Digital histopathology of tumor associated collagen signatures (TACS) in breast cancer tissue using phase imaging with computational specificity (PICS)

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ABSTRACT

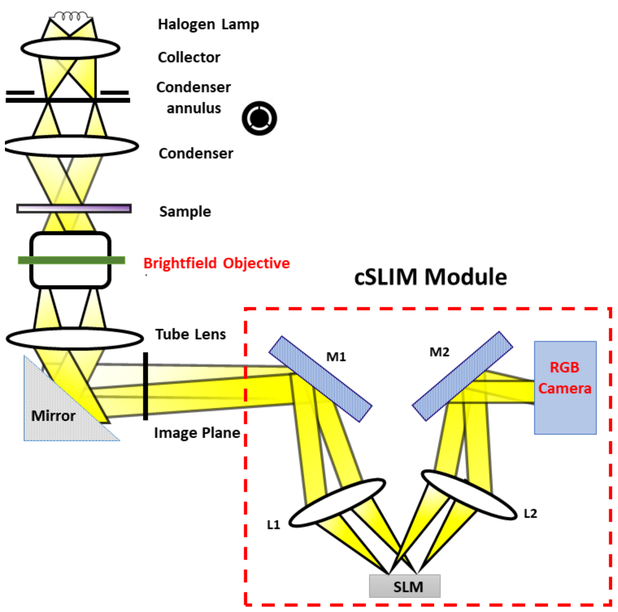
Treatment for breast cancer is highly dependent on a timely and accurate diagnosis and stratification of the disease. Microscopic analysis of a hematoxylin and eosin (H&E) counter-stained tissue biopsy is the traditional assessment procedure for diagnosing breast cancers, but it has the significant drawback of being time-consuming, needing considerable preparations, and exhibiting inter-observer variation. Significantly, H&E is not ideal for staining collagen fibers and, for this reason, specialized stains, such as picrosirius red (PSR), are used instead. We previously imaged H&E-stained human breast carcinoma TMAs using cSLIM, a quantitative phase imaging (QPI) technique that generates phase maps of the sample as well as their brightfield counterparts. Thereafter, we used a fiber analysis method to show that cSLIM can detect TACS-3. In this study, we demonstrate that the analysis of collagen fibers can be performed by integrating cSLIM with deep learning. We artificially stain the collagen fiber region associated with the PSR stain using a new approach: phase imaging with computational specificity (PICS). Taking the image acquired with SLIM as the input and the corresponding image acquired with polarization light microscopy (PLM) as the ground-truth, we trained the a translation GAN model extensively. We then used the algorithm CT-FIRE, an established technique for collagen fiber analysis, for mapping filamentous structures on the PICS-generated collagen image, without the need of specific stains.

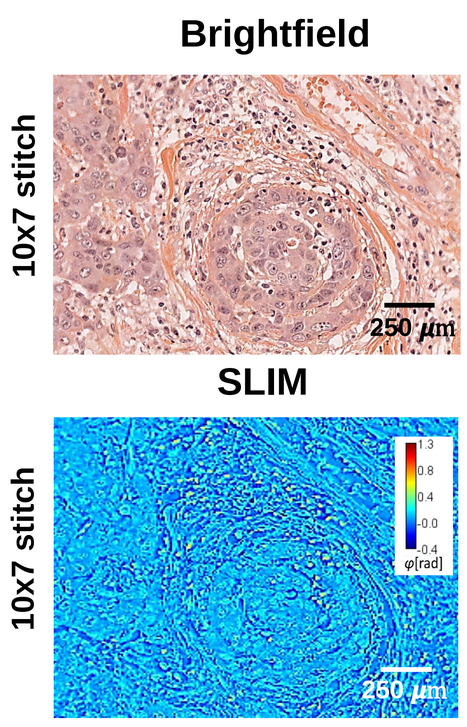
1. Motivation

- New quantitative approaches are needed to characterize tumor associated signatures in cancerous biopsies.
- The collagen properties of DCIS biopsies have never been computed from phase images.

2. Methods:

A: Color Spatial Light Interference Microscopy (cSLIM)

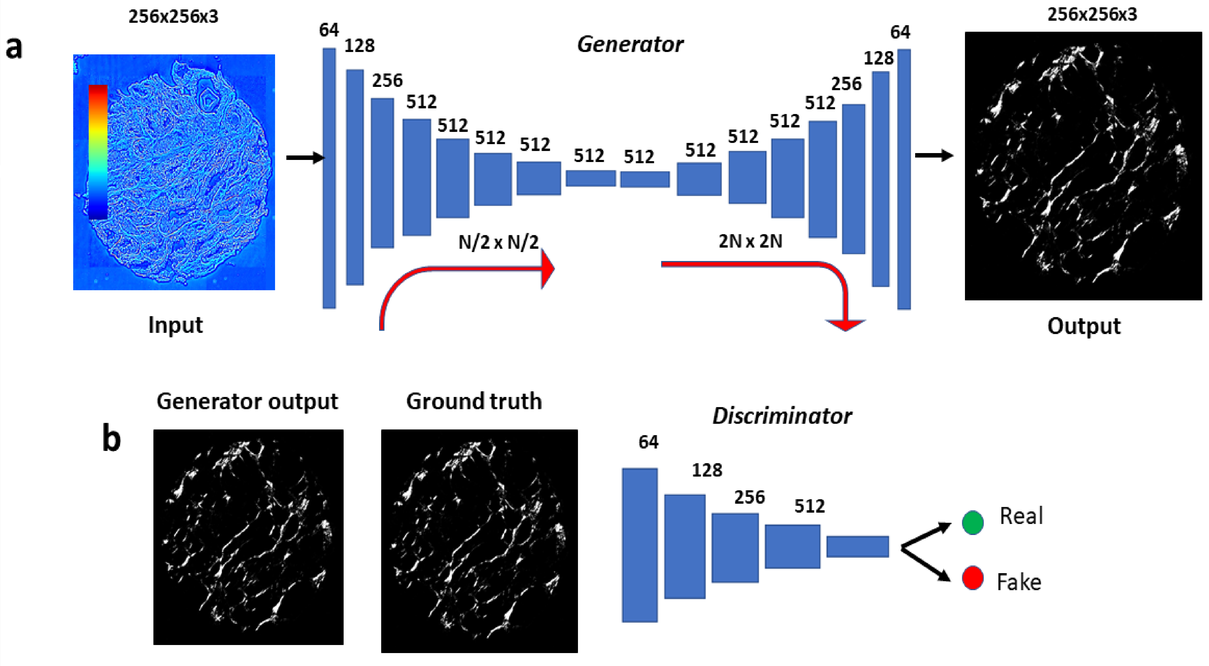




- cSLIM consists of an add-on QPI module to a commercial PC microscope, but uses a brightfield objective and RGB camera [1].
- Post-processing combines four shifted brightfield frames for quantitative phase [2].
- cSLIM generates both the brightfield and phase maps of identical fields of view.

$$\Delta\phi(x,y) = \tan^{-1}\left[\frac{I(x,y;-\pi/2)-I(x,y;\pi/2)}{I(x,y;0)-I(x,y;\pi)}\right]$$

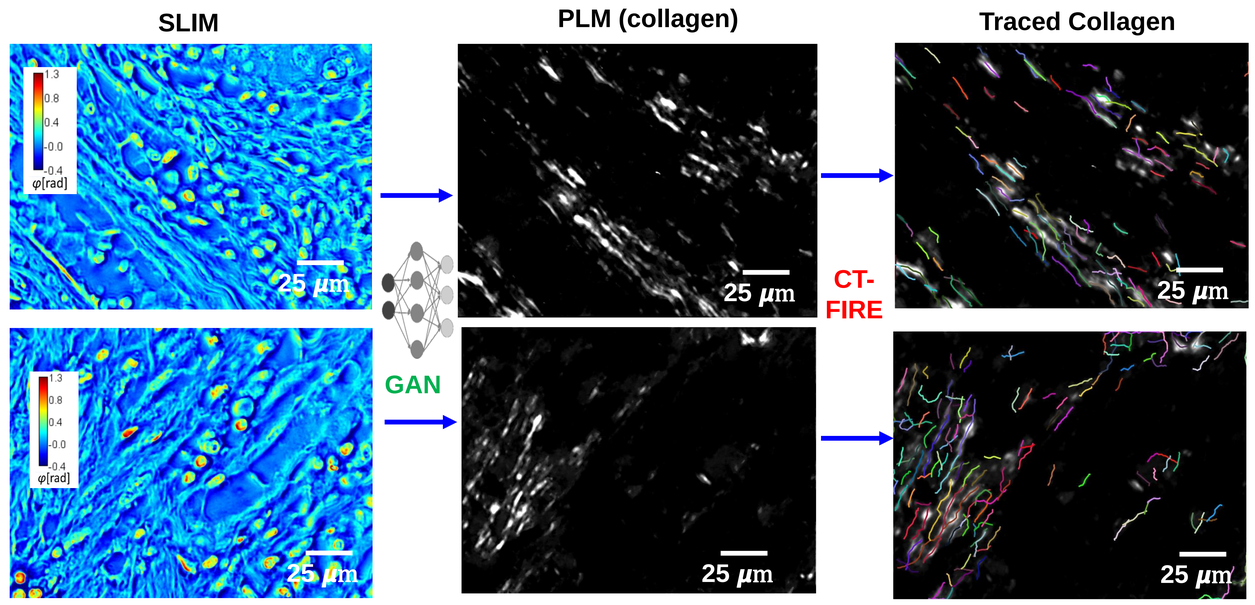
3. Image-to-image Translation using GAN



- A generative adversarial network (GAN), which comprises two opposing networks competing in a zero-sum dynamic, are employed in this study to convert the phase maps into their birefringent signals, which are associated with collagen fibers [3].
- The GAN model was trained with pairs of perfectly matched SLIM phase images of tissue cores with their corresponding polarization light microscopy (LPM) images, containing purely birefringent signals.

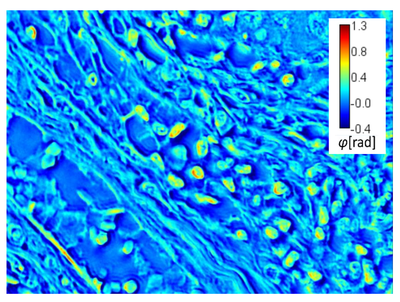
4. Workflow

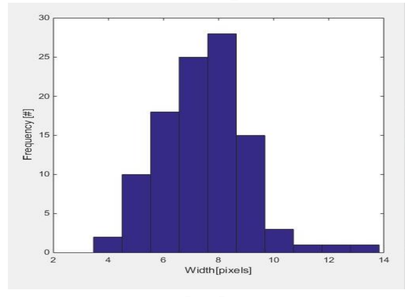
- 80 breast biopsies have been scanned and imaged in both brightfield and phase channels.
- The constructed SLIM phase images are first translated into collagen maps using the trained GAN model, and are then fed through the fiber segmentation algorithm CT-FIRE.

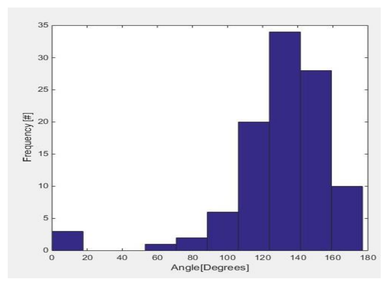


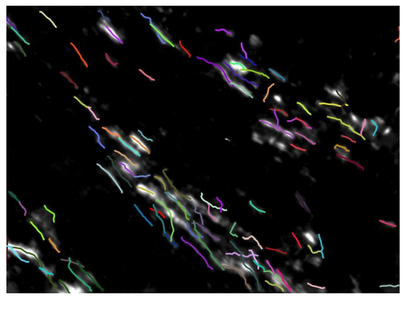
- The CT-FIRE fiber segmenting tool [4] is used to extract biomarker properties such as the angle, width, straightness, and length of the fibers. This algorithm has been used successfully in the past to predict prognosis in PDAC tissue [5].

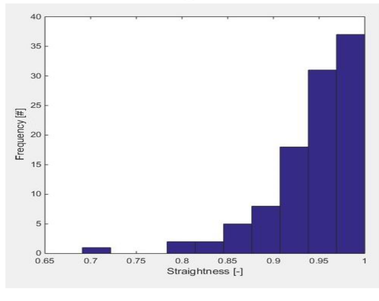
5. Extracted Fiber Properties

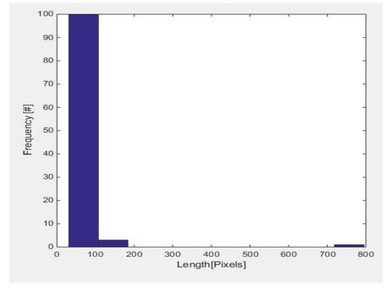












- In addition to the fiber structure properties above, the quantitative information contained in the SLIM phase maps, such as dry mass and scattering length, can be coupled to the overall analysis to leverage diagnosis and prognosis predictions.

6. Future Work

- Compile the results for over 200 DCIS biopsies and evaluate total patient statistics with CT-FIRE.
- Establish an end-to-end model for predicting fiber properties and associated survival statistics without the need for intermediary translation and segmentation steps.

References

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Acknowledgments

EBICS Emergent Behaviors of Integrated Cellular Systems
OPTICS from image to knowledge
NSF National Science Foundation WHERE DISCOVERIES BEGIN
LOCI