Retinal Blood Vessels Tortuosity Measurement

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***Abstract*— The degree of retinal blood vessels' tortuosity may indicate the progression of various diseases, such as hypertension or diabetic retinopathy. Therefore, observing the changes in tortuosity levels in retinal fundus images can be an effective biomarker for diagnosing diseases. However, tortuosity assessments performed by ophthalmologists are usually subjective and time-consuming. Thus, there is a need for a universally accepted tortuosity measurement standard. Several studies have proposed parameters or methods to measure blood vessel tortuosity, but these methods still have some drawbacks that can be improved to better describe tortuosity both in retinal arteries and veins. For that reason, this study aims to propose tortuosity measurement parameters that can increase the correlation between tortuosity assessments from ophthalmologists and automatic tortuosity measurement results. This research led to the development of a combined parameter incorporating some features that are included in previous studies, such as the comparison of arc length and chord length, as well as the angle values at the critical points of the curve structure. The proposed parameter has been applied to a retinal blood vessels dataset that consists of 60 fundus images (30 artery images and 30 veins images with similar length and caliber). The automatic measurement of each image's tortuosity level are compiled, ranked, and compared to the ground truth tortuosity ranks of each image provided in the dataset. The proposed parameter for retinal blood vessels tortuosity measurement achieved a Spearman rank correlation coefficient of 0.886 for arteries and 0.884 for veins.**

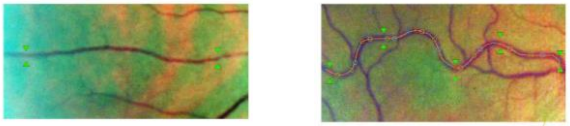
Keywords—tortuosity, blood vessels, correlation

I. INTRODUCTION

Tortuosity refers to the degree of tortuousness (twists and turns) of a curve structure. This property can be found in various curve structures in the human body, such as blood vessels and nerves.

The eye is the only organ in the human body that allows direct, non-invasive viewing of body blood vessels. Fundus photography can be easily done to observe any changes in retinal blood vessels. Changes in blood vessels that may lead to tortuosity may indicate the progression of some underlying systemic diseases.

Normally, retinal blood vessels appear as straight or slightly curvy lines. However, systemic or vascular diseases may cause blood vessels to be tortuous, which appear as curvy lines with more twists and turns (Fig. 1). The low tortuosity and high tortuosity retinal blood v Several studies suggest that elevated tortuosity in blood vessels may be associated with diseases such as diabetic retinopathy, hypertensive retinopathy, retinal vascular occlusions, and other diseases. Rousso and Souka [1] stated that dilated and tortuous retinal veins are usually associated with diabetes, hypertension, cardiovascular disease, anemia, arteriosclerosis, sickle cell disease, and other vascular diseases. Furthermore, tortuous and dilated retinal veins are usually present before and during the event of vascular occlusion. On the other hand, tortuous retinal arteries may also be associated with systemic vascular diseases.



(a) (b)

Fig. 1. Fundus image of retinal blood vessels, (a) as retinal blood vessel with low tortuosity and (b) as retinal blood vessel with high tortuosity (images from retinal tortuosity dataset in [8])

Diabetic retinopathy (DR) is one of the most common complications of diabetes, which the progression can be observed from the changes in retinal blood vessels tortuosity. Several studies suggested that retinal vascular tortuosity is sensitive to diabetes-related hemodynamic changes, including impaired blood flow, endothelial dysfunction, and increased production of VEGF (Vascular Endothelial Growth Factor). To find out more about the association of retinal vascular tortuosity with DR, Sasongko *et al.* [2] conducted a study to compare the DR patient's retinal vessel tortuosity with the severity of the patient's disease. The study states that patients with diabetes have retinal vessels that are more tortuous compared to patients without diabetes. In patients with diabetes, an increased degree of retinal artery tortuosity is associated with early and intermediate DR. Therefore, it can be concluded that retinal vascular tortuosity may be an early indicator of microvascular damage in diabetes. Hence, tortuosity of the retinal blood vessel may be a good biomarker to identify, predict, or monitoring patients for potential retinal and systemic risk [1].

The assessment of retinal blood vessels' tortuosity degree is usually done by ophthalmologists based on the difference in length, width, and number of turn curves between the patients' retinal blood vessels and normal blood vessels. Due to the differing experiences of ophthalmologists when assessing tortuosity, this results in subjective, inconsistent, and time-consuming assessments [3]. Therefore, there is a need to set a standard tortuosity measurement method that is universally accepted.

Some studies have proposed tortuosity measurement methods for retinal blood vessels. However, there are some drawbacks. For example, some of those methods only assessed tortuosity in certain aspects, such as the method proposed by Goh *et al.* [4] which only measured tortuosity from the angle variation of the blood vessels curve structure. Other than that, some methods were unable to produce an equal correlation between ophthalmologists' assessment and proposed measurement methods for arteries and veins. Therefore, a new tortuosity measurement method is needed to accurately capture the structural features of the vascular

curves and also produce equally high correlation values between the arteries and veins.

II. Tortuosity Measures

In clinical practice, ophthalmologists usually assess blood vessels' tortuosity degree by observing the number of convexity changes in the curves and the amplitude in each turn curve. A study done by Ramos et al. [3] showed that parameters such as neovascularization, vessel width, and the distinction between arteries and veins also play a role in determining how tortuous the retinal blood vessels are.

By following how doctors assess and define tortuosity, these are the several studies that proposed their methods in automatic retinal blood vessels tortuosity measurement.

A. Chandrinos et al. [5]

Chandrinos *et al.* proposed a tortuosity measurement metric based on local angle changes of blood vessels segment. For every pixel in the curve, P, the pixels that lie a set number of pixels behind and ahead of P (P-s and P+s) will form two vectors with P ((P-s, P) and (P, P+s)). Those two vectors will then be normalized and their dot product will be formed. Then, the inverse cosine of the dot product will be used to calculate the angle of each pixel. The tortuosity index of this study equals the average of the angle change calculated over the length of the vessel in reasonably discrete steps. The tortuosity metric is defined as in (1),

$$\mathrm{MAC} = \frac{1}{t_{length}-(2*step)} * \sum_{n=step}^{t_{length}-step} \arccos(UV(P_{n-\sigma step}, P_n)\cdot UV(P_n, P_{n+step})) \quad (1)$$

where t_{length} stands for the length of the curve and UV stands for unary vector.

Since this tortuosity metric is an angle-based metric, it can sometimes assign the same tortuosity value to two curves with different shapes that humans perceive as having different tortuosities, but with the same angle variation. Furthermore, vessel segments that lack direction variation do not contribute to tortuosity measurement.

B. Bullitt et al. [6]

Bullitt *et al.* proposed a tortuosity metric based on the number of inflection points in a curve. The inflection point is defined as a locus that exhibits a minimum of total curvature, or the point where the normal and binormal axes of the Frenet frame change orientation close to the π radian. An angle change of one π radian corresponds to a change in the curve's curvature sign. The tortuosity metric proposed in this study is defined as in (2),

$$\mathrm{CM} = (n_{ic}+1)\frac{L_x}{L_c} \quad (2)$$

where n_{ic} stands for the number of inflection points, L_x stands for chord length, and L_c stands for arc length.

Metrics that are solely based on inflection points sometimes produces inaccurate tortuosity value results. This is due to the inability to differentiate between high and low-amplitude curves. Additionally, the number of inflection points is not the only factor humans consider in evaluating tortuosity.

C. Hart et al. [7]

Hart *et al.* proposed a few tortuosity metrics, such as total curvature and total squared curvature. By defining curve $C = (x(t), y(t))$ on the interval $[t_0, t_1]$, these are some equations of the components used to construct the tortuosity metrics.

1) Arc length

$$\mathrm{s}(C) = \int_{t_0}^{t_1} \sqrt{x'(t)^2+y'(t)^2}\, \mathrm{d}t \quad (3)$$

2) Chord length

$$\mathrm{chord}(C) = \sqrt{\left(x(t_1)-x(t_0)\right)^2+\left(y(t_0)-y(t_1)\right)^2} \quad (4)$$

3) Curvature

$$\kappa(t) = \frac{x'(t)y''(t)-x''(t)y'(t)}{[y'(t)^2+x'(t)^2]^{\frac{3}{2}}} \quad (5)$$

4) Total curvature

$$\mathrm{tc}(C) = \int_{t_0}^{t_1} |\kappa(t)|\, \mathrm{d}t \quad (6)$$

5) Total squared curvature

$$\mathrm{tsc}(C) = \int_{t_0}^{t_1} \kappa(t)^2\, \mathrm{d}t \quad (7)$$

These components are used to form several tortuosity measures such as $\mathrm{s}(C)/\mathrm{chord}(C)-1$, $\mathrm{tc}(C)$, $\mathrm{tsc}(C)$, $\mathrm{tc}(C)/\mathrm{s}(C)$, $\mathrm{tsc}(C)/\mathrm{s}(C)$, $\mathrm{tc}(C)/\mathrm{chord}(C)$, dan $\mathrm{tsc}(C)/\mathrm{chord}(C)$. The experiments showed that the metric $\mathrm{tsc}(C)$ is the best choice for tortuosity measure, and was the closest to the ophthalmologist's notion of tortuosity.

Curvature-based tortuosity metrics may produce smaller tortuosity values for curves that may be perceived to be more tortuous. Additionally, these metrics do not include changes in curvature signs as one of the parameters, which ophthalmologists usually consider when evaluating tortuosity.

D. Goh et al. [4]

Goh *et al.* proposed a tortuosity measurement metric based on the number of direction changes. The direction change of each pixel in the curve is calculated by forming vectors of each pixel with the fifth pixel point before and ahead of the pixel. The steps to calculate the angle of the direction change can be seen in (8) and (9), and the direction of the vessel can be calculated with the formula seen in (10),

$$\boldsymbol{v}_{i+n} = \boldsymbol{d}_{i+n} - \boldsymbol{d}_i \quad (8)$$

$$\boldsymbol{v}_{i-n} = \boldsymbol{d}_{i-n} - \boldsymbol{d}_i \quad (9)$$

$$\theta(i) = \arccos(\boldsymbol{v}_{i+n}\cdot\boldsymbol{v}_{i-n}) \quad (10)$$

where $\boldsymbol{d}_i$ is the coordinate of the i^{th} centerline point of the vessel, $\boldsymbol{d}_{i+n}$ *and* $\boldsymbol{d}_{i-n}$ are the coordinates of the $(i+n)^{th}$ and (i-

n)[th] centerline point of the vessel, and θ(*i*) is the angle of the i[th] centerline point of the vessel.

In this study, the angle threshold is set to π/6, thus the tortuosity metrics formula is defined as in (11),

$$\mathrm{TN} = \sum_{i=1}^{n} \left(\theta(i) \geq \frac{\pi}{6}\right) \tag{11}$$

where n is defined as the number of the vessel's centerline pixels.

Similar to the metric proposed by Chandrinos *et al.*, this angle-based tortuosity metric may give inaccurate results due to the shape of the curves. In addition to that, the metric proposed in this study includes the use of a threshold in filtering the angle value, further diminishing the contribution of vessel segments with angle variation that is lesser than the threshold.

E. Grisan et al. [8]

Grisan *et al.* proposed a tortuosity measurement method based on the tortuosity density. This study defines a curve as a set of turn curves as the curvature of the curve equals zero. Once the curve is divided into *n* turn curves, the proposed tortuosity metric can be defined as in (12),

$$\tau(s) = \frac{n-1}{n} \frac{1}{L_c} \sum_{i=1}^{n} \left[\frac{L_{cs_i}}{L_{xs_i}} - 1\right] \tag{12}$$

where *n* is defined as the number of turn curves, L_c is the arc length, L_x is the chord length, L_{csi} and L_{xsi} are the arc length and chord length of each turn curve. This metric has a dimension of 1/*length* that may be interpreted as the tortuosity density.

This metric is dependent on the curve scale, so two curves with similar curvature but different sizes will produce two different tortuosity values. When this metric is used to calculate retinal fundus global tortuosity, short vessels with high tortuosity will increase the tortuosity of the entire image. In fact, those short vessels might appear insignificant compared to other vessels in the image.

F. Bribiesca [9]

Bribiesca proposed a tortuosity measurement method based on chain coding. Every curve segment of the blood vessels is described as a chain *a* which is an ordered sequence of *n* elements. The element of *a* (a_i) of a chain indicates the slope change of the segments of the curve in the element position. The slope change's range goes continuously from -1 to 1. The proposed tortuosity metric can be defined as in (13),

$$\tau = \sum_{i=1}^{n} |a_i| \tag{13}$$

where a_i is defined as the change in slope for the i[th] segments, and *n* is the number of segments in the curve. This metric is invariant under translation, rotation, scaling, origin of construction of the curve, and under mirroring image.

G. Khansari et al. [10]

Khansari *et al.* proposed a tortuosity measurement method named as the Vessel Tortuosity Index (VTI). VTI is sensitive to small changes in tortuosity, therefore it is very suitable for detecting small tortuosity changes in retinal vessels of OCTA (Optical Coherence Tomography Angiography) images. This tortuosity index proposed is defined as in (14),

$$VTI = \frac{0.1 SD_\theta \cdot N \cdot M \cdot L_A}{L_c} \tag{14}$$

where SD_θ is defined as the standard deviation of the absolute angle values between the line tangent to the centerline and a pre-determined reference axis, *N* is the number of the curve's critical points, *M* is the magnitude of the vessel's centerline, L_A is the arc length, and L_C is the chord length. Changes in the sign of curvature are used to determine the number of inflection points, which can be inaccurate for curves with many small curves.

H. Zhao et al. [12]

Zhao *et al.* proposed a tortuosity measurement method based on exponential curvature. The proposed method is tested on two corneal nerves datasets and a retinal blood vessels dataset. In this work, the corneal nerves image (CCM) is enhanced based on an extended Retinex model. The curvilinear data in the enhanced image is then mapped to a 3D space of positions and orientations, which create orientation scores. This method is used to better handle bifurcations and separate the crossing of line structures of the image. Next, the exponential curve fit is employed to align with the locally oriented structure. The tangent vector of the exponential curve is then used to compute the local curvature. Thus, the curvature-based metric proposed in this work is defined as in (15),

$$\kappa_{\exp} = \frac{1}{V} \int_{-\infty}^{\infty} \left|\kappa_{\mathbf{c}^*}\left(\mathbf{x}, \Theta(\mathbf{x})\right)\right| \hat{S}(\mathbf{x}) \mathrm{d}\mathbf{x}, \; with$$

$$\Theta(\mathbf{x}) = \arg\max_{\theta_i \in \frac{\pi}{No}\{1, \ldots, No\}} \{U(\mathbf{x}, \theta_i)\} \tag{15}$$

where $U(\mathbf{x},\theta)$ represents the orientation scores of the enhanced CCM image $\hat{S}$, $\kappa_{\mathbf{c}^*}$ is defined as the curvature of the tangent vector of the exponential curve, and *V* as the total image summation that is used for normalization. The method proposed in this work used a more direct approach to estimate the curvature of the images, which is useful to avoid potential errors in the images' pre-processing steps.

III. Methodology

The experiments were entirely carried out using MATLAB 2022a. The dataset used in this research is named RET-TORT, which is a publicly available dataset from the Department of Ophthalmology, University of Padova, Italy (https://bioimlab.dei.unipd.it/). This dataset contains 60 retinal fundus images, which consist of 30 arteries and 30 veins from normal and hypertensive patients. The retinal blood vessels that are included in this dataset are major arteries and veins that have minimal overlap with other surrounding vessels. The tortuosity of the veins and arteries images are manually estimated and ordered by a retinal specialist, Dr. S. Piermarocchi from the Department of Ophtlamology, University of Padova. The images were captured with a 50° fundus camera (TRC 50, Topcon, Japan),

which were then digitized to a resolution of 1100×1300 pixels using a scanner. The resulting images format are compressed JPG color images, and the preprocessed images are noncompressed color TIF images. The dataset also provides the coordinates samples of the manually traced vessel center line in ManualData.mat and the ordered images based on the degree of tortuosity in ClinicalOrdering.xls.

The proposed method in retinal blood tortuosity measurement is divided into two steps: the first step is tortuosity estimation and the second step is tortuosity metric evaluation.

1) Tortuosity estimation: The centerline coordinates of each blood vessel's image are available in the dataset expressed as = $[(x_1, y_1), (x_2, y_2), \ldots, (x_n, y_n)]$. However, the sample points are not dense enough to describe the blood vessels curve, hence they need to be upsampled to represent the actual vessel centerline. Sample points upsampling was carried out using the linear interpolation method, and the sample points were resampled to 3 times the number of initial sample points. Then, the upsampled curve is smoothed using the cubic smoothing spline interpolation method.

Ophthalmologists primarily consider the curve's number of turns and amplitude of turns when determining tortuosity. To define those aspects in the mathematical equations, the tortuosity metric proposed in this research combines other metrics that were proposed in previous work. Therefore, the tortuosity measurement metric in this research is defined as in (16),

$$\tau_C = \frac{L_c}{L_x} \times \sum_{i=1}^{n} \left[\frac{L_{c_{s_i}}}{L_{x_{s_i}}} - 1 \right] \times \frac{\sum_{j=1}^{m} \theta_j}{m-2} \tag{16}$$

where L_c and L_x are defined as arc length and chord length (definition is given in (3) and (4)), L_{csi} and L_{xsi} as the arc length and chord length of each turn curve of the blood vessels (the same as (12)), n as the number of turn curves (calculated based on changes in the curvature sign), m as the number of critical points (calculated based on gradient sign changes), and θ as the angle in the critical points of each curve.

For each sample points of the curve's centerline, the curvature of each sample points were calculated. The number of turn curves was calculated based on curvature sign changes (this method is adapted from Grisan *et al.* work). The gradient of each sample points were also calculated. The sample points where the gradient sign changes were considered as the critical points. Then, a simplified curve will be formed by the critical points and the first and last sample points. The θ angle in the equation was calculated by the vector formed by each points with the point before and ahead of the points of the simplified curve. The visual demonstration of the angle calculation is given in Fig. 2.

Fig. 2. Visual demonstration in determining the angle parameter used in the metric proposed in this research. (a) This is the original curve. (b) The sample points where the calculated gradient sign changes were considered as the critical points (black circles). (c) Simplified zig-zag line was created to clearly shows the path formed by the critical points and the first and last sample points. (d) The angle used in the metric was the angle that formed by each point (black circle) of the line.

The L_c/L_x ratio derived from Hart's proposed metric aims to calculate the ratio between the arc length and the chord length to make it easier to compare curves of different lengths. The ratio of arc length segments and chord length segments (derived from Grisan's metric (12)) aims to calculate the amplitude of each turn curve. Finally, angle calculations are performed at each sample point of the curve where the gradient sign changes. This aims to define how steep each turn curve that forms the blood vessel.

2) Tortuosity metric evaluation: Due to the dataset's images's tortuosity levels that are graded in ranks, the correlation between the ophtalmologist's gradings and the proposed method's measurement is used as the evaluation method. In the context of correlations among rankings, Spearman correlation coefficient is chosen to be the evaluation method of this work. Spearman correlation rankings is used to measure the strength between two sets of data [11]. The calculated tortuosity index of each image was sorted as ranks and compared to the actual ranking of the images' tortuosity index provided in the dataset. Then, the Spearman correlation coefficient will be calculated between the two rankings. The equation to calculate the coefficient is defined as in (17),

$$\rho = 1 - \frac{6 \sum d_i^2}{n(n^2-1)} \tag{17}$$

where d_i is defined as the difference in ranks of the i^{th} element and n is the number of cases between two variables. Spearman ranking coefficient correlation, ρ, ranges from 1 to –1, with 1 indicating the perfect association of rank, 0 indicating no association between ranks, and –1 indicating the perfect negative association between ranks. The closer the ρ value is to 0, the weaker the association between the ranks.

IV. Results and Discussion

Fig. 3 and Fig. 4 show the correlation plot between the images' ground truth tortuosity ranking provided in the dataset and the ranking calculated using the proposed tortuosity metric in this research.

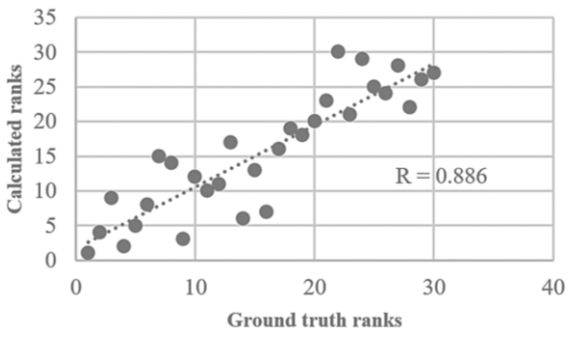


Fig. 3. Comparison between calculated ranks and ground truth ranks for artery images

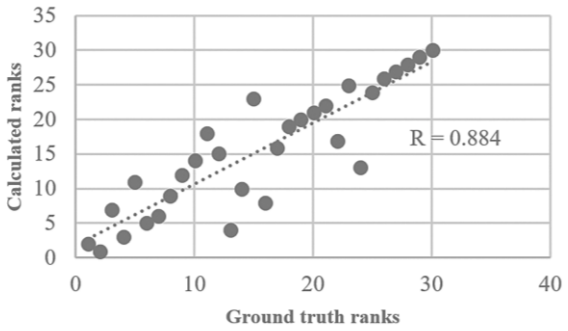


Fig. 4. Comparison between calculated ranks and groundtruth ranks for veins images

The Spearman's rank correlation coefficient for this metric is also compared to the coefficients produced by other metrics proposed in other works. Table I. shows the coefficient value for arteries and veins tortuosity estimation between previous works.

TABLE I. THE COMPARISON OF SPEARMAN'S RANK CORRELATION COEFFICIENT PRODUCED BY DIFFERENT METRICS FROM PREVIOUS WORKS

No.	Literature	Tortuosity metric	Spearman correlation coefficient	
			Artery	*Vein*
1	Hart *et al*. (1999)	$\frac{s(C)}{chord(C)}$-1	0.829	0.632
2		tc(C)	0.818	0.881
3		tsc(C)	0.844	0.876
4		tc(C)/s(C)	0.785	0.868
5		tsc(C)/s(C)	0.823	0.871
6		tc(C)/chord(C)	0.803	0.886
7		tsc(C)/chord(C)	0.838	0.876
8	Chandrinos *et al.* (1998)	MAC	0.675	0.482
9	Goh *et al.* (2001)	TN	0.877	0.644
10	Bullit (1998)	ICM	0.009	0.493
11	Grisan *et al.* (2008)	τ	0.723	0.834
12	Bribiesca *et al.* (2012)	SCC	0.868	0.596
13	Khansari *et al.* (2017)	VTI	0.901	0.810
14	Zhao *et al.* (2020)[a]	κ_{exp}	0.949	0.868
15	Proposed metric	τ_G	0.886	0.884

[a] The Spearman correlation coefficient is not recreated in this experiment but taken directly from the literature.

The coefficient values from other metrics shown in Table I. are obtained by recreating the experiments from the source paper (except the methods from Zhao *et al.* [12]). It is shown that the metric proposed in this research produced a more balanced correlation coefficient between arteries and veins compared to other works.

There are differences in the shape characteristics of arterial and venous vessels as the tortuosity level increases. As the arteries vessels become more tortuous, the number of turn curves tends to increase and the amplitude tends to decrease. In addition to that, the arteries vessels with low tortuosity do not appear as a straight line, instead, the curves display as a large, sloping, C-curve.

On the other hand, veins generally appear straighter than arteries. As the degree of tortuosity increases, the frequency of turns and the amplitude of the veins tend to increase. In the images of low tortuosity blood vessels, veins do not form large turning waves like arteries, but instead form many small waves. Due to these different characteristics, the tortuosity measurement metrics from previous works sometimes produce a Spearman correlation coefficient that is higher in arteries and lower in veins, and vice versa. Thus, metrics that include the number of turn curve in the equation are less accurate, because the increase in turn curves does not equal the increase of tortuosity.

However, metric proposed by Zhao et al. [12] produces a higher correlation coefficient in artery tortuosity measurement compared to the proposed metric's result. This may due to the direct approach of curvature calculation and the application of orientation scores, which may increase the accuracy of tortuosity estimation.

There are still several drawbacks from the method proposed from this research. The accuracy of automatic tortuosity measurement relies heavily on the sample points resampling step. Some resampling methods may produce small turn curves that are initially not seen in the original vessels, thus affecting the image's tortuosity value. Since this metric is also the results of the combination of other metrics proposed in other works, it also carries the same drawbacks as the other metrics. In addition, this metric is designed to produce a high correlation value to this specific dataset used in this research, so using a larger dataset will allow for a more thorough evaluation.

V. CONCLUSION

A combined version of several tortuosity measurement metric is proposed in this research. This metric is based on the ratio between arc length and chord length, the ratio between arc length and chord length segment, and the angle between each critical point in the curve. This parameter produced equally high correlation coefficients for arteries and veins. However, there is still room for improvement in formulating the parameter, and the different characteristics between veins and arteries in increasing tortuosity can also be considered in formulating the metric in the future. In addition, a larger set of images is required for a more extensive evaluation of the metric proposed in this research.

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