X-ray phase contrast CT with an amplitude modulated beam: moving towards clinical use

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***Abstract*—X-ray phase contrast (XPC) computed tomography (CT) provides access to an increased contrast for weakly attenuating samples, opening new application pathways. We have developed an XPC-CT approach based on amplitude modulation of the beam, achieved by using a mask with alternating absorbing septa and transmitting apertures placed immediately upstream of the scanned sample. Our approach can be implemented with two distinct sensing mechanisms: beam-tracking and edge illumination, applicable to different imaging scenarios and experimental constraints. Both are compatible with "single-frame" retrieval approaches, thereby enabling fast scans in which the sample is continuously rotated (flyscans). Our group has dedicated the best part of the last decade to developing the technique(s), and more recently has explored their potential clinical use in two applications (the real-time intra-operative scanning of excised breast and esophageal tissue). Here we provide an outlook on how recent technological advances, namely cycloidal and cycloidal-spiral CT, could further improve the method's performance, especially in terms of meeting clinical constraints on scan time.**

***Index Terms*—x-ray imaging, phase-contrast, computed tomography**

I. Introduction

Computed tomography (CT) is a versatile, non-invasive, imaging modality with applications ranging from clinical practice to biomedical research and material science. It can provide 3D information of the internal structure of materials with a spatial resolution covering a wide range of scales (mm to nm). However, it tends to suffer from weak contrast when imaging materials with a low atomic number (e.g., soft tissue).

While conventional CT is based on attenuation, x-ray phase contrast (XPC) CT is based on the phase changes that the x-rays undergo as they traverse the sample. Both effects are described by the complex refractive index, $n = 1 - \delta + i\beta$, where β and δ describe attenuation and phase shifts, respectively. XPC-CT exploits the fact that δ can be up to three orders of magnitude larger than β, which can result in substantially increased contrast, and therefore in the contrast to noise ratio at a fixed noise level. Phase effects can manifest on the pixel and sub-pixel scale; while the former give rise to x-ray refraction, the latter are responsible for the ultra-small angle x-ray scattering contrast channel, which is related to microscopic features in the sample.

II. Amplitude Modulation XPC-CT

Our XPC-CT method is based on amplitude modulation; the x-ray beam is structured into an array of physically separated beamlets created by an absorbing mask placed immediately upstream of the sample [1]. In this configuration, attenuation, phase (refraction), and scattering effects manifest as an intensity reduction, a shift, and a broadening of the beamlets, respectively.

Through the beam tracking sensing mechanism, each beamlet can be directly resolved by using a detector with sufficiently high resolution. Beam-tracking benefits from images in three contrast channels from a single exposure of the sample, which makes it compatible with flyscans. In the second sensing mechanism, edge illumination (EI), the pixels are typically much larger than the beamlets and each pixel receives at most one beamlet. To individually retrieve images in three-contrast channels, a second mask is required (placed immediately upstream of the detector) which acts as an analyzer. It is also necessary to acquire at least three frames per angle, each with a different offset between the two masks. However, we have developed an additional, approximation-based retrieval method for which only a single frame per angle is sufficient, which has been found to perform extremely well on biological samples consisting of similar soft tissues. In this talk, we compare the two sensing mechanisms in terms of their advantages and their limitations.

III. Previous Exploration of Potential Clinical Application

The ability to perform scans in reasonable acquisition times has opened the way to previously inaccessible applications. A key one, which has enabled early experimentation on human patients, is intra-operative specimen imaging; this has so far been trialed on excised cancerous breast and esophageal tissue, using the EI implementation in both cases.

In the context of breast tissue, we targeted Wide Local Excisions (WLEs), for which the clinical problem to be addressed is ensuring that the entirety of the tumor has been removed. An EI XPC-CT system was used in two ways. First, we scanned entire WLEs as they were extracted from patients undergoing breast conservation surgery, to demonstrate that the system could be used in an operational situation without disrupting the clinical workflow. Full-size (≤8 cm) specimens were scanned, with the "single-frame" retrieval approach, in 10

This work was supported by the Wellcome/EPSRC Centre for Interventional and Surgical Sciences (203145/Z/16/Z) and by EPSRC/UKRI (EP/T005408/1 and EP/P023231/1). Additional funding was obtained from the Wellcome Trust (200137/Z/15/Z). CKH was supported by the Royal Academy of Engineering, under the Research Fellowship scheme. PRTM was supported by the Royal Society under the University Research Fellowships scheme. AO was supported by the Royal Academy of Engineering under the Chairs in Emerging Technologies scheme.

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to 15 minutes without compromising the ability to detect tumour margins [2]. The second way, requiring longer scans, was used in a "virtual histology" study, in which the sample was laterally displaced at every projection angle in steps equal to the aperture size over a mask period (a process referred to as "dithering"); this enables us to achieve a resolution of the order of 10 μm over the entire specimens. A wealth of previously undetected features was revealed: alongside the detection of thinner tumor strands, which could to some extent be expected, it was also possible to detect the tissue response to chemotherapy [3]. While this currently requires significantly longer acquisition times, approaches to reduce these are discussed in the next section.

In oesophagectomy operations, we scanned entire oesophagi; the aim of this real-time imaging was the detection of involved margins and staging the tumor already during the operation. Both aims were achieved; as a result, this method has the potential to change patient pathways (for example by allowing the implementation of additional in-room interventions) [4].

IV. Recent advances

The "dithering" approach required to achieve aperture-size resolution has significant advantages when it comes to detecting minute details like tumor margins, strands etc. However, it prolongs scans due to the multiple exposures required at each projection angle, which also imposes a step-and-shoot scan i.e. it is not compatible with flyscans. To overcome this issue, we have been investigating solutions that allow performing EI or beam-tracking XPC-CT scans with sub-period resolution as flyscans, which would make higher resolution levels available to intra-operative specimen imaging.

So far, we have developed two novel approaches: cycloidal CT [5] and cycloidal-spiral CT [6]. These are acquisition schemes where the sample is translated horizontally, in cycloidal, or *both* vertically and horizontally, in cycloidal-spiral, simultaneously with being rotated; only a single exposure per angle is required. Both these schemes are therefore compatible with flyscans, so long as they are implemented with either beam-tracking, or edge-illumination with the "single-frame" retrieval method. Their associated "roto-translation" motion leads to a more evenly distributed spread of the acquired data in the sinogram.

The observation that resolution in an amplitude modulated XPC-CT scan can be realized by translating the sample while it rotates [5-6] suggests cycloidal and cycloidal-spiral approaches could provide a way of improving detection performance of intra-operative scans without exceeding the clinical constraints on scan time. The different implementation considerations for each of these two acquisition schemes will be discussed in the talk.

We will also cover recent work through which we have derived optimal sampling conditions for a cycloidal acquisition, in the sense of the Nyquist-Shannon theorem. Preliminary investigations of the cycloidal scheme at Nyquist-Shannon sampling, based on simulations, were performed. Comparisons with the fully-dithered step-and-shoot acquisitions were also made. These are shown in Fig. 1 and suggest that cycloidal acquisition can indeed yield high-quality μ-CT images, whilst being much quicker than their full sampling step-and-shoot counterpart.

In our talk, we will present the recently developed framework for sampling that complies with the Nyquist-Shannon theorem, show the corresponding results for both the cycloidal- and cycloidal spiral scanning schemes, and discuss their potential for clinical applications of XPC-CT.

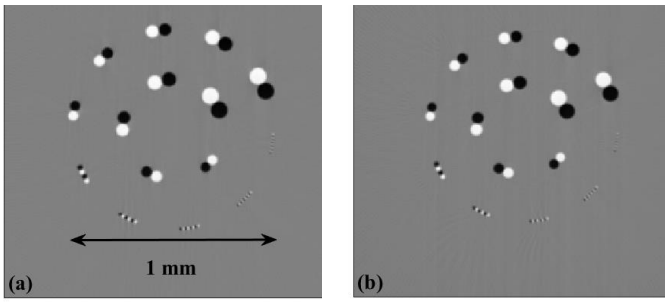

Fig. 1. Simulated results for XPC-CT using the edge illumination sensing mechanism. The axial slices show a numerical resolution phantom with features ranging from 8 μm to 83 μm obtained from dithered data (step-and-shoot) (left) and optimized cycloidal sampling (flyscan compatible) (right).

V. Conclusion

In summary, we have developed an amplitude modulation approach to XPC-CT, compatible with laboratory x-ray sources, that has shown early potential for clinical use, e.g., in the intra-operative imaging of excised breast and esophageal tissue. Two possible sensing mechanisms exist (beam-tracking, edge illumination), and both can be implemented as flyscans thanks to "single-frame" phase retrieval methods. While this implies that clinical constraints for scan times can be met, resolution had so far limited to the period of the sample mask. To increase this, lateral stepping of the sample at each rotation angle used to be required, inevitably prolonging scans. Our investigation into cycloidal and cycloidal-spiral acquisition schemes has led to opportunities for reducing scan times. We expect those schemes to significantly advance the clinical utility of amplitude modulation XPC-CT.

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