient experience, quality of life and convenience, reducing hospital visits and streamlining treatment[1]. As with other single-fraction studies, it's recognized that reducing the number of fractions required for APBI could impact patient throughput and improve access for those waiting for adjuvant breast RT.[3]

It's hoped that this novel radiation therapy protocol, delivered with the benefits of the MR-Linac, will greatly reduce the treatment burden and provide a safe and effective short course non-invasive option for women with early breast cancer in the future.

References

1. V. Batumalai, G.P. Delaney, J. Descallar et al. Variation in the use of radiotherapy fractionation for breast cancer: Survival outcome and cost implications. Radiotherapy and Oncology 152 (2020) 70–77. https://doi.org/10.1016/j.radonc.2020.07.038.
2. Meattini I, Marrazzo L, Saieva C, et al. Accelerated Partial-Breast Irradiation Compared With Whole-Breast Irradiation for Early Breast Cancer: Long-Term Results of the Randomized Phase III APBI-IMRT-Florence Trial. J Clin Oncol. 2020 Dec 10;38(35):4175-4183. doi: 10.1200/JCO.20.00650. Epub 2020 Aug 24. PMID: 32840419.
3. Rahimi A, Simmons A, Kim DN, et al. Preliminary Results of Multi-Institutional Phase 1 Dose Escalation Trial Using Single-Fraction Stereotactic Partial Breast Irradiation for Early Stage Breast Cancer. Int J Radiat Oncol Biol Phys. 2022 Mar 1;112(3):663-670. doi: 10.1016/j.ijrobp.2021.10.010. Epub 2021 Oct 25. PMID: 34710523.
4. Snellen T, van Duijnhoven F, van der Ploeg I M, et al. Preoperative accelerated partial breast irradiation in locally recurrent breast cancer patients. Eur J Cancer. 2024; 200(1):113719. https://doi.org/10.1016/j.ejca.2024.113719.
5. Magnetic Resonance Imaging-Guided Single-Fraction Preoperative Radiotherapy for Early Stage Breast Cancer (The RICE Trial): Feasibility Study (researchsquare.com)
6. Fisher ER, Anderson S, Redmond C, Fisher B. Ipsilateral breast tumor recurrence and survival following lumpectomy and irradiation: pathological findings from NSABP protocol B-06. Semin. Surg. Oncol.8(3), 161–166 (1992)

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