Optimization of pixel size and propagation distance in X-ray phase-contrast virtual histology

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Effects of pixel size and magnification on image noise in X-ray phase-contrast tomography: theoretical model

Propagation-based (PB) phase-contrast tomography (CT), combined to a suitable **phase retrieval (PhR)** filter, mitigates the dependence of noise on the pixel size, bringing to a major Signal to Noise Ratio (SNR) gain over conventional CT, especially at small pixel sizes [1,2]. A model that predicts the SNR dependence on pixel size and propagation distances [2] has been recently validated with experimental results obtained with monochromatic synchrotron radiation and employing a photon-counting detector featuring a quasi-ideal (box-like) Point Response Function (PSF) [3,4]. These results were obtained on breast mastectomy samples in the context of a clinically oriented breast CT project undergoing at Elettra (Trieste, Italy).

When measured in a homogeneous region portion of the CT image acquired at a fixed fluence, the SNR can be expressed as: $$SNR \propto \frac{h^2}{M^2}\frac{1}{f(A;d/h)};$$

where, **M** is the geometric magnification, **h** the detector pixel size, **f(A; d/h)** a dimensionless function that accounts for the tomographic process (filtering and interpolation), the detector's Modulation Transfer function (**MTF**) and the phase retrieval. Additionally, **d** is the FWHM of the detector's PSF.

The parameter **A** is different from 0 only when phase retrieval is applied, and depends on the refractive properties of the sample, on the setup geometry and on the detector pixel size as:

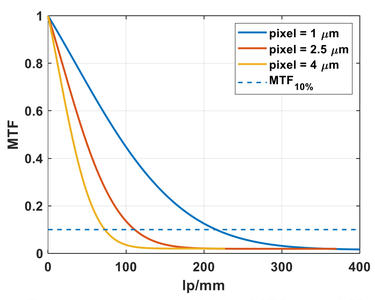
$$A = \pi\frac{\delta_1 - \delta_2}{\beta_1 - \beta_2}\lambda M R_2 \,/\, h^2$$

Where **λ** is the radiation wavelength, the subscripts 1, 2 in the **δ** and **β** and terms refer to an interface between two materials having given different refractive indices and $\mathbf{R_2}$ is the sample-to-detector (or propagation) distance.

The **validity of the model** applies in the near-field propagation regime, corresponding to **large Fresnel numbers, i.e., $N_F = d^2/(M^2\lambda R_2) >> 1$** (often this condition is relaxed down to N_F slightly higher than 1).

Aim of the work

Preliminary **experimental optimization of the propagation distance and the pixel size** in **virtual histology** experiments by using **polychromatic** (i.e., white) synchrotron X-ray beam and **sCMOS detector** with PSF far from being ideal. Both polychromaticity and broad PSF represent deviations from the model validated in [4].



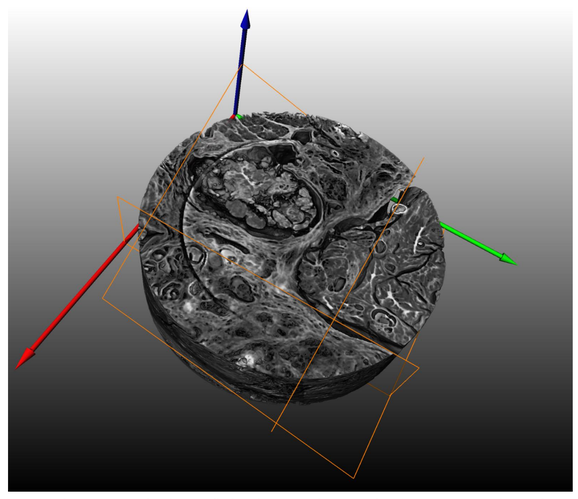
Gaussian fit of detector's MTF and 10% threshold at every pixel size

System characterization and processing

- MTF is measured for all the used pixel sizes through the slanted edge method. From the MTF, the PSF's FWHM is derived;
- TIE-Hom Phase-retrieval is applied prior to image reconstruction using a fixed δ/β = 350;
- Image reconstruction is performed via FBP and Shep-Logan filtration;
- CT Slices are processed via a de-trending procedure for beam-hardening correction.

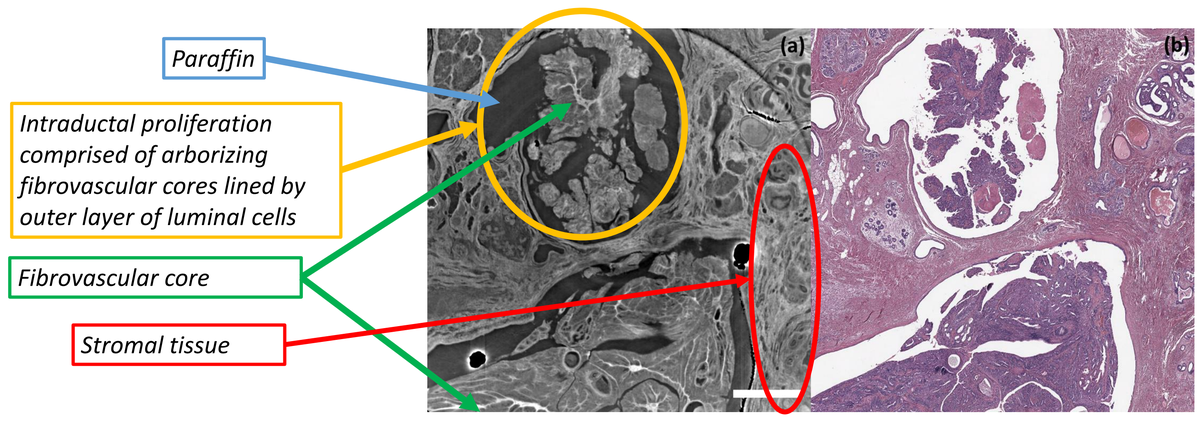
X-ray µCT for Virtual Histology

Computed Tomography at the micrometer scale (µCT) is becoming a viable solution in the field of virtual histology [5-6]. µCT can provide a complete 3D visualization of histological specimens which can be virtually sliced at any point and in any direction. This enables guided sectioning of tissues in histological analysis for selecting the most suitable cutting plane when dissecting specimens. The high sensitivity offered by X-ray phase-contrast technique enhances the contrast between soft tissues in biopsy specimens.

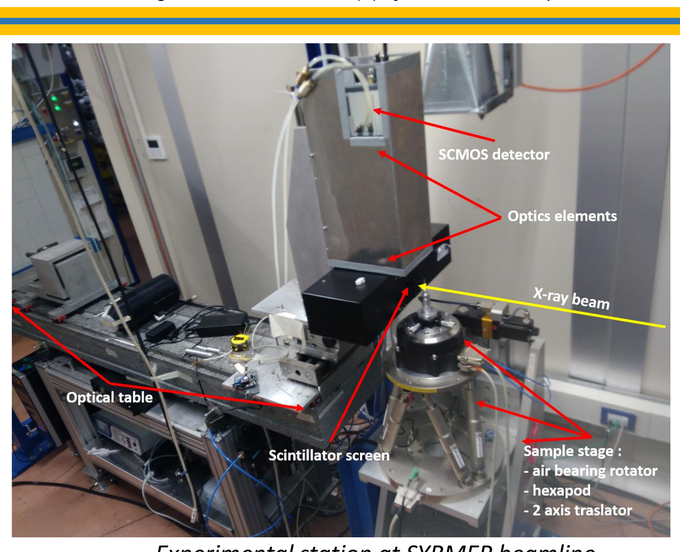


Volume rendering of the imaged sample. In orange virtual planes enabling pathologists to inspect the specimen in any arbitrary direction. Sample size (8.2 mm x 8.2 mm x 2.2 mm)

To be suitable for clinical evaluation, virtual histology images should have a spatial resolution in the micrometer scale to visualize small structures. This must be combined with high signal-to-noise ratio (SNR) to distinguish among similar tissues.



Comparison between X-ray phase-contrast image obtained with 4 µm pixel size (a) and the corresponding histological image obtained with a D-Sight F 2.0 slide scanner (b) of a breast tissue specimen with an intraductal papilloma. Scalebar in (a) is equal to 1 mm



Experimental station at SYRMEP beamline

Experimental setup

- Hamamatsu SCMOS detector coupled with a high numerical optic aperture.
- GGG:Eu scintillator screen.
- Pixel sizes: 1.0, 2.5, and 4.0 µm.
- Propagation distances: 45, 150, 250, 500 and 1000 mm.
- Average energy beam: 24 keV.
- 1800 projections over 180°
- 40 ms/projection

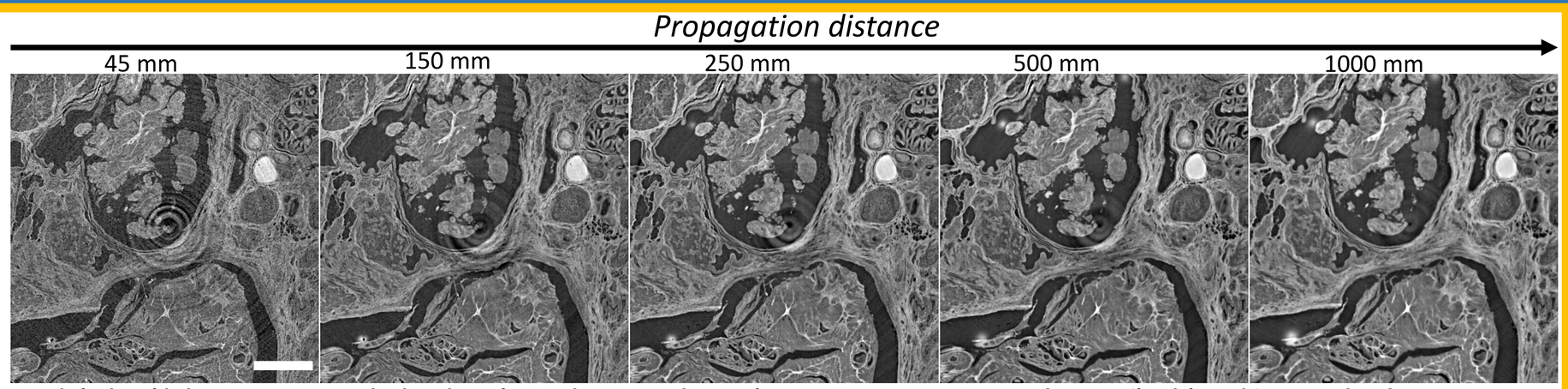
Acquired sample: *surgical specimen of pathologic (**intraductal papilloma**) breast tissues embedded in paraffin*

Results

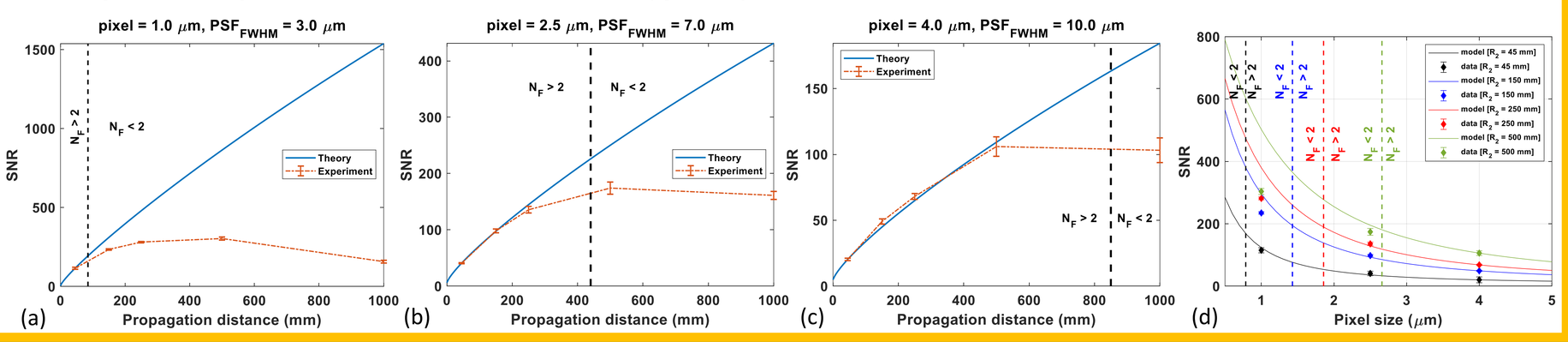
Thanks to the PhR a major SNR increase at larger propagation distances can be observed. **The experimental results match the SNR increase predicted by the model when the near field condition is satisfied** (a threshold N_F=2 is used for illustration purposes) as demonstrated in plots (a)-(c)

Similar consideration can be drawn in (d) where the measured SNR is plotted against the pixel size for all propagation distances.

In all cases deviations between experiment and theory are found when the near-field condition is no more fulfilled i.e. (N_F<2).



Detail of a slice of the breast specimen acquired with pixel size of 4 μm and propagation distance of 45 mm, 150 mm, 250 mm, 500 mm and 1000 mm (from left to right), respectively. At larger propagation distances, up to 500 mm, a major increase in SNR can be observed. Scalebar in the left panel is equal to 1 mm.



Remarks and Perspectives

Experimental results are in good agreement with the theoretical values for the SNR as predicted by the model for large Fresnel numbers (N_F > 2). The model well describes experimental data for all the geometrical configurations enabling to select the most appropriate propagation distance, once selected the pixel size, to generate images with the higher SNR.

This preliminary optimization will serve as **guideline in the choice of the best experimental parameters for** a future larger **virtual histology study**, aiming to assess the invasiveness of malignant diseases in various anatomical districts.

References

[1] Y I Nesterets *et al.*, Journal of Physics D: Applied Physics **51.11** (2018), 115402.
[2] T E Gureyev *et al.*, JOSA A **34.12** (2017), 2251-2260.
[3] L Brombal *et al.*, Physics in Medicine & Biology **63.24** (2018), 24NT03.
[4] L Brombal, JINST **15** (2020), C01005.
[5] J Albers *et al.*, Molecular Imaging and Biology **20.5** (2018), 732-741.
[6] P Baran *et al.* IEEE transactions on medical imaging **37.12** (2018), 2642-2650.