Update on Using Hair to Detect Breast Cancer

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In the 1990s, Australian physicist Professor Veronica James and colleagues were studying the structure of hair, and particularly its chief protein component, keratin, using synchrotron X-ray diffraction. Synchrotrons are large particle accelerators that generate enormously bright X-rays, allowing scientists to see much more molecular structure in objects than they had been able to using normal X-rays.

In 1999, they published a paper in *Nature* which showed consistent changes in the X-ray diffraction pattern of hair from women with breast cancer. A ring was noticeable in the pattern in the breast cancer samples that was absent in healthy women. This was followed by several other papers culminating in a 2005 paper in the *International Journal of Cancer* confirming the result in over 500 samples.

This scientific finding was intriguing enough for a group of investors to set up a company – Fermiscan – to further develop the science into a commercial, non-invasive test for breast cancer. The approach Fermiscan has taken is to undertake a comprehensive clinical trials program in order to test the technology in the "real world" setting. Fermiscan has completed three of these trials, bringing the total of women whose hairs have been screened by synchrotron X-ray diffraction for breast cancer to over 2,000 in a little more than 18 months. In that time, Fermiscan has secured long-term access to a synchrotron, essential for conducting the test; has re-designed the hair loading process to allow automation of the exposure; reduced the exposure time 6-fold; developed a screening test to help eliminate damaged hair; and set up collection centres for the trials in clinics from Newcastle to Geelong.

Now that the first three trials have been completed, it is time to summarise the findings and to determine what this means for bringing the Fermiscan Test to Australian women as an accessible option for a test for breast cancer.

Fermiscan Trial Results

The result of Fermiscan's first trial was published in the International Journal of Cancer this year, by Gary Corino and me. In that paper, we stated, "The results presented in this study confirm the existence of a correlation between an altered X-ray diffraction pattern of hair and the presence of breast cancer."

1. First study.

The results on hair from 39 women of confirmed breast cancer status are shown below. The samples were blinded prior to analysis.

	Positive by Mammography and biopsy	Assumed negative (by mammography)
Positive	12	3
Indeterminate (Damaged)	2	4
Negative	1	17
Total	15	24

In contrast to Dr James publications, we did not reach 100% sensitivity, as one breast cancer patient did not show a ring in the X-ray diffraction pattern of her hair. The reason for this is not known.

2. Sydney metastatic breast cancer trial.

In a second, open, trial in 2007 we assessed hair from women who had recently been diagnosed with breast cancer or who had metastatic disease to ascertain whether their hair contained the superimposed ring. Hair was collected from 17 women with early stage breast cancer and from 18 women with metastatic breast cancer. The mean age was 56.5 (range 34-84). In the early group 12 of

15 (80%) and in the metastatic 14 of 16 (88%) had the presence of the ring for breast cancer in the diffraction pattern in at least one hair."

3. Fer2k trial
In January 2007 Fermiscan began a blinded 2,000-patient validation trial with the support of major radiology and diagnostic groups in Australia. This trial was designed to assess the effectiveness of the test in a screening situation by testing the hair of women referred for breast imaging. Results compared mammogram and ultrasound followed by biopsy where indicated with the results from the hair test.

The key results were:

- Average age of the patients was 52
- Overall accuracy level of the Fermiscan Test in the 2,000 patient trial was 69%
- The Fermiscan Test provided a correct negative diagnosis for around 1500 women, (a 99% negative predictive value)
- The test correctly identified 20 out of 33 patients as positive for breast cancer
- The false positive rate was 24% (a 4%positive predictive value). The actual false positive rate will become clearer with long term follow up.

Fermiscan Test	**Mammogram negative**	**Confirmed positive for breast cancer**	**Total**
Fermiscan Positive	460	20	480
Fermiscan Negative	1,495	13	1,508
Total	1,955	33	1,988

- 170 women had breast biopsies due to a suspicious mammogram or ultrasound image. Of these, 137 were found to be negative. The Fermiscan test correctly identified 80% of these women as negative for breast cancer. This highlights the potential value of the test in conjunction with current screening methods to improve the accuracy of initial imaging-based diagnosis.

Fermiscan Test	**False Positive mammograms**
Total	137
Fermiscan Positive	20
Fermiscan Negative	117

13 patients found to be positive for breast cancer by a mammogram and biopsy were missed by the Fermiscan Test. In most of these cases there was evidence of damage to hair from treatments, which may explain the reason why most of these were missed by the test.

We believe that the accuracy of the test in the market will improve as women will prepare for the test by ensuring they have undamaged new growth of hair for testing (approximately 4 weeks-10.5mm in length is required). During the trial this could not take place as patients had no advance notice of the test and the requirements.

The value of the test for women of all ages was confirmed with patients covering a wider age group than current screening recommendations.

Conclusion
The Fermiscan Test is innovative, non-invasive, painless and is suitable for women of any age or breast composition and therefore may provide a reliable screening option for women under the age of forty years. In addition the Fermiscan Test relies on testing samples of the patient's hair, rather

than direct imaging of the breast therefore issues of concern regarding other radiology technologies such as long term safety and breast tissue density do not apply.
The Fermiscan Test could initially be used as an adjunct with routine screening options as early detection is the overall objective. The earlier breast cancer is detected the greater the benefits such as increased survival, increased treatment options and improved quality of life.

Preliminary work indicates that the technology has the potential to monitor the recurrence of breast cancer following treatment and may assist in improving the accuracy of mammography when used in conjunction with the Fermiscan Test.

Fermiscan is conducting further studies of cancer patients in Australia and internationally to expand the knowledge base of diffraction pattern images to increase the accuracy of the test.

Fermiscan and the Sydney Breast Clinic

In June 2008 Fermiscan Ltd acquired the Sydney Breast Clinic. The Sydney Breast Clinic, located in Bathurst Street, Sydney, has been operating for over 30 years as a leading provider of diagnostic services for women with symptoms of breast disease, and is a leader in the provision of risk assessment, breast screening and bone density testing.

The Clinic was a major participant in our 2,000 patient validation trial and its continued Involvement is a key element in the development and commercialisation of the Fermiscan test for breast cancer.

Originally published *BCAG Newsletter*, September 2008.

NOTE: We thank Fermiscan for agreeing to write this article for us. It follows items on Fermiscan which have appeared previously in our newsletter We do have concerns about inappropriate uses of this test and will be following up this issue in the future. We would be most interested in your comments.