Energy dispersive x-ray diffraction computed tomography of breast-mimicking test objects and breast tissue samples

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ABSTRACT

Breast lesions and normal tissue have different characteristics of density and molecular arrangement that affect their diffraction patterns. X-ray diffraction can be used to determine the spatial structure of such tissues at the atomic and molecular level. Energy Dispersive X-Ray Diffraction Computed Tomography (EDXRCT) can be used to produce 2-dimensional images of cross sections of the samples. The purpose of this work is to use an EDXRCT system to find the limiting visibility for details that simulate breast lesions. Results are presented for EDXRCT images of samples of different materials simulating breast tissue contrast and shapes. For simple circular details, the contrast between details and background in the images was measured with the goal of simulating the contrast between real breast tissue components. The limiting visible diameter was measured as a function of detail diameter for different combinations of scanning and geometrical parameters. Images of more complex test objects were assessed in terms of both contrast and accuracy of shape reproduction, evaluating the feasibility of using shape analysis as an additional parameter for lesion identification. The optimum combination of parameters are intended to be applied to the scanning of waxed breast tissue blocks.

Keywords: Energy-Dispersive X-ray Diffraction Computed Tomography, Breast Tissue Imaging, Pixellated Spectroscopic CdTe Detector.

1. INTRODUCTION

Breast cancer is the most widespread disease in women. In many parts of the world its incidence has increased continuously. Being a dominant cause of death among young women (average age of 33 – 55 years) ¹ there is a clear need for an early and more accurate diagnostic method in efforts towards saving life.

Alongside *in vivo* imaging methods, the need has arisen for quick and effective methods for *in vitro* tissue analysis to characterise excised lesions during surgery. Conventional pathology requires 24 hours for the tissue to fix, after it is embedded in paraffin, cut and assessed by a pathologist. This delay between excision and diagnosis results in distress for the patient and may require a recall operation for lymph node removal if the tissue is found to contain malignant cancer. It also implies increased costs for the healthcare services. The ideal scenario would be one in which the tissue is directly assessed in the operating theatre, enabling the surgeon to intervene when needed.

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X-ray diffraction (XRD) results from the interference of coherently scattered X-rays by tissue structures. Historically, XRD was used for characterising crystalline materials: the high degree of short-range order in such a material causes its diffraction pattern to feature sharp peaks, the position of which is related to the inter-atomic distances in the lattice. However, it has also been demonstrated that XRD is effective in the characterisation of amorphous materials that display a degree of short-range order: in this case, the diffraction patterns feature broader peaks, the position of which is still dependent upon the average inter-atomic distances in the materials. In particular, X-ray diffraction is effective in tissue characterization, as investigated by a number of authors²⁻⁸. The invasion of healthy tissue by cancer causes a loss of short-range order, as reflected in broadening of diffraction peaks, and alteration of inter-atomic distances, which reflects in changes of the position of peaks.

A diffraction pattern is a measurement of the intensity of scattered X-rays as a function of momentum transfer

$$\chi(nm^{-1}) = 1/\lambda \sin \frac{\theta}{2} \quad (1)$$

where χ is the momentum transferred to the photon causing it to deviate through an angle θ and λ is the wavelength of the beam⁹. A range of momentum transfer values can be achieved either by using a mono-energetic beam and varying the scatter angle (referred to as angle-dispersive XRD) or by keeping the scatter angle fixed and exploiting the information from the different energy components present in an X-ray beam from a conventional source (referred to as energy dispersive XRD), as in the present study¹⁰.

In the case of breast cancer, it has been shown that XRD allows differentiation between benign and malignant lesions, as well as cancer staging^{4 5 10-13}. However, characterizing thick tissue samples (above a few mm) becomes difficult due the contribution to the diffraction signal from different tissue components at different depths. Computed tomography solves this problem due to its ability to provide a three-dimensional map of the distribution of tissue differential scattering coefficients. However, due to the limited availability of multi-element spectroscopic detectors, to-date diffraction CT acquisitions have been based on rotational and translational motion for the sample, in the so called “first generation CT” geometry. In this paper, a proof of concept method will be presented for an EDXRDCT system based on one-shot acquisition of a CT projection by using a fan beam and a pixellated spectroscopic detector.

2. MATERIALS AND METHODS

An energy dispersive X-ray diffraction (EDXRD) system was used, based on a conventional W- anode X-ray source (COMET MXR-225/22) operated at 70kVp, pixellated spectroscopic detector, a 1 mm × 10 mm fan collimator made of brass positioned at 40.5 cm from the source, a scatter collimator made of brass that is attached to the detector (referred to as the HEXITEC detector). The HEXITEC consist of an 80×80 array of pixels 250 μm in side. The signal from each pixel is processed with a charge sensitive amplifier. A two dimensional readout ASIC is used for signal processing and readout^{14 15}. The detector used in this project is a 1 mm thick Schottky anode CdTe detector manufactured by ACORAD¹⁴. The detector with the attached scatter collimator sits on a goniometer that allows the change of detection angle. 6° and 8° are the two scatter angles which are presented in this paper. The information from several angles can be summed to improve the statistics providing the diffraction patterns are comparable after correction for incident spectrum and, where applicable, for absorption in the sample. Figure 1 shows a schematic diagram of the experimental setup. The sample was held on a rotational/translational stage (miCos VT-80 and DT-80). The optimum distance between sample and detector has been defined as the one giving the highest scattered intensity from a uniform sample (in this present case 4.3cm).

Figure 1. Experimental setup of the X-ray diffraction system.

The scatter collimator consists of 17 holes ($0.5\text{mm} \times 0.5\text{mm}$) separated by 0.5mm gaps, each of which has a different angle to trace the beams coming through the primary collimator and the sample. A beam trace diagram is shown in figure 2 to illustrate the angles and dimensions of the system.

Figure 2. Beam trace diagram of the scatter fan collimator.

The primary collimator was aligned using a CCD camera and the scatter collimator was aligned subsequently to the detector alignment. The angular resolution of the system in this case is 0.64° and 0.62° for the scatter angles 6° and 8° respectively. These values for the angular resolution were calculated using the procedure presented by Pani et. al.¹⁰. When these values of angular resolution are converted to momentum transfer, the range is from 0.06 nm^{-1} to 0.3 nm^{-1} and 0.05 nm^{-1} to 0.2 nm^{-1} at the angles of 6° and 8° respectively.

2.1 System primary characterisation

Calibration of the detector was carried out by measuring the peak position of the characteristic lines for Ag, Ba and Mo from a Variable Energy X-ray (VEX) radionuclide source based on ^{241}Am . Figure 3 shows the calibration line, with an R^2 value of 0.99 and the calibration equation:

$$\text{Energy} = 0.285 \times \text{Channel number} + 2.52 \quad (2)$$

Figure 3. Calibration graph.

The actual scatter angle was identified by identifying the position of diffraction peaks for caffeine and by converting energy into momentum transfer, using calibration equation 2 and substituting the value in to equation 1. A caffeine sample of 1 cm thickness was irradiated for 10 minutes to verify the actual scatter angle. Since the diffraction pattern of caffeine is known to have peaks at 0.65nm^{-1} and 1.29nm^{-1} ¹⁶, the angle for a nominal 8° position was found to be $8.04^\circ \pm 0.04$, agreeing with the nominal angle.

2.2 Scatter collimator test

A flat 1 cm thickness sample of polyethylene was irradiated for 30 minutes to test the scatter collimator holes uniformity. The resultant image is shown in figure 4.

Figure 4. A diffraction image detected by the HEXITEC detector from a 1cm thick polyethylene sample irradiated for 30 minutes.

The efficiency differs from one hole to another, being limited by manufacturing capability and by the alignment between holes and detector pixels. Figure 5 shows a profile plot for the normalized efficiency of the holes, averaged across four different trials. These values were used to correct the data acquired subsequently.

The uniform sample that was scanned using the EDXRDC system consists of a polymethylmethacrylate (PMMA/Perspex/Plexiglass) cylinder of 5 mm diameter with a 2 mm hole filled with water along the central axis. The combination of the cylinder material and water simulate the contrast between adipose tissue and malignant cancer at 1.1 nm^{-1} ¹⁷.

Due to the cylindrical symmetry of the object, CT acquisitions were carried out with the sample stationary in front of the detector for this proof-of-principle study. 180 projections were acquired for each sample, for an acquisition time of 60 seconds/projection. Each CT projection was a 17 x 300 array, where 300 is the number of channels in each spectrum, and 17 is the number of collimator holes. After individual energy calibration, the spectrum for each hole was obtained by summing the spectra from all pixels corresponding to a hole. The data were combined into a 3-dimensional array (spectral sinogram) in which the three dimensions are the number of holes x number of projections x number of channels in each spectrum.

The aim of this work is to optimize the system in preparation for scanning of real tissue samples. In a preliminary test, a waxed block containing liver tissue was scanned using the EDXRD system that contains a conventional W-anode X-ray source operated at 70kVp and 30 mA, a 1mm primary collimator, a pinhole CdTe detector (AMPTTEK XR-100T), a 6° diffraction collimator and a MiCos VT-80 linear sample stage . The scan was performed by acquiring a diffraction spectrum for 3 minutes for each 1 mm step across the sample. A transmission CT image of the sample was also acquired in order to determine the fractional content of tissue versus wax along each projection line.

3. RESULTS AND DISCUSSION

3.1 Uniform samples with details

Diffraction CT images were obtained at two different momentum transfer values (0.8 nm^{-1} and 1.5 nm^{-1}). The reason for this choice is that at 0.8 nm^{-1} the contrast between Perspex and water reproduces that between adipose tissue and tumor at 1.1 nm^{-1} ¹⁷ while the value 1.5 nm^{-1} refers to the position where the diffraction pattern of water has a maximum value. Figures 6 and 7 show diffraction images of the sample at two different scatter angles, as well as the profiles across the central line. It is apparent from all images that the detail is clearly visible at a momentum transfer value for which the difference in the diffraction pattern of water and Perspex is significant, while it becomes barely visible when the diffraction pattern of the materials become close together.

Detail contrast was measured by selecting the central region of the detail and the region around the maximum in the detail material and calculated using equation 3. Contrast between Perspex and water was found to be 0.70 ± 0.02 at 6° and 0.55 ± 0.03 at 8° . The contrast values represented are in agreement with the data from single point measurements¹⁷.

$$\text{contrast} = \frac{I_2 - I_1}{I_2} \quad (3)$$

where I_1 is the average signal from the detail region and I_2 is the average signal from the background. The arrow S in the figures shows the region of maximum contrast.

Figure 6. Perspex CT images at 0.8 nm^{-1} for different scatter angles: (a) at an angle 6° and (b) at an angle 8° . Arrow S, in the profiles (c) and (d) for angles 6° and 8° respectively, refers to the regions used for the contrast analysis between different angles.

Figure 7. Perspex CT images at 1.5 nm^{-1} for different scatter angles: (a) at an angle 6° and (b) at an angle 8° . Arrow S, in the profiles (c) and (d) for angles 6° and 8° respectively, refers to the regions used for the contrast analysis between different angles.

Diffraction patterns of the materials were obtained by extracting, for each reconstructed image in the stack, the average value for the same regions of interest used for contrast measurement in the previous section. For all materials, figure 8 shows a comparison of the diffraction patterns obtained from the image at 6° and 8° and their sum to increase statistics. The diffraction patterns at the two angles show good agreement, indicating that negligible loss in the momentum transfer resolution occurs when the diffraction patterns at different angles are summed. However, the diffraction patterns do not match fully the diffraction patterns shown in previous literature. The main reason for this is the high level of cross talk between different collimator holes. This signal alters the background and prevents a correct normalisation by the incident spectrum, thus warping the actual diffraction pattern shape. This will be addressed in future by a collimator design that allows it to be as close as possible to the sample (the current distance is 4.3 cm), thus making the scattering angle under which adjacent pixels are seen large, and allowing any photons scattered beyond the relevant hole to be absorbed by the collimator septa.

Figure 8. Comparison between diffraction patterns extracted from CT images and the summed data at different angles. (a) Perspex and (b) water.

3.2 Preliminary test of real tissue

Figure 9 shows the diffraction patterns obtained from different positions of the waxed tissue block. Each pattern results from a thin strip of the sample cross-section. Patterns for step 8 shows wax with wire, step 15 represents wax with the tissue and step 24 for wax only. These initial results confirm the feasibility of scanning waxed samples rather than fresh ones, the diffraction patterns from regions containing the sample being clearly distinguishable from those containing wax only. Further work will address CT acquisition and reconstruction of composite tissue samples and the limiting visibility for different tissue types.

Figure 9. Diffraction pattern of scanning the waxed tissue block. The different steps shown presents the diffraction pattern of radiating step 8: wax and the wire, step 15: liver and wax and step 24: wax only.

Figure 10 shows 360° projections of a micro CT image of the liver waxed block which helped in determination of the percentage representation of each detail in each of the scanning steps. The normalised average signal per unit length of wax and liver in the sample presented in figure 11.

Figure 10. Transmission micro CT image of the liver waxed tissue block. The black circle on step 8 represents the position of the metal wire that was used for position determination.

Figure 11. Average signal per unit length of wax and liver from the sample shown in figure 6.

4. CONCLUSION AND FUTURE WORK

The results demonstrate the capability of the method in differentiating between materials and in extracting diffraction patterns from diffraction CT reconstructions. Statistics was increased by summing the diffraction pattern at 6° and 8°. Points to be addressed are the high background from neighbouring image pixels, reducing contrast and altering the diffraction patterns, as well as the limited spatial resolution of the system. Both points will be addressed with the use of a new collimator design, proposed for the next stage of this work.

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