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BREAST CANCER

Targeted intraoperative radiotherapy—one pit stop for breast cancer treatment

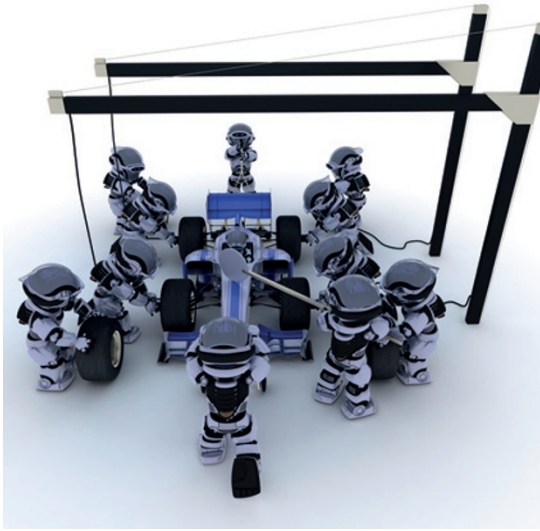
The current standard of care for women with small breast carcinoma (up to 3.5 cm) is a lumpectomy followed by adjuvant external beam radiotherapy (EBRT) for several weeks after surgery. Despite the length of treatment and its adverse effects, EBRT is considered necessary to decrease local tumour recurrence. Two new studies, one published in *The Lancet* and the other in *The Lancet Oncology*, have identified targeted intraoperative radiotherapy as an alternative protocol to treat women with early stage breast cancer. Both studies arise from the staggering reality that many women face mastectomy—despite having a tumour that is suitable for conservative breast surgery—because of the logistical and financial difficulties of a 6-week course of post-operative radiotherapy.

Lead author of one of the studies, Jayant Vaidya, explains how previous findings showed that "breast cancer seems to recur mainly at the site of the original tumour," which led to the idea of developing an instrument that would deliver radiation to the tumour bed during lumpectomy. Vaidya and colleagues developed a new technique—TARGIT (TARGeted Intraoperative radioTherapy)—and designed a risk-adapted trial to achieve a personalized approach to adjuvant radiotherapy. The TARGIT-A trial, launched in March 2000 and closed in June 2012, accrued a total of 3,451 women aged ≥45 years with invasive ductal carcinoma who were suitable for conservative breast surgery. Patients were randomly assigned to receive TARGIT or EBRT. Patients assigned to the TARGIT group, were subjected to lumpectomy, immediately followed by a single dose of radiation (20 Gy), delivered under the same anesthetic.

"TARGIT given to the fresh, undisturbed tumour bed also changes the surgical wound fluid—the tumour microenvironment—making it less favourable for cancer growth and spread," says Vaidya. Importantly, he continues, "our risk-adapted design meant that on final histological examination, if high risk factors were found, then whole breast radiotherapy was added—this occurred in about one in five women." This approach ensured that every patient received a treatment tailored for her specific cancer.

The results of the TARGIT-A trial proved the effectiveness of TARGIT in reducing local recurrence when given during lumpectomy (similar to EBRT), as 80% of patients were able to complete their treatment in one hospital visit. Although breast-cancer-specific mortality was the same in the two groups, the local toxicity in the TARGIT group was lower, as were deaths from other causes (1.3% versus 4.4%). According to Vaidya, "these results give confidence to offer TARGIT to suitable women in daily clinical practice."

The second study, conducted by Umberto Veronesi and colleagues, enrolled women (aged 48–75) diagnosed with early stage breast cancer (tumour diameter <2.5 cm) who were suitable for breast-conserving surgery. Between November 2000 and December 2007, 1,305 patients were randomly assigned to receive either EBRT or electron-based intraoperative radiotherapy (ELIOT). Patients in the ELIOT group received a single dose of radiation (21 Gy) directly to the tumour bed after tumour resection and mobilization of the mammary gland for optimal exposure of the target. Veronesi's team found that ELIOT resulted in a significantly higher local recurrence rate of 4.4% versus 0.4% with conventional EBRT, although this difference was within the prespecified equivalence margin of 7.5%. The researchers reported a similar overall survival rate in both groups and a similar number of distant metastases and deaths. Consistently, however, fewer adverse effects were noted among women in the ELIOT group.



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Of note, the different results obtained in the TARGIT and ELIOT trials might be due to differences between the studies, such as the radiotherapy techniques, patient selection (the ELIOT trial included slightly more high-risk patients) and trial design (ELIOT was not a risk-adapted trial). Nonetheless, both studies indicate that intraoperative radiotherapy should be considered a treatment option for suitable patients.

These options for 'one-stop' breast-conserving cancer treatments are welcome news for many women. As this technology continues to be refined, the cost-savings are likely to be considerable, as are the benefits to women with cancer—justifying the change in clinical practice and the acquisition of the new equipment from many hospitals.

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Original articles Vaidya, J. S. *et al*. Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial. *Lancet* doi:10.1016/S0140-6736(13)61950-9 | Veronesi, U. *et al*. Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial. *Lancet Oncol.* doi:10.1016/S1470-2045(13)70497-2