Decline in extent macroscopic cerebral Vasculature with Age quantified using Computerized Automatic Vessel Tracking

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Introduction It is well-known that human brain size decreases with advance into middle and old age and this process is accelerated by some dementias. Structural MRI has proved to be a sensitive method for detecting this loss in volume. Also, although vascular disease increases in the aging brain this is detected on MRI rather than direct observation of the vasculature through MR angiography (MRA). While it is well known that both perfusion and blood velocity in major arteries decline with old age [1], the general pattern of macroscopic cerebral vascular changes with age has not, to our knowledge, been a subject of previous study. We have developed an automated computerized technique to extract information about the centre lines of vessels detected by time of flight MRA (TOF-MRA) [2]. In this study we applied this methodology to study the length of arteries detected from TOF-MRA in 40 subjects aged from 21-70 years to explore the impact of age on extent of the detected vessels.

Method All TOF-MRA images were acquired using a 3T Philips Intera system (Best, Holland) with a standard 6 channel head array coil. The MR sequence parameters were as follows: multi-slab 3D TOF field echo sequence: TR 16.62 /TE 5.75ms, FOV 240, matrix $512\times 512\times 100$, flip angle 15°, voxel size $0.47\times 0.47\times 0.8mm^3$. All images were first interpolated to isotropic voxels before any image processing. A vessel tracking method was then applied to extract the whole cerebral vasculature for every subject. The approach consists of three steps. **a) Ridge detection:** a modified ridge traversal method originally presented in [3] was developed to extract vessel centrelines. The method starts from a seed point near the vessel centre and moves to a ridge point by minimizing a ridgeness function $J(\vec{x}) = (\vec{v}_1 \cdot \nabla \boldsymbol{I})^2 + (\vec{v}_2 \cdot \nabla \boldsymbol{I})^2 \approx 0$ where $\boldsymbol{I}$ is image intensity and $\vec{v}_1$ and $\vec{v}_2$ are normalized eigenvectors corresponding to the k-th smallest eigenvalues of the Hessian matrix of second derivatives of $\boldsymbol{I}$ at $\vec{x}$. **b) Seed generation**: to automate this process, we developed a seed production method based on the ZBS algorithm [4]. The algorithm computes a roughness K that quantifies the rate of variation of a local Z- or depth buffer for each point in the maximum intensity projections (MIP). Because vessel regions normally have lower roughness than background, a threshold is used to pick up low roughness points as vessel seed points. **c) Vasculature length measurement**: Following automatic detection of voxels along the centre lines of the complete vascular tree, the extracted data was manually checked to ensure all visible vessels were included and to delete any erroneously detected centreline voxels. The total extracted vessel length was then calculated in mm. Brain volumes for all subjects were also measured from the T2w images acquired in the same scan session as the TOF datasets. A dimensionless normalized vasculature length (NVL) was computed for each subject by dividing the total length of vessels by a characteristic brain length taken as the cube root of brain volume.

Results TOF-MRA images of 20 males and 20 females who had been imaged as part of the IXI cohort of normal adult subjects (www.ixi.org.uk) were processed to extract whole cerebral vasculatures. The mean age for males is 39.5 ±12.4 (24 – 60 yrs) and 43.1±16.6 (21 to 70yrs) for females. Fig. 1 shows a representative example of an extracted vessel tree. Visual inspection confirmed that the extracted vasculatures are precisely centred on the vessels and are virtually complete with even tip branches extracted. If necessary more seeds were provided manually to ensure that any remaining unsegmented peripheral vessels were included. The tolerance for minimizing J was 1.0e-4 and K is 1.5 for all subjects. Fig. 2 shows the measured normalized vasculature length (NVL) versus age for all subjects – the data showed much more scatter when not normalised. There is a clear decline in NVL with age in both men and women and this was found to be consistent with a linear trend (correlation coefficient r = -0.511, p=0.0008).

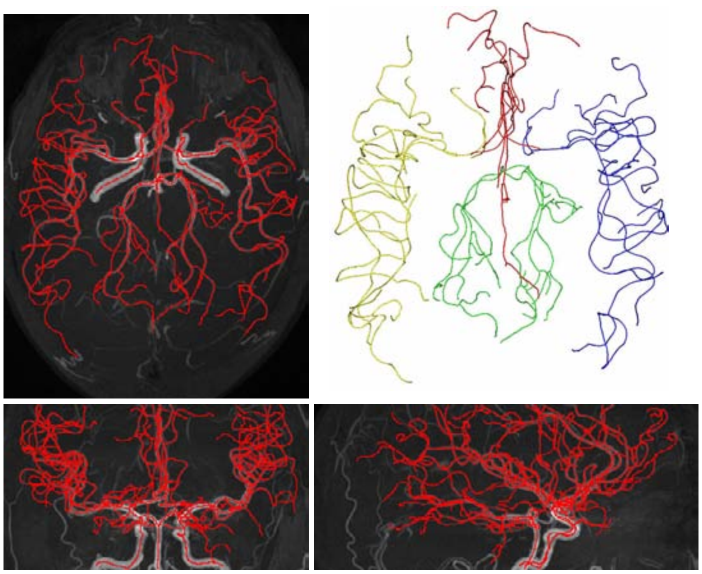
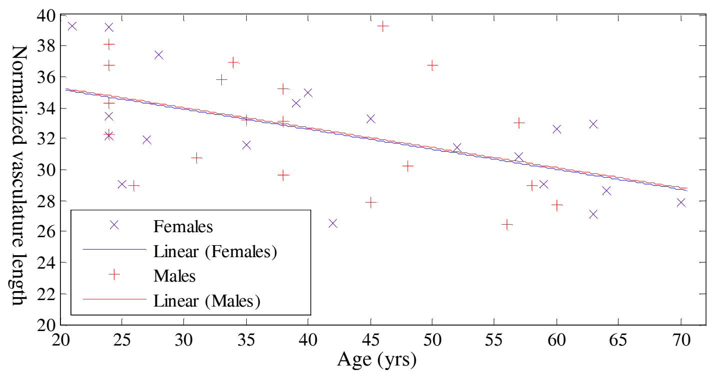


Fig. 1. An example of extracted cerebral vasculature. A female aged at 47 years was scanned to acquire the 3D TOF-MRA image. Note that there are peripheral vessels in the MIP images that are not part of the cerebral arterial tree.



Linear trend lines were fitted independently for each gender and these both show consistent slopes of -0.13 with an offset projected back to zero of ~37.8. This slope represents a decline in NVL of ~0.3% per year and was not consistent with zero change (95% CI: -0.20 to -0.06).

Conclusion This study shows a linear decline in detected vessel extent with age during the whole of adult life. A parallel pattern of decline occurs in brain volumes, with an initial rate of 0-0.2%/yr from 30-50yrs increasing to 0.3-0.5% /yr by age 70-80yrs [5]. Although we normalised to brain volume, our segmentation was not designed to be precise enough to be sensitive to this rate of normal tissue loss. In considering this result it is important to be aware that TOF-MRA is a velocity dependent method and that the NVL represents only the extent of those vessel that could be detected in the images. There may be several reasons why the detected vessel length could decline. These include reductions in vessel diameter of distal branches so that they are no longer adequately resolved in the images and/or reductions in flow rates that lead to a progressive loss of visibility of vessels in older subjects [1]. Thus although the results are unequivocal, their significance remains to be further investigated.

References

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