Fractal dimension and vessel complexity in patients with cerebral arteriovenous malformations

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INTRODUCTION:

The fractal dimension (FD) can be used as a measure for morphological complexity in biological systems [1]. A fractal set can be defined as a set, whose FD is greater than its topological dimension which is zero for a point, one for a curve and two for a plane. The aim of this study was to proof the usefulness of this quantitative parameter in the measurement of cerebral vascular complexity. Cerebral arteriovenous malformations (AVMs) are defined by arteriovenous shunting though a nidus of coiled and tortuous vessels, that directly connect feeding arteries to draining veins [2]. Due to the increased number of vessels, the vascular network shows a higher structural complexity. Based on skeletonized MIP images from 3D-TOF MRI data, we quantified the vascular complexity by means of FD using the Minkowski dimension (Dm) [3]. Furthermore, we investigated the relation between FD and the vascular dynamic of AVMs. MIP images from DSC-MRI data were analyzed with respect to contrast media transit, quantified through the maximum slope. A correlation analysis was performed to study if FD can be associated with this physiological parameter.

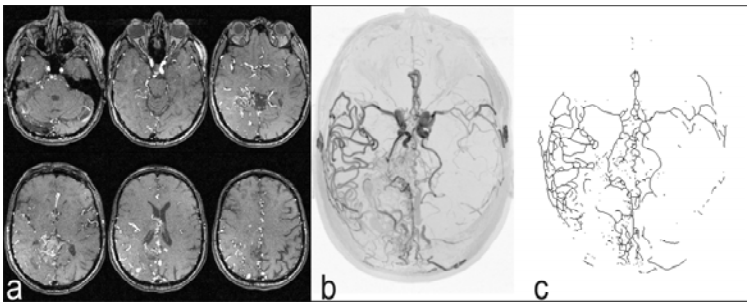

Figure 1: 3D-TOF images (a); MIP images (b); After segmentation and *skeletonizing binary images (c) are obtained that serve as input for the FD analysis. ((b) and (c) inverted view)*

METHODS:

Ten patients (P), seven male, three female, (mean age 44.1±18.5 years) showing a unilateral AVM (8 left sided, 2 right sided), which was confirmed by an experienced neuroradiologist, and ten healthy controls (HC), four male, six female (mean age 51.4±13.1 years) showing no cerebral vascular abnormalities, were included in this study. 3D-TOF MR angiograms of the circle of Willis and vertebral arteries were obtained with the following parameters: TR = 22 ms, TE = 3.68 ms, flip angle = 18°, FOV = 200 mm, phase FOV = 75%, image matrix = 384 x 288, number of slabs = 3, slices/slab = 40; slice thickness = 0.65 mm. DSC-MRI was acquired with a 3D-FLASH sequence (TR = 2.73 ms, TE = 1.02 ms, flip angle = 20°, FOV = 230 mm, image matrix = 320 x 240, slices = 12; slice thickness = 6 mm).All measurements were carried out on a 3T Tim Trio system (Siemens Medical Systems, Erlangen, Germany) using a 12 channel head coil. An affine 12 parameter model was applied to coregister the 3D-TOF data sets to a template (MNI152_T1_0.5mm) resulting in spatially normalized 3D data sets with an matrix size of 364 x 436 x 364 each. To capture the vascular tree and remove the background from the MIP images, a k - means clustering algorithm was applied. Afterwards the images were converted into binary images and skeletonized (Figure 1) using the ImageJ software (Wayne Rasband, National Institutes of Health, USA). Both, the images from the patients and from the controls were divided into two halves for the FD analysis with a resolution of 182 x 436 each. MIP DSC-MRI data from patients were also divided into two halves where the maximum slope of the contrast media was evaluated for each half by differentiation the contrast tracer concentration-time curve. The Minkowski or Minkowski-Bouligand dimension was evaluated according to [4]. A 2 x 2 mixed-design ANOVA test with a within-subjects factor of hemisphere (for patients: AVM, no AVM, for healthy controls: left, right) and a between-subject factor of group (P, HC) was performed to reveal significant differences in FD between groups. A correlation analysis was performed including FD values of the hemisphere with and without AVM and the maximum slope of contrast media transit in the hemisphere with and without AVM.

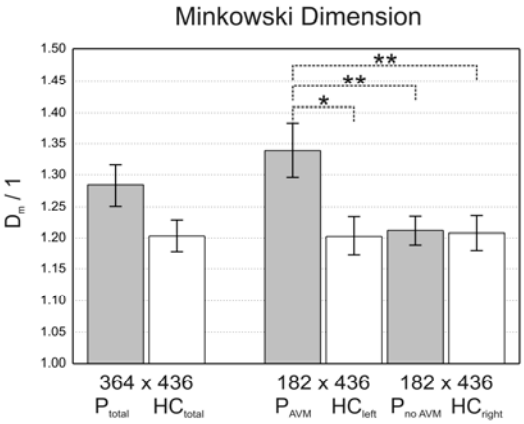

Figure 2: D_m *comparing patients* (P_{total}) *with healthy controls* (HC_{total}) *for the whole image, and both hemispheres* (P_{AVM}, $P_{no\ AVM}$, HC_{left}, HC_{right}). * $p<0.05$, ** $p<0.01$

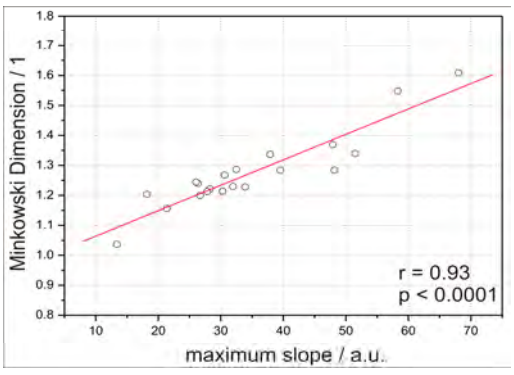

Figure 3: *Correlation between FD and the maximum slope of contrast media transit from DSC-MRI data.*

RESULTS:

Posthoc-analysis of ANOVA using Bonferroni adjustment for multiple comparison indicated that patients had significant higher FD values in the hemispheres with AVM compared with the hemisphere without AVMs ($p = 0.002$). Healthy controls had similar values for FD in both hemispheres with no significant differences in FD ($p = 0.892$). No significant differences were observed comparing the non affected hemisphere of patients with healthy controls (HCleft: $p = 0.918$, HCright: $p = 0.872$) but significant differences when comparing the patients hemisphere with AVM with the hemispheres of healthy controls (HCleft: $p = 0.020$, HCright: $p = 0.024$) (Figure 2). Patients compared with controls showed a statistical trend of elevated Dm ($p = 0.067$) in patients for the whole image. A strong correlation was found between values of FD and the maximum slope of contrast media transit from DSC-MRI data ($r = 0.93$, $p < 0.0001$) (Figure 3).

CONCLUSION:

In this work we set out to proof the usefulness of FD as a quantitative parameter in the measurement of cerebral vascular complexity. Our results indicate that FD, assessed by the Minikowski dimension, is related to structural vascular complexity due to feeding arteries in patients suffering from AVM. We successfully demonstrated that FD is significantly higher in the hemispheres with AVM compared to the hemispheres without AVM. The correlation between FD and the slope of the contrast tracer transit in DSC-MRI data underlines the physiological significance of this parameter. FD analysis is a simple and robust technique that may yield an objective measure for vascular complexity. However, further studies are needed including more patients to determine the sensitivity of this method.

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