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Morphometric, Geographic and Territorial Characterization of Brain Arterial Trees

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Abstract

Morphometric information of the brain vascularization is valuable for a variety of clinical and scientific applications. In particular, this information is important when creating arterial tree models for imposing boundary conditions in numerical simulations of the brain hemodynamics. The purpose of this work is to provide quantitative descriptions of arterial branches, bifurcation patterns, shape and geographical distribution of the arborization of the main cerebral arteries as well as estimations of the corresponding vascular territories. For this purpose, subject-specific digital reconstructions of the brain vascular network created from 3T magnetic resonance angiography images of healthy volunteers are used to derive population averaged morphometric characteristics of the cerebral arterial trees.

Introduction

Detailed knowledge of the brain vascular architecture is important for gaining insight into a variety of vascular pathologies and brain diseases [1]. In particular, knowledge of the distribution of hemodynamic quantities in the cerebral arteries is important to understand the pathophysiology and pathogenesis of cerebrovascular diseases such as intracranial aneurysms [2]. The hemodynamics in cerebral arteries has been studied with subject-specific computational fluid dynamics models [3, 4]. These numerical simulations require specification of appropriate outflow boundary conditions [5–7]. The flow division among the different arteries is largely determined by the relative impedance of the distal vascular beds. Thus, researchers have estimated these impedances by developing arterial tree models [5, 8, 9]. A variety of methods have been developed to build realistic arterial trees [9–13] and scaling laws for vascular trees have been proposed [14, 15]. Recently Blanco et al. [13] proposed a method for concurrently generating arterial networks in vascular territories using a constrained constructive optimization (CCO) method. A given vascular territory fed by several inflow vessels is first partitioned into sub-domains by solving an inverse problem that assigns each vascular voxel with one of the feeding arteries. Then a modified CCO technique is applied to fill each one of the sub-domains with a vascular tree. These approaches require not only the specification of constraints related to the arterial branch geometry and bifurcation characteristics, but also geometric characteristics of the different vascular territories.

Vascular brain territories have been studied using magnetic resonance techniques such as arterial spin labeling [16–18], which provide information about brain perfusion from individual arteries. Recent advances have made also possible to assess collateral perfusion [18]. However these studies do not provide geometric characteristics of the vascular territories and the watershed zones.

The purpose of this paper is to present morphometric, geometric, branching and territorial characteristics of human brain arterial trees based on *in vivo* image data of a population of 61 healthy subjects. This information is important to guide models of arterial trees and estimations of distal impedances in hemodynamics models of the cerebral circulation. This paper complements and extends the data presented previously by Wright et al. [1] by including branch geometry and bifurcation metrics typically used in arterial tree modeling, as well as by describing the population averaged shape and geographic distribution of the brain arterial trees based on a probabilistic vascular atlas.

Methods

Vascular Reconstructions

A total of 61 digital reconstructions of healthy human arterial networks were created from 3T magnetic resonance angiography (MRA) images [1]. These images were acquired with a field of view that spanned the entire brain at an isotropic voxel resolution of 0.6 mm. The brain arterial network of each subject was manually traced using Neuron_Morpho (www.personal.soton.ac.uk/dales/morpho) a software tool originally designed for reconstruction of neuronal trees (www.neuromorpho.org) [19]. This tool was implemented as a plug-in extension of the ImageJ software developed at the National Institute of Health (<http://rsbweb.nih.gov/ij/>). The centerline and diameter of each arterial branch were reconstructed by interactively selecting voxels on the MRA image rendered as 2D slices in three orthogonal planes by one of the researchers (SW). More details of the imaging protocols, methods used for vascular reconstruction as well as information about the subject population and comparisons between genders and age groups have been reported by Wright et al. [1].

Arterial branches and bifurcations were digitally represented as a set of interconnected tapering cylinders characterized by the x, y, and z coordinates along their centerlines and corresponding radius, and connection to the parent branch or node. The arterial reconstructions have been made publicly available at <http://cng.gmu.edu/brava>. At the level of detail of this study, no anastomoses between the different arterial trees were identified and/or incorporated into the vascular reconstructions.

The vascular reconstructions were systematically checked and verified by running a battery of tests in order to detect defects such as intersecting arterial segments, zero diameter branches, overlapping or duplicated branches, disconnected nodes or branches, etc. More details are given in [20]. The reconstructions were also checked by visual inspection of the vascular model overlaid to the MRA slices and to volume renderings of the 3D MRA images in order to verify the topology and geometry of the vascular models by another researcher (FM). When detected, the errors were corrected by interactively editing the models (by SW

using the same Neuron_Morpho software) to remove incorrect connections, doubly defined branches or intersecting branches, etc. Once corrected the tests were run again until no new problems were found.

Subsequently, the vascular models were smoothed and re-parameterized by passing cubic splines along the centerline of each arterial branch. Finally, the arterial trees corresponding to the six main cerebral arteries emanating from the circle of Willis were identified and labeled: left (L) and right (R) anterior cerebral artery (ACA), middle cerebral artery (MCA) and posterior cerebral artery (PCA).

The reconstruction process is illustrated in Figure 1. The top row shows an axial slice of the MRA dataset of one of the subjects at the level of the circle of Willis (a), a maximum intensity projection (MIP) of the vasculature (b) and a volume rendering of the brain arteries (c). The bottom row of this figure shows the reconstructed arterial centerlines colored with the vessel radius (d), the reconstructed arterial model rendered as a 3D surface (e), and the labeling of the main arterial trees (LACA=green, RACA=yellow, LMCA=cyan, RMCA=red, LPCA=magenta, RPCA=blue) of the vascular model (f).

Arterial Tree Characterization

The nodes of each arterial tree were classified as: a) the root node (node at the origin of the tree with no connection to a parent node), b) terminal nodes (with no children nodes), c) internal nodes (with only one child node and one parent node), and d) bifurcation nodes (with two children nodes and one parent node). Arterial branches were then identified as the set of connected internal nodes between root, bifurcation or terminal nodes. Arterial branches and bifurcation nodes were assigned a branch order or generation number by recursively traversing the tree starting at the root node and incrementing the generation number at each bifurcation node. The geometry and branching pattern of the tree were then characterized by measuring quantities defined at each branch and at each bifurcation (see schematics in Figure 4). The geometry of each branch was characterized by its geodesic length (S) computed as the sum of the arc length of segments comprising each branch, its Euclidean length (L) calculated as the Euclidean distance between the end points of the branch, the mean radius along the branch (R), the branch tortuosity ($T=S/L$), and its aspect ratio ($A=S/R$). Bifurcations were characterized by measuring parent-children and children-children ratios of branch lengths ($LR=L_0/L_i$ $i=1,2$ and L_1/L_2), mean radius ($RR=R_0/R_i$ $i=1,2$ and R_1/R_2), bifurcation law (n such that $R_0^n=R_1^n+R_2^n$), and bifurcation angles between the parent and each of the children branches. The bifurcation angles were calculated from the arc cosine of the inner product of the tangent directions of each branch emanating from the bifurcation point. Here 0 represents the parent branch, i represents each child branch ordered by size (1 is larger, 2 is smaller).

Vascular Atlas and Territories

In order to build probabilistic vascular and territorial atlases, the 61 vascular reconstructions were aligned to a common reference frame. For this purpose, a landmark point (the tip of the basilar artery) was manually identified in all models and used as the origin of the reference frame. Then, three main directions (left-right, anterior-posterior, and inferior-superior) were

identified using a principal component analysis. Specifically, the left-right direction was found by performing a principal components analysis that computed the plane that best separates the nodes belonging to the left and right arterial trees. Then, the anterior-posterior direction was found with a principal components analysis that computed the perpendicular plane that best separated the nodes belonging to the anterior cerebral from those of the posterior cerebral arterial trees. The inferior-superior direction was then defined as perpendicular to the other two directions. Next, all vascular models were translated to the common origin (basilar artery tip) and rigidly rotated to make their principal directions coincide.

Once the vascular reconstructions were aligned, a population averaged or generic brain region was created. First, the bounding box enclosing all 61 aligned vascular models was computed (min/max coordinates of all trees of all subjects). This 3D box was then subdivided into isotropic voxels with the same resolution as the original MRA images. Next, each arterial tree of each subject was voxelized, i.e. voxels intersected by any branch of any tree of any subject were labeled as “brain”, while empty voxels not crossed by any branch were labeled as “empty”. Then, a population averaged brain region or mask was created using a rasterization algorithm. Briefly, rays were cast in each of the three coordinate directions until they hit a “brain” voxel or traverse the entire volume. In rays that intersect “brain” voxels, the “brain” voxels with the minimum and maximum coordinates along the ray were identified and all voxels between these were also labeled as “brain”. The result of this process consists in a region (defined by the “brain voxels”) that represents a generic average brain volume for the entire population. A probabilistic vascular atlas for each of the six cerebral arterial trees was then created by computing the occupancy probability of each voxel in the rasterized brain region.

Vascular territories, i.e. regions perfused by each arterial tree, of each subject were approximated by assigning each voxel of the population averaged brain to the closest arterial tree using a multiple-seed region growing technique. Briefly, starting from voxels crossed by the vascular reconstructions (seeds), neighbor voxels not yet visited are progressively labeled and the process is repeated until all voxels have been assigned to a vascular territory. Territorial probability maps, i.e. probabilistic territorial atlases, were then computed from the vascular territories of the 61 subjects by counting the number of times a voxel belongs to the vascular territory of a given tree. Watershed regions between pairs of territories were identified by finding voxels with non-zero probabilities of belonging to the two adjacent territories. Relative volumes of all territories and watershed regions were calculated.

The process is illustrated in Figure 2 that shows: the alignment of the vascular models of two subjects (a), the alignment of the arterial trees of all 61 subjects (b), the arterial trees of one subject superposed to the rasterized or population averaged brain region (c), and the vascular territories of the left (transparent red) and right (transparent cyan) middle cerebral arteries of one subjects along with the corresponding arterial trees. In this figure, the vascular territories (d) and the brain volume (c) were rendered by extracting an iso-surface corresponding to 0.5 probability of belonging to each region and plotting these iso-surfaces with transparency.

Results

Branch Geometry

Geometric characteristics, including geodesic and Euclidean length, mean radius, aspect ratio, and tortuosity were calculated for each branch of each of the vascular trees and for all subjects. Population averages were computed for each branch order or generation of each of the brain arterial trees. Averages were computed over all subjects and both hemispheres. The results are presented in Figure 3. This figure shows how the population average of the branch geodesic length (a), mean radius (b), aspect ratio (c), and tortuosity (d) varies along the generations of each arterial tree. We can see that branch radius decrease with branch order and that lengths and aspect ratio peak between generations 4 and 7 and then continue to decrease as the generation order increases. Branch tortuosity increases up to about generation 8 and then seems to stabilize or slightly decrease in the terminal branches. The average variabilities of these metrics among subjects (for all trees and all generations) were in the following ranges: 64%–73% for geodesic length, 18%–21% for mean radius, 66%–82% for aspect ratio, and 21%–25% for vessel tortuosity.

Bifurcation Characteristics

Similarly, bifurcation characteristics were computed by averaging over subjects (population average) and hemispheres for all bifurcation generations of each arterial tree. The branching pattern characteristics of each arterial tree are presented in Figure 4. This figure shows the variation of the population average of the length and radius ratios, the bifurcation power law exponent between parent and children branches, and the parent-child angles along each tree (i.e. as a function of the branch or bifurcation generation). We can see that all these values remain roughly constant after about the third generation, except for the power law exponent of the PCA trees which exhibits a larger variation. These results indicate that the largest child, i.e. with larger mean radius, has roughly a length 130% of the parent branch length (panel a) and a radius about 90% of the radius of the parent branch (panel b). Conversely, the smallest child has a length of about 50% of the parent branch length (panel a) and a radius about 75% of the radius of the parent branch (panel b). Additionally, for each arterial tree the smallest child tends to bifurcate with a larger angle (above 55 degrees) than the largest child (angle below 50 degrees), as can be seen in panel c: red and magenta curves for ACA, green and cyan curves for PCA, and blue and brown curves for MCA. This suggests that the trees do not bifurcate symmetrically. Instead, when each artery reaches a bifurcation point, it curves and gives off a thinner and shorter branch, and continues with roughly the same radius for a longer distance. This branching pattern is schematically illustrated in panel e. Interestingly, the bifurcation power law exponent (panel d) remains roughly constant for all generations with a value around 2.5 (except for larger variations seen in the PCA trees). This value seems to indicate that the branching pattern satisfies a principle of minimum work. Another interesting observation is that on average the bifurcation characteristics of the cerebral arterial trees seem to remain roughly constant for generations beyond 3, i.e. they exhibit a roughly fractal behavior. The average variability of bifurcation quantities among subjects (for all trees and generations) were in the following ranges: 96%–125% for length ratio, 17%–19% for mean radius ratio, and 39%–48% for bifurcation angle. Length ratios (as well as branch geodesic lengths) exhibited larger variabilities for smaller generations (closer

to the tree origin near the circle of Willis) than for larger generations. The power law exponents exhibited a large variability among subjects and trees of over 400%.

Tree Shapes

The shapes of the arterial trees of each subject were characterized using a principal component analysis. The shape of each tree of each individual was quantified by computing the extension of the tree along three orthogonal principal directions of elongation. The distribution of sizes along the three principal components of each tree is presented in Figure 5. In this figure each point corresponds to one tree of one subject. Different colors were used for the ACA, MCA and PCA trees. Clustering of the shapes of the ACA, MCA and PCA trees can be clearly observed. This means that the trees of different subjects have similar shapes. The range, mean and standard deviation of the three principal directions of each group of trees computed over the subject population are given in Table 1. The trees closest to the mean of each cluster are shown at the right of Figure 5. These are representative examples of the shape of the trees in each group. In particular, the ACA trees appear flatter (one dimension much smaller than the other two), the PCA trees appear more isotropic (all three dimensions are similar), and the MCA trees appear elongated (one dimension longer than the other two).

Territory Characteristics

The probabilistic atlases computed from the vascular reconstructions of the 61 subjects are presented in Figure 6. In order to visualize the probabilistic vascular atlas of each arterial tree, the probability that a voxel belong to a given arterial tree was encoded with a grey level value and displayed using volume rendering techniques (six leftmost panels). Thus, the grey level values in these images represent the probability of occupancy of each voxel by a branch of each arterial tree. The territorial probabilities (rightmost panel) were visualized by plotting transparent iso-surfaces corresponding to probability of belonging to each territory > 0.5 .

The probabilistic geographic partition of the brain volume into vascular territories corresponding to each cerebral arterial tree is presented in Figure 7. This figure shows the territories of the ACAs, MCAs, and PCAs from three orthogonal viewpoints.

Relative volumes of the territories with respect to the PCA territory are presented in Table 2 for the left and right hemispheres. The volumes of the vascular territories were estimated by thresholding the probabilistic territorial atlas (denoted Atlas in the table) as well as by averaging the territories of all subjects in the population (denoted population average in the table). Both estimates are in good agreement: they coincide well within one standard deviation. These results indicate that the territories of the MCAs are about 2.5 to 3 times larger than those of the PCAs. Similarly, the territories of the ACAs are about 1.3 to 1.6 times larger than those of the PCAs.

The geographic locations of the watershed regions are presented in Figure 8. This figure shows regions that have probabilities above 0.5 of belonging simultaneously to the territories of the ACA and the MCA (denoted $ACA \cap MCA$), the MCA and PCA (denoted $MCA \cap PCA$), and the PCA and ACA (denoted $PCA \cap ACA$). The relative volumes of the

watershed zones with respect to the $PCA \cap ACA$ (smallest watershed region in each hemisphere) are presented in Table 3. These results show that the watershed region between the MCA and the ACA are the largest and is about 16 times larger than the PCA and ACA, followed by the MCA and PCA watershed region which is about 12 times larger than the PCA and ACA. Although the size of the watershed areas could be affected by the choice of the probability threshold, the relative volumes are not expected to be significantly affected as the regions would grow/shrink proportionately with increases/decreases of the threshold.

Discussion

In vivo morphometric characteristics of the arterial vascularization of the human brain have been extracted from MRA images of healthy subjects. These characteristics include geometric properties of the arterial branches of the main cerebral arteries as well as their bifurcation or branching pattern and their geographical and territorial distributions. Generic values of a variety of geometric and bifurcation parameters were given as population averages at each generation along the arterial trees of the ACA, MCA and the PCA. The results indicate that the geometric properties of arterial branches follow similar variations along the generations of the different cerebral artery trees (see Figure 3). Likewise, these trees seem to follow similar asymmetric bifurcation patterns in which the main arterial trunk gives off smaller branches as it extends on the brain surface (as illustrated in Figure 4 – panel e). The bifurcation characteristics were found to be roughly constant after about the third generation for all trees, suggesting a “fractal” branching pattern (i.e. invariant along arterial generations). However, the vascular trees of the ACA, MCA and PCA have in general different shapes (Figure 5) and cover territories of different extensions (Figure 7).

Additionally, the artery radius seems to follow a power law at arterial bifurcations (Figure 4 – panel d). Conservation of mass at a bifurcation implies $Q_0 = Q_1 + Q_2$, where Q_0 , Q_1 and Q_2 represent the volumetric blood flow in the parent and children branches, respectively. The principle of minimum work applied to a straight circular cylinder under steady flow conditions implies $Q = A \times r^3$ (Murray's law), where A is a constant, and r the radius of the artery. This law was obtained by minimizing the energy required to move a volume of blood through a straight artery with a steady flow (i.e. Poiseuille's flow) [21]. An optimal value of 3 has been proposed for laminar flow and 2.33 for turbulent flow [5]. Values ranging from 2 to 3 have been suggested for pulsatile flows [22]. Similarly, an extension of Murray's law for non-Newtonian flows suggests a value between 2.42 and 3 [23]. In this work, a power law of the form $r^n_0 = r^n_1 + r^n_2$ was proposed and the value of n was fitted at each bifurcation and population averaged for each generation along the different arterial trees. It was observed that n fluctuated between 2 and 3 for all generations greater than 3 of all trees (except for the PCA trees that exhibited larger variations). Thus, the arterial trees of the brain seem to obey a principle of minimum work, i.e. they are close to the optimal design for transporting blood with the minimum possible energy. However, it is not exactly clear which form of the principle of minimum work is the most appropriate to describe the branching pattern observed in the data presented in this paper. Additionally, our results indicate that bifurcation angles cluster around a value of 50–55 degrees. These values are consistent with optimal values estimated to minimize work in vascular trees [24].

The information and quantitative values provided in this paper are important for a variety of applications. In particular, they are useful for specifying morphometric parameters required by different techniques used for generating computer models of brain arterial trees. For instance, arterial tree models have been generated using fractal structured trees [5, 9], or using constrained constructive optimization techniques [10, 11, 25]. These models require specification of the bifurcation law exponent, length to radius ratios, etc. These models have been constructed, for example, with the objective of estimating impedances of the distal vascular beds and imposing outflow boundary conditions in computational fluid dynamics models of the brain circulation. The data presented in this paper is not only useful to prescribe the values of required parameters but also to impose constraints to the geometric, bifurcation and geographic characteristics produced by these algorithms, as well as evaluating the anatomical and physiologic realism of the generated trees.

The current study has several limitations that could affect the values of morphometric characteristics calculated and should be taken into consideration when interpreting the results presented in this paper. The limited resolution of the MRA images used to build the digital reconstructions of the brain vascular network can affect the estimations of geometric and bifurcation characteristics of the arterial trees, especially in the smallest arteries. This can be observed as larger variability of the morphometric parameters with increasing branch generation, especially beyond generation 10. The reconstruction method approximates vessel cross sections as circular. This assumption can have an important effect if the reconstructions are used for instance to calculate hemodynamic parameters along the trees. The digital reconstructions were created from 3T time-of-flight MRA images. These images suffer from artifacts related to signal loss in regions of low flow or disturbed flow patterns, which can affect the estimations of the diameter of the arteries in these regions. However, other parameters such as branch length, vessel tortuosity, tree shapes, etc. are not expected to be affected by these artifacts. Time-of-flight MRA techniques may also suffer from additional signal void artifacts because they detect flow perpendicular to the slice orientation and not within the plane of the slice. Although other imaging modalities such as computed tomography angiography (CTA) or 3D digital subtraction angiography (3D-DSA) have higher resolution, they are more difficult to use in healthy subjects since they are either invasive (e.g. catheter angiography) and/or use ionizing radiation (e.g. CTA). In contrast, MRA is noninvasive and does not use ionizing radiation, and furthermore all the images used in this study are publicly available through the International Consortium for Brain Mapping (ICBM) [26]. The vascular territories were estimated by partitioning a generic brain volume instead of each subject's brain volume, and they were identified by computing the distance to the closest blood vessel instead of estimating flow distributions. Blanco et al. [13] identified vascular territories by estimating the flow distribution from a given set of source arteries. This approach is useful to estimate a partition of the brain into territories when the arterial trees are not known or to further subdivide the distal territories. In our work, the vascular territories were estimated in a purely geometric manner from the reconstructed arterial trees. The assumptions made for this purpose can affect the estimations of the relative volumes of the vascular territories of each cerebral artery. It is worth noting that some parameters are likely less affected by these sources of errors. For example, estimations of the length of arterial branches, or bifurcation angles, are likely less

affected by limited resolution or flow related imaging artifacts than estimations of the arterial diameters. Despite these limitations and potential sources of inaccuracy, this study provides quantitative values of a number of important morphometric parameters based on measurements performed on 3D images acquired *in vivo* in human subjects.

Conclusions

Geometric characteristics, bifurcation patterns, and shape and geographical distributions of brain arterial structures were quantified from MRA data of normal subjects. Population averaged quantities are independent of the brain hemisphere, subject's gender or age, and therefore can be considered a normative set of generic values valid for all subjects in these groups. The parameters that characterize the brain vascularization are useful to guide and/or constraint methods for building realistic arterial tree models and to evaluate whether such models are capable of reproducing the morphometric characteristics extracted from *in vivo* human data presented here. Additionally, these vascular and territorial characteristics can be useful for comparing normal to pathological conditions, and help understand the effects of different diseases and their treatments.

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References

1. Wright SN, Kochunov P, Mut F, Bergamino M, Brown KM, Mazziotta JC, Toga AW, Cebral JR, Ascoli GA. Digital reconstruction and morphometric analysis of human brain arterial vasculature from magnetic resonance angiography. *NeuroImage*. 2013; 82C:170–181. [PubMed: 23727319]
2. Sforza D, Putman CM, Cebral JR. Hemodynamics of Cerebral Aneurysms. *Ann Rev Fluid Mechanics*. 2009; 41:91–107.
3. Oshima M, Torii R, Kobayashi T, Taniguchi N, Takagi K. Finite element simulation of blood flow in the cerebral artery. *Computer Methods in Applied Mechanics and Engineering*. 2001; 191(6–7): 661–671.
4. Cebral JR, Castro MA, Soto O, Löhner R, Alperin N. Blood flow models of the circle of Willis from magnetic resonance data. *Journal of Engineering Mathematics*. 2003; 47(3–4):369–386.
5. Olufsen MS. Structured tree outflow condition for blood flow in larger systemic arteries. *Am J Physiol Heart Circ Physiol*. 1999; 276:257–268.
6. Cebral JR, Castro MA, Soto O, Löhner R, Alperin N. Blood-flow models of the circle of Willis from magnetic resonance data. *Journal of Engineering Mathematics*. 2003; 47(3 – 4):369–386.
7. Cebral, JR.; Löhner, R.; Burgess, JE. ECCOMAS. Barcelona, Spain: 2000. Computer simulation of cerebral artery clipping: relevance to aneurysm neuro-surgery planning.
8. DeVault K, Gremaud PA, Novak V, Olufsen MS, Vernieres G, Zhao P. Blood Flow in the Circle of Willis: Modeling and Calibration. *Multiscale Modeling & Simulation*. 2008; 7(2):888–909. [PubMed: 19043621]
9. Olufsen MS, Peskin CS, Kim WY, Pedersen EM, Nadim A, Larsen J. Numerical Simulation and Experimental Validation of Blood Flow in Arteries with Structured-Tree Outflow Conditions. *Annals of Biomedical Engineering*. 2000; 28(11):1281–1299. [PubMed: 11212947]
10. Karch R, Neumann F, Neumann M, Schreiner W. A tree-dimensional model for arterial tree representation, generated by constrained constructive optimization. *Computers in Biology and Medicine*. 1999; 29(1):19–38. [PubMed: 10207653]

11. Bui AV, Manasseh R, Liffman K, Sutalo ID. Development of optimized vascular fractal tree models using level set distance function. *Med Eng Phys.* 2010; 32(7):790–4. [PubMed: 20472487]
12. Dokoumetzidis A, Macheras P. A model for transport and dispersion in the circulatory system based on the vascular fractal tree. *Ann Biomed Eng.* 2003; 31(3):284–93. [PubMed: 12680726]
13. Blanco PJ, de Queiroz RA, Feijoo RA. A computational approach to generate concurrent arterial networks in vascular territories. *Int j numer method biomed eng.* 2013; 29(5):601–14. [PubMed: 23576397]
14. Kassab GS. Scaling laws of vascular trees: of form and function. *Am J Physiol Heart Circ Physiol.* 2006; 290(2):H894–903. [PubMed: 16143652]
15. Zamir M. On the fractal properties of arterial trees. *J Theor Biol.* 1999; 197:517–526. [PubMed: 10196094]
16. van Laar PJ, Hendrikse J, Golay X, Lu H, van Osch MJ, van der Grond J. In vivo flow territory mapping of major brain feeding arteries. *NeuroImage.* 2006; 29(1):136–44. [PubMed: 16095923]
17. Kansagra AP, Wong EC. Quantitative assessment of mixed cerebral vascular territory supply with vessel encoded arterial spin labeling MRI. *Stroke.* 2008; 39(11):2980–5. [PubMed: 18703809]
18. Dang Y, Wu B, Sun Y, Mo D, Wang X, Zhang J, Fang J. Quantitative assessment of external carotid artery territory supply with modified vessel-encoded arterial spin-labeling. *AJNR Am J Neuroradiol.* 2012; 33(7):1380–6. [PubMed: 22345497]
19. Brown KM, Donohue DE, D'Alessandro G, Ascoli GA. A cross-platform freeware tool for digital reconstruction of neuronal arborizations from image stacks. *Neuroinformatics.* 2005; 3:343–360. [PubMed: 16284416]
20. Halavi M, Hamilton KA, Parekh R, Ascoli GA. Digital reconstructions of neuronal morphology: three decades of research trends. *Front Neurosci.* 2012; 6:49. [PubMed: 22536169]
21. Murray CD. The Physiological Principle of Minimum Work. *Proceedings of the National Academy of Sciences of the United States of America.* 1926; 12(3):207–214. [PubMed: 16576980]
22. Painter PR, Eden P, Bengtsson HU. Pulsatile blood flow, shear force, energy dissipation and Murray's Law. *Theor Biol Med Model.* 2006; 3:31. [PubMed: 16923189]
23. Revellin R, Rousset F, Baud D, Bonjour J. Extension of Murray's law using a non-Newtonian model of blood flow. *Theor Biol Med Model.* 2009; 6:7. [PubMed: 19445663]
24. Huo Y, Finet G, Lefevre T, Louvard Y, Moussa I, Kassab GS. Which diameter and angle rule provides optimal flow patterns in a coronary bifurcation? *J Biomech.* 2012; 45(7):1273–9. [PubMed: 22365499]
25. Schreiner, W.; Karch, R.; Neumann, F.; Neumann, M. *Scaling in biology.* Oxford University Press; Oxford, UK: 2000. Constrained constructive optimization of arterial tree models; p. 145-165.
26. Mazziotta J, Toga A, Evans A, Fox P, Lancaster J, Zilles K, Woods R, Paus T, Simpson G, Pike B, Holmes C, Collins L, Thompson P, MacDonald D, Iacoboni M, Schormann T, Amunts K, Palomero-Gallagher N, Geyer S, Parsons L, Narr K, Kabani N, Le Goualher G, Boomsma D, Cannon T, Kawashima R, Mazoyer B. A probabilistic atlas and reference system for the human brain: International Consortium for Brain Mapping (ICBM). *Philos Trans R Soc Lond B Biol Sci.* 2001; 356(1412):1293–322. [PubMed: 11545704]

Figure 1.

Reconstruction of vascular trees from MRA image data: a) slice of MRA at the level of the Circle of Willis, b) maximum intensity projection of MRA image, c) volume rendering of MRA image, d) tracing of arterial network, e) reconstruction of arterial networks, f) labeling of arterial trees. Views in b–f are from inferior to superior.

Figure 2.

Vascular atlas and territories: a) alignment of vascular trees of two subjects, b) alignment of vascular trees of 61 subjects, c) rasterized brain volume and arterial trees of one subject, d) vascular territories corresponding to left and right MCA trees of one subject.

Figure 3.

Geometric characteristics of arterial tree branches as functions of branch order: a) branch geodesic length along trees, b) branch mean radius along trees, c) branch aspect ratio along trees, d) branch tortuosity along trees.

Figure 4.

Bifurcation characteristics as functions of branch order: a) daughter to parent length ratios, b) daughter to parent radius ratios, c) daughter to parent bifurcation angles, d) bifurcation power law, e) schematics showing the general characteristics of arterial bifurcations.

Figure 5. Principal component analysis of arterial tree shapes: a) distribution of tree sizes along three principal size directions, b) example of ACA tree closest to the mean, c) example of MCA tree closest to the mean, d) example of PCA tree closest to the mean.

Figure 6.
Probabilistic vascular atlases (left) and probabilistic territorial atlas (right).

Figure 7.

Probabilistic territorial atlas from 61 subjects corresponding to each cerebral arterial tree (ACA, MCA and PCA), from three orthogonal viewpoints (superior/inferior, frontal/occipital, and left/right).

Figure 8. Probabilistic atlas based on data from 61 subjects of watershed zones between vascular territories of main cerebral arteries, from three orthogonal viewpoints (superior/inferior, frontal/occipital, and left/right).

Table 1

Distribution of height, depth and width of brain arterial trees.

Arterial tree	Value	Height	Depth	Width
ACA	Mean	72.45	109.07	25.97
	Standard dev	7.44	14.31	5.40
	Min	49.6	51.46	10.23
	Max	97.96	148.8	48.05
MCA	Mean	69.40	105.55	38.48
	Standard dev	5.57	10.01	3.02
	Min	51.46	76.88	32.86
	Max	84.63	127.1	48.05
PCA	Mean	52.43	66.27	30.50
	Standard dev	10.22	6.69	6.86
	Min	21.39	51.46	15.5
	Max	74.09	85.56	49.29

Table 2

Relative volumes of vascular territories.

Territory	Side	Relative volume	
		Atlas	Population average
MCA/PCA	Right	2.99	2.8 (± 0.51)
	Left	2.53	2.42 (± 0.42)
ACA/PCA	Right	1.59	1.54 (± 0.42)
	Left	1.28	1.37 (± 0.32)

Table 3

Relative volumes of watershed regions.

Watershed territory	Side	Relative volume
$(MCA \cap ACA) / (ACA \cap PCA)$	Right	16.57
	Left	16.34
$(MCA \cap PCA) / (ACA \cap PCA)$	Right	11.62
	Left	12.39