3-D Reconstruction of Tumor Vascular Networks

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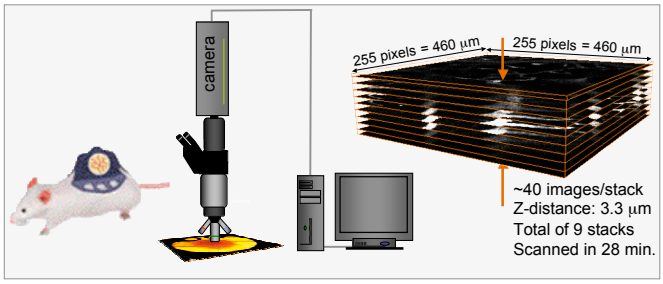
INTRODUCTION

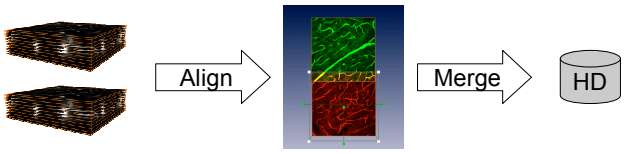
Most solid tumors consist of optically dense tissue. Therefore intravital visualization of its complete vasculature with topological and morphological details is difficult. We propose a method to reconstruct tumor vascular networks using confocal intravital microscopy and a dedicated software system.

EXPERIMENTS



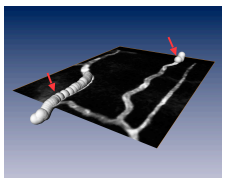
Human squamous cell carcinoma xenograft line (FaDu) were implanted in the skinfold window chamber of a nude mouse Confocal imaging started after 10 days

IMAGE STACKS – ALIGNMENT AND MERGING



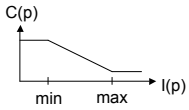
- Blockwise acquired image stacks are aligned – based on grey values or interactively
- All blocks are merged to a single image volume which is stored on disk (*out-of-core*)
- Any subvolume is available for visualization and analysis
- Processing of large data with small memory footprint

VASCULAR MIDLINES – INITIALIZATION

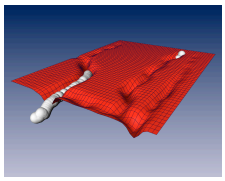


I(p)

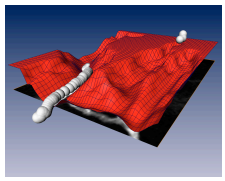
- Anchor points (↘) are selected by user
- At position p, a cost function C(p) is assigned to local Intensity I(p) (user specifies min & max)



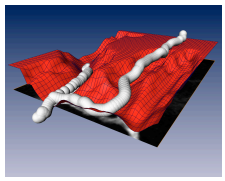
- *Dijkstra Shortest Path* algorithm minimizes ∑ C(p) to compute connection



C(p)



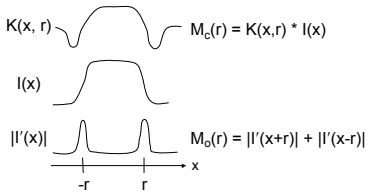
$\sum_{p \in Path} C(p)$

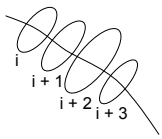


Walk downhill to find connection

MIDLINES - OPTIMIZATION AND DIAMETER FITTING

- A *Snake Model* optimizes the centerlines and fits diameters
- It minimizes ∑ α $E_{ext}(i)$ + (1- α) $E_{int}(i)$ with respect to positions p_i (perpendicular to skeleton) and radii r_i using a gradient descent method
- External energy E_{ext} depends on *Measures of Medialness* (M_c, M_o) which are computed from Intensity I, its derivative I′ and a kernel K



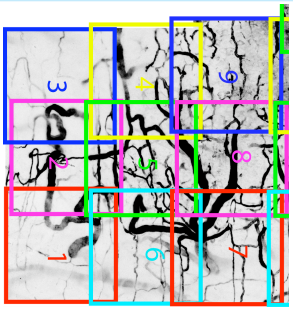


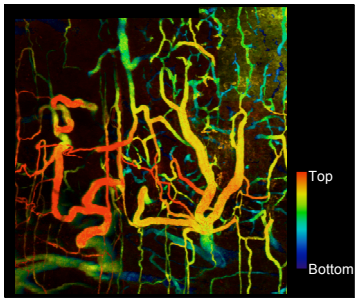
$E_{ext}(i) = -(\lambda M_c + (1-\lambda) M_o)$

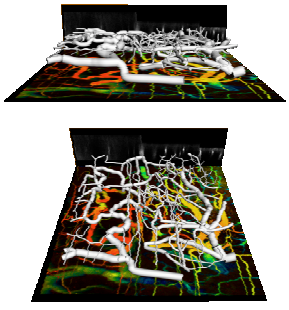
$E_{int}(i) = \beta(p_i - p_{i+1})^2 + (1-\beta)(r_i - r_{i+1})^2$

S. Schmitt, J.F. Evers, C. Duch,M. Scholz, K. Obermayer: New Methods for the Computer-Assisted 3D Reconstruction of Neurons from Confocal ImageStacks. Neuroimage (2004), in press.

RECONSTRUCTED NETWORK







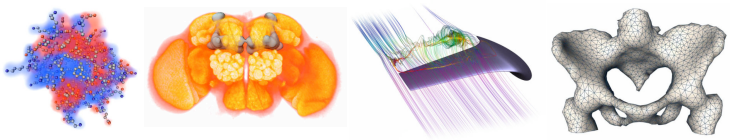
Left: Mosaïk of all fields created from projection of the 9 z-stacks

Middle: the 9 z-stacks merged, color coded for depth

Right: reconstruction of the tumor vasculature with 287 vascular segments, of which 76 are boundary segments, with a mean vascular diameter of 13.8 µm, total vascular length of 23 mm, and volume of 6.6e-3 mm^3

AMIRA

- 3D Visualization
- Geometry Reconstruction
- Developer API
- http://amira.zib.de



CONCLUSION

Reconstruction of tumor vascular networks in optically dense tissue with disorganized topology is possible using semi-automatic software. This application provides a useful tool to help understanding the mechanisms of tumor angiogenesis and tumor growth.

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