# Quantifying the vascular profile of a tumor by 3D Euclidean distance maps

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**Introduction:** The complexity of the vascular morphology of tumors presents a quantification problem to identify vascular changes in MRA studies that image tumor vasculature to understand the effects of treatment. A practical quantification method to analyze the vascular data will considerably benefit these studies. We propose a computationally robust approach that quantifies the vasculature based on the distribution of 3D Euclidean distance from each voxel in the vascularized regions of the tumor to their nearest vessel boundary and show that such a Euclidean Distance Map [EDM] provides a useful quantification measure to monitor the changes in the tumor vasculature.

**Rationale:** The major difference in this approach is that the vasculature is characterized by the region in which the vessel branches are contained as opposed to the anatomical parameters of the vessels such as number of branches and their respective diameters. The rationale for choosing such an approach is that it provides an objective way of studying how the changes in vasculature have altered the spatial distribution of the surrounding region in terms of their relationships to the vessel branches and there by monitor the changes in the vasculature.

**Methods:** Orthotopic xenograft models were grown in female SCID mice by injecting $10^6$ of human breast carcinoma MDA-MB-231 cells into the mammary fat pad of the animal. Animals bearing tumors (~120 $mm^3$) were given different forms of cytotoxic therapy. MR images were acquired pre-, 5 and 10 day post-treatment. To obtain the angiogram of the tumor, pre and post contrast images with Albumin-GdDTPA as contrast agent were acquired on a horizontal bore Bruker Biospec 9.4T Spectrometer using 3D fast low-angle shot (FLASH) imaging sequence with following parameters: FOV: 13x13x13 mm; Matrix: 128x64x64 (zero filled to 128x128x128 for the analysis); Echo time: 2.5 ms; Repetition time: 8 ms; Number of averages: 8. The vasculature was visualized as the difference image between the co-registered pre and post contrast images (Fig. 1b).

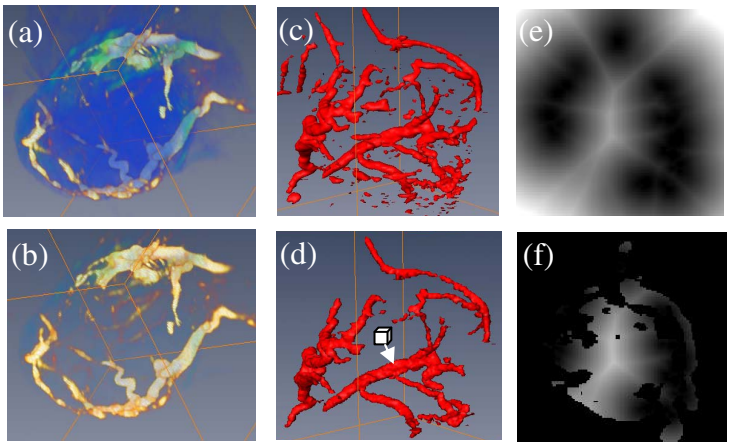


**Fig. 1** (**a**) 3D rendering of the tumor and its vasculature (**b**) vasculature as derived from the co-registered pre and post contrast data (**c**) threshold based segmentation of the vasculature (**d**) noise filtered vascular data in which, EDM - distance to nearest vessel boundary at every voxel, is calculated (**e**) EDM displayed as an image data,- the intensity maps the distance to nearest vessel boundary (**f**) tumor boundary mask applied on the EDM to discard voxels outside the tumor in the histogram analysis

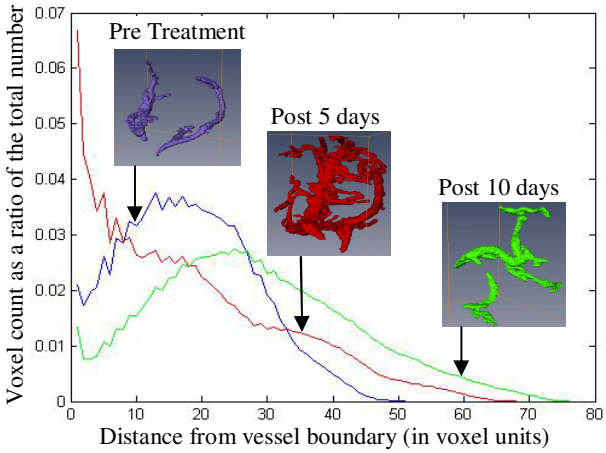


**Fig. 2** Normalized histogram plots of the Euclidean distance maps of the vascularized regions from pre-treatment, 5 and 10 day post treatment data illustrate the progressive changes in the vasculature. Distances are binned at one voxel unit intervals to generate the histogram and the plots are normalized by the area under the curve.

Using proper threshold for the vascular data the vessels were segmented (Fig. 1c) and spurious segments were removed based on their voxel cluster size (Fig. 1d). 3D distance maps (EDM) was constructed by finding the distance from every voxel to its nearest vessel boundary (Fig. 1d,1e). The boundary of the tumor is used as a mask to discard EDM voxels outside of the tumor (Fig. 1f). A normalized histogram of EDM was generated to plot the relative distribution of the distances among the total number of data points in the EDM (Fig. 2). The software for this analysis was developed in Matlab (MathWorks, Inc, USA). Image registration and 3D renderings were performed on Amira software (Visage Imaging, Inc, USA).

**Results:** The EDM analysis was performed to quantitatively display the changes associated with the tumor vasculature from different set of experiments in which the tumors were given various forms of cytotoxic therapy to study their effects. Fig. 1 illustrates the sequence of steps in the analysis. Fig. 2 compares the results of the EDM analysis of the progressive changes in response to the therapy. The observed trend in the voxel population toward larger distances from the vessel boundary indicates the increasing sparseness in the vascular data following the treatment thus providing a means for quantifying its effect.

**Conclusion:** The EDM provides a practical quantification approach to track the progression of changes in the tumor vasculature which can benefit imaging studies that focus on the vasculature to monitor the effects of treatment. The computation time for EDM currently takes less than a minute on a 2.4Ghz processor system with 3GB of memory. Techniques such as EDM try to leverage the computational and memory capabilities of the recent generation of systems to offer new approaches to address image quantification problems.

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