

A brief description of the TARGIT-A trial by Jayant S Vaidya on behalf of the TARGIT group

For most women with breast cancer, the standard treatment includes surgery, which removes the tumour with a margin of normal tissues (lumpectomy), and radiotherapy, which reduces the chances of the cancer coming back.

Radiotherapy is usually given as a 3-6 weeks course (whole breast external beam radiotherapy - EBRT). A new development could significantly change the way breast cancer is treated.

Based on our clinical and pathological studies, we suggested in 1995 that radiotherapy restricted only to the tissues around the original tumour, and given at the time of surgery, may be as effective.

In the late 1990s, we designed a new device (called Intrabeam®) in collaboration with a specialist manufacturer, and developed the operative technique to deliver single-dose radiotherapy either during the lumpectomy or at a second operation soon afterwards. We called this novel approach TARGeted Intra-operative radioTherapy (TARGIT). In this technique, radiation is given directly to the site, the spherical device being placed where the lump was, and over half an hour, radiation is administered to the tissues that surrounded the tumour – the ‘tumour bed’, from within the breast.

We first treated a breast cancer patient with this technique on 2 July 1998. Our initial study of 25 women was expanded to 300 cases. TARGIT was given as a substitute for the usual tumour bed boost and all patients also received a shorter course of EBRT. TARGIT boost was found to be feasible, safe, and according to a recent analysis may even yield a better clinical outcome.

In March 2000 we launched a large international randomised clinical study (TARGIT-A trial) that took 10 years to complete and directly compared the TARGIT approach with conventional EBRT given over 3-6 weeks. The TARGIT approach was to give single-dose TARGIT to every patient, and, if a higher than acceptable risk was found (for example many positive lymph nodes) whole breast EBRT was added. The control group consisted of whole breast EBRT over 3-6 weeks

for every patient. Patients could also be entered in the trial after the tumour had been removed for example, at another hospital. For such patients, TARGIT was delivered by re-opening the wound as an additional surgical procedure.

It is important to recognise that the TARGIT-A trial compared TARGIT (with added whole breast EBRT as per the individual risk) vs. whole breast EBRT in all. In other words it compared risk-adjusted radiotherapy vs. whole-breast-radiotherapy-for-all. Within the trial, overall, 14% patients who received TARGIT also received EBRT. Amongst those who received TARGIT at the time of the first operation, 21% also received EBRT. Thus nearly 4 out of 5 such patients did not need any further radiotherapy.

In total, 2232 women from 28 centres in 9 countries participated in the trial: 1113 were allocated the TARGIT approach and 1119 the conventional radiotherapy approach. Our manuscript describing the results was fast tracked and published in *The Lancet* (online first on 5 June and in the print on 9 July 2010)¹. We found that the local recurrence rates in the two groups were very low and similar at 4 years, by which time the greatest risk of local recurrence had passed (EBRT group 0.95% and TARGIT group 1.2%)*. We also found that the TARGIT approach had less radiotherapy related side effects. We concluded in the *Lancet* that “For selected patients with early breast cancer, a single dose of radiotherapy delivered at the time of surgery by use of targeted intraoperative radiotherapy should be considered as an alternative to external beam radiotherapy delivered over several weeks”

Given the similar outcome and lower side effects, one cannot overemphasise the obvious advantages to the patient and the healthcare system of completing the radiotherapy in a single session at the time of the cancer operation; in addition the equipment is less expensive and there would be lower greenhouse gas emissions from avoiding 3-6 weeks’ of daily trips for EBRT.

*The statistics: The actual difference between the TARGIT and EBRT groups was 0.25% (10 times less than our original acceptable limit of 2.5%) at 4 years. As is usual while reporting clinical trials, not all patients have reached the follow up period of 4 years, so a standard statistical method was used to estimate a range around the 0.25% difference. This range, called 95% confidence interval, was -1% to +1.5%, which means that, with a 95% probability, at worst TARGIT is 1.5% worse than EBRT and at best TARGIT is 1% better than EBRT.

1. Vaidya JS, Joseph DJ, Tobias JS, Bulsara M, Wenz F, Saunders C, Alvarado M, Flyger HL, Massarut S, Eiermann W, Keshtgar M, Dewar J, Kraus-Tiefenbacher U, Sutterlin M, Esserman L, Holtveg HM, Roncadin M, Pigorsch S, Metaxas M, Falzon M, Matthews A, Corica T, Williams NR, Baum M. Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial. *The Lancet*. 2010;376(9735):91-102.