Three-dimensional imaging improves mammogram accuracy

New findings have shown that adding 3D breast imaging technology, called tomosynthesis, to digital mammography can increase diagnostic accuracy by finding more cancers missed by standard mammography while decreasing recall rates for non-cancer cases.

Two studies compared the effects of combined tomosynthesis and digital mammography versus digital mammography alone. The studies included 997 women presenting at five screening clinics (780 screening cases and 217 biopsy cases). Study 1 involved 312 cases (48 cancer cases) and 12 radiologists; study 2 involved 312 cases (51 cancer cases) and 15 radiologists. Diagnostic accuracy increased by 6·8% for study 1 and 7·2% for study 2. Significant reductions in recall rates were 38·6% and 17·1% for studies 1 and 2, respectively. Sensitivity increased most for invasive cancers by 15% and 22%, but 3% for in situ cancers for both studies.

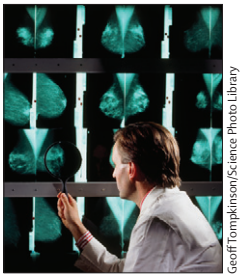
"What's exciting is that this study advances our understanding of how to improve breast cancer detection," says Martin Yaffe (University of Toronto, Toronto, Canada). "Overlapping breast tissues from various planes tend to create structures that can hide a cancer or look like there's a cancer present even when there isn't. Going to a 3D-image format eliminates that interference, so you get a clearer picture of whether cancer is present, as well as its location, and you avoid false positives."

Yaffe adds, however, that combining the techniques did not allow for the individual evaluation of tomosynthesis, and that the radiation dose for tomosynthesis was somewhat artificially lowered, "so it isn't clear whether those doses were optimised."

Lead study author, Elizabeth Rafferty (Massachusetts General Hospital, Boston, MA, USA) explains that combining the techniques and consequently reducing the radiation exposure was necessary to aid radiologists' transition to the new technology. The researchers have subsequently been able to generate a synthesised 2D mammogram from the 3D tomosynthesis images, so radiologists will still have those comparative data.

"The next step will be to eliminate standard mammography and use tomosynthesis alone," says Rafferty, pending approval from the US Food and Drug Administration over the next several months. "Tomosynthesis represents the next phase of mammography," says Rafferty. "It's a truly substantive change that addresses the flaw of mammography."

Angela Pirisi



Geoff Tompkinson/Science Photo Library

Published **Online**
December 7, 2012
http://dx.doi.org/10.1016/S1470-2045(12)70562-4

For the **study** see *Radiology* 2012; published online Nov 20. DOI:10.1148/radiol.12120674

Ponatinib for resistant Ph chromosome-positive leukaemia

Ponatinib is a third-generation tyrosine kinase inhibitor designed to target the BCR-ABL fusion protein encoded by the Philadelphia (Ph) chromosome. It also evades the kinase-domain mutation T315I that confers resistance to tyrphostins approved to treat Ph chromosome-positive leukaemias. In a phase 1 study of ponatinib published in the *New England Journal of Medicine*, a complete haematological response was seen in 98% of patients with heavily pretreated, chronic-phase chronic myeloid leukaemia (CML), and a major cytogenetic response was seen in 72% of these patients.

Lead author Jorge Cortes (MD Anderson Cancer Center, Houston, TX, USA) said that, "The response rate is very impressive. A 72% rate of cytogenetic response is a very, very high rate...[This drug] addresses resistance for a lot of patients." Co-author Moshe Talpaz (University of Michigan, Ann Arbor, MI, USA) was "very impressed with this drug...Most patients had been heavily treated—most had received two drugs and many had received three drugs. A high response rate was seen in [these] patients with long-standing disease...Virtually all of the patients with the gatekeeper [T315I] mutation responded to ponatinib."

Further clinical studies have been undertaken since this study established the maximum tolerated dose (45 mg of oral ponatinib once a day). The PACE phase 2 trial is ongoing, and preliminary results presented at the 2012 ASCO Annual Meeting in June showed that 54% of patients with treatment-resistant chronic-phase CML had a major cytogenetic response to ponatinib, with a 70% response rate seen in a subgroup harboring the T315I mutation.

Talpaz emphasised, "When we work with targeted therapy, we've learned that tumours are not succumbing to the treatment—they are outsmarting the treatment. With this drug, we can overcome this."

John Goldman (Imperial College London, London, UK) noted that "It is impressive that this drug has been made basically from scratch. The result is a largely engineered molecule...Ponatinib passed its first test with flying colours in CML patients who failed previous treatment. A new phase 3 study is underway, so a year from now we'll have a very good idea of its efficacy in previously untreated patients, where it may have an important role. It could also turn out to be a big boon to patients with advanced-phase disease, as it seems to be effective in Ph chromosome-positive acute lymphoblastic leukaemia".

Judith A Gilbert

Published **Online**
December 7, 2012
http://dx.doi.org/10.1016/S1470-2045(12)70563-6

For the **ponatinib study** see *N Engl J Med* 2012; **367:** 2075–88

For **the PACE trial** see *Proc Am soc Clin Oncol* 2012; **30** (suppl)**:** abstr 6503