Texture and shape quantification to characterize angiogenesis in tumour tissue

Marco D. Dominietto, Peter Thalmann, Sabrina Lang, Simone E. Hieber, Georg Schulz, and Bert Müller

Biomaterials Science Center, University of Basel, Switzerland.

INTRODUCTION: Derivation of quantitative information descripting tissue morphology and physiology is critical for the detection and staging of a disease, as well as for treatment follow-up.[1] The aim of this work is to present a mathematical framework that explicitly considers the spatial variability within data sets. Such framework consists of two classes of geometrical estimators[2]. The texture class allows estimating the fractal dimension (FD), a measure of the self-similarity at lengths from 50 µm to 10 mm, and the lacunarity (L), which quantifies the relative distribution of substructures within the tissue. The shape class yields measures of the compactness, which describes the deviation of a mass from spherical symmetry, and the signature, which is a measure of the branching (or infiltration) of the tumor into the surrounded healthy tissue.

METHODS: The analysis was applied to tissues of twelve mice injected with C51 tumor cells: Six mice were treated with a pro-angiogenic drug (dimethyloxalylglycine, DMOG) and six with a placebo (saline). We analyzed physiological parameters describing the tumor vasculature derived from magnetic resonance imaging: i) vascular permeability, ii) blood volume distribution, iii) blood flow, and iv) vascular size index (VSI). This analysis was complemented by a detailed study of the vascular architecture using synchrotron radiation-based micro computed tomography (SRµCT).

RESULTS & DISCUSSION: We found significant differences in the FD and L values between treated and non-treated group for both the permeability and perfusion maps (Table 1).

*Table 1: Quantification of treatment effects on FD and L. Values are given as mean±SD; * indicates significant difference between the two groups*

		DMOG	Placebo
FD	pre	2.16±0.18	2.00±0.17
	post	2.58±0.04*	2.07±0.22
L	pre	7.70±4.61	7.86±3.35
	post	6.81±0.37*	3.22±1.06

The FD values increased significantly in response to treatment. A higher level of FD means smaller self-similarity and therefore more chaotic structure, which may reflect angiogenesis, i.e. an expansion of the chaotic capillary network. The L values remained unchanged in the DMOG group and significantly decreased in placebo treated mice. Interestingly, no effect of drug treatment has been found comparing volume averaged values: this illustrates the superior sensitivity of the texture analysis in identifying morphological differences.

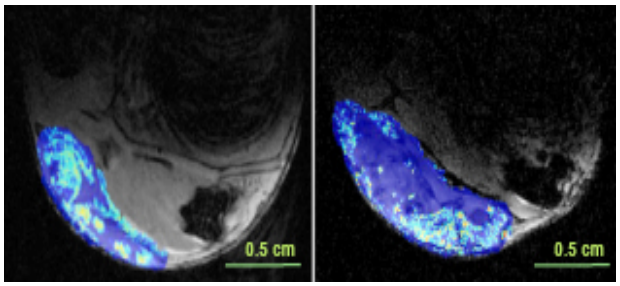

Fig. 1: Blood volume distribution (high value in red, low value in blue) for a mouse treated with drug (L = 6.5, left) and with placebo (L=3.11, right).

The increase in FD values is corroborated by the structural analysis of the tumor vasculature: VSI showed a persistent predominance of capillaries during tumor growth, but no formation of bigger vessels indicating the absence of hierarchical organization. This is in line with the SRµCT results, which reveal a high number of highly tortuous capillaries in C51.

CONCLUSIONS: The use of non-biased mathematical methods enables the quantification of changes in tissue heterogeneity. Such changes can be masked when analyzing volume averaged data sets.

This approach can be easily applied to monitor angiogenic cascade in regenerative treatment of damaged tissues.

REFERENCES:

[1]S. Lang, B. Müller, M.D. Dominietto (2012), *Microvascular Research* ***84****: 314-322.* [2]M.D. Dominietto (2012) *Multimodality approach to study the fractal physiology of tumor angiogenesis*, Lambert Academic Publishing, pp 63-69

ACKNOWLEDGEMENTS: The authors thank M. Rudin, S. Lehmann, and R. Keist for their support.