EUROPEAN SYNCHROTRON RADIATION FACILITY

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Experiment Report Form

The double page inside this form is to be filled in by all users or groups of users who have had access to beam time for measurements at the ESRF.

Once completed, the report should be submitted electronically to the User Office using the **Electronic Report Submission Application:**

http://193.49.43.2:8080/smis/servlet/UserUtils?start

Reports supporting requests for additional beam time

Reports can now be submitted independently of new proposals – it is necessary simply to indicate the number of the report(s) supporting a new proposal on the proposal form.

The Review Committees reserve the right to reject new proposals from groups who have not reported on the use of beam time allocated previously.

Reports on experiments relating to long term projects

Proposers awarded beam time for a long term project are required to submit an interim report at the end of each year, irrespective of the number of shifts of beam time they have used.

Published papers

All users must give proper credit to ESRF staff members and proper mention to ESRF facilities which were essential for the results described in any ensuing publication. Further, they are obliged to send to the Joint ESRF/ ILL library the complete reference and the abstract of all papers appearing in print, and resulting from the use of the ESRF.

Should you wish to make more general comments on the experiment, please note them on the User Evaluation Form, and send both the Report and the Evaluation Form to the User Office.

Deadlines for submission of Experimental Reports

- 1st March for experiments carried out up until June of the previous year;
- 1st September for experiments carried out up until January of the same year.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report, in English.
- include the reference number of the proposal to which the report refers.
- make sure that the text, tables and figures fit into the space available.
- if your work is published or is in press, you may prefer to paste in the abstract, and add full reference details. If the abstract is in a language other than English, please include an English translation.

ESRF	**Experiment title:** **Measurement of trace element distribution in adipose healthy and diseased breast tissue using XRF**	**Experiment number**: **28-01-656**
Beamline: BM28	**Date of experiment**: from: **18/05/04** to: **20/05/04**	**Date of report**:
Shifts: 9	**Local contact(s)**: **Simon Brown**	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

Dr Michael Farquharson*, School of Allied Health Science, City University London

Report:

Experiment 28-01-656 on beamline BM28 followed a series of measurements on the same station all pertinent to certain properties of breast tissue with a focus on the differentiation between healthy and different types of diseased tissue. The first two experiments (in 2000 and 2001) used X-Ray Fluorescence (XRF) as an instrument for the quantification of four elements, potassium, iron, copper and zinc, in over 100 specimens. The analysis of these results strongly suggested the elevation of the levels of these elements in cancerous tissue. In 2002 the measured quantities of these metals where evaluated for properties such as homogeneity of distribution within a sample and reproducibility of the quantification procedure. The elemental quantification studies have been reported in Geraki *et al* (2004a). In 2003 a different type of measurement was combined with the metal quantification. A scintillation detector was used for Angular Dispersive X-Ray Diffraction (ADXRD) measurements, taken on the same part of tissue as the elemental XRF readings. The purpose for ADXRD was double; the results were used for correction of the XRF data but also to provide additional information about the sample properties. The diffraction profiles obtained over a suitable range of momentum transfer reveal characteristic molecular structures and these were investigated for the presence of variation between healthy and diseased tissue (Ryan and Farquharson 2004). Quantitative analysis of the diffraction

spectra suggested a differentiation between healthy and diseased specimens in terms of the relevant amounts of adipose and fibrous tissue they contain (Geraki *et al*, 2004b). Further features introduced in this experiment were the inclusion of a new sample category (benign-fibroadenoma) and a more accurate quantification of the element with the fluorescence x-rays of the lowest energy (potassium) due to the use of a silicon detector with a resolution, at these energies, superior to the previously used germanium one.

The latest experiment, in May 2004, concentrated on comparing specimens from the same individuals and from the same disease sites in an effort to assess the variability of findings. The parameters compared were the levels of the four elements of interest and the scatter profiles. There were seven cases (three carcinomas and four benign fibrocystic changes) while four samples were taken from each case. An XFlash silicon drift detector (Röntec) was used to collect full spectra for the estimation of the quantities of the four elements while a NaI detector was used on the 2-theta arm of the diffractometer for the ADXRD measurments. The angular range for these was 5-45 degrees.

The variation of the metal levels was assessed using the Median Absolute Deviation (MAD), a measure of group variability equivalent to the standard deviation but more appropriate for data that cannot be described by a normal distribution. The MAD, as a percentage of the median group concentration, was calculated for each element and each case (four samples/case). Table 1 shows the ranges of MAD recorded for each element as well as the median MAD that can be used as a measure representative of the overall variability of each element.

Table 1: Variability of elemental levels in samples from same individuals

MAD (%)	K	Fe	Cu	Zn
Min	13	3	13	4
Max	65	50	43	39
Median	39	21	17	27

The spread of the recorded diffraction patterns can be seen by directrly comparing the spectra acquired by the four samples constituting each case. The overall picture suggests significant inter-case variations, examples of which are shown in figures 1 and 2.

It is evident that both regarding the elemental levels and the difraction patterns there is significant variation between different specimens originating

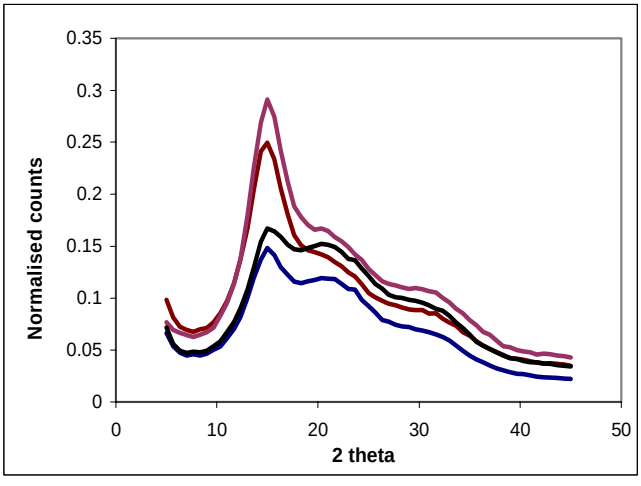

Figure 1: Inter-case variation of a fybrocystic change group of specimens

from the same disease site. It is hypothesized that such variations are due to the fact that a bulk specimen contains several types of diseased and healthy tissue, therefore x-ray measurements on a limited volume of a sample cannot guarantee a reading representative of the bulk specimen. These results suggest serious implications regarding the collection of tissue material from histolology laboratories where, to date, a gross examination of the specimens was deemed sufficient for the classification of the samples according to the type of disease previously diagnosed. As the project moves to a more fine-tuned classification of specimens these findings command a reassessment of the protocols for the collection of surgery specimens, pointing towards a precise histological examination of each specimen before the x-ray measurements. The requirements for the size of the samples will also have to change to ensure a volume sufficiently small to limit inhomogeneity effects and facilitate the accurate correlation between histology and the x-ray measured parameters.

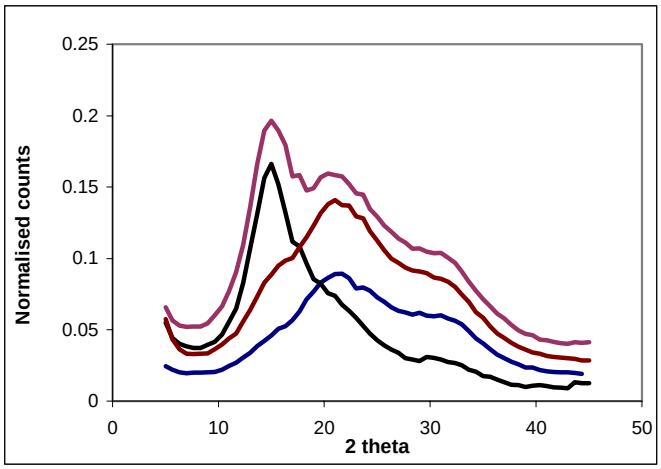

Figure 2: Inter-case variation of a carcinoma group of specimens

On the other hand it is not believed that these findings contest the previous results that showed significant differentiation between healthy and tumours. The strong point of these measurements was the large sample number which ensured that the obsreved statistical differentiations reflected the true situation. Particularly for the elemental concentrations similarly large group deviations have been taken into account in previous analyses and the statistical differences between groups, although somehow reduced, remained highly significant.

References

Geraki K., Farquharson M.J. and Bradley D.A., 2004. X-ray fluorescence and energy dispersive x-ray diffraction for the quantification of elemental concentrations in breast tissue. *Physics in Medicine and Biology* 49(1) 99 – 110

Geraki K., Farquharson M.J., Bradley D.A. and Hugtenburg R.P., 2004. A synchrotron XRF study on trace elements and potassium in breast tissue. N*uclear Instruments and Methods in Physics Research Section B-Beam Interactions with Materials and Atoms* 213 564-568

Ryan E. and Farquharson M.J., 2004. Angular dispersive X-ray scattering from breast tissue using synchrotron radiation. *Radiation Physics and Chemistry* 71(3-4) 971-972