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

The use of Computed Tomography at the micrometre scale (μCT) is becoming a viable solution in the field of virtual histology [1-2]. In principle, μCT can provide a complete three-dimensional visualization of histological specimens which can be virtually sliced at any point and in any direction. This, if not a diagnostic tool per se, can enable guided sectioning of tissues in histological analysis for selecting the most suitable cutting plane when dissecting specimens in order to obtain, e.g., the largest cross-section of the pathological area of interest. One of the challenges of virtual histology is related to the poor X-ray attenuation contrast that exists between the soft tissues commonly encountered in biopsy specimens. In this context, the high sensitivity offered by X-ray phase-contrast imaging techniques, such as propagation based (PB) imaging, can overcome this limitation. To be suitable for clinical evaluation, virtual histology images should have a spatial resolution high enough to distinguish small structures but, at the same time, cover a sufficiently large volume to enable the inspection of biopsy specimens, usually having sizes of 4-5 cm3, in a single or very few μCT acquisitions. Considering the standard dimensions of commercial detectors (4-8 MP), the aforementioned requests translate in acquisitions with pixel size of few microns (1-5 μm). To provide adequate visibility of soft-tissue structures in the virtual slices, such high spatial resolutions must be combined with high signal-to-noise ratio (SNR).
In conventional attenuation-based CT the image noise is strongly dependent on the detector pixel size and the geometrical magnification. Recently published theoretical models [3-4] showed that PB phase-contrast tomography, with the application of phase-retrieval (PhR) in the near field regime, mitigates the dependence of noise on the pixel size bringing to a major SNR gain at small pixel sizes. Similarly, the model predicts a steep increase in the SNR for increasing propagation distances. In two recent papers [5,6] this model was quantitatively compared with experimental results obtained with monochromatic synchrotron radiation and employing a photon-counting detector having a quasi-ideal (box-like) response function. The measured SNR gain due to the PhR application showed a good agreement with the theoretical prediction by varying both the pixel size and the propagation distance. This quantitatively demonstrated that a careful optimization in terms of pixel size and propagation distance is required to fully exploit the advantages of PB and PhR. On the other hand, considering current limitations in the manufacturing process, the level of spatial resolution required by virtual histology cannot be achieved with photon counting detectors. Another limitation in their use comes from the extremely high X-ray fluxes which are needed to provide high SNR at high resolution, that is commonly achieved at synchrotrons by employing white (i.e. polychromatic) beams. These features require the use of small-pixel indirect-conversion detectors, such as CCD or sCMOS, usually coupled with magnifying optical elements, leading to a detector's response function that is far from being a 1-pixel wide function. Both polychromaticity and wide response function represent deviations from the model validated in [6].
In this context, we present a preliminary experimental optimization of propagation distance and pixel size obtained in virtual histology imaging experiments performed at the SYRMEP beamline of the Italian Synchrotron facility Elettra (Trieste, Italy). Experiments were carried out by using a white beam from a bending magnet source with an added filtration of 1 mm of Si, resulting in an average energy of 24 keV. Samples were surgical specimens of pathologic breast tissues embedded in paraffin. The imaging system was a Hamamatsu sCMOS camera (2048×2048 pixels) coupled with a GGG:Eu scintillator and a high numerical aperture optic enabling to adjust the pixel size between 0.9 and 6.5 μm. In the study we used three different pixel sizes: 1, 2.5 and 4 μm. For each pixel size we performed CT scans, collecting 1800 projections over 180o, at 5 sample-detector distance: 4.5, 150, 250, 500 and 1000 mm. For each image, noise and SNR were measured within homogeneous regions of the sample and optimal combinations of pixel size and propagation distance were identified. Experimental results were compared to the theoretical model which has been adapted to the imaging system-specific point-spread function. 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.

Figure 1 Detail of a slice of the breast specimen acquired with pixel size of 4 μm and three different propagation distances: 45 mm (a), 150 mm (b) and 500 mm (c). The slice at largest propagation distance shows a much higher signal to noise ratio with slightly worse sharpness. Scalebar in (a) is equal to 0.5 mm.

Figure 2 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.

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