4D Flow MRI for intracranial hemodynamic assessment in Alzheimer's Disease

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Target Audience: Researchers and clinicians interested in MR flow imaging, potential derivative biomarkers, and dementia.

Purpose: There is increasing evidence that cerebral arteries are often morphologically altered and dysfunctional in Alzheimer's disease (AD) [1]. Therefore, there is growing interest in the non-invasive assessment of cranial hemodynamics as potential systemic indicators of AD [2]. Recent advances in MR hardware, data acquisition, and reconstruction have facilitated 4D flow MRI in clinically feasible scan times, thereby providing dynamic velocity vector maps with volumetric coverage. With adequate spatial and temporal resolution, such 4D flow MRI approaches seem ideally suited for comprehensive hemodynamic assessment. In this pilot study, we investigated intra-cranial flow features, particularly mean flow and pulsatility index, in patients with AD and in healthy controls.

Methods: ***Subjects***: The study population consisted of 11 AD patients (age 61-91y, mean = 74.6, 4 F) and 26 normals (age 47-89y, mean = 60.8, 18 F). With IRB approval and HIPAA compliance, informed consent was obtained for all study subjects. ***MRI:*** Volumetric, time-resolved PC MRI data with 3-directional velocity encoding were acquired on a 3T clinical MRI system (MR750, GE Healthcare, Waukesha, WI) with a 3D radially undersampled sequence, PC VIPR [3] with the following imaging parameters V_{enc} = 80 cm/s, imaging volume = 22x22x11 cm^3, 0.7 mm^3 acquired isotropic spatial resolution, TR/TE=7.4/2.7ms, 14,000 projection angles, scan time ~ 7 min, retrospective cardiac gating into 20 cardiac phases with temporal interpolation similar to view sharing [4]. ***Flow analysis:*** Vessel segmentation was performed in MIMICs (Materialize, Leuven, Belgium) from PC angiograms while flow visualization and quantification was performed in EnSight (CEI, Apex, NC). Flow analysis planes where interactively placed orthogonal to the vessel orientation in 11 locations as shown in Fig. 1: 5mm below posterior curve of the Internal Carotid Artery(ICA) (left&right), 5 mm above the posterior curve of the ICA (l&r), 5mm above the basilar artery formation, 5 mm from the Middle Cerebral Artery/ Anterior Cerebral Artery (MCA/ACA) bifurcation (l&r)), within 5 mm of Posterior Cerebral Artery (PCA) and Basilar Artery (l&r), 5-10 mm from the 'proximal' PCA plane(l&r). 2D cine images series with through plane velocities were generated from the 4D flow MRI data and analyzed in a customized Matlab (The Mathworks, Natick, MA) analysis tool [5]. Mean flow and pulsatility index (PI = (Qmax-Qmin/Qmean)) were calculated for all vessel segments and compared between normal and AD patients with Student's t-test (statistical significance for $p<0.05$). In addition, the PI was calculated for 4 age brackets of the normal subjects: (40-49 (n=2), 50-59 (n=9)m 60-69 (n=12), >70 (n=3)).

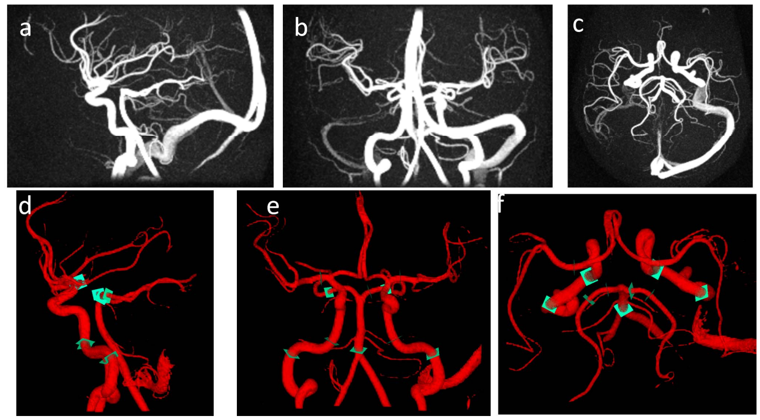

Figure 1: PC VIPR data shown as(a) sagittal, (b) coronal, and (c) axial MIP image and corresponding view of the segmented vessels with eleven flow analysis planes placed perpendicular to the vessel path (d,e,f).

	Normal PI	AD PI	Normal flow (mL/s)	AD flow (mL/s)
Distal ICA	1.11 ± 0.23	1.44 ± 0.25	3.74 ± 0.53	2.68 ± 0.51
MCA	1.04 ± 0.21	1.66 ± 0.43	2.33 ± 0.17	1.41 ± 0.33
Basilar	1.11 ± 0.17	1.41 ± 0.38	2.31 ± 0.39	1.46 ± 0.41

Table 1: Pulsatility index (PI) and mean flow for patients with Alzheimer's disease (AD – grey) and the normal control group. For AD patients, the mean flow is decreased and the PI increased with statistical significance in all five vessels (left and right branch of MCA and ICA are reported together.

age	40-49y	50-59y	60-69y	<70y
	2	9	12	3
Distal ICA	0.87 ± 0.07	1.09 ± 0.06	1.08 ± 0.27	1.68 ± 0.30
MCA	0.78 ± 0.14	1.13 ± 0.07	1.00 ± 0.23	1.53 ± 0.31
Basilar	0.89 ± 0.20	1.11 ± 0.23	1.15 ± 0.19	1.46 ± 0.23

Table 2: Pulsatility index vs age group of the normal control group. The PI increases with age.

Results and Discussion: Fig. 1 shows a representative imaging study with the PC angiogram and the cut planes for flow analysis superimposed on the segmented arterial tree. Results for the flow and PI analysis are summarized for five vessels (distal ICA (l&r), MCA (l&r), basilar) in Table 1. There is a statistically significant decrease in mean flow and increase in PI for the AD patients vs the normal control group. These results are similar to those reported in a study based on intracranial ultrasound and are thought to be a consequence of increased arterial rigidity, decreased arterial compliance, combined with putative age-associated cardiovascular output declines [2]. Table 2 shows the PI for the 4 age brackets of the normal subjects, which increases with age.

Conclusions: This pilot study demonstrates the feasibility of hemodynamic analysis over a large vascular territory in the context of Alzheimer's disease with 4D flow MRI. Significant differences were demonstrated in the pulsatility index and mean flow between AD patients and a normal control group. A larger subject population is needed for more detailed analysis including age effects in the AD population as well as incorporating anatomical variances in the cranial vasculature [6]. With the large volume coverage and high temporal and spatial resolution demonstrated here, 4D flow MRI can provide additional biomarkers of vascular health that can contribute to the identifying patients who could benefit from interventions to improve circulatory system functions.

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