Some hints into Fellgiebel's work “Basilar Artery Diameter is a Potential Screening Tool for Fabry Disease in Young Stroke Patients” (Cerebrovasc Dis 2011;31:294–299 297 )

Fabry disease (FD) is a rare hereditary lysosomal storage disease that has been highlighted as a possible etiology of stroke at a young age. The prevalence of ischemic stroke has been reported to be about 12 times greater in FD patients than that expected in a comparable general population. Cerebrovascular events in males typically occur at an early age and preferentially within the territory of the posterior circulation. In females, cerebrovascular events occur a mean of 10 years later.

The neurological hallmarks of Fabry disease include small fiber neuropathy as well as cerebral micro- and macroangiopathy. Conventional MRI shows micro- and macroangiopathic changes such as progressive white matter lesions at an early age, increased signal intensity in the pulvinar on T1-weighted MRI (‘pulvinar sign’) as well as tortuosity and dilatation of the larger vessels. Enlarged basilar artery diameters (BADs) have been demonstrated to be higher in FD compared to healthy controls and Fellgiebel and coworkers have recently showed that, among other MRI findings which are known to be indicative for FD, especially white matter lesions, the enlarged BAD was by far the best MR morphological characteristic to separate FD patients from normal controls.

In particular, using a BAD cutoff of 2.67 mm derived by receiver-operating curve (ROC) analysis, patients could be separated from controls with an accuracy of 87%. This favorable diagnostic utility was clearly superior to all other applied structural MR measurements such as global white matter lesion load, global mean diffusivity and diameters of the remaining larger vessels of the circle of Willis.

There is evidence that the proportion of undiagnosed FD within the cohort of young cryptogenic stroke patients is much higher (5% of males and 2.4% of females aged 18–55 years in cryptogenic stroke, corresponding to 1.2% of all young stroke patients) than previously expected.

In some cases, ischemic stroke at a young age is the first manifestation of the disease. Therefore, a reliable and easily detectable screening parameter for FD in young cryptogenic stroke patients would be highly desirable. An enlarged BAD might serve well as this parameter. However, diameters of the cerebral blood vessels between FD and common stroke patients have not yet been systematically compared. The aim of Fellgiebel et coll. study was to determine the reliability and diagnostic utility of BADs for the identification of FD in a mixed cohort of patients with FD, young non-FD stroke patients and healthy controls.

BADs were measured on a 1.5-tesla system using MR angiography (time-of-flight sequences) in 3 age- and gender-matched groups: 25 FD patients, 26 non-FD stroke patients and 20 healthy controls.

Men with FD had a significantly larger BAD (3.88+/−0.64 mm) than women with FD (3.08+/−0.31 mm, p = 0.006). BADs did not differ significantly between men (2.78+/−0.42 mm) and women (2.38+/−2.52mm) within the stroke group. Both men and women with FD had increased BADs compared to the age-matched stroke patient group (p=0.0005).

The subgroups of FD men and women could also be distinguished significantly from sex-matched stroke patients by ROC analyses of BADs.

FD patients could be significantly separated from stroke patients by BADs while diameters of all larger vessels did not differ significantly between patients and healthy controls. Whereas a number of etiological factors has been suggested for the FD-associated microangiopathy, the nature of macroangiopathy in FD, especially the pronounced involvement of the basilar artery, is still unclear.

It has been suggested that autonomic dysfunction is a leading mechanism for the dilatation of the larger brain vessels and causes, possibly enforced by secondary hemodynamic changes, the pronounced involvement of the basilar artery.
Eighty-six percent of all subjects could be correctly classified by BADs (sensitivity 84%, specificity 88.5%). Therefore, enlarged BADs were able to detect FD within a cohort of FD, stroke patients and healthy controls. BAD measurement could be an easily obtainable and sensitive screening tool for FD in young stroke patients.

Rapid diagnosis is highly desirable in light of the possible therapeutic intervention. It is noteworthy that enzyme replacement therapy (ERT) is available and has already shown beneficial effects on renal, cardiac and peripheral nerve function in FD. Thus, beyond etiological and prognostic evaluations, young stroke patients should be screened systematically for FD to initiate both sufficient reinfarction prophylaxis with regard to the specific needs of FD patients and ERT to improve or stabilize the course of the disease. Although pathologically increased cerebral blood flow in FD could be reversed under ERT, it remains to be studied if ERT can reduce the progression of brain structural alterations or the probability of subsequent cerebrovascular events.

In addition to the highlighted diagnostic utility, some additional aspects contribute to the qualification of basilar artery measurements using MR angiography (TOF sequences) as feasible routine tool for the screening of FD in young stroke patients. Firstly, analyses are not time-consuming (duration of 1 measurement including data processing about 5–10 min), and the MR angiography is broadly available, noninterventional and without contrast agent.

Moreover, studies validating TOF MR angiography measurements of the cerebral vessel diameters by phantom studies, animal models or by digital subtraction angiography showed sufficient concordance of the different measures. One has to mention that the TOF angiography without the use of contrast agents is especially sensitive to fast-flowing blood, because only unsaturated blood produces a high signal. The disadvantage is that slowly flowing blood is more difficult to detect by just applying TOF techniques. Thus, it seems possible that the technique might overestimate vascular diameters in the case of FD, especially in the posterior circulation where the blood flow is known to be significantly elevated. This potential weak point concerning the validity of the BAD must not necessarily imply a disadvantage of the technique for the diagnostic screening of FD in the young stroke population. On the contrary, the use of the increased blood flow information could improve the diagnostic accuracy of the parameter compared to the exclusively morphological information.