Computerized image analysis of Glioblastoma vascular network for improving diagnosis and disease prediction

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Background:
In Glioblastoma multiforme (GBM) treatment with Bevacizumab prevents linkage between the vascular endothelial factor (VEGF) and its endothelial receptor thus preventing tumor neoangiogenesis and edema. The response to Bevacizumab is heterogeneous in GBM patients.

Objectives:
To use computer assisted image analysis in order to assess the role of tumors vascular network complexity and of tumor blood vessels shape in predicting response to Bevacizumab treatment in patients with GBM.

Patients and methods:
Retrospective study including 26 patients with progressive GBM treated with Bevacizumab. Tumor were immunohistochemically stained for the endothelial Marker CD31. Images were captured and digitized with a Retiga 2000 camera (QIMAGING, Canada). Vessel network complexity was assessed by the Fractal Dimension (FD) computed using the box-counting method implemented by the Image J program. The roundness of the vascular contours was calculated using the Image Pro Plus vs 7 program (MediaCybernetics, USA) (see figure 1).

FD = 1.4, Roundness = 5.2
FD = 1.53, Roundness = 6.3

Statistical analysis:
Survival analysis was performed using Kaplan Meier curves, and statistical comparison between subgroups were computed using the Log-Rank test. The Cox multivariate test was used to adjust for confounding variables. P values of 0.05 or less were considered to be significant. For the statistical analysis, the SPSS vs. 20 program was used.

Results:
Patients with a more complex vascular network (higher FD) and with lower vascular contours displayed lower survival rates as compared to patients with simpler vascular architectures and more round vessel contours, as shown in figure 2. The Cox multivariate test also confirmed the FD and the vascular countours to independently predict tumor response to Bevacizumab.

Conclusion:
Our study demonstrated that analysis of vascular network complexity and vessels shape may predict response to Bevacizumab treatment in GBM patients.

Figure 1.
A. Low vessel complexity and low roundness
B. High vessel complexity and higher roundness
C. Applying the box counting method to calculate the F.D

Figure 2. Survival analysis