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Revealing the Morphology of Coronary Arteries to Design Nanocontainers for Targeted Drug Delivery

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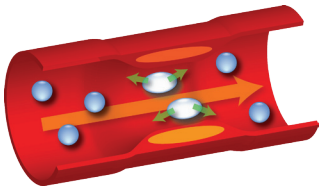
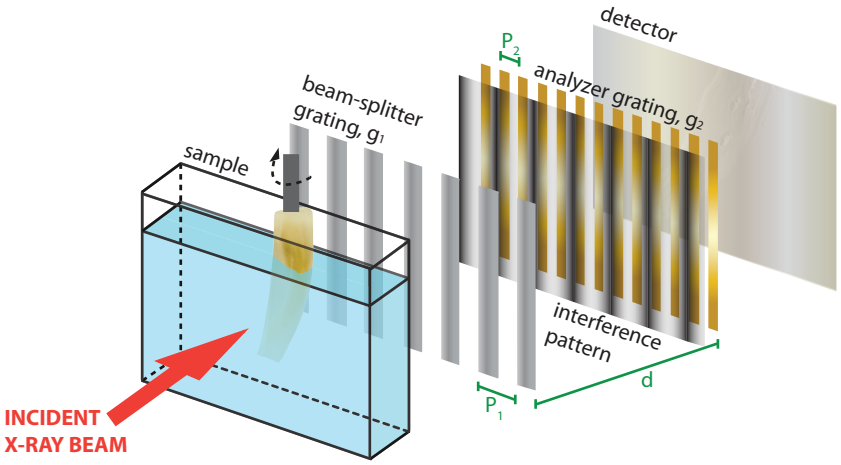
INTRODUCTION



Cardiovasular diseases are the most common cause of death worldwide, causing 30% of all deaths in 2008 [1]. In the acute case of heart attack, treatment by vasodilators such as nitroglycerine is essential to open occluded arteries and restore blood flow before the onset of myocardial ischemia. However, the unspecific systemic actions of such drugs lead to systemic vasodilation and undesirable secondary effects such as hypotension and diminished perfusion of blood to the heart. Localized delivery of such vasodilators to the constricted arteries could be realized using the increased endogenous shear forces as physical trigger [2]. These shear stresses are intrinsically dependent on the morphology of the constricted artery.
Synchrotron radiation micro computed tomography (SRμCT) and SRμCT in phase contrast mode is a tool that facilitates the imaging of biological samples in 3D down to the true micrometer level. We applied this technique to human coronary arteries to obtain specific information about the morphology of a constricted artery to better understand flow dynamics and local shear stresses.

SRμCT IN PHASE CONTRAST MODE

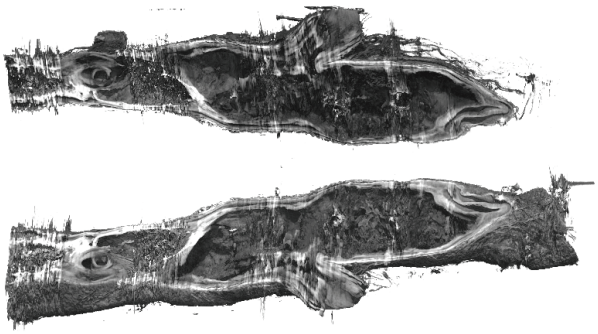
The human coronary artery was first fixed in formaldehyde, decalcified and embedded in paraffin.



Schematic representation of the setup of SRμCT in phase contrast mode [3]. Periodicity of the beam splitter grating, p_1 = 4.785 μm, and analyser grating, p_2 = 2.400 μm. Distance between gratings, d = 481 mm. The beam splitter grating induces fringe patterns in the x-ray intensity distribution to give an interference pattern. The sample induces slight shifts in the interference pattern. The analyser grating is necessary to detect deflection angles too small to be detected by the 5 μm pixel size detector alone. Setup for SRμCT in normal (absorption) mode does not require any gratings.

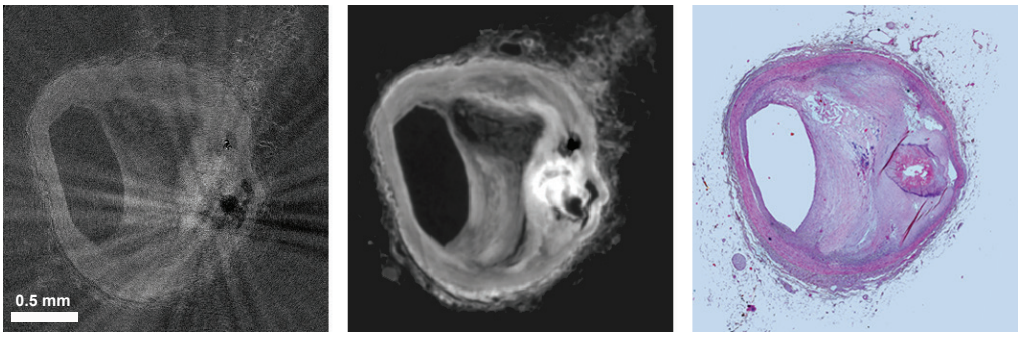
EXTRACTING THE 3D MORPHOLOGY

SRμCT: The area of interest around a bifurcation was recorded using 1441 projections over 360°. Using a photon energy of 14 keV, the pixel size and the spatial resolution corresponded to 2.95 μm and 5.28 μm, respectively [4].
SRμCT in phase contrast mode: 999 projections were recorded over 360°. Using a photon energy of 23 keV, the effective pixel size corresponded to 5.4 μm [5].



Above: 3D representation of a human coronary artery measured with SRμCT in phase constrast mode.
Different tissue types and lumen morpholgy are visible. Blood flow is from left to right.

RESULTS



Images were reconstructed using standard filtered back-projection algorithms and, in the case of phase contrast mode, a modified filter kernel (Hilbert transform). Specific δd values to plaque, muscle and fatty tissues can be assigned in this mode.
Finally, the artery was prepared in 2 to 4 μm lateral slices on glass slides, which were colored with H&E stain.

Left: Lateral slices from a decalcified human coronary artery measured using SRμCT (left), SRμCT in phase contrast mode (middle) and by histological preparation and H&E stain (right).

CONCLUSION AND ACKNOWLEDGEMENT

SRμCT allows segmentation of the inner artery lumen with a higher spatial resolution than SRμCT in phase contrast mode, but it contains strong artifacts from the remaining traces of highly X-ray absorbing plaque. Phase contrast allows for the differentiation between the various tissue types. The anatomical features visible in the tomography data are validated using the highly detailed two-dimensional histology slice. The obvious advantage of the SRμCT over histology is the ability to reconstruct 3D images. Additionally, it is a non-destructive method and avoids artifacts such as tissue pleating. The combined results are used to reconstruct the morphology of the inner lumen wall for modeling of flow dynamics and localized shear stresses.

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[1] Fact sheet N°317, www.who.int. (World Health Organisation, September 2011) [2] M.N. Holme et at, Nature Nanotechnology, accepted [3] T. Weitkamp et al., Opt. Express 13, 6296 (2005)
[4] F. Beckmann et al, Proceedings of SPIE 7078, 70781D (2008) [5] F. Pfeiffer et al, Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment 580, 925 (2007).