Optimization of a Custom-Built Confocal Microscope for Imaging of Human Cancer

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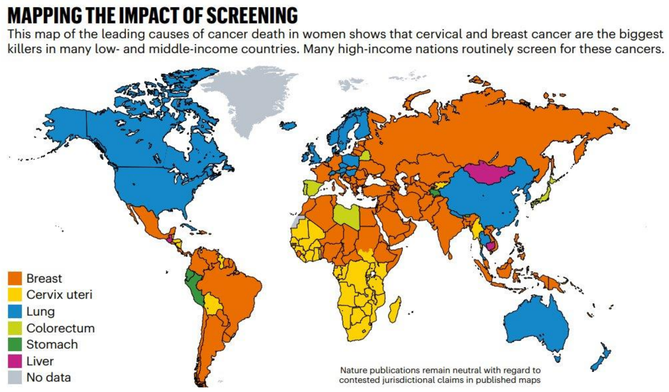
INTRODUCTION

More than 75% of cancer-related deaths will occur in low-income and middle-income countries, and the biggest killers worldwide include breast, cervix uteri, and lung cancer, as shown on the map below. [1]



Here we discuss computational advancements implemented toward a custom confocal imaging system that can accompany screening tools to provide prognostic information in low- and middle-income regions.

METHODS

The mechanical inertia of galvanometer mirrors at higher frequencies results in ghostly artifacts of the sample that distort images (Figure 1).

This effect worsens exponentially as scan frequency increases limiting the acquisition time and FOV of usable, accurate images The figures below show the scan speed dependance of the column separable artifacts.

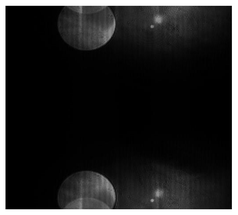


Figure 1a: 5000Hz

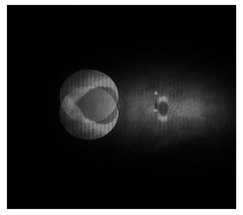


Figure 1b: 2000Hz

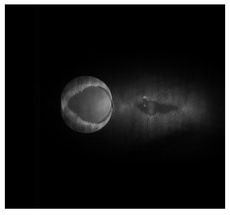


Figure 1c: 1000Hz

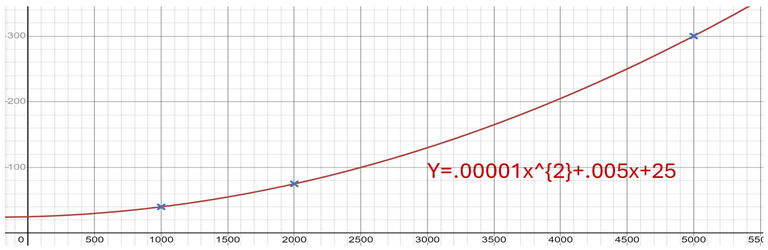


Figure 2: Line of Best fit Approximated to Estimated Column Shifts (Y-Axis in micrometers) at each scan frequency (X-Axis in Hz).

METHODS (cont'd.)

The column separability of these artifacts allows us to separate the image and artifact content, shift them to alignment and then reconstruct a true to sample image. Figure 3 shows a series of four images of a control slide documenting the process of computationally correcting for the scan speed dependent motion artifacts.

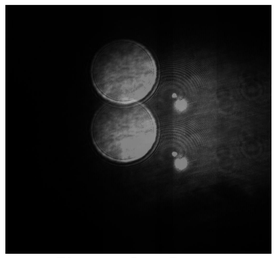


Figure 3a: Raw Confocal Image

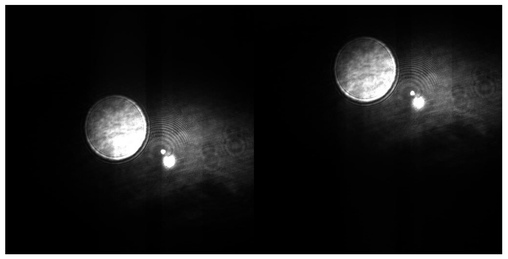


Figure 3b: Image Split by Even and Odd Columns

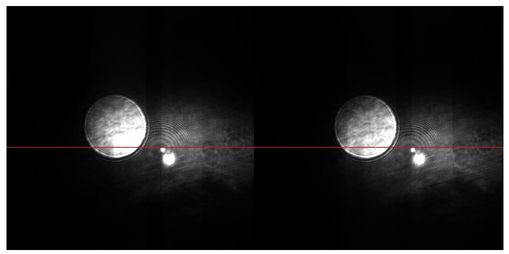


Figure 3c: Image Split Shifted to Proper Y-Alignment

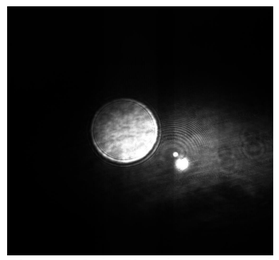


Figure 3d: Final Image after Concatenation

Additionally, another method used the following steps to improve image quality further. Given the limited image FOV we cropped and zero padded the image to artificially restore resolution around the window of sample data.

We then convolved the image with a regimen of smoothing and edge detecting kernels to denoise and enhanced edges and contrast in the image. Figure 4 shows diagrams visualizing the concept and process of zero padding and convolution which were done in the Fourier Domain after cropping the image in standard form.

0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0						0	0
0	0						0	0
0	0						0	0
0	0						0	0
0	0						0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0

Figure 4a: [2] Zero-Pad Visualization

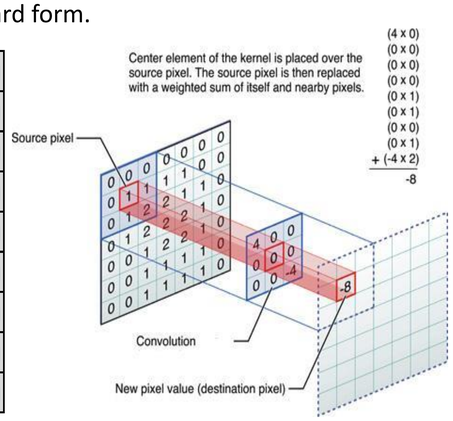


Figure 4b: [3] Convolution Visualization

RESULTS

Images were collected from fixed histological tissue slides. Compared to the raw images, the images using the postprocessing techniques show fewer artifacts, signal-to-noise ratio (SNR) improvements, and greater overall image quality.

Figure 5 shows progression of image quality from the raw image throughout postprocessing stages along with a histogram comparison of image SNR values.

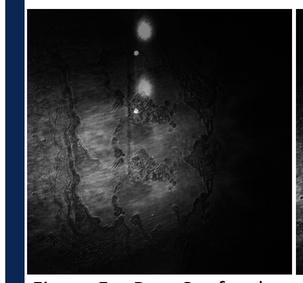


Figure 5a: Raw Confocal Image of Lung Carcinoma Slide showing artifacts

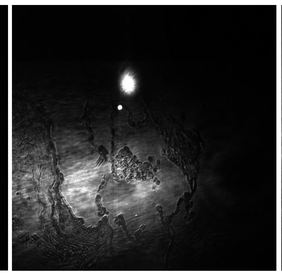


Figure 5b: Pre-FFT Confocal Image of Lung Carcinoma Slide with artifacts removed

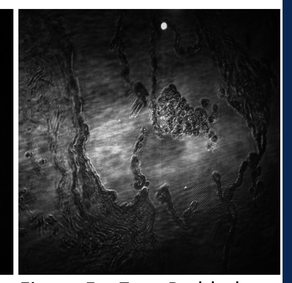


Figure 5c: Zero Padded Confocal Image of Lung Carcinoma Slide

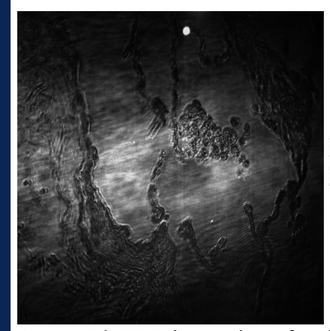


Figure 5d: FT Enhanced Confocal Image of Lung Carcinoma Slide

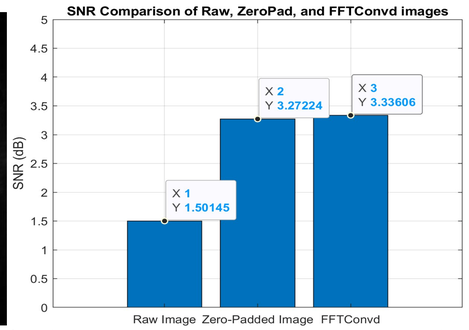


Figure 5e: Mean-to-Variance SNR comparison at each stage of enhancement processing

DISCUSSION

Our devised methods are sufficient for recovering accurate sample image data as well as denoising, enhancing contrast, and improving mean to variance SNR. These computational processes achieve clearer, more reliable imaging results, which can enhance the analysis, interpretation, and diagnostic potential of low-intensity reflectance confocal images.

The artifact correction relies on physical aspects of our system that limit our FOV and accessible scan rate. This defines a direction for future research working to expand our accessible scan frequencies and FOV physically and computationally.

REFERENCES

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