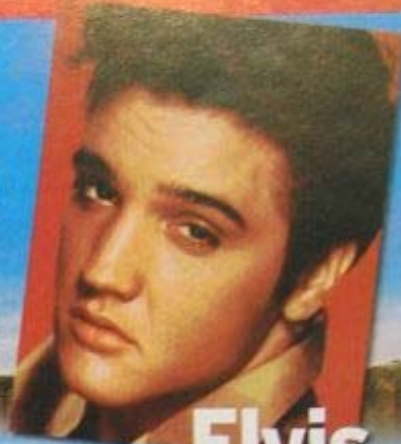


Breast Cancer: New Hopes, New Cures

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Curing Breast Cancer

BY ELIZABETH
ADLAM

We're nearly there, thanks to
five new treatments

IN AN OPERATING THEATRE in London's Middlesex Hospital, Linda Lines lies unconscious. Sterile green gowns drape her body, leaving exposed only her right breast and outstretched arm. Linda has breast cancer; in the upper part of her breast, a mass of runaway cells has grown to about the size of a pea. Given her age—55—and the size of her tumour, Linda is typical of the 40,000 British women expected to be diagnosed with invasive breast cancer this year. But her experience is about to take a sharp turn from the typical.

After the tumour is neatly excised, surgeon Jayant Vaidya reaches for a slim probe with a tiny metal sphere at one end and inserts it into Linda's breast. He is going to deliver radio waves directly on to the tumour site.

Satisfied with the probe's position, he signals for the electron generator to be switched on. To the sound of a gentle bleep, it begins generating "soft" X-rays which pass out through the sphere.

Five minutes, then ten. Twenty-five minutes, Vaidya removes the probe and inspects the small incision. He nods to the team: "Looking great." With



Linda Lines

When businesswoman Linda Lines learned she had breast cancer, she "refused to panic" and went ahead with a family holiday in Thailand. There, Linda read up on treatments, eating healthily and getting fit. When her London surgeon asked her if she'd heard of Targit, a one-off therapy without any follow-up, she said she'd have some of that. She became the first patient to opt for the therapy—a courageous decision that has paid off. Four years on, she is clear of cancer.

a couple of stitches he closes it up.

If all has gone well, not only has the tumour in Linda's breast been destroyed, but any rogue cells have been mopped up, eliminating the need for weeks of radiotherapy. This is targeted intra-operative radiotherapy (Targit). It's a far cry from the early days of treatment, when surgeons routinely removed not just a woman's breast but the muscles of her chest, lymph nodes and some fat and skin, disfiguring and frequently disabling her. Targit is based on the premise that, since 90 per cent of early breast cancer recurrences occur at the site of the original tumour, it makes sense to limit therapy to that spot.

This approach, part of a study, is just one of a number of new treatments that are gentler on the body—and, it is hoped, better able to save lives. With deaths from breast cancer continuing to fall—from 15,400 to 12,800 in a decade—here are some of the most promising treatments to be found in hospitals and research institutions across the country.

Surgery: A Total Treatment

The notion of bathing breast tissue with protective radio waves at the same time as surgery is exciting, though still experimental. Jayant Vaidya originally hit on the idea as a way of offering treatment in one go for patients in his native India. "Targit offers a degree of precision impossible with traditional

irradiation delivered externally," he says. "The surgeon can see where to direct the rays. It delivers an even dose and doesn't endanger heart or lungs."

Three years into a UK-led global trial, results are promising—only two patients of 185 treated so far have experienced relapses, with tumours appearing elsewhere in the breast. (Patients wishing to take part in the trial can ask to be referred to the Middlesex or Guy's Hospital in London.)

Targit is set to transform treatment for early breast cancer patients. It could be routinely available on the NHS in five years and potentially save £15 million a year.

A Kinder Cut

In 1983, after Jeanne Tassis had a breast tumour removed, she had two months of radiation therapy and returned to her life as a teacher and mother. But two years later she began to suffer a painful side effect of her treatment: her left arm started swelling, eventually growing to three times its size. She became increasingly prone to potentially life-threatening infections. For a time, she was being hospitalised every few weeks. "All I could think of was I survived the cancer and I'm going to die from this," she says.

Jeanne had a moderately severe case of lymphoedema. When the surgeons cut out her tumour, they also took lymph nodes from her armpit to check for spreading cancer cells.

One escape route for malignant cells is provided by the lymph system, a fluid-filled highway for immune cells, oxygen, nutrients and cell waste. Lymph nodes trap bacteria and viruses so that white blood cells can kill them—that's why they sometimes swell when a person has an infection. And they collect cancer cells as well. For many years, surgeons would routinely remove ten to 20 nodes from the network under the arm and send them to the lab. If cancer was found, it meant a whole-body treatment such as chemotherapy was in order.

But all that cutting can damage the system of tiny vessels that drains lymph fluid, and radiation can do further harm. The build-up and stagnation of fluid can cause minor numbness and swelling, or lead to great pain, dangerous infections and disability.

A new procedure may protect

women. When Philomena Whittle had a lumpectomy at the Royal Surrey County Hospital, her surgeon, consultant Mark Kissin, removed just one lymph node. The approach, known as sentinel node biopsy (SNB), is based on the realisation that lymph fluid travels in an orderly way from one node to the next. Find the node first in line to drain the region and this sentinel will signal the cancer's spread or give the all-clear.

Three days later, Philomena, from Godalming in Surrey, went home with a small incision in her armpit, another in her breast and without the drains that are needed after standard node clearance. Philomena's node was found to be cancer free. Over the next

Philomena Whittle

Every woman should be aware of changes in her breasts. Philomena Whittle's fears were confirmed when she checked out the lumpiness of a mosquito bite which "felt different" and a biopsy revealed a tumour. The 36-year-old Surrey nurse volunteered to join a trial of a new, safer surgical technique called sentinel node biopsy. After the lump in her right breast was removed, surgeons took just one of the nearby lymph nodes to see if the cancer had spread. It hadn't. "I was so lucky, the whole procedure was relatively mild." Four years on, her right arm is unaffected. "I work out at the gym regularly, cycle. It never felt better."



18 months she had her arm measured regularly to check for lymphoedema, but there was no swelling whatever.

While proof is still to come that SNB is as reliable as taking the whole lymph network, a five-year trial of 1,000 patients across Britain seems certain to provide it. Four years in, the cancer recurrence rate in patients who have had SNB is less than five per cent. "It's a win-win situation," says Professor Robert Mansel of the University of Wales College of Medicine, Cardiff, who is heading up the trial. "When women know these results, they'll all want this treatment."

The skill and experience of leading SNB surgeons such as Mark Kissin and Robert Mansel are crucial for a good result. "Surgeons taking part in our trials must have performed at least

40 sentinel node biopsies, achieving pinpoint accuracy," says Mansel. "Our success rate in locating the sentinel node is 99 per cent—a world best."

Women across Britain are being recruited for this final phase of the SNB trial. Mansel is confident that less than five years from now an early breast cancer patient will be a hospital day case. Small cancer, small incision, sentinel node biopsy, home.

Gentler, Safer Radiation

"Time and time again, I'd patients who'd become increasingly low even though they were clear

Margaret Bates

A tragic family history of breast cancer meant that Margaret, 66, was not surprised when a tumour showed up in her left breast. "I vowed there was no way I was going to die of cancer like my mother and eldest sister," she says.

Margaret jumped at the chance to take part in the trial of IMRT, a way of tailoring radiotherapy to the shape of the breast, making treatment briefer and more effective. She was happy to spend 15 minutes every weekday over six weeks having a mechanical arm rotate for less than a minute over her breast. "What really amazes me is that my breast looks and feels marvellous—I can hardly see a scar."



Crucial to the early detection of breast cancer is X-ray mammography, offered by Britain's national screening programme to every woman over 50. In the next five years, even better digital mammography (DM) should come on line throughout the NHS.

DM still uses X-rays, but depends on sensitive digital receptors to record images, and computers to

help detect abnormalities. The image is manipulated to change contrast and density, making abnormalities easier to detect. But the biggest plus, says Dr Robin Wilson, clinical director of breast services at Nottingham City Hospital, is that "computers don't get tired or lose concentration".

Two other imaging techniques offer hope for better diagnoses. The

first, magnetic resonance imaging, is offered to women with a high genetic risk of breast cancer. It produces detailed 3D images made up of many planes or "slices". The second, ultrasound, is a screening "add-on" to assess mammogram queries. Both techniques can easily "see" through the dense breast tissue that can confound traditional mammography.

breast cancer," says Professor John Yarnold, clinical oncologist at London's Royal Marsden Hospital. Something was badly wrong.

These patients were suffering the damaging long-term effects of intensive radiotherapy. Though it's a highly effective treatment, some patients can find that their breasts change shape, become discoloured and chronically sore. So Yarnold decided to search for a new way of delivering post-operative radiation therapy.

Conventional radiotherapy beams waves along straight lines. But a woman's breast is not geometrically shaped, Yarnold reasoned, hence the potential for damage. His solution: to sculpt radiotherapy dose volumes to suit the actual shape of each individual breast—an approach called Intensity Modulated Radiotherapy (IMRT).

The patient's details are fed into a special computer programme. Using sophisticated imaging it judges the depth and density of tissue, then works out a treatment plan that gives all parts of the breast an equal dose.

After two years of a study comparing 300 women treated with IMRT against conventional radiotherapy, the new treatment is proving highly effective, particularly in women with larger breasts where the radiotherapy dose tends to be more uneven. Women are 30 per cent less likely to suffer side effects or physical damage.

IMRT is offered at the Royal Marsden Hospital, Ipswich General Hospital and in a modified form at Torbay Hospital in Devon. But Yarnold hopes that a proposed national research trial will lead to its introduction into routine clinical practice in under

three years. "IMRT will have a real impact on a woman's quality of life," he says. Great news for any woman with a battered self-image.

Starve the Tumour

In the fight against breast cancer, two recent drug developments are making startling advances. The first belongs to a class of drugs called aromatase inhibitors, and it may represent not just a step but a leap.

As you might guess, the drugs inhibit aromatase, an enzyme. Aromatase converts testosterone and related hormones into oestrogen. Block the enzyme and you block the manufacture of oestrogen.

Women think of oestrogen as the female hormone. But it can also act as fuel to the 70 per cent of breast cancers that are oestrogen-positive. So one approach is to kill breast cancer cells by starving them of oestrogen. Breast cancer patients sometimes have their ovaries removed to reduce levels of the hormone. More often, following surgery, they take tamoxifen, which does the job chemically by blocking the cancer cells' docking site for oestrogen. Tamoxifen cuts a woman's chances of relapse without causing the nausea, hair loss and exhaustion frequently associated with chemotherapy drugs.

Now, after 20 years in which tamoxifen has been the gold standard hormonal treatment, a new drug—an

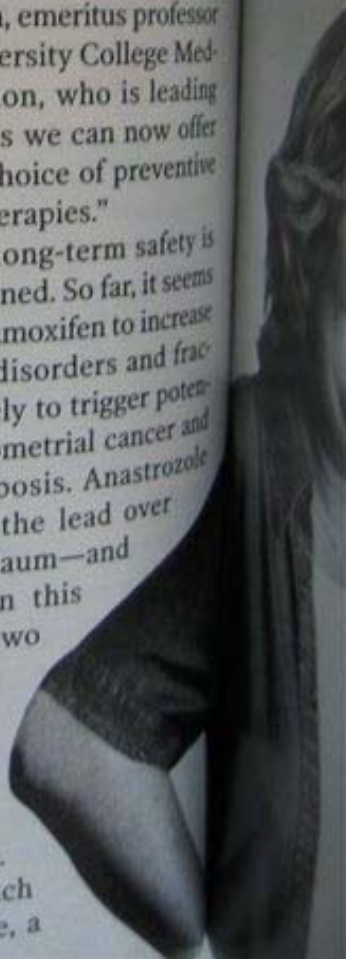
aromatase inhibitor called anastrozole—is challenging its supremacy. Four years into a five-year global study involving 9,000 women from 300 countries, researchers compared the results from women who were taking either tamoxifen, anastrozole or a combination of both.

While tamoxifen lowers the risk of breast cancer recurrence by as much as 40 per cent with no add-on therapy, the scientists found that women who took anastrozole brought down their risk of tumour recurrence by another 22 per cent.

"These results are truly exciting," says Michael Baum, emeritus professor of surgery at University College Medical School, London, who is leading the trial. "It means we can now offer women a viable choice of preventive hormonal drug therapies."

Anastrozole's long-term safety is still being determined. So far, it seems more likely than tamoxifen to increase musculoskeletal disorders and fractures, but less likely to trigger potentially deadly endometrial cancer and deep vein thrombosis. Anastrozole appears to have the lead over tamoxifen, says Baum—and the finish line in this race is less than two years away.

The second advance is an impressive chemotherapy drug—epirubicin. For oncologists such as Dr Chris Poole, a



consultant at Queen Elizabeth and City Hospital, Birmingham, chemotherapy remains a vital line of defence for the majority of patients—particularly younger women, whose tumours spread faster.

“Patients view chemotherapy with great reluctance,” says Poole, “since it comes with a bucketful of side effects. But it can be a key to survival”

Now results of the largest trial of its kind, involving some 2,000 women at 75 cancer centres, have shown that when women treated with a combination of chemotherapy drugs

are also given epirubicin, they are a third less likely to relapse or die. “These are staggering findings,” says Poole. “And the wonderful thing is, this drug is licensed—so every single woman who needs it can get it.”

THIRTY YEARS AGO, the official five-year survival rate for women with a tumour in the breast was 54 per cent. These days it's more than 90 per cent for early breast cancer. Even when cancer has spread to nearby areas of the body, women have a survival rate of 78 per cent.

Couple that news with gentler and more potent treatments, and you can almost envisage a day when a diagnosis of breast cancer has truly been sapped of its terror.

Christine MacArthur

A professor of epidemiology at Birmingham University, Christine MacArthur, 45, was diagnosed with “multifocal” breast tumours—tumours that had sprung up in a number of places within her breast.

Knowing there was a real risk they might spread, Christine agreed to be injected with a new drug being trialled—epirubicin—followed by standard chemo. Seven years later, she is still cancer free.

