# An evaluation of the clinical potential of tissue diffraction studies

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**Abstract.** Medical imaging is a long established part of patient management in the treatment of disease. However, in most cases it only provides anatomical detail and does not provide any form of tissue characterisation. This is particularly true for X-ray imaging. Recent studies on tissue diffraction have shown that true molecular signatures can be derived for different tissue types. Breast cancer samples and liver tissue have been studied. It has been shown that diffraction profiles can be traced away from the primary tumour in excised breast tissue samples and that potentially 3mm fat nodules in liver tissue can be identified in patients at acceptable doses.

## 1. Background

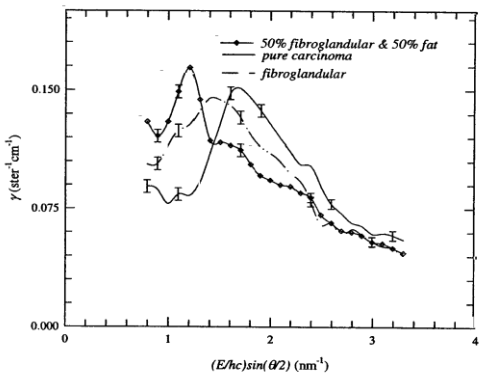


Figure 1: Diffraction signatures (indirect measurements of molecular form factors) for different breast tissues.

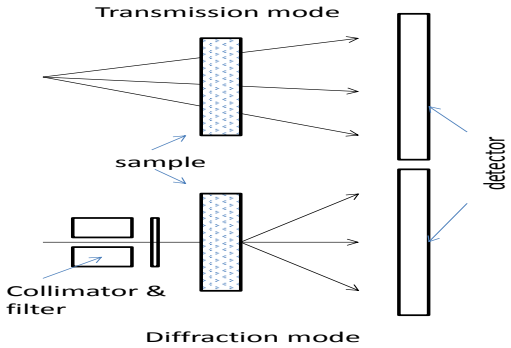


Figure 2: Angular dispersive X-ray Diffraction system using the DynAMITe detector. The sample – detector distance was 135mm and the X-ray beam reduced to ~2mm diameter.

One of the common medical diagnostic procedures is an X-ray examination. In most cases the image information is interpreted by considering subtle changes in X-ray transmission leading to information about the shapes and internal features in different organ structures. Considerable experience is required to convert this information into a diagnosis that can be used for patient management. One aspect is that the shape and appearance of a given structure is the only information available for classifying the tissue and with early stages of many diseases, changes in shape and appearance can be very subtle. This makes classifying a given tissue as diseased difficult.

Tissue diffraction using X-rays has, over the past 20 years, shown potential for classifying different disease states for a range of organs or tissues and hence could be used to quantify the status of disease. For example Figure 1 is for breast tissue (taken from Kidane *et al.* (1999)). In the current paper we look at two clinical problems and suggest how tissue diffraction measurements made with two different diffractometers could aid patient management - firstly breast cancer surgery and analysis of a wide local excision (WLE) and secondly assessment of fat nodules in liver tissue.

## 2. Breast tissue analysis

Early breast cancer is usually treated by breast conserving surgery, chemotherapy and radiotherapy. However, despite advances in modern personalised treatments the recurrence rates are generally ~20-40%[1]. The problem is thought to be due to inadequate removal of tissue during surgery. One possible approach to ensure complete removal whilst minimising the tissue removed is to study the

diffraction profiles associated with suspicious regions in the WLE. To study this, several WLEs have been analysed with the diffraction system shown in Figure 2. The system consists of a tungsten target X-ray tube with a collimator system that can be introduced remotely to reduce the X-ray beam from a

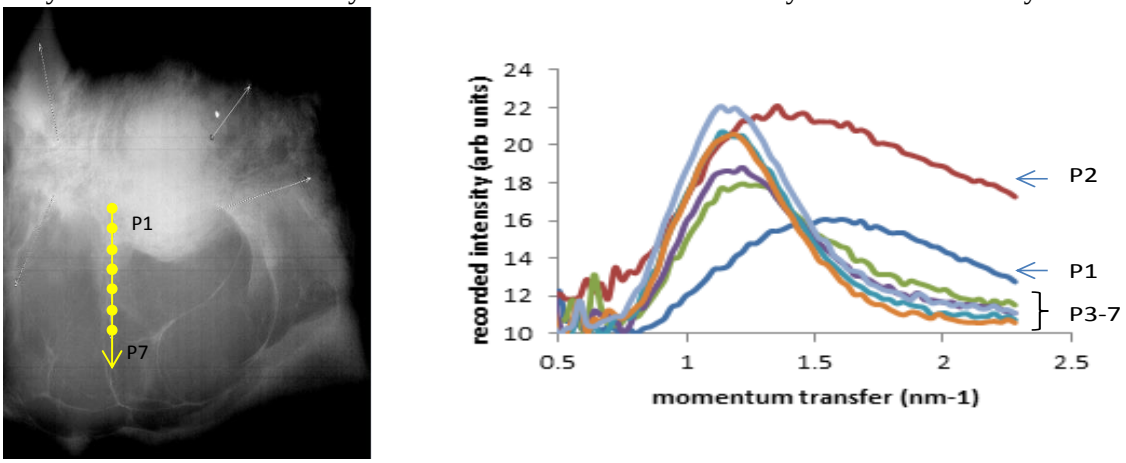


**Figure 3: Diffraction analysis of a WLE tissue sample. (a) high resolution transmission image, (b) diffraction signatures.**

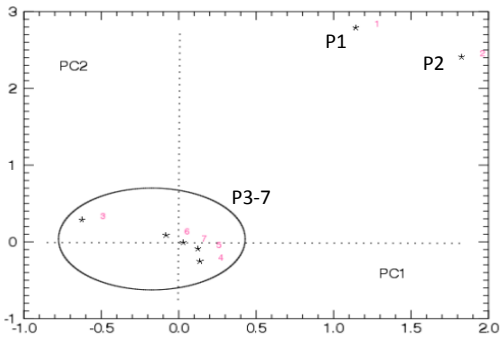


**Figure 4: PC1 vs PC2 for the diffraction profiles shown in Figure 3.**

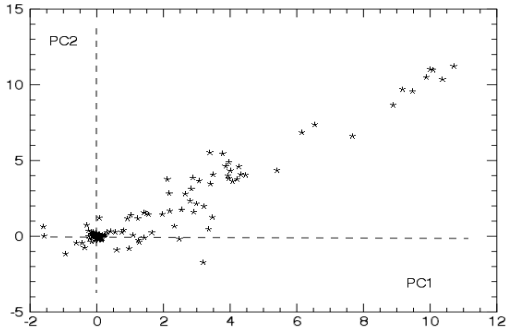


**Figure 5: PC1 vs PC2 for diffraction profiles from 41 samples. These profiles were taken from the centre of the primary tumour moving towards the periphery in 1mm steps.**

wide cone to a 2mm diameter pencil beam. Without the collimator, a conventional transmission image can be recorded on the detector system. When the collimator is introduced the pencil beam can be used to analyse small, selected regions of tissue where a diffraction pattern is recorded on the same detector used for transmission imaging. Generally two images are taken in the diffraction mode using two different filter materials, i.e. 0.1mm Samarium (Sm) and 0.2mm Tin (Sn). This combination of filters (i.e. balanced filtration) gives an effective narrow band of X-ray energies when the two images are subtracted. The detector system used for these measurements is called DynAMITe (Dynamic range Adjustable for Medical Imaging Technology) - see [2]. Typical results are shown in Figure 3. Figure 3(a) shows part of a high resolution transmission image of a breast tissue WLE. The primary tumour is in the upper part of the image. One of the infiltrating branches of the tumour has been subjected to diffraction analysis at a series of points (P1 to P7) indicated in the figure. At each of these points a diffraction signature has been measured and these are shown in Figure 3 (b). To obtain the 1D profiles shown in Figure 3(b) the 2D diffraction pattern recorded by the detector has been radially averaged. The radius of

integration has been converted to momentum tranfer using the scattering angle and an estimate for the mean energy of the X-ray beam using the balanced filters described above. It can be seen that the diffraction signatures change as the point of measurement moves along the structure in the image. Comparison with Figure 1 suggests these changes in the profiles are related to the fraction of different tissues present at each point. Peaking at lower values of momentum transfer are the profiles measured some distance from the primary tumour whereas those from within the tumour have peaks close to 1.5nm$^{-1}$. Principal component analysis (PCA) shows that more than 97% of variance is explained by PCAs 1 and 2. The scores plot given in Figure 4 shows clear separation between diffraction signatures (L3P3-L3P7) and L3P1 and L3P2. In total 41 samples have been looked at and results are shown in Figure 5. All breast tissue samples were taken from breast wide local excisions provided by the Tissue Bank at St. Bartholomew's Hospital, London, UK, under ethical approval from the local Research Ethics Committee (East London and The City REC Alpha). All patients had given informed consent for the use of redundant tissue from excision specimens for research purposes. Comparing Figures 4 and 5 suggests that tissue away from the primary tumour occupies a region close to the origin of the plot whereas tumour involvement moves towards the top right hand corner. Thus analysing a tissue sample removed during surgery to ensure the borders are clear of tumour would require the analysis to place the result close to the origin of Figure 5.

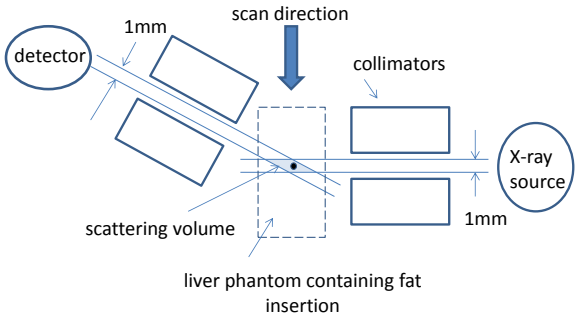


**Figure 6: The diffraction system used for the analysis of liver samples. The scattering angle is 5$^0$**

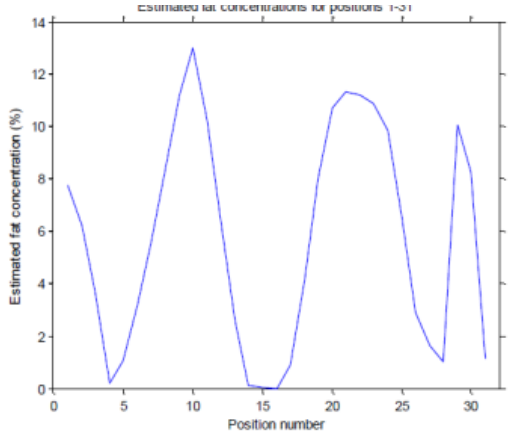


**Figure 7:The predicted percentage of fat occupying the scattering volume as the sample is scanned across the X-ray beam. 31 steps separated by 1mm were used.**

**3. Fat content in liver tissue.** Identifying normal tissue at the borders of a WLE is an investigation on an excised tissue sample, generally small in size. Quantifying the fat content of liver tissue would be a measurement made upon a patient. Hence, in this work, the analysis of liver tissue was approached in a different way. Small test phantoms were built and evaluated using a transmission energy dispersive X-ray diffraction system. The clinical potential was investigated by modelling based upon the results from the small-scale phantoms. The diffractometer uses a tungsten target X-ray source operated at 70kVp, a set of collimators that restrict scattering to 5$^0$ and an HpGe spectrometer. Figure 6 shows the equipment set-up. The two collimators allow phantoms up to 40mm thick to be examined. Frozen pig liver had different diameter cylinders of lard (4,5 and 6mm) inserted. Diffraction profiles were collected at 1mm intervals as the phantom was scanned a total of 31 different positions across the X-ray beam. The set of diffraction profiles were subjected to PCA analysis. The residuals, following subtraction of the mean of the diffraction profiles, generate curves that have the same shape but differ in their scales. This is typical behaviour of a two-component, additive system. Hence when PCA models the data, it estimates the shape of the common curve (loading vector) and the multiples of that curve present in each individual diffraction profile (the scores). These factors were then used to build a model to predict the percentage of fat present at each measurement point. The result of these estimations is shown in figure 7. Fat inclusions of 6, 5 and

4mm are shown as peaks at positions 10, 22 and 30 respectively. The predicted percentage of fat depends upon the diameter of the insert and the fraction of the scattering volume the insert occupies. The scattering angle was $5^0$ leading to a total length for the scattering volume of ~23mm. As the inserts are significantly less than the scattering volume, a partial volume effect reduces the predicted occupancy to significantly less than 100%. To estimate whether or not these measurements could be made in a patient, the diffraction profiles measured with the phantoms were used as input to a model that allowed additional tissues to be added. The effect of these additional tissues would be to attenuate both the incident and scattered beams and to generate additional multiple scatter. The simple model ignored the multiple scatter but attempted to include the statistical quality of the data. Attenuating the beam would mean less photons would be recorded and hence the statistical quality of the data reduced unless the input flux, and hence dose, increased. Hence a range of patient sizes and a range of effective doses were simulated and the results subjected to the same analysis. The results are shown in Figure 8. Each curve is the result of the analysis described above divided by the result given in Figure 7. The top left hand corner of Figure 8 is for the smallest sized patient and the highest dose. As the resultant curve is a straight, horizontal line it means there no differences compared to the result in Figure 7, i.e., the small experimental phantom. Moving across the set of curves displayed in Figure 8 the patient becomes larger (going from child to large adult), moving down the set of curves the dose is reducing (going from an entrance surface dose of (3.2mGy to ~0.32mGy). The lower right hand corner (larger patients, lower doses) demonstrates large differences in detecting the fat inserts as their locations are incorrectly predicted. In the upper left section the curves only show small departures from predicting correctly. The results suggest that for conditions to the left of the dotted line in Figure 8 useful estimates of fat content could be made.

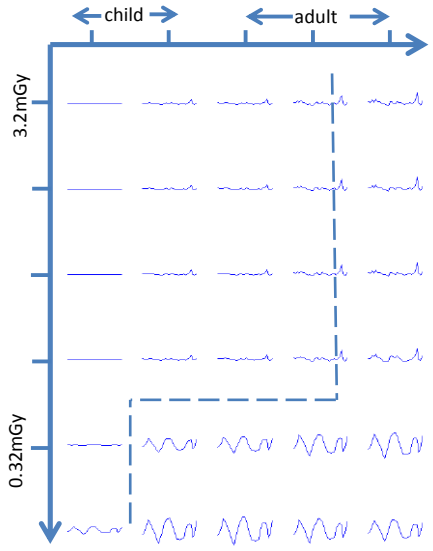


**Figure 8: Modelled results for 5 different sized patients and 6 different dose levels using the experimental result in Figure 7 as input to the model. To highlight any changes from the detectability demonstrated in Figure 7 each result has been divided by the result in Figure 7.**

## 4. Conclusions

Tissue diffraction measurements can provide useful clinical data. It has been shown that tissue removed during breast cancer management could be analysed in a way that could demonstrate that all the tumour has been removed. Our preliminary results show an ability to identify normal tissue from tumour in WLE. Analysing liver tissue to quantify the fat content has also been studied. The results, from a combination of experimental measurements and modelling, show that estimates at acceptable doses are only likely in the case of small adults or children.

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## References

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