



Newsdesk

Targeted intraoperative radiotherapy for breast cancer

There is no doubt that breast cancer patients would rather not endure the gruelling 6 weeks of radiotherapy which follows most breast-conserving surgery procedures. Radiotherapists and surgeons alike have been discussing the possibility of shorter, or less intense treatment schedules, with little success. But now, two research groups from Britain and Italy plan to give the radiotherapy in the operating theatre during surgery instead.

Breast-conserving surgery and radiotherapy are well-established treatments for breast cancer. If the tumour is below a critical mass, then the surgeon can remove it along with some of the surrounding tissue, while leaving the remaining breast intact. Afterwards, the patient is encouraged to attend daily radiotherapy sessions, which can take 1–2 hours a day for 6 weeks, to kill any cancerous cells which were not removed by surgery.

For patients, this routine is an incredible strain, not only physically and emotionally, but also because of the time and effort it takes to get to the hospital. For this reason, many people in remote areas such as parts of Australia and India, where there is no radiotherapy unit nearby, opt for a mastectomy rather than trying to save any of the healthy breast tissue.

The concept of combining radiation and surgery into a single procedure is not a new one. However, until recently, giving the two treatments at the same time presented logistical problems. "All intraoperative radiotherapy techniques before now involved wheeling the patient from the operating theatre to the radiotherapy unit, which is often a long way", says Jayant Vaidya, Middlesex Hospital, London, UK, who is working on a study of intraoperative radiotherapy (IORT) in the UK. But this problem has been overcome by the design of mobile radiotherapy units specifically for use in the operating room.

Two medical device companies Photoelectron Corporation (USA) and Hythesis SpA (Italy) have independently developed miniature radiation machines named PRS400 and NOVAC-7, respectively. These machines enable radiation treatments

to be delivered inside the tumour cavity during an operation, thus minimizing irradiation to surrounding healthy tissue and skin.

The British team, led by Michael Baum at the Middlesex Hospital, London, UK, is using the PRS400 model in clinical trials. "The really new concept we are testing is only treating the quadrant around the tumour", says



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Vaidya. Before joining Baum in the UK, Vaidya was looking at the distribution of tiny occult tumours in breast tissue to identify the areas of likely recurrence. Surprisingly, despite the presence of many small tumours scattered all over the breast, 91% of recurrences seen were in the index quadrant, where the primary tumour had been (*Br J Cancer* 1996; 74: 806–14). "Looking at the occult tumours, the obvious conclusion is that everyone should have a double mastectomy to remove the risk!", says Vaidya. "But the high rate of recurrence in the index quadrant suggested that all the tiny tumours elsewhere were not important, and therefore there was no argument for mastectomy."

A group in Italy is investigating a similar approach. "The equipment we are using consists of a mobile linear-accelerator with a robotic arm which is easily adapted to the site to be irradiated in the breast", explains Umberto Veronesi, Italian Minister for Health, who pioneered work with the NOVAC-7 model. "We can be more precise in defining the exact area to be irradiated in the mammary gland and

by working intraoperatively, we can spare the skin from irradiation", he said.

Both groups have begun randomised trials of IORT as a stand-alone treatment (for the UK trial protocol see *The Lancet* website <http://www.thelancet.com>), but it has not been easy to convince people that targeting radiotherapy to the tumour bed is sufficient to protect against recurrence. "There has been a lot of resistance to the concept of only treating the index quadrant, especially in the USA – even in the UK not all radiotherapists were happy", Vaidya said.

But data from both groups suggest that any worries are unfounded. "We have treated some 1300 patients in 12 months without any serious side-effects", says Veronesi. Vaidya and his colleagues have also obtained positive results (*Ann Oncol* 2001, in press). "We started a pilot study with 26 patients in 1998 and tested the feasibility of giving IORT in the operating theatre as a boost to the tumour area, in addition to whole breast radiotherapy over 5 weeks. At median follow-up of 23 months there were no complications and we haven't seen any recurrences yet", Vaidya said.

However, there are limits to this approach. An earlier trial at the Christie Hospital in Manchester, UK, compared local-field to wide-field radiotherapy. There was an increased risk of local recurrence when local-field treatment was given to patients with lobular cancers and those with an extensive intraductal component (*Clin Oncol* 1993; 5: 278–83).

Both Veronesi and Vaidya are confident that targeted IORT will be a success. "We expect that if the randomised trial yields favourable results, we may translate the procedure into routine practice in 5 to 7 years" comments Veronesi.

Vaidya is also adamant that this technique will save a lot of money for hospitals. "Breast cancer makes up almost a third of the work load in radiotherapy units worldwide, and removing 6 weeks post-operative radiotherapy could save about £15 million [\$21.5 million]", he says.

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