Harnessing X-Ray Diffraction for Non-Invasive Breast Cancer Detection

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Abstract

Background: Conventional breast cancer screening methods face several limitations including missed detections, false positives, and exposure to X-rays. There is a clear need for an alternative screening method that is non-invasive, rapid, and cost-effective.

Objective: This study aims to explore the use of X-ray diffraction (XRD) to detect structural biomarkers in the extracellular matrix (ECM) of breast tissues, which could serve as a basis for a new breast cancer screening technology.

Methods: We performed a systematic analysis using XRD on 292 diffraction scans from 38 breast cancer patients. The samples, obtained from biopsies and lumpectomies, were processed with a custom-built transmission-mode diffractometer. Data were divided into a training set of 30 patients and a blind test set of 8 patients. A detection algorithm employing machine learning techniques was developed to differentiate between healthy and cancerous tissues based on the XRD patterns.

Results: Our analysis revealed significant differences in the XRD patterns between normal and cancerous tissues, notably a broader peak in cancerous tissues. The machine learning model demonstrated high accuracy, with a sensitivity of 95.9%, specificity of 93.5%, and a positive predictive value (PPV) of 95.1% in the training set. The blind test set results were similarly robust, with a sensitivity of 97.4%, specificity of 87.2%, and PPV of 88.4%.

Conclusion: The study confirms the potential of XRD as a reliable tool for breast cancer screening, offering significant improvements over traditional methods by potentially reducing unnecessary biopsies and enhancing diagnostic precision. These results encourage the integration of XRD analysis into routine breast cancer screening protocols, promising a significant step forward in the early detection of breast cancer.

Introduction

Despite advancements in early detection of breast cancer, conventional screening methods exhibit limitations, including missed detections, false positives, unnecessary pain, exposure to X-rays, and overdiagnosis. Hence, there is an unmet medical need for a non-invasive, patient-friendly, quick, and economical solution for breast cancer screening. In this work, we present a systematic analysis of human breast tissue samples using X-ray diffraction (XRD) to determine the structural biomarkers associated with the changes in extracellular matrix (ECM). Many components of ECM, such as glycoproteins, lipids, collagen, and keratin, exhibit a periodicity, leading to pronounced XRD patterns. These components experience cancer-induced changes, which the XRD measurements can monitor.

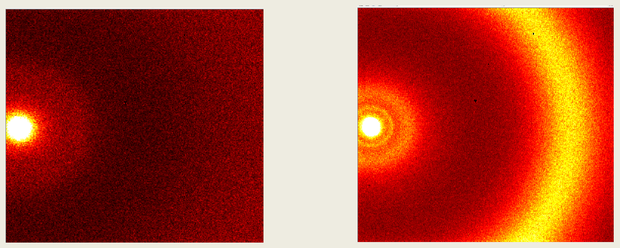

Fig 1: (Left) tumor-like diffraction pattern (Right) control-like diffraction pattern

Fig 2: XRD instrument used at EosDx

Methods and Materials

Breast tissue samples (biopsies and lumpectomies) were obtained following regulatory standards. Tissues were microscopically examined and manually probed, guided by pathology reports, in order to identify control-like or tumor-like regions. Appropriately sized sample holders were selected based on tissue dimensions, and each was labeled with a unique barcode for tracking purposes. For data collection, we used a simple, custom-built, low-cost, transmission-mode diffractometer comprising a Xenocs source, Genix 3D Cu, an Advacam MiniPIX TPX3 detector, and a sample stage. Breast tissue samples were scanned for 2 or 4 minutes at various sample-to-detector distances. In this work, we present the WAXS (wide-angle X-ray scattering) results obtained with a distance of approximately 12 mm. The analysis aimed to produce a detection algorithm capable of taking a raw diffraction input image and outputting a binary cancer prediction. We used data from 38 cancer patients with 292 diffraction scans in total. We randomly selected 30 patients for training and 8 patients for testing (the "blind" set).

Results

Significant differences in XRD patterns between healthy and cancerous breast tissues were found. Additionally, a machine learning analysis demonstrated an even more precise differentiation between control and cancerous clusters. XRD has been demonstrated to distinguish between normal and tumorous tissue and it should be noted that the most prominent peak in the control-like sample is sharper, whereas the most prominent peak in the tumor-like sample is broader.

Dataset	Sensitivity	Specificity	PPV	F1
Training	95.9%	93.5%	95.1%	0.955
Blind	97.4%	87.2%	88.4%	0.927
Overall	**96.3%**	**91.6%**	**93.4%**	**0.948**

Table 1: Algorithm performance on the training set, blind set, and entire dataset

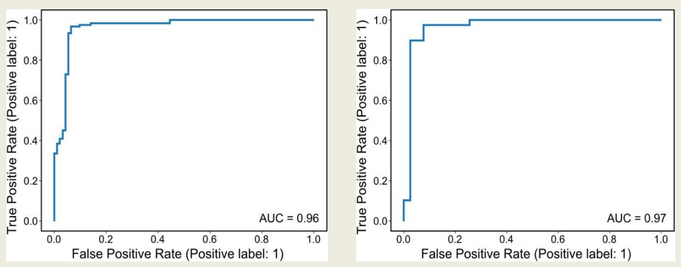

Fig 4: ROC curves on training (left) and blind (right) data, with the AUC values indicated.

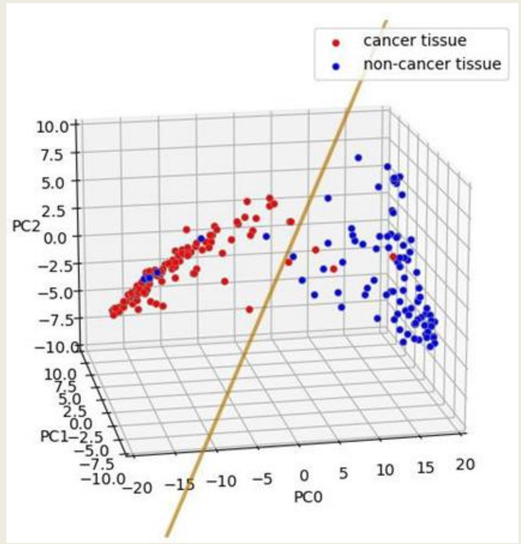

Fig 3: PCA-transformed data in 3 dimensions and the decision boundary.

Discussion

The XRD patterns were examined using principal component analysis and logistic regression. We achieved 95.9% sensitivity, 93.5% specificity, and 95.1% positive predictive value (PPV) for our training set. For the blind set, the results are 97.4%, 87.2%, and 88.4%, respectively. It should be emphasized that a separate team performed the blind set analysis. Our results represent a promising step towards adoption of diffraction technology for early cancer detection, potentially functioning as an intermediary tool to complement the Breast Imaging Reporting and Data System (BI-RADS) scoring system and enhancing mammography outcomes to minimize the need for unnecessary biopsies.

Conclusion

The findings of this study highlight the potential of X-ray diffraction (XRD) as a transformative tool for breast cancer screening. XRD's ability to detect subtle structural changes in the extracellular matrix (ECM) of breast tissue offers a promising avenue for distinguishing between healthy and cancerous tissues. This capability is underscored by the pronounced differences in the XRD patterns observed between control and tumor-like samples, particularly the sharpness and breadth of the peaks, which are indicative of underlying molecular changes. The high sensitivity (97.4%) and specificity (87.2%) achieved in our blind test set suggest that XRD could serve as a complementary technique to mammography, potentially advancing the accuracy of current screening protocols and reducing reliance on invasive biopsies. Overall, the implementation of XRD in breast cancer screening facilitates timely intervention at the most treatable stage of cancer development, thereby enhancing patient outcome.

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