Low Dose X-Ray Diffraction Imaging with Real Time AI Classification

Aika Tanaka, Audrey Nguyen, Mark Pegram, Masroor Khonkhodzhaev, Slava Shcherbakov, Daryl Hoffman
Alexander Lazarev, Byron Aram, Thomas Lomis, Prashant Chawla, Lev Murokh, Pavel Lazarev
Abstract #1891

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.

Background

X-ray diffraction detects nanoscale structural alterations in collagen, lipid, and water that indicates breast neoplasia. EoScan™ is a diffraction breast scanner that captures Bragg signatures through intact tissue and classifies malignancy using a convolutional neural network (CNN) trained on >12,700 spectra.



Fig 1: XRD instruments used at EosDx

Materials and Methods

Breast samples including malignant (n = 161) and benign (n = 131) obtained at Valley Breast Care (Los Angeles, USA) and Keele University (Keele, UK). A total of 12,730 diffraction patterns were collected at EosDx (Menlo Park, CA) and Queen Mary (London, UK) respectively. Malignant samples include infiltrating and in-situ types. Healthy control tissue was donated by patients undergoing reconstructive surgery performed by Dr. Daryl Hoffman (Campbell, CA); all samples were collected under the same IRB-approved protocol. For all samples, pathology testing was conducted by the Valley Breast Care Pathology Department to confirm the disease status. Standard immunohistochemistry testing is conducted for information on hormone receptor status. FISH results are also reported. The analysis aimed to produce a detection algorithm capable of taking a raw diffraction input image and outputting a cancer prediction.

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.

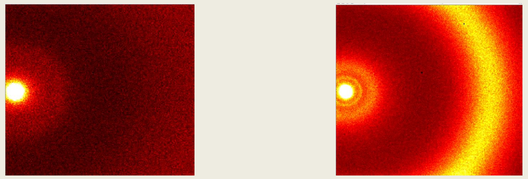


Fig 2: (Left) tumor-like diffraction pattern (Right) control-like diffraction pattern

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

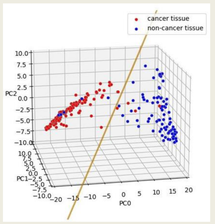


Fig 3: PCA-transformed data in 3 dimensions and the decision boundary.

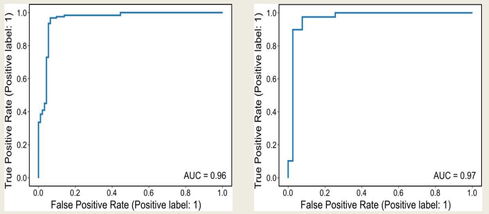


Fig 4: ROC curves on training (left) and blind (right) data with the AUC values indicated.

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.

*Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from SABCS® and the author