Micro-computed tomography optimised for soft tissues: first steps towards early diagnosis of colorectal cancer

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Introduction - One in five patients who suffer from Inflammatory Bowel Disease (IBD) for more than 20 years will eventually be diagnosed with inflammation-associated colorectal cancer (CRC) [1, 2]. Even though CRC is treatable if diagnosed at an early stage, it is the third most lethal cancer worldwide and the second in Europe [3]. Moreover, although IBD patients are usually screened by regular surveillance colonoscopies (annually or bi-annually) and random multiple biopsies, advanced stages of CRC are still reported [1]. To better understand the early stage of CRC, we propose the use of high-resolution computed tomography (μCT) to identify the early onset of structural changes in the gut mucosa. The goal of this study is to investigate if soft tissue-optimised μCT of standard formalin-fixed and paraffin-embedded (unstained) tissue [4], as used in clinical histopathology, can reveal microstructures of the colon in a mouse model for inflammation-associated CRC.

Methods - An azoxymethane/dextran sodium sulphate mouse model [5, 6] is used to mimic the conditions of IBD/CRC in patients. Murine colonic tissue samples have been collected at different stages of CRC and fixed in 10% formal saline. One group of samples was first stained using 25% Lugol's iodine [7, 8] ("stained" group), a diffusible contrast agent that increases X-ray absorption and thus CT image contrast, and embedded in paraffin wax blocks according to standard procedures. The second group of samples was embedded unstained in paraffin wax ("unstained" group). All samples have been imaged using a prototype μCT scanner, provided by Nikon Metrology UK, optimised for soft tissue X-ray contrast imaging [9].

Results and Discussion - Preliminary results show that it is possible to obtain high-fidelity 3D images of the colon (Figure 1: stained, Figures 2&3: unstained), including the underlying mucosal layer structure (Figures 2&3: unstained).

Conclusion and Outlook - 3D high-resolution imaging of the colon using soft-tissue optimised μCT can reveal microstructural details in a mouse model for CRC. Clinical translation will be facilitated as the proposed imaging approach is fully compatible with standard clinical workflows. In this spirit, we will start investigating

abnormalities on the colonic microstructure as precursors of CRC and potential phenotypes for early diagnosis of the disease.
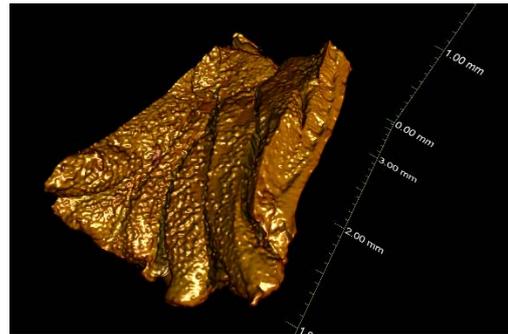

Figure 1: 3D rendering of murine colon tissue sample stained in 25% Lugol's iodine. High contrast and spatial resolution reveal the surface texture and the tissue structure. Voxel size of μCT scan = 5.5 μm.

Figure 2: 3D rending of unstained murine colon tissue sample. Structure and surface texture of the mouse colon can clearly be identified. Voxel size of μCT scan = 3.25 μm.
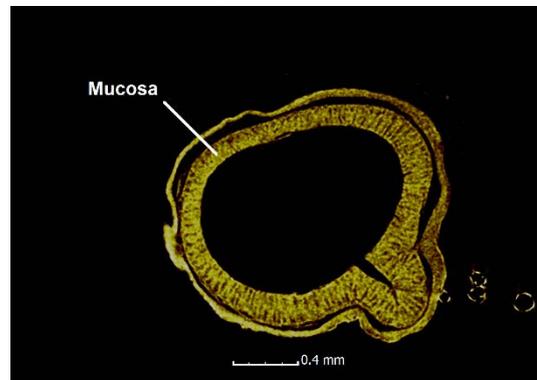

Figure 3: Rendering of unstained murine colon tissue sample. Microstructure is visible in the mucosal layer. Voxel size of μCT scan = 4 μm.

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