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Imaging of the Tumor Vascularization using μCT

Sabrina Lang[1], Marco Dominietto[2], Hans Deyhle[1], and Bert Müller[1]

[1] Biomaterials Science Center, University of Basel, Basel, Switzerland
[2] Institute for Biomedical Engineering, ETH Zürich, Zurich, Switzerland

INTRODUCTION

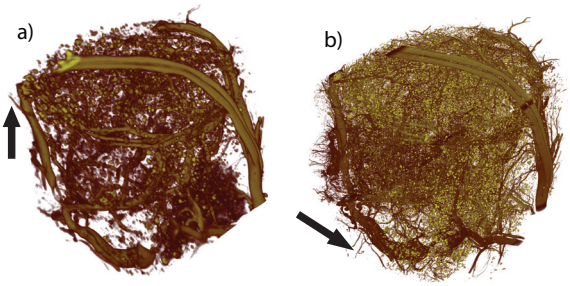
The vascularization of cancerous tissues is of key importance to understand tumor formation, tumor growth and, finally, to successfully treat cancer patients. Morphological parameters such as vessel bifurcation frequencies and distances support the quantification of tumor angiogenesis. The deep understanding of the growth mechanisms will allow developing strategies to prevent or inhibit proliferation of cancerous tissue. Micro computed tomography belongs to the techniques that allow the visualization of the three-dimensional (3D) structure of tumors with the spatial resolution in the micrometer range, including all vessels down to the smallest capillaries. Because the contrast between the vessel tree and the surrounding tissue is often insufficient, staining or casting is applied to the specimens prior to measurement.

METHOD & MATERIALS

Tomography data of the C51 tumor casts, made at the Institute of Zoology, University of Zurich, Switzerland using PU4ii resin [1], were acquired using a SkyScan 1174 (SkyScan, Kontich, Belgium) at 35 kV and 800 mA. Data reconstruction was carried out using a modified Feldkamp algorithm. The same specimens were measured at the TOMCAT beamline, (SLS, PSI, Switzerland) with a pixel lengths of 5.92 μm, 0.74 μm and 0.37 μm using a photon energy of 15 keV. Because the tumor dimensions exceeded the available field of view, local tomography measurements were performed. Global and local data reconstructions are based on a filtered back-projection algorithm.

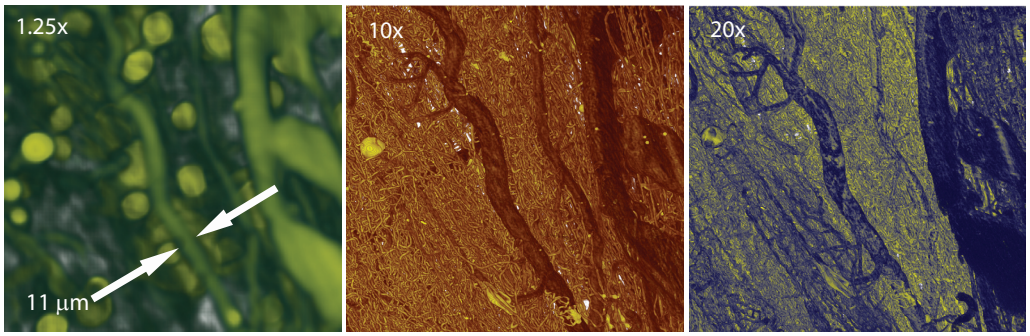
CONVENTIONAL vs. SRμCT

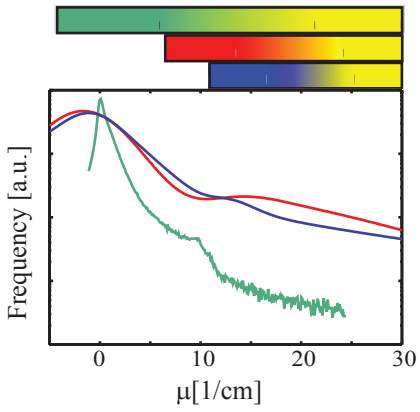
Both conventional and synchrotron radiation-based micro-tomography allow visualizing the 3D structure of an appropriately prepared cast from the vascular network of tumors. The SkyScan 1174 scanner has the advantage of availability combined with relatively short acquisition time (below 1h) and easy operation.



The diameter of the smallest distinguishable vessels was around 30 μm (arrow at (a)). The global tomography at TOMCAT permits to uncover vessels down to a diameter of 15 μm (arrow at (b)). Capillaries down to 3 μm could only be visualized using local tomography.The improvement in the spatial resolution by almost 2 orders of magnitude, however, led to significantly increased acquisition times.

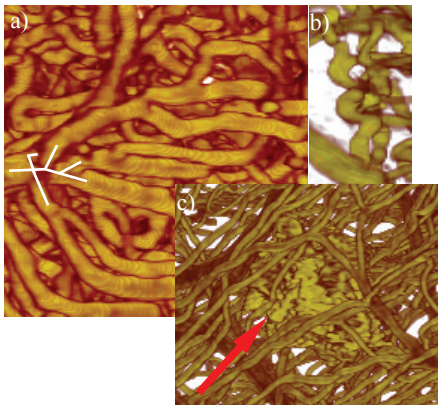
SPATIAL VS. DENSITY RESOLUTION





The images show volume rendered images of the tumor vessels measured at TOMCAT with 1.25, 10 and 20 fold magnification. In the 10 fold magnification tomograms capillaries can be identified, while they were merged with the background in the lower resolution data. Histograms reveal that the improvement in spatial resolution comes at the cost of a reduction in the density resolution. The peaks in the histograms of the 10 fold magnification tomograms are slightly broadened in comparison to the ones of the 1.25 fold magnification. Broadenings resulted from the different optics used. Further improvement of the spatial resolution, as for the 20 fold magnification, did not reveal additional information, but caused decreased density resolution and further reduced the field of view.

TUMOR VESSELS



(a) Strong bifurcation with more than two branches can be found in the tumor vessel system. The vessel show additionally strong deviation in diameter while the diameter for healthy vessel is more or less constant. Many vessels in the cancerous section appear twisted (b), while they are better ordered in the healthy tissue. The casting elastomer penetrated into the cancerous tissue outside the vessels at several locations (c), presumably as the result of vessel wall damages in the necrotic part of the tumor.

CONCLUSION & ACKNOWLEDGEMENT

Using erosion casts, the vessel tree of tumors can be made visible down to the capillary level using micro-tomography in absorption contrast mode. The SkyScan 1174 offers availability for overview scans, where moderate spatial resolution is desired. For high-resolution imaging down to the smallest capillaries, synchrotron radiation sources are better suited. The tomography data can be converted into vectorized format for quantifying the bifurcation networks and vessel shapes. Although the vessel diameters are included in the tomography data, their exact diameter is not directly accessible, because the casting procedure induces shrinkage, which has to be calibrated. Therefore, the morphological parameters including lengths and diameters of differently sized vessels can only be estimated.

We kindly acknowledge Alexandra Ulmann and Eric P. Meyer for the corrosion cast of the vessels and Marco Stampanoni and Federica Marone for their support during data acquisition at TOMCAT.

[1] T. Krucker, A. Lang, E.P. Meyer, New polyurethane-based material for vascular corrosion casting with improved physical and imaging characteristics, Microscopy Research and Technique 69 (2006) 138–147.