



## Breakthrough for breast cancer patients

A commentary by  
Professor Jayant S Vaidya



### “New treatment heralds breakthrough for breast cancer patients”

“A pioneering breast cancer therapy developed by UCL clinicians, which requires just one shot of radiotherapy rather than conventional weeks-long treatment, has proven to be as effective for most women in treating the disease.”<sup>1</sup>

*Professor Jayant Vaidya is a breast cancer expert and considered a leading consultant surgeon, and oncology expert in diagnosis and treatment of all breast conditions. He presents a commentary by behalf of all authors on A pioneering breast cancer therapy*

**B**reast cancer is one of the commonest forms of cancer and its treatment has been improving over the last century. These improvements have led to improved survival and far fewer women are now dying from breast cancer. Over the twenty-year period from 1987 to 2017 the number of women dying from breast cancer has nearly halved from 60 to 33 per 100,000 per year. As women with breast cancer are living longer, and the objectives of research in the last 2 to 3 decades has focussed on reducing the harmful side effects of treatments by optimising them to be targeted and personalised: optimum treatment for maximum benefit and minimum risk.

Radiotherapy is a necessary part of treatment of breast cancer especially when it is treated by removing only the cancerous lump and some surrounding normal tissue with an operation called lumpectomy. Traditionally, the lumpectomy operation is followed by a post-operative course of external beam radiotherapy (EBRT) which normally is delivered from outside the body via a radiotherapy machine, once every day for 3 to 6 weeks. Each of these treatments is given over a few minutes, but requires 15 to 30 hospital visits, which could be a significant distance from where the patient lives. Trying to reduce the number of days of therapy by giving larger doses (for example, larger doses every day given for just 5 days) can result in higher toxic side effects such as making the breast hardened.

Furthermore, giving radiotherapy to the whole breast also means that surrounding normal vital organs such as the heart, lung, the food pipe (oesophagus) all receive unnecessary and potentially harmful ‘scatter’ radiation. Such radiation has been shown to cause heart attacks and cancers. Unfortunately, cancer of the lung and oesophagus have poor outcomes. Moreover, smokers given radiotherapy for breast cancer face a 1 in 4 risk of dying from a heart attack or lung cancer over a 30-year period – a very unfortunate event when she is already cured of breast cancer!

Of course, the other option which breast cancer patients have is to have a mastectomy – i.e., remove the whole breast. Unfortunately, if it isn’t possible for the patient to commit the prolonged radiotherapy treatment then mastectomy is the only option, drastically altering their quality of life.

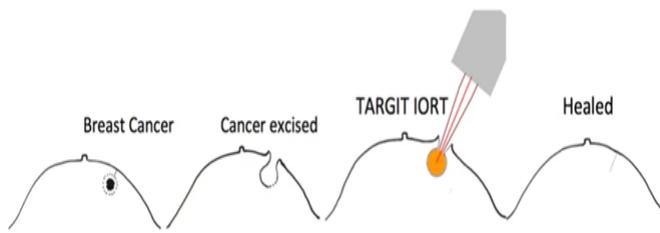
- Patients who are diagnosed with a small breast cancer are normally treated by surgically removing the lump followed by treatment of the whole breast with radiotherapy (WBRT)
- TARGeted Intraoperative radioTherapy (TARGIT-IORT) treatment developed by Professors J Vaidya, M Baum and JS Tobias is given during the cancer operation and gives radiotherapy to only the area around the tumour. It is completed at the same time as the cancer surgery.
- TARGIT-IORT avoids delays, has fewer side effects and leads to an improved quality of life.
- The results of the large international randomised clinical trial (TARGIT-A trial) show that WBRT can be effectively substituted by the single-dose TARGIT-IORT with similar long-term local and distant control of breast cancer, breast preservation and breast cancer survival.
- TARGIT-IORT avoids unnecessary harmful radiation to nearby organs such as the heart and the lungs that inevitably accompanies WBRT.
- With TARGIT-IORT, there are fewer deaths from causes such as cardiovascular and lung problems and other cancers.
- Following this research, TARGIT-IORT has been offered to patients with breast cancer in 38 countries and over 45,000 patients have been treated

When I worked in India in the 1990, at the Tata Memorial Hospital in Mumbai, I faced this problem on a daily basis. Many of my patients had to have a mastectomy only because they could not stay in Mumbai for the 6 weeks of post-operative radiotherapy- it was a very sad situation.

Our laboratory work suggested that we may be able to focus radiotherapy only around the tumour. So, in the late 1990s, working with Professors Mike Baum and Jeff Tobias at University College London, in collaboration with Photoelectron Corp (USA) we developed a new machine to give radiotherapy during the lumpectomy operation, under the same anaesthetic. We called this new operation TARGeted Intraoperative radioTherapy, TARGIT-IORT in short.

Then, in collaboration with expert clinicians and scientists, we performed a very large clinical trial called the TARGIT-A trial.

TARGIT-A is not an industry sponsored trial. It was prompted by academic insight and run with foresight, enthusiasm, and hard work from each of the investigators, many of whom made significant contributions to different aspects of TARGIT-IORT. Such a large trial was only possible committed long-term international collaboration with open minded and dedicated colleagues all over the world.



In addition, I cannot emphasise enough the remarkable contribution of so many patients with breast cancer.

They provided vital insight as members of our committees, as well as willingly participating in the trial itself.

In the TARGIT-A trial, we asked whether giving TARGIT-IORT targeted only to the tumour bed during the cancer operation, could completely avoid the whole breast radiotherapy course in a large proportion of women with breast cancer.<sup>2</sup>

TARGIT-IORT is delivered immediately after lumpectomy (tumour removal), via a small ball-shaped device placed inside the breast, directly where the cancer had been. The single-dose treatment lasts for around 20 to 30 minutes and replaces the need for extra hospital visits, benefiting both patient safety and well-being.

To establish TARGIT-IORT's long-term effectiveness, 2,298 women aged 45 or over with invasive ductal carcinoma (breast cancer) and a tumour of up to 3.5cm in size, were randomly assigned to receive either TARGIT-IORT or the traditional EBRT.

This large clinical trial, designed and run from UCL, involved 32 hospitals and medical centres in ten countries: the UK, France, Germany, Italy, Norway, Poland, Switzerland, United States, Canada and Australia.

The trial started in March 2000, which has enabled us to publish these long-term results. The findings show that with TARGIT-IORT therapy, eight out of every ten patients had no need for any further post-operative radiotherapy treatments. There was also no detriment to survival from breast cancer and no increase in the likelihood of the cancer returning.

In addition, with TARGIT-IORT, significantly fewer women died from causes other than breast cancer. Previous studies have shown that TARGIT-IORT has fewer radiation-related side effects compared with conventional whole breast radiotherapy, with less pain, better cosmetic outcome and a better quality of life.

Significantly, at long-term follow up (average 9 years, maximum 19 years) breast cancer outcomes with risk-adapted single-dose

TARGIT-IORT given during lumpectomy were comparable with the long-course of post-operative whole breast radiotherapy.

No difference was found between the two treatments for local or distant control of breast cancer, breast preservation and deaths from breast cancer.

An important finding was that women allocated to receive TARGIT-IORT had a substantial reduction in deaths from causes other than breast cancer (e.g. cardiovascular causes and lung problems and other cancers), a reduction from 9.85% to 5.41% by 12 years from the operation.

With TARGIT-IORT, women can have their surgery and radiation treatment for breast cancer all at the same time. This reduces the amount of time spent in hospital and enables women to recover more quickly, meaning they can get back to their lives more quickly. With TARGIT-IORT, a large proportion of patients with breast cancer will never need to make the repeated daily visits to the radiotherapy centre. They avoid side effects of whole breast radiotherapy. TARGIT-IORT also reduces the burden on overstretched radiotherapy departments.

During the past 20 years TARGIT-IORT has been used worldwide in over 260 medical health centres in 38 countries, helping to treat more than 45,000 patients. It is expected that this treatment will be made much more freely available.

Patients should ask about this treatment before their surgery for breast cancer is performed.

Funding for the trial was provided by the National Institute for Health Research (NIHR) Health Technology Assessment programme, <https://www.nihr.ac.uk/news/international-trial-shows-single-dose-radiotherapy-as-effective-for-treating-breast-cancer-as-conventional-treatment/25517> UCL Comprehensive Biomedical Research Centre, and Cancer Research UK.

- Excerpts from <https://www.ucl.ac.uk/news/2020/aug/single-dose-radiotherapy-effective-treating-breast-cancer> and <https://blogs.bmj.com/bmj/2020/08/19/targeted-intraoperative-radiotherapy-for-early-breast-cancer-new-evidence>
- A video (<4min) explanation <https://youtu.be/5Xby04NBanY>
- Full paper at British Medical Journal (BMJ) <https://www.bmj.com/content/370/bmj.m2836.full.pdf>
- The clinical trial confirmed the long-term effectiveness of Targeted Intraoperative Radiotherapy (TARGIT-IORT): a breast cancer treatment which is increasingly available throughout the world.
- More information at <https://www.targit.org.uk>



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