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Original article

Hemodynamic parameters and vessel tortuosity: an investigation with a mesenterial vascular network

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Abstract

Purpose: The effect of hemodynamic parameters on vessel tortuosity remains unclear. Here we investigate the correlation of tortuosity with a set of hemodynamic parameters in a mesenterial vascular network.
Methods: A mesenterial vascular network of 389 vessels (131 arteries, 132 veins, and 126 capillaries) was imaged. Eleven hemodynamic parameters were measured (pressure, wall shear stress, diameter, blood velocity and flow, viscosity, haematocrit, partial oxygen saturation, oxygen saturation, wall thickness, and local vessel density). Tortuosity was assessed quantitatively with a validated algorithm and correlation computed with subsets of hemodynamic parameters selected by a lasso regressor.
Results: Results suggest that tortuosity is related to pressure, wall shear stress, diameter, blood velocity, viscosity, partial but not full oxygen saturation, and wall thickness for the arteries; diameter, blood flow, hematocrit, and density for the veins; and viscosity (but not hematocrit), partial and full oxygen saturation, and density for the capillaries. The combination of hemodynamic parameters correlating best with tortuosity is the set of all parameters except density (r = 0.64, p < 0.01), using as tortuosity definition the set of tortuosity features (geometric measures) correlating best with a single hemodynamic factor for the arteries.
Conclusion: This pilot suggests two general conclusions. First, the quantitative definition of tortuosity (*i.e.*, the set of geometric features adopted) should be tuned to the

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specific data and problem considered. Second, tortuosity is caused by a combination of hemodynamic factors, not a single one.

Keywords: hemodynamic factors, physiogenesis of tortuosity, tortuosity models, vascular tortuosity

1. Introduction

Vessel tortuosity is a qualitative clinical index associated with the degree of bendiness of a vascular network or segments thereof. Changes in retinal vessel tortuosity have been associated with several conditions, both systemic and eye-specific, and several computational models of tortuosity developed.[1–5] The physiological causes of tortuosity are, however, not completely understood. In this paper, we investigate the correlation between a set of 11 hemodynamic factors and vessel tortuosity, estimated by a validated algorithm, in a mesenterial vascular network.

Several studies have shown the association of tortuosity with elevated blood pressure.[6–10] Kylstra *et al.*[6] modeled the deformation of a blood vessel experimentally using a latex tube resting on a horizontal surface. They measured shape changes of the tube following variations of the pressure inside the tube. They observed that diameter changes dominate over tortuosity ones as long as the pressure remains below a certain level; beyond this level, buckling occurs and tortuosity increases more rapidly than diameter.

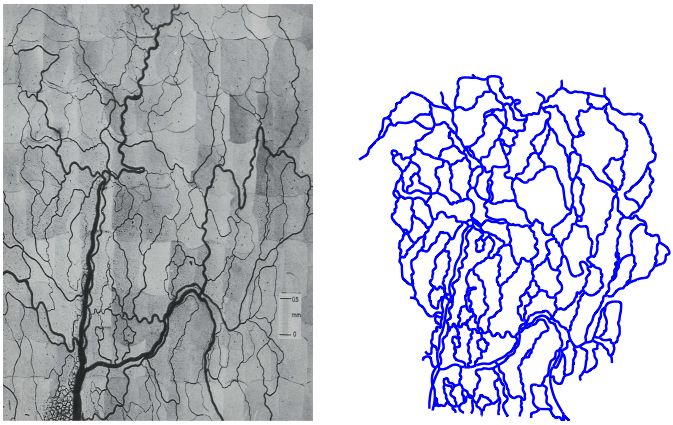
Growth has also been investigated as a possible cause of increased tortuosity. In particular, when a vessel has its endpoints fixed, growth beyond a certain level would inevitably lead to buckling and tortuosity. Jackson *et al.*[7] investigated this aspect thoroughly with rabbit carotid arteries *in vivo* and found that tortuosity increased only after very potent growth inputs. Their explanation was that most arteries, for instance, exhibit a substantial *in-situ* axial stretch of 40% to 60%, thus needing to offload this axial strain before buckling. In order to investigate the consequences of a partial offloading of longitudinal tension on the shape of vessels, they reduced the axial stretch in rabbit carotid arteries from 60% to 30% using interposition grafts. They observed the following:

1. No normalisation of axial strain within 12 weeks;

2. All the arteries displayed tissue growth and remodelling that caused tortuosity (despite persistent and lower axial stretch); and

3. Structural changes, namely an enlargement of the internal elastic lamina, a key layer of the vessel wall[11] including holes (*fenestrae*), which contribute to the overall stiffness of a vessel.

Repeating the same experiment with an inhibitor preventing changes in vessels structure, they observed no tortuosity, suggesting that structure is strongly related to tortuosity. This important observation led to complex mathematical tortuosity models that take into account the tissue surrounding the vessel wall.[8]



(a) *(b)*

Fig. 1. (a) Mesentery network; (b) full-resolution network reconstruction after spline interpolation from sampling points.

Recently, Hathout and Do[9] investigated which shape properties distinguish physiological from abnormal tortuosity. Based on an optimality criterion, they found that tortuous vessels deviating from a sine-generated curve (a modified sinusoid) are abnormal. The chosen criterion serves to minimize the average curvature per unit length, which minimizes the changes of direction for the blood flowing through the tortuous vessel.

2. Materials and methods

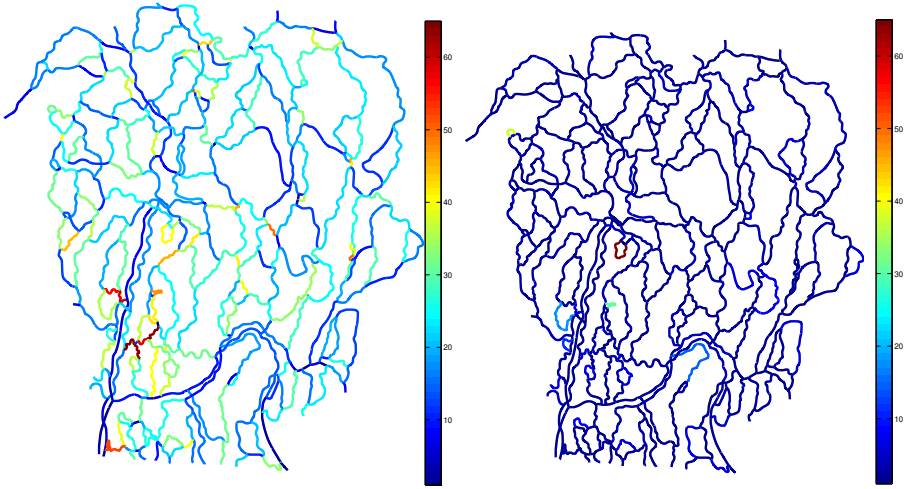
2.1 Materials

A mesenterial vascular network including 389 vessels (131 arteries, 132 veins, and 126 capillaries) was made available at Charité - Medical University of Berlin (Berlin, Germany) and imaged. As shown in Figure 1a, the network contains a variety of tortuosity levels and is therefore suitable as a data source for our study. For each vessel, 11 hemodynamic parameters were measured or simulated: pressure (Pre), wall shear stress (Wss), diameter (Dia), blood velocity (BV), blood flow (BF), viscosity (Vis), hematocrit (Hem), partial oxygen saturation (PO2), oxygen saturation (SO2), wall thickness (Wt), and local vessel density (Den).

2.2 Methods

The vessels in the image were sampled manually at regular intervals and the sample points interpolated by cubic splines to obtain an analytical model of the whole network (Fig. 1b).

Tortuosity was computed automatically using an algorithm reported elsewhere.[5]



(a) *(b)*

Fig. 2. Tortuosity maps obtained by colour encoding the mean curvature at spatial scale 1 (a) and 10 (b) .

Briefly, the algorithm computes the curvature analytically from the parameters of the spline reconstruction of the vessels, then computes three tortuosity features (mean and max curvature, and density of inflection points) at ten spatial scales, resulting in a pool of 30 features from which the lasso regressor selects by cross-validation the subset correlating best with hemodynamic parameters, as described below.

To set the maximum spatial scale to consider, we plotted tortuosity maps for each tortuosity feature (see example in Fig. 2; tortuosity is encoded by color). Vessel density was measured as the ratio of the total number of vessel pixels in a 1000×1000 square region to the area of the region in pixels. The region size was determined empirically. Vessel width was not taken into account. An example of a density map is shown in Figure 3.

Correlation was computed between tortuosity and hemodynamic factors, both individually and in combination, using a lasso-based regressor[12] to identify weights automatically. Associations were tested in two ways:

1. *Experiment (1):* Finding the definition of tortuosity (*i.e.*, the set of geometric features) best associated with each individual hemodynamic parameter; and

2. *Experiment (2):* Finding the combination of hemodynamic parameters best associated with a tortuosity definition (*i.e.*, the subset of features from the 30-strong pool identified by the lasso regressor).

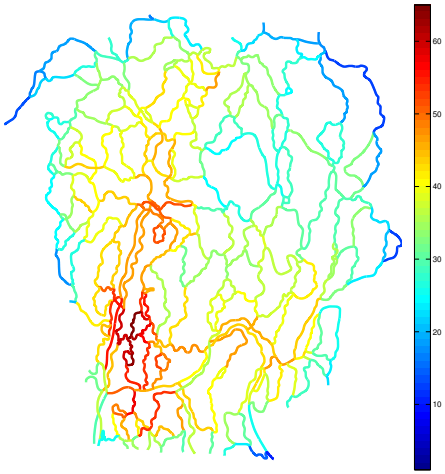


Fig. 3. Density map of the mesentery network in Figure 1b.

3. Results

Table 1 reports the correlations related to Experiment (1). These results suggest that tortuosity is related to: pressure, wall shear stress, diameter, blood velocity, viscosity (although the correlation with haematocrit is not as high as expected given previous studies), partial but not full oxygen saturation, and wall thickness for the arteries; diameter, blood flow, hematocrit (for viscosity correlation is lower), and density for the veins; viscosity (but not hematocrit), partial and full oxygen saturation, and density for the capillaries.

The motivation behind Experiment (2) is that correlations between each tortuosity feature and each hemodynamic factor (not reported in detail due to space limitations) are typically low (*i.e.*, < 0.3), suggesting that tortuosity is caused by a combination of hemodynamic factors, not a single one. To investigate, we ran exploratory experiments to determine the combination of hemodynamic factors correlating best with a specific tortuosity definition. We observed that, using as tortuosity definition the combination of tortuosity features giving the highest correlation with a single hemodynamic factor for the arteries, the best combination of hemodynamic parameters is the set of all parameters except density, for which correlation reaches 0.64.

4. Discussion

It is worth noting that the definition of tortuosity found automatically by the lasso-based regression, *i.e.*, which geometric features of the vasculature are included in the tortuosity model, changed with the set of hemodynamic parameters and vessel type. It is likely that this adaptation occurs to accommodate the different structural char-

Table 1. Experiment (1): Correlation measures of the best combination of tortuosity features with each hemodynamic parameter separately. "NS" replaces correlations whose p-value was greater than 0.01.

	Pre	**Wss**	**Dia**	**BV**	**BF**	**Vis**	**HEM**	**PO2**	**SO2**	**Den**	**Wt**
Art	0.46	0.48	0.48	0.45	0.37	0.47	0.38	0.47	0.26	NS	0.48
Vei	NS	0.26	0.47	0.24	0.51	0.33	0.41	0.23	0.28	0.49	0.39
Cap	NS	0.38	0.36	NS	0.29	0.50	NS	0.46	0.45	0.41	NS

acteristics of the blood vessels (arteries, veins, and capillaries are functionally and structurally different) and, potentially, the different impact of the specific hemodynamic factor on tortuosity. Therefore, results seem to suggest that *the definition of tortuosity should be tuned to the specific vascular data considered, which is best done by an adaptive algorithm*. This departs from the prevailing approach to modeling tortuosity, which aims to determine a one-fits-all definition. Results also indicate that *tortuosity is caused by a combination of hemodynamic factors, not a single one*.

This pilot study has several limitations. First, the vascular data available for this study are specific to the mesentery and do not include retinal vessels; in spite of this, we feel that our results may provide initial insights into the physiogenesis of tortuosity in the retina, to be tested by further, specific work. Second, a more thorough statistical analysis (beyond correlation) is needed. Third, the correlations found in Experiment (2) may be arguably due to the specific (incomplete) set of hemodynamic parameters considered, and could be improved considering further parameters.

5. Conclusions and future perspectives

We have presented a pilot study of the correlation of vessel tortuosity, estimated with a validated automatic algorithm, with a set of hemodynamic parameters. The main overall conclusions are that the quantitative definition of tortuosity (which geometric features to include) should be tuned to the specific data and problem considered, and that tortuosity is most likely caused by a combination of hemodynamic factors, not a single one. Further studies are needed to confirm our findings, including a more detailed statistical analysis and retinal vascular networks.

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