#4044 Targeted intraoperative radiotherapy (TARGIT) yields very low recurrence rates when given as a boost.

Jayant S Vaidya¹, Michael Baum², Jeffrey S Tobias², Frederick Wenz³, Samuele Massaruti¹, Olive Murphy⁴, Basil Hilaris⁵, Joan Houghton⁵, Christobel Saunders⁶, Tammy Corica⁶, Uta Kraus-Tiefenbacher³, F Melchart⁵, Mohammed Keshgat⁵, Richard Sainsbury³, Michael Douek⁵, Ellie Harrison⁵, Alastair Thompson⁵, John Dewar⁵ and David Joseph⁶

UNITED KINGDOM ¹Surgical Oncology, CRO, Aviano, USA ²Radiation Oncology, Our Lady of Mercy Medical Center, New York, AUSTRALIA ³Radiation Oncology, Our Lady of Mercy Medical Center, New York, ITALY ⁴Surgical Oncology-CRO, Aviano, Italy, ⁵Radiation Oncology, Our Lady of Mercy Medical Center, New York, AUSTRALIA ⁶Radiation Oncology, Sir Charles Gairdner Hospital, Perth

Abstract

Patients and Methods

The value of tumour bed boost after breast conserving surgery has been well demonstrated, especially in those with higher risks of local recurrence. However, accurate targeting of this boost is difficult and the risk of a ‘geographical miss’ is estimated to occur in 50% to 80% of cases, substantially contributing to local recurrence.

Beginning in 1998, we have been treating patients of early breast cancer suitable for breast conserving surgery with TARGIT and intraoperative radiotherapy (TARGIT) using the Intrabeam™ system. This was a pilot series to test the feasibility and safety of the new approach as a prelude to the randomised trial which would test if intraoperative radiotherapy would be sufficient for local control in selected patients. This series now includes patients from the UK, USA, Italy and Germany. Patients suitable for breast conserving surgery were given intraoperative radiotherapy at the time of surgery, using the Intrabeam™ system, delivering 20 Gy to the surface of the tumour bed, followed external beam radiotherapy (EBRT) as per local guidelines, but excluding the boost. 310 patients have been treated. The median follow up is 24 months (longest 10 years). The treatment is well tolerated and the local recurrence rate is less than 2%.

Discussion

We found that the local recurrence rate with Targeted Intraoperative radiotherapy yields a very low recurrence rate (1.6%) at the median follow up time of 2 years. The patient population is representative of the usual patient who is suitable for breast conserving therapy with (T1-75% and T2-21%) and 28% patients were node positive. About a third of these patients were pre-menopausal.

The cosmetic outcome of a small subset of these patients has been analysed and was found to be excellent. An analysis of the patient with recurrence suggests that 2 recurrences may have been missed due to the timing of radiotherapy immediately after surgery which is not possible for other methods of partial breast irradiation. This is very encouraging.

We believe that the low recurrence rate is achieved due to such accurate targeting. In addition the timing of radiotherapy immediately after surgery may also have contributed to this result.

The time is ripe for a randomised trial to test whether the conventional external boost should be replaced by Tar1g1t, especially in high risk women. We are planning to commence this superiority study - TARGIT-B (Boost) to run in parallel with the ongoing TARGIT-A (Allo) equivalence trial.

Background

Over 90% of local recurrence after breast conserving surgery and postoperative radiotherapy occurs in the area around the primary tumour (TARgeted) Radiotherapy boost to the tumour bed is therefore part of the standard protocol. However, accurate targeting of this boost is difficult. A “geographical miss” has been shown to occur in 50-80% of cases and this may account for a large proportion of local recurrences.

We have developed a novel technique of delivering intraoperative therapeutic radiotherapy called TARGIT. With this technique using the Intrabeam™ system the TARgeted tumour-the tumour bed is wrapped around the radiotherapy source which delivers radiotherapy (Intrabeam) to the bed.

Our approach ensures excellent conformation and dosimetry and almost completely eliminates a “geographical miss”. Patients participating in the TARGIT trial have treated over 300 patients with the new technique using Intrabeam as a boost dose. These pilot cases tested the feasibility of giving intraoperative radiotherapy and the safety of adding the standard external beam radiotherapy as a boost. This paper will describe the efficacy of intraoperative radiotherapy as a tumour bed boost in terms of local recurrence.

Introduction

The Intrabeam™ system is likely to be the only and elegant intraoperative technique shown on the right

Results

 Patients suitable for breast conserving surgery were approached and consented to part in the pilot studies at each centre. Each patient had her breast conserving surgery as per local protocol – which typically was wide local excision of primary tumour and axillary surgery.

Intraoperative radiotherapy was delivered to the tumour bed immediately after surgical excision during the same anaesthesia as previously described. In some patients especially in the Australian cohort, due to logistic reasons, this procedure was performed as a second operation within a few weeks.

Various sizes of applicators (2.5 cm to 5 cm diameter) were used. The radiation dose received by the tumour bed was between 15 to 20 Gy. The dose at 1 cm was 18 Gy. The additional time required for intraoperative radiotherapy was between 30 and 50 minutes, depending on the size of the applicator. After completion of radiotherapy, the wound was closed in usual and patients discharged home at the usual time.

Patients were planned to receive external beam radiotherapy to the whole breast as per local protocols, but excluding the boost. All patients were planned to receive external beam radiotherapy to the whole breast as per local protocol, delivering 50 Gy at 25 fractions over 5 weeks. Some patients were given external beam radiotherapy and these are given in a separate table.

The following patients are excluded:

1. Patients who had a mastectomy soon after the primary surgery
2. Patients who had re-excision and conventional EBRT
3. Patients who had Tar1g1t as the only radiotherapy

Patients with positive margins were advised re-excision and mastectomy and were treated according to local protocols.

Patients suitable for breast conserving surgery were approached and consented to part in the pilot studies at each centre. Each patient had her breast conserving surgery as per local protocol – which typically was wide local excision of primary tumour and axillary surgery.

Intraoperative radiotherapy was delivered to the tumour bed immediately after surgical excision during the same anaesthesia as previously described. In some patients especially in the Australian cohort, due to logistic reasons, this procedure was performed as a second operation within a few weeks.

Various sizes of applicators (2.5 cm to 5 cm diameter) were used. The radiation dose received by the tumour bed was between 15 to 20 Gy. The dose at 1 cm was 18 Gy. The additional time required for intraoperative radiotherapy was between 30 and 50 minutes, depending on the size of the applicator. After completion of radiotherapy, the wound was closed in usual and patients discharged home at the usual time.

Patients were planned to receive external beam radiotherapy to the whole breast as per local protocol, delivering 50 Gy at 25 fractions over 5 weeks. Some patients were given external beam radiotherapy and these are given in a separate table.

The following patients are excluded:

1. Patients who had a mastectomy soon after the primary surgery
2. Patients who had re-excision and conventional EBRT
3. Patients who had Tar1g1t as the only radiotherapy

Patients with positive margins were advised re-excision and mastectomy and were treated according to local protocols.

Total evaluable patients included in this paper are 310

Patients who had a mastectomy soon after the primary surgery 12

Patients who had re-excision and conventional EBRT 4

Patients who had Tar1g1t as the only radiotherapy 69

(outside the TARget trial)

Patients with positive margins but refused further surgery are not excluded

Total number of patients treated during the pilot phase 395

Further reading: www.tar1g1t.org.uk and www.rig.ac.uk/tar1g1t_targ1t_home.htm

Corresponding author: J.S. Vaidya, j.s.vaidya@dundee.ac.uk

References


Intrabeam™ is manufactured by Carl Zeiss Inc., has FDA approval and CE mark.