# NEWSROUND

Selected press reports compiled by the ESO Cancer Media Centre

## New surgical technique for malignant glioma

➜ Lancet Oncology

A novel technique that uses a fluorescent marker to guide surgery in malignant gliomas has been shown to enable surgeons to remove more of the tumour and improve progression-free survival.

Malignant gliomas have a poor prognosis. This may be because surgeons often have difficulty in seeing exactly where the tumour stops and healthy tissue starts, making complete removal difficult. Numerous new techniques have been developed to try and solve this problem; however, they have not fulfilled expectations – frameless stereotaxy (image-guided surgery) is too expensive and intraoperative MRI is too cumbersome to use in every case.

Researchers from the ALA-Glioma Study Group investigated a new way to detect the tumours during surgery, by using a drug called 5-aminolevulinic acid, which causes fluorescent compounds to accumulate in cancerous tissue. The tumour can then be seen with a modified microscope during neurosurgery, in a simple, economical procedure.

The study compared two groups of patients; one group was operated on with fluorescence-guided surgery and the other group received the usual surgical procedure under white light. They found that after a median follow-up of 35.4 months, the percentage of patients who had their tumours removed completely was higher in the group that received fluorescence-guided surgery than in those who received usual surgery (65% vs 36%).

In the fluorescence-guided surgery group, more people survived to 6 months without progression of their tumour (41% vs 21%). Furthermore, there was no difference in serious side-effects between the groups.

"This technique is an advance over older, traditional methods, because it is simple, cheap, can be performed in real-time, and has now been put to a truly prospective test," claims coordinating investigator Walter Stummer.

In an accompanying article, Fred Barker, of the Massachusetts General Hospital, Boston, USA, welcomed the trial, but added that, "this study alone cannot definitively establish that the more extensive removal, and not some other unanticipated effect of the drug, led to the improved clinical results."

Although the drug is not yet available commercially worldwide, he concludes that the trial is likely to "encourage surgeons in pressing for more complete resections of malignant gliomas using the various technological adjuncts that have become widespread over the last 10-15 years, such as intraoperative MRI and frameless image-guided surgery."

■ Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: a randomised controlled multicentre phase III trial. W Stummer, U Pichlmeie, T Meinel, et al for the ALA-Glioma Study Group. *Lancet Oncology* 7: 392–401, published online 13 April

## Alcohol blamed for a large part of cancer deaths

➜ International Journal of Cancer

New research carried out by the International Agency for Research on Cancer (IARC), based in Lyon, France, shows that alcohol-related cancers are responsible for around 1 in 30 cancer deaths worldwide each year.

The researchers analysed data from 2002 on the prevalence of drinkers obtained from the World Health Organization Global Burden of Disease. The information based on relative risks of cancers of the oral cavity, pharynx, oesophagus, liver, colon, rectum, larynx and female breast was examined and the researchers estimated the number of cancer cases and deaths attributable to alcohol drinking.

The study found that, worldwide, almost 390,000 cases of cancer are attributable to alcohol drinking, this represents almost 4% of all cancers. Among women, breast cancer appeared to make up 60% of alcohol-attributable cancers.

The authors cautioned that the estimates were based on simplified assumptions; however, they highlight the need for alcohol-associated cancer to be taken seriously, and raise questions about whether public health recommendations on alcohol drinking need to be reviewed.

■ The burden of cancer attributable to alcohol drinking. P Boffetta, M Hashibe, C La Vecchia, et al. *Int J Cancer*, published online 23 March, doi: 10.1002/ijc.21903

## New hand-held device to detect oral cancers

➔ Journal of Biomedical Optics

A new, simple, hand-held device may help dentists detect high-risk precancerous and early cancerous lesions by shining a light that causes fluorescence in oral tissue.

Tumours developing in the mouth are often easily visible; however, determining whether a sore is benign or potentially cancerous has remained scientifically problematic. Early identification of high-risk disease could greatly reduce both mortality and morbidity due to oral cancer. This new device can help dentists tell whether a lesion is likely to become cancerous and thus avoid needless biopsies. Oral cancers are particularly prevalent in India, where the technology to perform biopsies is expensive and impractical in rural villages.

The Visually Enhanced Lesion Scope (VELScope), which was developed with support from the National Institute of Dental and Craniofacial Research, emits a cone of blue light into the mouth that excites various molecules within the cells, causing them to absorb the light energy and re-emit it as visible fluorescence.

Changes in the natural fluorescence of healthy tissue are generally caused by light-scattering biochemical or structural changes indicative of developing tumour cells. The VELScope allows dentists to shine a light onto a suspicious sore in the mouth and watch directly for changes in colour through an attached eye piece. Normal oral tissue emits a pale green fluorescence, while potentially early tumour, or dysplastic, cells appear dark green to black.

The device was tested in 44 people, and in 43 of them it was found to distinguish correctly between normal and abnormal tissue, classified on the basis of biopsy and standard pathology.

"The natural fluorescence of the mouth is invisible to the naked eye," said Miriam Rosin, a senior author on the paper. The VELScope literally brings this natural fluorescence to light, helping dentists to answer in a more informed way a common question in daily practices: To biopsy or not to biopsy."

Rosin said her group is now engaged in a larger follow-up study in Vancouver that will further evaluate the VELScope. "Laboratories are developing similar devices to detect lung and cervical cancer," said Rosin. "That means that the same basic technology is now being used to evaluate three tumour sites, and we can begin hopefully to pool our data and fine-tune the characteristics and meaning of the changes in fluorescence."

■ Simple device for the direct visualization of oral-cavity tissue fluorescence. PM Lane, T Gilhuly, P Whitehead, et al. *J Biomed Optics* 10 April, 11:024006

## Children need more information to deal with cancer in the family

➔ British Medical Journal

Children whose mothers have been recently diagnosed with breast cancer need more age-appropriate information about the disease to cope better, according to a recently published study. More than a quarter of women in the Western world will have children living at home when they are diagnosed with breast cancer. It is important for a child's psychological wellbeing to understand their mother's diagnosis and treatment.

British researchers separately interviewed 37 mothers and 31 of their children aged between 6 and 18 years to find out about their attitudes to the mother's recent breast cancer diagnosis. The study found that parents may underestimate their children's needs for information in order to protect them. Evidence from paediatric cancer shows that giving children appropriate information about diagnosis and treatment reduces anxiety. The more children are prepared and informed, as appropriate for their age and development, the more it seems to help them cope.

Even before their mother's diagnosis, children from seven years old were more aware of the life-threatening nature of cancer than their parents and other adults realised. Talking about cancer and death may help relieve children's apprehension. Children had sometimes picked up skewed information about cancer through the media, including TV adverts and soap operas. For example, many children linked smoking to all kinds of cancers, including breast cancer, and were troubled when family members continued to smoke.

Many of the children said they were unprepared for the consequences of their mother's treatment – particularly the side-effects of chemotherapy, such as the loss of their mother's hair, and the length of treatment. Visits after surgery were also an area of anxiety.

Children were unprepared for their mother's drowsiness, the number of tubes around the bed and even the blood on the sheets and in the drainage tubes. Children who had visited their mothers before the operation in hospital and then at least two days after the operation seemed to cope better with visiting times.

Some of the older children expressed a desire to talk to a health professional so that they could learn more about their mother's disease, and a few also expressed a desire to talk to their mother's doctor. Older children wanted a list of websites to look at for more information.

The study recommends that parents with newly diagnosed cancer need to be supported to think about how they will talk to their children. Some families may need their doctor and nurses to take part in the discussions with the children. Families should be routinely offered age-appropriate

information, and more literature needs to be developed for younger children.

■ Breast cancer in the family – children's perceptions of their mother's cancer and its initial treatment: qualitative study. G Forrest, C Plumb, S Ziebland. *BMJ* 29 April, 332:998–1003

## Potential new target to prevent metastasis

➜ Nature

Researchers from Stanford University School of Medicine, USA, have identified a protein vital for the spread of cancer from one part of the body to another. The research may help scientists develop new targeted anti-cancer drugs.

Most deaths from cancer occur from metastasis. Scientists have been trying to find out what makes cancer cells spread to help develop targets for anti-cancer therapies.

Cancerous tumours contain areas low in oxygen. This seems to make the cells particularly prone to metastatic growth, although scientists are unsure why. The new research shows that the enzyme lysyl oxidase (LOX) is produced at high levels in oxygen-starved human breast, head and neck tumours.

They found that patients with tumours producing high levels of LOX are more likely to suffer metastases and tend to have poorer survival.

The research demonstrated that LOX promoted the spread of cancer cells by helping cells invade new tissue. In a mouse model, it was also found that inhibiting the LOX enzyme blocked the spread of breast cancer. Further research is needed to see whether inhibiting the LOX enzyme in humans would prevent the spread of cancer cells.

■ Lysyl oxidase is essential for hypoxia-induced metastasis. JT Erler, KL Bennewith, M Nicolau, et al. *Nature* 27 April, 440:1222

## EMEA gives positive opinion for Herceptin

➜ European Medicines Agency

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMEA) has given a positive opinion to extending the use of Herceptin (trastuzumab) to include adjuvant treatment of early breast cancer (invasive, non-metastatic) over-expressing HER2 following surgery, chemotherapy (neo-adjuvant or adjuvant) and radiotherapy (if applicable).

This was the first accelerated assessment by EMEA under new EU legislation introduced in November 2005. The application was submitted in February 2006 and a decision made at the end of April. Also for the first time, EMEA supplied a separate question-and-answer document relating to the extension of Herceptin's indication.

Manufacturers Roche will be asked to perform further studies on the long-term effects of treatment with the product, particularly its cardiovascular risk. Efforts will also be made to identify patients at higher risk of cardiotoxicity and define monitoring requirements. A final decision on extending Herceptin's indication now has to be made by the European Commission. Normally this takes a further 1–2 months.

Other decisions of the CHMP include a positive opinion on Bayer Healthcare's Nexavar (sorafenib tosylate) for the treatment of advanced renal cell cancer in patients who have failed to respond to prior interferon-α or interleukin-2 based therapy or are considered unsuitable for such therapy. The CHMP also adopted the first positive opinion on the granting of a conditional marketing authorisation under new EU rules on conditional approvals that came into force at the beginning of April 2006. It recommended that Pfizer's Sutent (sunitinib malate) should be approved for the treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST) after failure of imatinib mesylate treatment due to resistance or intolerance, and for advanced and/or metastatic renal cell carcinoma (MRCC) after failure of interferon- α or interleukin-2 therapy. A marketing authorisation under conditional approval means that further evidence on the medicinal product is awaited. In the case of Sutent, this relates to the product's effect in terms of progression-free survival in patients with MRCC, for which a study is being conducted. EMEA will review new information within one year and update the product information as necessary. The European Commission will now consider these recommendations and should make a decision on the marketing authorisation of both products within two months.

## Stopping chemo early halves survival time in colon cancer

➜ Journal of Clinical Oncology

New research from Columbia University Medical Center in New York has found that as many as 30% of patients with stage III colon cancer who were prescribed six months of chemotherapy with a combination of 5-fluorouracil and leucovorin stop their treatment prematurely. Early termination of chemotherapy for colon cancer was shown to be equivalent to receiving no treatment at all. The findings add to the arsenal of reasons why colon cancer patients, and all cancer patients, need to complete their chemotherapy regimens whenever possible.

Previous studies have shown that not completing chemotherapy regimens for breast cancer is associated with shorter survival. This is the first study to look at a link between mortality rates from colon cancer and treatment adherence.

"The intuitive thinking is that if you complete most of a treatment regimen, you should get most of the treatment benefit. But these findings are significant because

they indicate that completing treatment is as critical for colon cancer as it is for breast cancer – and we need to do better to ensure that patients who can, complete treatment as intended," said Alfred Neugut, one of the leaders of the study.

The research team used the Surveillance, Epidemiology, and End Results (SEER)-Medicare database to identify stage III colon cancer patients who were at least 65 years of age or older, and who received between one and seven months of fluorouracil-based adjuvant chemotherapy treatment.

Among the 1,579 patients who survived eight months or longer, the 1,091 (69.1%) who underwent five to seven months of treatment survived nearly twice as long as the 488 (30.9%) who received only one to four months of treatment. Patients who were older, unmarried and had co-morbid conditions, were more likely to receive less than five months of treatment.

■ Duration of adjuvant chemotherapy for colon cancer and survival among the elderly. AI Neugut, M Matasar, X Wang. *J Clin Oncol*, published online 17 April, doi: 10.1200/JCO.2005.04.5005

## Some melanoma patients at risk of additional tumour within two years

➔ Archives of Dermatology

Approximately 8% of patients with melanoma may develop an additional melanoma within two years of their initial diagnosis, and those with atypical moles appear to be at higher risk, according to a recent study.

Cutaneous (skin) melanoma begins in cells known as melanocytes, which produce the pigment that gives skin its colour. Previous studies have evaluated the recurrence of melanoma among patients already diagnosed with the disease; most have estimated that less than 4% of them will develop additional tumours in the year following diagnosis.

Linda Titus-Ernstoff, of the Dartmouth Medical School, New Hampshire, USA, and colleagues, assessed the frequency of and risk factors for recurring cancer among 354 New Hampshire residents with a first diagnosis of cutaneous melanoma. Participants completed a 40-minute telephone interview, during which they answered questions about medical history, demographics, eye and hair colour, sun exposure and whether their skin tanned, burned or freckled in the sun.

They then underwent a skin examination, during which a physician identified and catalogued benign and atypical moles. Atypical moles have at least three of the following features: a diameter larger than 5 mm, redness, an irregular or ill-defined border, a variety of colours or a portion that is flat.

By examining pathology records, the researchers found that 20 (6%) of the participants developed an additional melanoma within one year of diagnosis and 27 (8%) developed an additional melanoma within two years. Sixty-three percent of those who developed additional tumours and 37% of those who did not had at least one atypical mole. The more atypical moles an individual had, the more likely he or she was to develop additional melanomas – three or more atypical moles indicated four times the risk. Lifetime history of sun exposure did not appear to influence the risk of recurring melanoma.

"The importance of studying risk for additional primary tumours within a defined population-based study group is underscored by our findings," they conclude. "These findings, which indicate a higher frequency of second primary melanomas than suggested by previous studies, also underscore the importance of close surveillance of patients with melanoma."

■ Multiple primary melanoma: two-year results from a population-based study. L Titus-Ernstoff, AE Perry, SK Spencer, et al. *Arch Dermatol*, April 2006, 142:433–438

## WHO announces new standards for clinical trial registration

➔ World Health Organization

The World Health Organization (WHO) is urging research institutions and companies to register all clinical trials, including phase I trials, whether they involve patients or healthy volunteers. As part of the International Clinical Trials Registry Platform, a major initiative aimed at standardising the way information on medical studies is made available to the public, WHO is also recommending that 20 key details be disclosed at the time studies are begun.

Before making the recommendations, the Registry Platform initiative consulted with all concerned stakeholders, including representatives from the pharmaceutical, biotechnology and device industries, patient and consumer groups, governments, medical journal editors, ethics committees, and academia over a period of nearly two years.

Currently, there are several hundred registers of clinical trials around the world. The planned Registry Platform will not be a register itself, but rather will provide a set of standards for all registers. It has not only standardised what must be reported to register a trial but is creating a global trial identification system that will confer a unique reference number on every qualified trial.

"Registration of all clinical trials and full disclosure of key information at the time of registration are fundamental to ensuring transparency in medical research and fulfilling ethical responsibilities to patients and study participants," said Timothy Evans, Assistant Director-General of the WHO.

Later this year, the WHO Registry Platform will launch a web-based search portal where scientists, patients, doctors and anyone else who is interested can search among participating registers for clinical trials taking place or completed throughout the world.