# Flow Sensitive 4D MRI: Descending Aortic Retrograde Flow and Embolization Risk in Acute Stroke Patients

**M. Markl[1], C. Strecker[2], P. Dudler[2], A. Nußbaumer[2], J. Bock[1], A. F. Stalder[1], A. Frydrychowicz[1], A. L. Stroh[3], C. Weiller[2], J. Hennig[1], and A. Harloff[2]**

[1]Dept. of Diagnostic Radiology, Medical Physics, University Hospital, Freiburg, Germany, [2]Dept. of Neurology, University Hospital, Freiburg, Germany, [3]Dept. of Cardiology, University Hospital, Freiburg, Germany

**Introduction:** Previous studies have shown that atherosclerosis and thus increased aortic stiffness results in marked increase of diastolic retrograde blood flow in the aorta [1]. Recent echocardiography and MRI studies in patients with embolic stroke and plaques in the descending aorta demonstrated retrograde flow channels directed towards the brain feeding arteries. It was hypothesized that retrograde embolism from the proximal descending aorta into the brain would be theoretically possible [2, 3]. However, a significant retrograde flow leading to cerebral embolization was only considered for the rare coincidence of high-grade aortic valve insufficiency [4, 5].
It was the purpose of this study to evaluate individual retrograde flow patterns in 63 acute stroke patients by flow sensitive 4D MRI [6]. We hypothesized that in presence of progressive aortic atherosclerosis and thus reduced aortic compliance descending aortic retrograde blood flow could be far more pronounced than expected. As a result, it would be necessary to consider high risk plaques (maximum thickness ≥4 mm) in the descending aorta as novel high-risk source of brain ischemia as previously shown for plaques localized in the ascending aorta and the aortic arch [7].

**Methods:** Transthoracic and echocardiography (TTE) was used to assess aortic valve-insufficiency (grade I-IV), systolic ejection fraction and diameter of the ascending aorta in 63 acute stroke patients (age 17-85 y). Additional exams were performed using a 3T MR system (TRIO, Siemens, Germany). T1-weighted fat-saturated 3D gradient echo imaging (T1 3D-GRE) with near-isotropic spatial resolution ($0.8x1.1x1.1mm^3$) was used for plaque detection, localization and analysis of maximum aortic wall thickness (AWT) of the ascending/descending aorta and aortic arch [8]. For the assessment of time-resolved 3D blood flow in the entire thoracic aorta, flow-sensitive 4D MRI was employed: venc =150cm/s, spatial res. = 2.1 x 3.2 x $3.5mm^3$, sagittal oblique 3D volume, $\alpha = 15°$, TE =3.5ms, TR = 6.1ms, temporal res. = 45ms. Respiration and wall motion artifacts were minimized by ECG and respiratory gating. The extent of retrograde flow originating in the proximal descending aorta was evaluated using 3D flow visualization (EnSight, CEI, Apex, USA) [4, 6]. To evaluate maximum retrograde flow, analysis was based on time-resolved 3D particle traces originating from a series of emitter planes virtually positioned distal to the origin of LSAO with an inter-plane distance of 10mm. Time-integrated 3D particle traces were successively calculated to identify the maximum reach of retrograde flow (figure 1), which was defined as the most distal location for which particle traces connected the emitter plane and the LSA, e.g. emitter plane 4 in figure 1.

**Results:** The extent of retrograde flow in the proximal descending aorta in all 63 patients was 24.8 ±12.8mm (median 20mm, range 10-60mm) which was chosen as cut-off for the distribution of patients into group 1 (<25 mm) and group 2 (≥25 mm) in table 1. Logistic regression analysis revealed a stepwise increase of the risk of retrograde flow ≥25 mm with increasing age: adjusted OR=1.92 (95% CI 1.16–3.19) for each decade. Except for age, however, the extent of retrograde flow did not significantly correlate with other TTE or MRI findings. Most noticeably, no correlation of the extent of retrograde flow and the severity of aortic valve insufficiency was found (figure 2A). Even for the 13 of 63 patients with the most pronounced retrograde flow (>40 mm) only 1 patient suffered from high-grade (III) valve insufficiency. Further, AWT as a measure for the severity of atherosclerotic disease did not correlate with the extent of retrograde flow.
Most noticeably, in 33/63 patients with high risk plaques ≥4 mm, retrograde flow lengths closely matched the distance between the high risk sources the descending aorta and the LSA outlet. Of these 33 patients, 26 (79%) suffered an embolic stroke and a direct retrograde embolization pathway connecting the high risk source and the LSA was found in 18 patients (69%). Further, MRI revealed potential retrograde embolization in 7/29 (24%) patients with previously undetermined etiology. Individually detected stroke risk via retrograde embolization closely matched clinical findings, i.e. involvement of the posterior circulation or left hemisphere in 15/18 patients (83%) with embolic events and 6/7 patients (86%) with undetermined etiology.

**Discussion:** The results of this study demonstrate that marked retrograde flow is a very frequent finding in stroke patients. Contrary to current clinical considerations, retrograde flow of several centimeters was frequently observed in patients with normal aortic valves. Further, 4D MRI was successfully used to establish a direct link between high risk plaques in the descending aorta and embolic stroke for individual patients.
Our findings helped to provide a potential explanation of stoke in 25% of all patients with previously undetermined etiology. Therefore, complex aortic plaques 25 mm distal to the LSA should be taken into account as a potential high-risk source in stroke patients. The combination of plaque location in the descending aorta and formation of retrograde flow channels initially passing the left supra-aortic arteries are in close agreement with the observed higher incidence of ischemic events involving the left hemispheric or posterior circulation. Since, except for age, no other cardiovascular risk factors were found, MRI may be the methods of choice for stroke risk assessment, i.e. identification of plaque location and retrograde flow analysis by 4D MRI, to safely determine stroke risk for individual patients.

| Characteristic | Retrograde flow <25 mm, n = 39 | Retrograde flow ≥25 mm, n = 24 | P Value |
|---|---|---|---|
| Age [years] | 56.5 ±14.4 | 65.3 ±7.8 | 0.008 |
| Hypertension, no. (%) | 28 (71.8) | 20 (83.3) | n.s. |
| CAD, no. (%) | 4 (10.3) | 1 (4.2) | n.s. |
| PAD, no. (%) | 2 (5.1) | 2 (8.3) | n.s. |
| Maximum AWT [mm] | 3.73 ±1.42 | 4.05 ±1.54 | n.s. |
| Mean maximum AWT [mm] | 2.80 ±0.96 | 3.12 ±1.05 | n.s. |
| Systolic ejection fraction [%] | 57.3 ( ±5.6 | 58.2 ±4.3 | n.s. |
| Aortic diameter [mm[ | 32.7 ±4.1 | 34.0 ±3.5 | n.s. |

**Table. 1**: Characteristics of the 63 study participants. CAD = coronary artery disease, PAD = peripheral artery disease, AWT = aortic wall thickness, mean AWT = all aortic segments, p-values by Fischer`s exact and unpaired t-test.

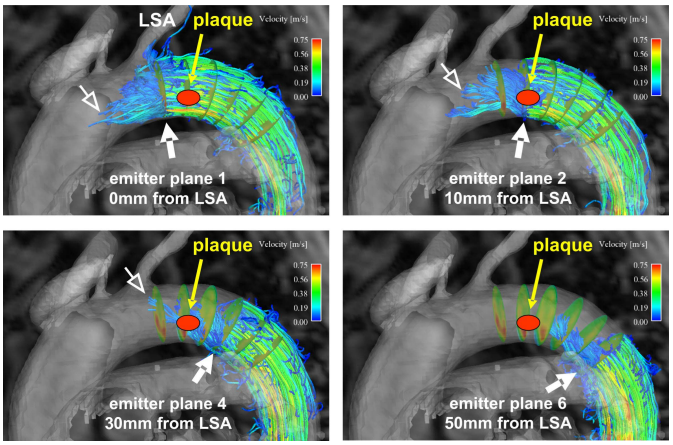


**Fig. 1**: Assessment of maximum retrograde flow by 3D particle traces originating from the emitter planes 1-6. For emitter plane locations 1-4, marked retrograde flow reaching at least as far as the left subclavian artery (LSA) can be identified (open white arrows). In this patient a complex plaque ≥4 mm was detected 10mm distal to the LSA (red marker) which was thus considered a high risk source of embolic stroke via retrograde embolization.

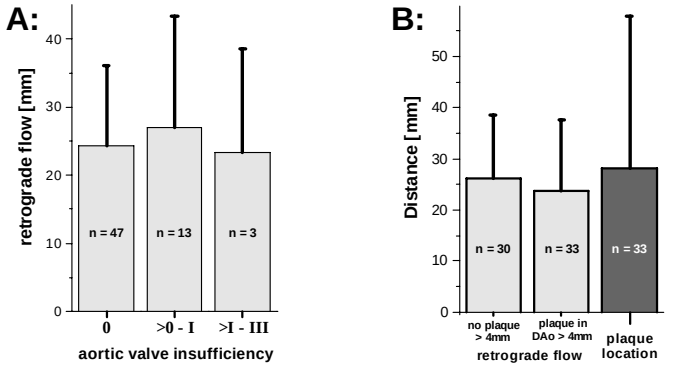


**Fig. 2**: **A:** Mean retrograde flow distances demonstrated no correlation with aortic valve insufficiency (p>0.05). **B:** Mean lengths of retrograde flow for all 63 patients and mean plaque location for 33 patients with high-risk sources ≥4 mm (dark gray column). The extent of retrograde flow was independent from the existence of high-risk plaques (p>0.05).

**References:** **1.** Bogren HG, et. J Magn Reson Imaging 2004;19:417-427. **2.** Tenenbaum A, et al. Chest. 2000;118:1703-1708. **3.** Harloff A, et al.. J Magn Reson Imaging, 2007, in press. **4.** Kronzon I, et al. Circulation. 2006;114:63-75. **5.** Reimold SC, et al. J Am Soc Echocardiogr. 1996;9:675-683. **6.** Markl M, et al.. J Magn Reson Imaging 2007;25:824-831. **7.** Cohen A, et al. Circulation. 1997;96:3838-3841. **8.** Harloff A, et al. J Neurol Neurosurg Psychiatry 2007, in press.