



Re. Multimodality breast cancer screening in women with a familial or genetic predisposition

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Earlier this year in *Current Oncology*, Trop and colleagues added new information to support the claim that screening with magnetic resonance imaging (MRI) for breast cancer is superior—in terms of sensitivity—to routine mammography¹. This news should be welcome to women who are found to carry a mutation in the *BRCA1* or *BRCA2* gene and should encourage more women to undergo genetic testing. Two emergent technologies—one in imaging and one in laboratory medicine—have come together to advance the translation of cancer genetics into cancer control.

In the Trop paper, genetic testing using BRCAPRO [Berry D, Parmigiani G. Duke SPORE (Specialized Program of Research Excellence) in Breast Cancer. 1999] software was offered to women with a 30% risk of having a *BRCA1* mutation. This conservative approach will identify only a minority of carriers in the French-Canadian population, because many mutation carriers have no family history—or only a modest one. But because of the presence of a small number of *BRCA* founder mutations in the French-Canadian population, Quebec is now in a unique position to offer rapid, efficient, and inexpensive genetic testing to women in the province so as to identify most women with a *BRCA* mutation². And Quebec scientists are in a unique position in Canada (and the world) to lead large-scale genetic epidemiology studies.

About 5% of French-Canadian women with breast cancer carry a *BRCA* mutation; most of those have a BRCAPRO probability that falls below 30%². Under conventional guidelines, those women would not have been offered genetic testing. Does it not make sense to offer genetic testing to all French-Canadian women with breast or ovarian cancer, with the aim of identifying their unaffected relatives, who may then be offered intensified screening, such as with MRI?

In Ontario, genetic testing has been offered to all Jewish women in the province, regardless of personal or family history of cancer³. The underlying philosophy was to maximize the number of mutation carriers identified before they developed cancer, in the hopes of preventing the disease. However, approximately 1% of Jewish women carry a mutation, compared with just 1 French-Canadian woman in 500².

The goal of breast cancer screening is to identify cancers when they are small (<2 cm, and preferably <1 cm) and node-negative. However, having a small cancer is not a guarantee of cure. For some cancer types, including those that occur in *BRCA1* carriers, the relationship between tumour size and outcome is not highly correlated⁴. Also, mammographically-detected cancers appear to be intrinsically less aggressive than those that mammograms leave behind⁵. In the Henrietta Banting database in Toronto, 13% of women with a breast cancer less than 1 cm at diagnosis eventually died of their disease. The mortality rate was much less (7%) for women with mammographically-detected cancers than for those with palpable cancers of the same size. This observation suggests that mammography preferentially identifies cancers with a low growth rate, a fact that could help to explain why data from screening trials in young women are less than compelling^{6,7}. Ideally, a screening test will identify all small breast cancers equally, independent of metastatic potential. If a screening test picks up all small cancers, then mortality should be reduced. It is to be hoped that such a reduction will prove be the case with MRI screening, and it is important that future cohort studies of women undergoing MRI screening, such as the study by Trop *et al.*, evaluate the technology from that point of view.

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