

## Breast Cancer Overtreated

Up to 29% of women diagnosed with invasive cancers following mammography screening actually have non-invasive cancers, leading to overtreatment according to a new study. Earlier research had also suggested that overdiagnosis is occurring but was criticised for failing to take into account other possible explanations.

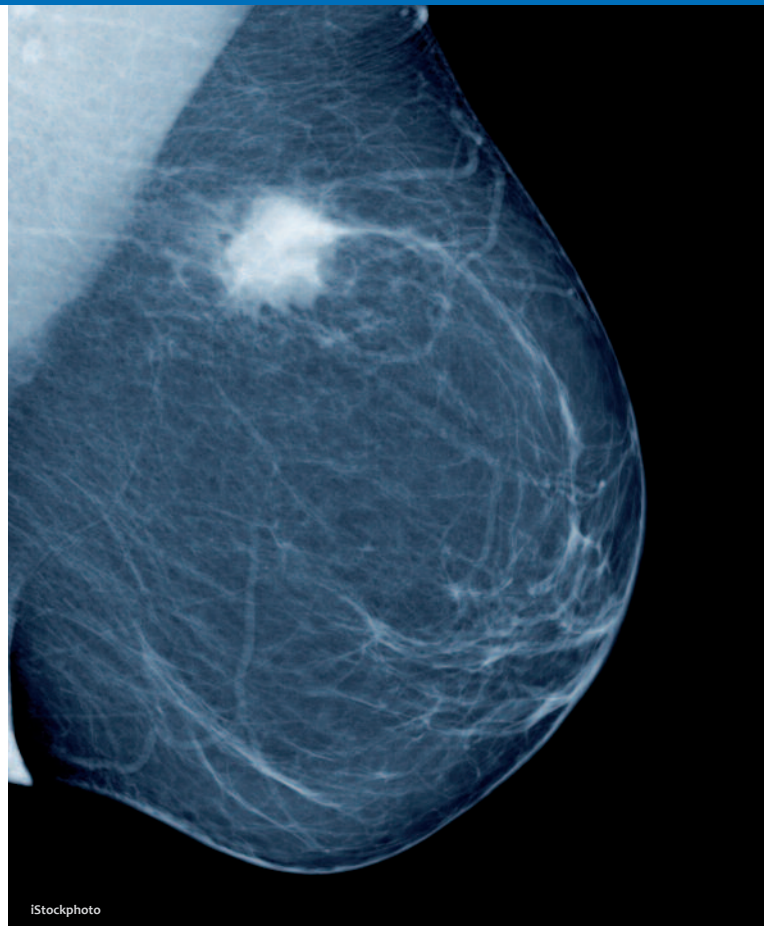
A/Prof Alex Barratt of the University of Sydney conducted the new study by looking at the rates of invasive cancer observed in NSW women before screening became common. These were projected forwards to allow for an ageing population, as other researchers have done, but Barratt says her results are more robust. “They take into account risk factors such as hormone replacement therapy and obesity, both of which have increased the prevalence of breast cancer,” she explains.

Barratt says the cases concerned are genuine cancers. However, the overdiagnosis represents non-invasive cancers where a watch-and-wait approach would be preferred to immediate treatment.

“There are three implications from this,” Barratt says. “Firstly there has been a lot of debate over whether overdiagnosis exists once you allow for changing risk factors. We’ve confirmed that it does, and it’s important for doctors and policy-makers to know and consider as a downside of screening.

“Secondly, breast cancer programs give women information about the benefits of screening as well as the drawbacks, and this needs to be included.

“Finally, it demonstrates we need a better test to distinguish



whether women have invasive or non-invasive cancers. Ideally this would be at the screening stage so it doesn’t pick up non-invasive cancers, but it could also be a triage test after the screening has been done.”

The study did not consider ductal carcinoma *in situ*, which makes up 18% of breast cancers found in NSW screening.

## Brain Cancer Causes Aggression

Brain cancers contribute to high levels of aggression among those who suffer from them, and a new study indicates that this does not depend on whether the cancer is malignant or benign.

“We found that all brain cancer patients are susceptible, regardless of the type or severity of their cancer, even those with benign tumours,” says Dr Eng-Siew Koh of the South-West Sydney Clinical School.

“Their behaviours are varied and include

everything from apathy to anger, aggressive behaviour and loss of inhibition.”

Carers were more likely to report anger symptoms than the patients themselves by a margin of 31% to 20%. One in five patients with brain cancer in the study was physically aggressive. The sample size was just 54, but Koh suspects that the symptoms may be underestimated since more than 100 patients were approached to take part, and those more affected were

probably less likely to participate.

Perhaps the most surprising finding is that the location of tumours did not seem to affect the extent or form of emotional disturbance, but Koh acknowledges that this may be because the sample sizes of subcategories were small.

Koh believes that changes in behaviour may be of some use as a trigger prompting further investigation, but says that many other factors can cause similar effects and hence “only a brain scan can be definitive”.

## Change to Publication Schedule

In 2010 *Australasian Science* will continue to be published 10 times per year but the cover dates of some editions will change.

- Instead of a combined November/December issue there will be individual issues in November and December.
- There will now be a combined winter edition in July/August instead of individual editions in these months.

The changes have been made to spread the frequency of editions throughout the year.

## RNA Approach to Asthma and Arthritis

For the first time, the inflammation leading to an asthma attack has been prevented by blocking malfunctioning microRNA molecules. The announcement could lead to better ways to treat asthma and other inflammatory diseases including rheumatoid arthritis.

Asthma and rheumatoid arthritis are caused by inflammation brought about by imbalances in protein levels. These proteins are regulated by microRNA molecules, and malfunctions in the molecules can trigger the protein imbalances.

“Based on the understanding that malfunctioning microRNA molecules may lead to asthma or other types of inflammation, our research team has been looking at ways to inhibit their function,” says Prof Paul Foster of the University of Newcastle’s Priority Research Centre for Asthma and Respiratory Diseases.

Foster has blocked the faulty microRNA using an antagomir treatment in mice. Antagomirs are small synthetic

RNA sequences that are specific to their microRNA target. Trials on human tissue are now underway.

If an antagomir treatment can be produced it will eliminate the problem that current steroid-based treatments are harmful in the long term at the doses required by people with severe asthma.

Although the method of treatment will take some time to confirm, Foster says: “Testing in the model found that delivery via the airways was very effective at inhibiting inflammation”.

He thinks asthmatics might continue to use puffers for health maintenance, but these will eventually carry less side-effects. The antagomir works quickly enough that top-up doses might be used prior to an event that might trigger conditions, such as exercise.

Foster adds that a model has been created for rheumatoid arthritis but results are not yet available as to the effectiveness of treatments.



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## DNA Circles Found in ALT Cancers

The identification of a molecule associated with certain cancers should help to track the progress of cancer treatments and improve the accuracy of prognoses. Potentially it may lead to more targeted treatments of the cancers in question.

In normal cells the telomeres at the ends of cells shorten each time they divide. Cancers operate by interfering with this shortening. When the telomeres don’t shorten, cells can divide indefinitely and become immortal.

In most cancers this occurs when the enzyme telomerase provides an RNA template to extend the telomeres. However, 15% of cancers are driven by the alternative lengthening of telomeres (ALT) process using a DNA template.

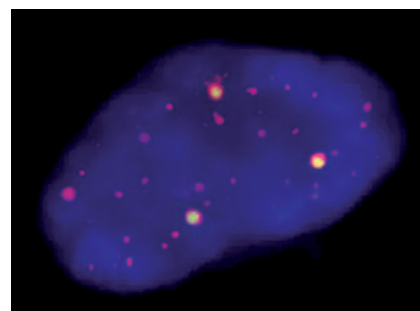
Previously it has been difficult to distinguish cancers caused by the two

mechanisms. Moreover, the proteins involved in the ALT mechanism are also important in healthy cells, so there has been less hope for ALT-targeted treatments than against cells containing high levels of telomerase.

However, James Hansen of the Children’s Medical Research Institute in Sydney has found that ALT cancer cells have circles of partly single-stranded, partly double-stranded DNA. The number of these circles reduces when ALT is inhibited, which Hansen says may make it possible to “track the effectiveness of chemotherapy in real time”.

It is not yet known why the circles are produced. “An educated guess is that they are intermediates in the ALT mechanism,” Hansen says. “They could be the template for lengthening the telomeres.”

Whatever their role, the DNA circles



The green stain (appears yellow over the red stain) indicates the presence of C-circles, which are markers of specific forms of cancer. Nuclear bodies are red and the cancer cell nuclei are blue. The rest of the cancer cell is present but not visible as it is not stained.

offer a great opportunity for escalating the speed of assays of potential ALT-suppressant drugs, as well as offering a possible marker to enable treatments to target cancer cells while ignoring healthy cells.

Moreover, since ALT bone cancers shed into the bloodstream there are possibilities for non-invasive diagnosis.