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Clinical validation of three-dimensional tortuosity metrics based on the minimum curvature of approximating polynomial splines

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Abstract

The clinical recognition of abnormal vascular tortuosity is important in the diagnosis of many diseases. Metrics based on three-dimensional (3D) curvature, using approximating polynomial spline-fitting to "data balls" centered along the mid-line of the vessel, minimize digitization errors and give tortuosity values largely independent of the resolution of the imaging system. We applied two of these metrics to a number of clinical vascular systems, using both 2D and 3D datasets. Using abdominal aortograms of low tortuosity, we established their validity by their strong correlation with the ranking of an expert panel of three vascular surgeons. The values of the Spearman rank correlation coefficient between our rankings, using a data ball radius of one-quarter of the local vessel radius, and the average ranking of the expert panel were 0.96 (with a 95% confidence interval of [0.91, 0.99]) for the mean curvature and 0.98 ([0.94, 0.99]) for the root-mean-square (RMS) curvature. These confidence intervals indicate that our automated analysis is producing rankings whose reliability is similar to that of a human expert, and is significantly better than that achieved with existing algorithms. The metrics provided good discrimination between vessels of different tortuosity for both 2D and 3D datasets, and produced values sufficiently discriminating to assess the relative utility of arteries for endoluminal repair of aneurysms.

Keywords: Tortuosity; Blood vessels; MRA; Endoluminal repair

1. Introduction

Vascular diseases surpass cancer as the major cause of morbidity and mortality in the Western world. Many vascular disease processes including diabetes, hypertension and the vasculopathies [1] produce increased tortuosity of the blood vessels although the mechanism is often incompletely understood. The tortuosity of large blood vessels results in haemodynamic changes that have been implicated in the development of atherosclerotic lesions [2,3] and aneurysms [4]. Vascular malformations and malignant tumours produce localized clusters of abnormally tortuous vessels, whose tortuosity can be successfully reduced by anti-angiogenic agents [5]. Even in conditions where the etiology of the tortuosity is not understood, the severity of the disease and its progression with time and/or treatment can be inferred by measuring the tortuosity of the blood vessels.

A number of tortuosity measures have been proposed, but none has gained universal acceptance. They include the distance factor [6,7], the number of inflection points [8], the sum of angle changes along segments [9,10] and various line integrals of local curvature values [8,11,12], which may be more conveniently computed from second differences of the vessel mid-line [13]. We proposed tortuosity metrics in terms of the curvature of a unit speed curve obtained by approximating polynomial spline-fitting to the discrete data points representing the mid-line of the vessel [14]. Our analysis was construed directly in three dimensions (3D) so that it could be applied to 3D datasets, which are increasingly becoming available due to the thin contiguous images now obtainable with helical computed tomography (HCT) and magnetic resonance angiography (MRA). Our method avoids the arbitrary filtering of mid-line data needed with other tortuosity indices to minimize errors introduced during digitization. Our met-

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rics are sensitive to morphology and satisfy intuitive notions of tortuosity, e.g. they are scale invariant, so that their values are independent of the image size.

The aim of this study was to find suitable data ball sizes for fitting the polynomial splines and to test the validity of our metrics for a variety of clinical images from different vascular regions by comparing their values with the ranking of tortuosity as judged by an expert panel of three vascular surgeons.

2. Methodology

2.1. Definitions

The *length* of a unit speed function *f*, denoted *L*(*f*), is given by

$$L(f) = \int_a^b |f'(t)|\,\mathrm{d}t = \int_a^b 1\,\mathrm{d}t = b - a,$$

The *mean curvature* of *f*, denoted *M*(*f*), is defined by:

$$M(f) = \int_a^b |f''(t)|\,\mathrm{d}t \qquad (1)$$

and the *mean square curvature*, denoted *J*(*f*), is defined by:

$$J(f) = \int_a^b |f''(t)|^2\,\mathrm{d}t \qquad (2)$$

The normalized root-mean-square (RMS) curvature, denoted *K*(*f*), is defined by:

$$K(f) = \sqrt{L(f)J(f)} = \sqrt{(b-a)\int_a^b |f''(t)|^2\,\mathrm{d}t} \qquad (3)$$

For real (i.e. noisy) data there exists a unique shortest path which passes through "data balls" of radius r_i, centered on the points, x_i, defining the mid-line, and which minimizes *L*(*f*); and this shortest path is a unit speed piece-wise linear function [14]. The radii of the data balls can be specified in terms of the local radius of the vessel, R_i. This "shortest path", f_1, between the data balls is used to calculate the mean curvature, *M*(*f*). Once this is obtained, an algorithm is used to find the "smoothest path", f_2, connecting these data balls which is appropriate for calculating *J*(*f*) and *K*(*f*). The putative tortuosity metrics were tested on a simulated 2D blood vessel and synthesized 3D helices [14]. *M*(*f*) and *K*(*f*) were shown to be scale invariant and additive, insensitive to digitization errors and largely independent of the resolution of the imaging system; the mean square curvature, *J*(*f*), was found not to be scale invariant and has not been considered here.

The spline fitting technique, which has been described and analyzed in reference [14], has been tailored to suit the nature of the particular metric. In fitting curves to sampled data points, there is always the danger that the length of the fitted curve is too long. We have resolved this by looking at all possible curves and finding the minimal value of tortuosity. For *M*, this corresponds to the shortest path. Given a sequence of "data balls" which mark the midline, we compute the value *M* by applying Eq. (1) to the curve defined as the shortest path passing sequentially through the data balls. This shortest path happens to be a parametric linear spline and is well-suited (in terms of stability) to the computation of *M*. This shortest path is ill-suited for the computation of *J* or *K* because applying Eq. (2) to the shortest path would yield a *J* value of infinity. Rather, the minimum tortuosity corresponds to the "smoothest path" through the data balls which turns out to be a parametric cubic spline and this is well-suited to the computation of *J* and *K*.

2.2. Mid-line tracking algorithms for 2D and 3D images

Accurate determination of the vessel mid-line is important for analyzing tortuosity. However, our use of approximating polynomial spline fitting is tolerant of inaccuracies in the mid-line extraction, and does not require the sampled points to be regularly spaced.

There are many methods for extracting the mid-line axis of a vessel automatically, including using the medial axis transform [13], matched filtering [15,16], region-growing [17] and incremental search [18], and a sector-search algorithm [19]. However, some of them are less useful near bifurcations, in regions of low signal-to-noise ratios (SNR) and in tortuous vessel regions. We are experimenting with various vessel tracking techniques in order to automate this procedure, which would be a prerequisite for clinical implementation.

For two-dimensional (2D) data we located the mid-line of a vessel from its more easily defined vessel edges, obtaining the boundary pixels by Sobel masking followed by local adaptive thresholding. The images were then magnified (×8, in both *x*- and *y*-directions) to show individual pixels and the (*x*, *y*) co-ordinates of the vessel boundaries recorded, using interpolation when the boundaries were obscured by crossing vessels. With the boundary pixels partitioned into two disjoint sets, the "left boundary pixels" and the "right boundary pixels", the location of each pixel taken as its centre and interpolated points added to each set, the mid-line curve was calculated as the set of points equidistant from both boundary sets (where the distances were measured to the closest points in the boundary sets). The mid-line was begun at one end of the vessel and sequentially extracted one point at a time: given a "current point", one constructs an arc with the centre at this point and having a small radius. The "next point" is then the point on this arc which is equidistant from the two boundary sets. The vessel radius (*R*) at each point was defined to be the (equal) distance from the point to the boundary sets. The algorithm is robust and computationally efficient.

There are a number of specific algorithms for automatically segmenting and finding the mid-line for 3D datasets [20–23]. However, we used a simple, manual method for tracking such mid-lines so that we could link vessels across sections. With 3D datasets, vessels which are locally cylindrical intersect the slice plane to give elliptic cross-sections. Eight points were manually traced around the circumference