‘We will help you live until you die’

Joanna Lyall

Cicely Saunders touched the lives of millions of terminally ill patients through her promotion of hospices and palliative care. Though she died this summer at the London hospice she founded in 1967, her fight for all patients to have the right to live well and die pain free and in dignity goes on.

Shortly before her death in St Christopher’s Hospice this summer, Cicely Saunders took part in a television programme that called for better access to good palliative care in the UK. Few who knew her would be surprised that at 87, and only weeks away from her own death from cancer, she still accepted the opportunity to speak out on the issue to which she had dedicated her life.

Born in 1918, months before the end of the First World War, Saunders is widely recognised as a pioneer of the modern hospice movement, founding the trail-blazing St Christopher’s hospice in south London in 1967. Though the concept of offering a place of support and comfort for the dying was not new, such hospices as existed at that time were mainly run by nuns. Saunders’ unique contribution was to insist that the medical profession had an equal responsibility to help their dying patients live as full and pain-free lives as possible for as long as possible.

It was a hard battle to win, and, as is clear from her correspondence, published in paperback earlier this year, Saunders recognised the message of palliative care is one that needs constant reinforcement.

In a letter written in 1972, she warned that, “Unless we teach students even more widely than we are doing and continue battling away with those already trained, patients will simply not get the quality of care they should receive.”

It was due to her work that palliative medicine was first recognised as a specialty by the Royal College of Physicians in 1987, 20 years after she started St Christopher’s hospice as a centre for treatment, teaching and research.

Robert Twycross, who worked as a research fellow at St Christopher’s, from 1971 to 1976, says “When Cicely first became involved, doctors largely neglected the dying. There was no systematic approach to pain and symptom management and the idea that patients had to ‘earn’ their analgesia was still prevalent.”

Twycross, now emeritus clinical reader in palliative medicine at Oxford University, says that as well as being “an excellent physician and a charismatic figure with a superb brain… she was extremely effective at engaging powerful allies and spreading the knowledge she had gained.”

Saunders, he says, saw the benefits of pain relieving drugs being given regularly, pre-empting pain. She initiated research which showed the effectiveness of morphine and spread what she had learned.

“She was a visionary and also a

ST CHRISTOPHER'S HOSPICE

She was a great advocate for research and made the case that morphine is the gold standard

propagandist and disseminator of knowledge. She always said she didn't found the hospice, it found her, and certainly it was an idea whose time had come. But without her in the background there would not have been a recognition of palliative medicine as a specialty.

"She was also a gifted teacher. Her concept of 'total pain', introduced in an article in 1964, encouraged students and health professionals to consider the mental, spiritual and social dimensions of the patient's feelings.

"Cicely was never just a symptomatologist," he says.

Pain and palliation

Twycross' research at St Christopher's in the 1970s showed that morphine was as effective in preventing and relieving pain as the mixture of diamorphine, cocaine and anti-emetic in chloroform water, then known as 'the Brompton cocktail'. Importantly, it also showed that there were no problems of addiction when morphine was given for pain relief.

"In the 1970s we killed the Brompton cocktail and were essentially using morphine in tap water and an anti-emetic in selected patients," recalls Twycross. This had considerable implications for pain control in countries where diamorphine could not be prescribed.

Saunders had already seen the benefits of pre-empting pain by giving drugs regularly when she worked as a volunteer nurse in the evenings at St Luke's hospital, in central London between 1948 and 1955. But the practice was not widespread, and she saw that part of her task was to act as a catalyst to promote better care both in the UK and beyond.

Her background gave her a special perspective from which to do this. Forced to give up nursing because of a back problem, she trained as a hospital almoner (medical social worker) and worked at St Thomas's hospital (south London), on a cancer ward, before starting medical school at the age of 33, qualifying in 1957, at the age of 38.

Some of her first articles, written well before the opening of St Christopher's, were for the nursing press in the 1950s, and her writings stressed the role of nurses in hospice care. She believed it was the nurses at St Luke's who came up with the idea

ST CHRISTOPHER'S HOSPICE

"You matter because you are you, and you matter until the last moment of your life"

of giving drugs regularly to patients with advanced cancer to prevent pain.

It was Saunders' concept of 'total pain' that sparked the modern palliative care movement, according to Phil Larkin, lecturer in palliative care at the National University of Ireland in Galway and vice-president of the European Association of Palliative Care (EAPC).

"She could speak to a number of levels, and as a nurse she hugely validated the role of nurses in palliative care. She was also a great advocate for research and made the case that morphine is the gold standard," he says, adding that some doctors still need to be reminded that prevention is better than trying to treat pain when it has already occurred.

Pain is still a problem

However, regulation is still hampering effective palliative care in many parts of the world, he says. "Despite clear evidence that morphine remains the gold standard for pain relief and may be administered safely and with relatively little expense, excessive and unnecessary regulation of opioids still prevents its use where it is most needed."

Geoffrey Hanks, professor of palliative medicine at the University of Bristol, and honorary president of the EAPC, agrees that many patients with cancer pain still do not benefit from the advances made many years ago. "We have the knowledge to relieve pain in about 80–90% of patients with cancer. But the prevalence of unrelieved cancer pain is 50%."

He argues that pain relief is still poorly understood by many, and that some patients are wary of taking morphine. "Our problem is still the inadequate use of powerful drugs by non-specialists. And the reluctance of patients to take these drugs."

But while it may be depressing to see how little has changed for some cancer patients since Saunders started her campaign, a head of steam is clearly building up to force a change of attitudes at the highest level. A group of pain specialists from 16 countries, known as the Opioids and Pain European Network of Minds (OPENMinds), is calling for "a positive educational programme to change attitudes on the medical use of opioids, extending from the core curriculum of medical students to patients taking opioids and their families."

In a report to the European Parliament in June, the group pointed out that many European countries demand special prescription forms for strong opioids, different from those for other drugs.

In Italy, Poland, Portugal and parts of Spain, doctors must travel to regional offices in order to access the prescription forms used to prescribe strong opioids. In Austria, Germany, Portugal, Italy and Switzerland triplicate forms must be filled in.

The report concludes that "These unnecessary regulations reinforce an outdated viewpoint associating these medicines with addiction, abuse and death, despite considerable evidence showing the efficacy of their use in managing chronic pain," and it calls for a loosening of bureaucratic regulations that restrict doctors' freedom to prescribe effective pain relief.

A GLOBAL VIEW

While wanting to spread the idea of high quality care for the dying as widely as possible, Saunders always stressed that the pattern of services, should be determined at a local level. She lectured widely and fostered international networks and received thousands of visitors to St Christopher's, but did not want it to be taken as a global template, saying her main aim was "to encourage people to do this work in whatever way is most suited to their circumstances."

Later in her career, reviewing global developments in hospice care, Saunders said: "a worldwide spread has shown that the basic principles can be interpreted in widely differing cultures and with few resources other than the family values of the developing world."

CICELY SAUNDERS

Cicely Saunders was born in London on 22 June 1918, the eldest child of a successful estate agent. Educated at Roedean, a girls' private boarding school, she went to Oxford to read philosophy, politics and economics, but left when war broke to train as a nurse at St Thomas's Hospital, South London, qualifying in 1944. Forced to give up nursing because of a back problem, she trained as an almoner (medical social worker) and it was while working at St Thomas's in 1948 that she met David Tasma, a 40-year-old agnostic Polish Jew who was dying of cancer. In the months before his death, she fell in love with him. They discussed the needs of the dying and he left her £500 and said "I'll be a window in your home."

Soon afterwards she went to work as a volunteer in the evenings at St Luke's hospital, in central London. It was at St Luke's, which had been founded as the Home for the Dying Poor in 1839, that she saw the benefits of pain relieving drugs being given regularly. When she told a surgeon colleague that she wanted to go back to nursing, he said: 'Go and read medicine, it's the doctors who desert the dying.' At the age of 33, with no background in science, she was accepted to read medicine at St Thomas' and qualified in 1957, at the age of 38. Two years later, having worked at St Joseph's Hackney, a hospice established by the Irish Sisters of Charity in 1905, she drew up a plan for her own hospice at an estimated cost of £200,000. St Christopher's opened in 1967.

1944 Qualifies as state registered nurse
1945 BA (war degree) Oxford
1945 Diploma in Public and Social Administration
1947 Works as an almoner (medical social worker) at St Thomas's Hospital
1957 Qualifies as a doctor
1958–1965 Works at St Joseph's Hospice, east London
1967 Founds St Christopher's Hospice and is awarded the Order of the British Empire
1974 Becomes a fellow of the Royal College of Physicians
1980 Is made Dame of the British Empire
1980 Marries Marian Bohusz-Szyszko. She was 61 and he was 79
1989 Is awarded the Order of Merit
1981 Is awarded the Templeton Foundation Prize
2001 Is awarded the Conrad N Hilton Humanitarian Prize
2002 The Cicely Saunders Foundation is established at King's College London
2005 Dies in St Christopher's Hospice, July 14

ST CHRISTOPHER'S HOSPICE

The entrance to St Christopher's hospice, founded by Saunders in 1967

Carl Johan Furst, director of the EAPC Centre For Palliative Care Support in Eastern Europe, hopes that her emphasis on local patterns of care, forging international links and learning from each other, will be maintained by her successors.

Colleagues in eastern Europe need support to fight for recognition for palliative care and basic drugs, he says. "The main issue is morphine availability. Basic morphine tablets costing about 10 cents are just not available."

He hopes forming links with centres in eastern Europe and inviting healthcare professionals to conferences will strengthen the development of palliative care services. "And surely we in western Europe can learn too. How do you provide palliative care without the basic drugs? What sort of qualities do you draw on?"

In his introduction to her letters, Canadian oncologist Balfour Mount says Saunders "has been the catalyst for a paradigm shift in global health care." The lessons from her work on pain and symptom control may need constant reinforcing to successive generations, but there can be little doubt that she had a huge effect on attitudes to care of the dying. Her focus was on quality of life, listening to the patient, helping them to feel safe and involving the family. "You matter because you are you, and you matter until the last moment of your life. We will do all we can, not only to help you die peacefully, but also to live until you die," she said.

Looking back on her own therapeutic journey, which began on the wards of St Thomas's in 1941, she concluded, "Whatever happens it will still matter that we go on listening and we continue our questioning. Above all, my experience emphasises that the practice of medicine includes more than specific treatments."

Marilene Filbet, president of the EAPC and director of the palliative care unit at the Centre Hospitalo-universitaire, Lyon, France, believes Saunders was responsible for 'a silent revolution' and that her focus on listening to and comforting the patient is a model which could be applied to a wide variety of settings, including care of the elderly, people with AIDS and the severely disabled. "Before, we had the paternalistic model of medicine with the doctor deciding what was good for you. Cicely Saunders' stress on communication, teamworking, listening and freedom of choice for the patient and holistic care was revolutionary."

Filbet remembers being somewhat taken aback when she met Saunders. "I had somehow expected someone gentle, and was struck by her dynamism and force of character. This was clearly someone who had battled…"

Saunders would not demur. When someone observed in her last portrait (now in the National Portrait Gallery in London) a look of "love and steel" she said: "Love and steel, how kind. Anyone doing hospice work will need plenty of both."

A new European report calls for doctors to be given the freedom to prescribe effective pain relief

What's coming up in breast cancer?

Experts piece together the big picture

Mary Rice

In a follow-up to the first Breast Cancer Observatory, held in 2004, international names in radiotherapy, surgery, medical oncology, genetics and patient advocacy gathered again in Milan this June to predict the major changes for the year ahead.

With so much new information published every week on every aspect of cancer research and cancer care it is enough of a challenge for clinicians and researchers to keep up to speed in their own specialist area. Yet the implications of the new knowledge can be lost if it is not seen in the context of what is happening in the field as a whole.

To try to address this problem, last year, the European School of Oncology initiated an Observatory session at the annual Milan Breast Cancer Conference hosted by the European Institute of Oncology. The Observatory provides a platform where experts from many fields can present an overview of where they feel the most significant progress can be expected in the coming year.

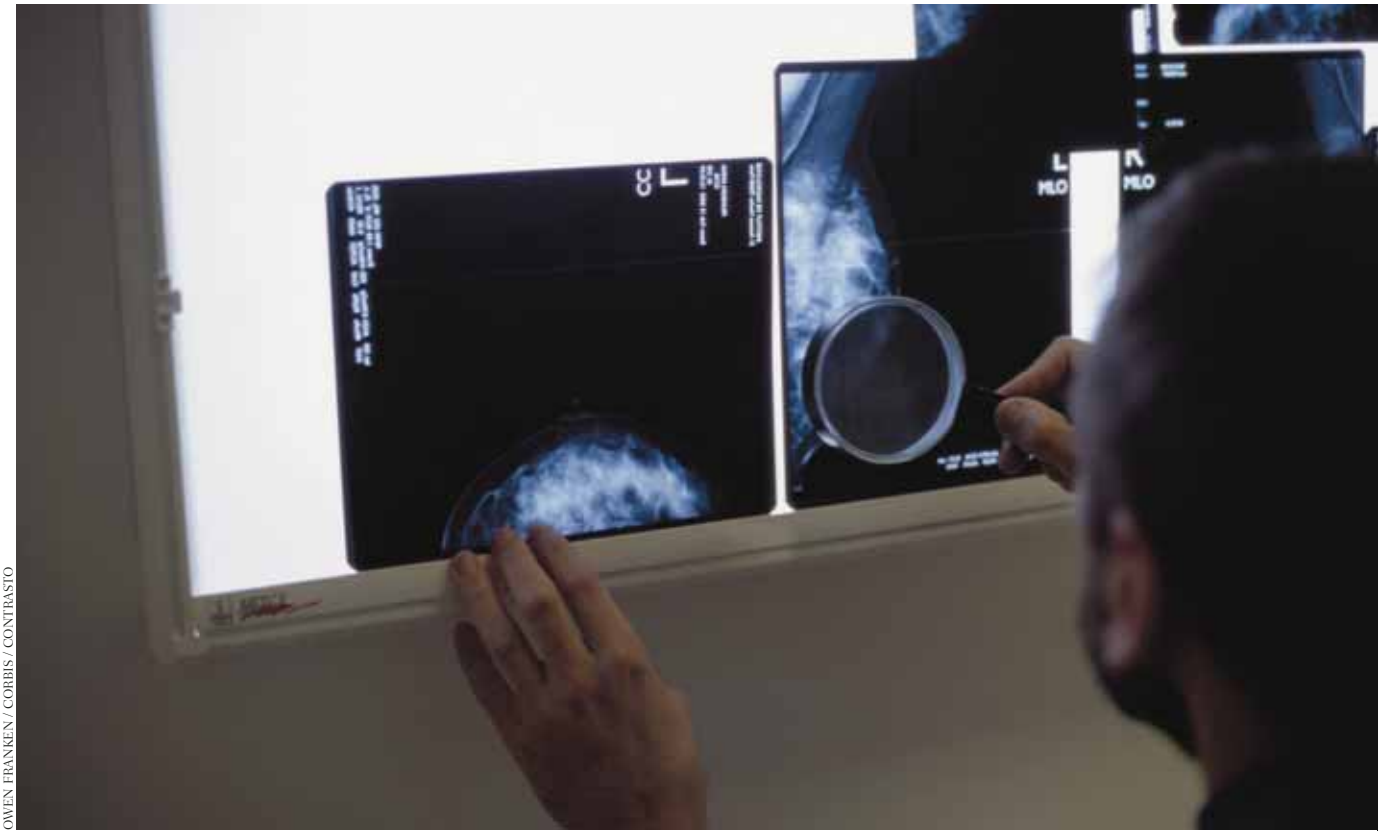
This June, a second Observatory was held, which brought together leaders in their fields from all over the world, representing surgery, radiotherapy, medical oncology, basic science, clinical trialists, and patient groups.

This year's Observatory revealed a sense that the molecular biology approach to cancer is finally beginning to make itself felt in the clinic in the areas of diagnostics, prognostics, treatment selection, and available therapies. As it does so, the financial implications of this new high-tech era are becoming an increasing factor in access to top quality cancer care.

Benefits from recent developments in 'targeted' radiotherapy, which concentrates the dose on the malignancy, sparing healthy tissue, were also flagged up, as was the slow but steady progress in greater patient involvement and in implementing European guidelines and recommendations for improving breast cancer screening and care.

From description to prediction

Patrick Borgen, of the Memorial Sloan Kettering Cancer Centre, New York, predicted that, overall, the trend in 2006 would be towards disease class prediction. The traditional descriptive definition of breast cancers will be replaced by a functional one, with cancers being defined according to risk of recurrence, allowing treatment to be tailored to individual tumours. Crucially, new testing technologies that can be conducted in a pathology lab are set to bring genetic fingerprinting of tumours into everyday clinical use. Tests such as Oncotype DX, which are just coming into use in the US, use polymeric chain reaction (PCR) to identify tumour genetic signatures



OWEN FRANKEN / CORBIS / CONTRASTO

"Breast cancers will be defined according to prediction of risk of recurrence"

based on a very limited number of genes. At a current cost of around $3,200–$3,500 (euros 2,750–3,000) a go, they are much cheaper than the microarray technique being used in clinical studies.

Aron Goldhirsch of the European Institute of Oncology, Milan, agreed that using specific targets via molecular and pathological identification remains the great hope for 2006. "Genetic signatures and other molecular characteristics, like altered proteins, will aid in the definition of types of cancers according to prediction of response to specific therapies," he said. "These features, together with age, will radically change the way treatment decision making for individual patients is performed."

Tumour markers and genomic profiles have a number of other uses, he added.

They can help improve monitoring treatment effects and might aid assessment of efficacy for pre-operative systemic therapies, providing more women with the chance of breast preservation. They can also be used to identify sub-groups of patients at high risk of recurrence in order to modify treatment. This may help in identifying patients with in-situ carcinoma, who should be spared radiation therapy after tumour excision. "Avoiding unnecessary damage to normal tissue is vital," he emphasised.

Combination therapies

New opportunities for improving the

"There will be increased use of aromatase inhibitors and trastuzumab at all stages of disease"

use of therapies for patients with advanced breast cancer by using the novel targeted treatments together with cytotoxic agents are becoming available, said Goldhirsch. Novel agents with several biological targets, which include overexpressed receptors, cellular pathways particularly active in tumour cells, and molecules responsible for tumour vessel formation (angiogenesis) have all shown some efficacy in controlling disease progression.

The role of some of these new compounds, used as single agents or in combination with cytotoxics, is already being tested in women with advanced disease. They include tyrosine kinase inhibitors like erlotinib (Tarveca), targeted to the epidermal growth factor receptor (EGFR), or lapatinib, a dual EGFR and ErbB-2 (Her2/neu) inhibitor, and anti-angiogenic antibodies such as bevacizumab (Avastin). Their potential impact as an effective adjuvant treatment will be explored in the very near future.

Adjuvant therapy

Roberto Labianca of the Ospedali Riuniti, Bergamo, Italy, talked about the implications for adjuvant therapy. Not so long ago, whether or not to prescribe adjuvant treatment was decided on standard criteria such as age and menopausal status, and the spread of disease.

In the near future, he said, whether or not a patient needed adjuvant treatment on a more personalised or 'tailored' basis would be decided by looking at the biology of the tumour and its genetic profile. Key to this would be access to genomic testing, such as the new Oncotype DX test. This 'new biological frontier' would spare many women from unnecessary chemotherapy and lighten the burden on health budgets.

Novel biological compounds, such as the monoclonal antibody trastuzumab (Herceptin) will soon enter the adjuvant setting. Targeted treatment will therefore go beyond the domain of endocrine therapies. More work will be needed to address the issue of resistance.

Alan Coates from the University of Sydney, Australia, said aromatase inhibitors, either alone or in sequence with tamoxifen, will become the standard adjuvant treatment for women with steroid hormone-receptor-positive breast cancer. "There will be increased use of aromatase inhibitors and trastuzumab at all stages of disease," he said, adding that adjuvant chemotherapy regimens will continue to be refined with particular attention paid to the selection of drugs and dosage, and to the treatment schedule.

Targeted radiotherapy

Following the huge advances made in breast-conserving surgery, there is now a great deal of interest in finding ways to minimise the amount of tissue exposed to radiotherapy.

One way this is done is to minimise the irradiated area. Jacques Bernier, from the Institute of Oncology in Bellinzona, Switzerland, said, "Until fairly recently the idea was widespread that surgery to the whole mammary gland was the right way to go. With surgery now often limited to the index quadrant, this means that we can limit radiation treatment to that area." This, says Bernier, will have a major effect on quality of life, not to mention economic benefits to healthcare systems.

Increased use of high-conformality radiation therapy is another way in which clinicians are trying to spare healthy tissue. By delivering doses

OBSERVATORY PANEL

- **Jacques Bernier**, radiotherapist, Switzerland
- **Patrick Borgen**, surgeon, US
- **Alan Coates**, medical oncologist, Australia
- **Alberto Costa** (chair): European School of Oncology, Italy
- **Aron Goldhirsch**, medical oncologist, Italy
- **Marie Claire King**, geneticist, US
- **Stella Kyriakides**, patient advocate, Cyprus
- **Roberto Labianca**, medical oncologist, Italy
- **Umberto Veronesi**, surgeon, Italy

With intraoperative radiotherapy, patients will be spared the need to report for daily treatment for several weeks following conservative surgery

from many different angles it is becoming possible to target the radiation increasingly precisely on tumour while sparing surrounding areas. This is particularly important in avoiding cardiac damage to breast cancer patients.

There are also moves to try to define more closely patients who really need post-mastectomy radiation, in order to spare patients who are unlikely to benefit. A study looking at the impact of radiotherapy to the axillary nodes in patients at intermediate risk post-mastectomy, is set to start later in the year.

Another highly significant development Bernier pointed to is the introduction of intraoperative radiotherapy. Early trial results, he said, are very encouraging, though the technique is not suitable for all patients.

"We can irradiate the surgical bed for 20–25 minutes, and once again this has major advantages for the patient in terms of quality of life as well as in terms of savings to healthcare providers."

Organisational changes

Changes were predicted in the way care is delivered and the way clinical trials are planned. Coates predicted that patients will be treated in ever greater numbers in specialist centres offering multidisciplinary treatment planning and care. Formal accreditation of breast units throughout Europe will be done by the European Society of Mastology (EUSOMA) through a codified process including site visits and with the full participation of the patient advocacy group Europa Donna.

In addition to their role in the breast unit accreditation process, Stella Kyriakides, President of Europa Donna (the European Breast Cancer Coalition), also predicted greater patient involvement in the planning of clinical trials. Advocates are being asked more often to sit on trial committees, she said, but further work is needed to ensure that their input is valued and taken into account in all appropriate areas.

Coates predicted that details of the outcomes of clinical trials will become more available to the general public, and patients would be increasingly interested in participating in trials.

Economic toxicity

One warning note raised by some speakers was the cost of improvements in cancer therapies and the likely social repercussions. Borgen, from the Memorial Sloan Kettering, presented some chilling figures. Treating one patient who metastasises with breast conservation, chemotherapy and tamoxifen costs between $50,000 and $75,000 (41,000 and 62,000 euros). But treatment with the angiogenesis inhibitor bevacizumab alone could be as high as $130,000 (107,500 euros) a year. That cost will multiply if treatment is with cocktails of different types of targeted and non-targeted drugs.

"Intraoperative radiotherapy has major advantages in terms of quality of life"

"Patients will be treated in ever greater numbers in specialist centres"

Add on to that the costs of the increasingly high-tech investigations needed to characterise the cancer in order to establish which therapies may be appropriate, and real questions emerge about whether societies with universal public health systems will be prepared to foot the bill, opening the possibility that these therapies may be available only to those who can afford to pay privately. Health insurance systems may start offering two-tiered premiums, restricting expensive targeted treatments to patients paying the higher rate.

However, better selection of the patients could offset some of the higher costs of the therapies, by ensuring that therapies are used only in patients who are known to be likely to respond. In both developed and developing countries, clinical prediction for the appropriate use of specific drugs in cohorts of patients with a predictable highest yield of treatment will become increasingly important. This may help access to appropriate medical care even for the less cared-for populations.

Ethical toxicity

Goldhirsch made the point that with so much at stake, the pressure for unethical marketing will increase. "There are people out there pushing information who have a financial or political interest in 'breakthroughs'," he said. The point was reinforced by Borgen, who referred to the case of a woman with bone metastases refractory to hormone ablative strategies who qualified for an experimental trial of taxane plus Avastin (bevacizumab). Her comments that she suffered no side effects and that her quality of life was much improved were widely reported. However, later it transpired that she had transferred her entire investment portfolio into Roche, the company that makes Avastin, raising questions about how impartial her comments about the drug really were.

A message of hope

Observatory Chair Alberto Costa, from the European School of Oncology, summed up the changes expected in the fields of medicine, radiotherapy, surgery, diagnostics, clinical research and organisation of care (see box). "The overall picture," he said, "is hopeful – for better working together, learning from each other, and providing the very best service to the patient."

10 PREDICTIONS FOR 2006

- Breast cancer will gain more acceptance as a genetic disease. Technology will detect more mutations; competition will start among testing technologies
- Research will tackle the issue of interactions between tumour and stroma and normal tissues, looking for new targets for therapies
- Interest in the value of local control will increase, leading to more diagnoses of ductal carcinoma in situ (DCIS)
- Assessment of tumour characteristics to guide therapy choice will become increasingly common and accurate
- Systemic therapies will continue to become less toxic, the use of cytotoxic chemotherapy in patients with small node-negative breast cancers will decrease
- Use of trastuzumab (Herceptin) and studies of Avastin will expand quickly and dramatically. Taxanes will be monitored.
- The issue of treatment duration and maintenance of response will be tackled separately for endocrine responsive and endocrine non-responsive tumours
- Competition and cross-fertilisation will increase between partial breast (PBI) and whole breast irradiation (WBI)
- The real impact of post-mastectomy irradiation will be challenged, biological response modifiers will be back
- Formal accreditation of breast units will start in Europe through a codified process, including site visits and with the full participation of advocates