

People and Publications

The Neurovascular Laboratory of the Department of Neurology, Albert-Ludwigs-University Freiburg is the pioneering institution for neurosonology in Germany. In Freiburg, ultrasonography is traditionally employed as a practical tool for identification and quantification of vascular pathology in close conjunction with clinical neurology. Since 1990 A. Hetzel is the head of a highly qualified team comprising medical researchers, vascular technicians and high end technology. Cerebral autoregulation is one of the main interests of the group. (M. Kaps)

Cerebral Autoregulation in Acute Stroke

by **A. Hetzel**

The assessment of cerebral autoregulation has experienced dramatic changes over the last years. With the introduction of transcranial Doppler sonography (TCD) an equipment exists, which enables noninvasively with a high-time resolution a measurement of dynamic responses of cerebral blood flow velocity (CBFV) to transient changes in blood pressure [1,2]). Such spontaneous changes occur especially in a low frequency range around 0.1 Hz. Transfer function analysis in the frequency domain [3] and correlation coefficient methods in the time domain [4,5] are used to reveal parameters for dynamic cerebral autoregulation from these spontaneous fluctuations.

TCD measurements enable bilateral non-invasive monitoring of dynamic cerebral autoregulation in acute stroke from spontaneous blood pressure fluctuations [2,6]. Dynamic autoregulation itself has been shown to correlate closely to the classical static autoregulation and thus represents an elegant method for serial assessment of autoregulation dynamics [7]

An important limitation is that transcranial Doppler sonography can assess the MCA territory only as a whole. Focal areas of autoregulatory impairment cannot be ruled out. Therefore dynamic autoregulation measured within the first 5 days after stroke in minor MCA stroke did not found MCA dysautoregulation [6]. Other studies found a diffuse MCA dysautoregulation on affected and unaffected sides lasting for at least fourteen days independent of underlying MCA or posterior cerebral artery stroke and stroke severity [8,9]. A recent investigation showed a dynamic dysautoregulation over affected sides in large MCA strokes and a presumably preexisting bilateral dysautoregulation in lacunar stroke due to small vessel disease [10]. These studies measured autoregulation once within 72 hrs of onset not allowing observing a temporal evolution during the first days of stroke.

During the initial stages of vessel occlusion and early reperfusion, tissue lactate acidosis impairs the autoregulatory mechanism in the ischemic core and periinfarct area [7]. Observation of the temporal evolution of dynamic autoregulatory impairment in the territory of the basal arteries will help us in understanding of stroke evolution within the first three days. Cerebral autoregulatory impairment may play a significant role during stroke evolution with reperfusion and hyperperfusion [11]. Disturbance of the cerebral autoregulatory mechanism in the contralateral hemisphere in acute stroke has been

described previously [12]. Recent investigations did not show altered dynamic autoregulation in acute major MCA stroke in the contralateral hemisphere suggesting no relevant general affection of the cerebral autoregulatory mechanism in acute stroke [10].

As a practical result of these data we suggest for clinical practice that blood pressure strategies will be optimal if specific attention is paid to the status of vessel recanalization and autoregulatory capacity.

References:

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The Group, the Topics and the Papers

History: the neurovascular lab in Freiburg was founded by Freund, von Büdingen und von Reutern during the early years of ultrasound. Since these days the philosophy of neurovascular ultrasound in Freiburg was ultrasonography as practical tool for identification and quantifications of vascular pathology and as an extension of the clinical examination. Since 1990 this guideline and ultrasound as a research tool was continued by A. Hetzel and supplemented together with his colleagues by the following emphasis:

Wolf-Dieter Niesen: Sonoperfusion in acute stroke

Transcranial ultrasound plays an important role in acute stroke patients. Due to the introduction of ultrasound contrast enhancers the detection of acute MCA occlusion and branch occlusion has a high sensitivity. Additionally, by applying contrast media the visualization of the microcirculation is possible and several studies were able to detect perfusion deficit in acute stroke patients. Whilst initially the detection of perfusion was possible ipsilateral to the probe only nowadays a bilateral approach is used. Thus the depiction of cortical perfusion deficit as well as leptomeningeal collateral perfusion is possible.

Our study group uses transcranial perfusion sonography in a bilateral approach in several clinical settings. Studies on acute stroke patients before and following thrombolysis are just being published. Comparison of perfusion deficit with other perfusion weighed methods seems promising. Also the depiction of “penumbral flow” in different types of bleeding is an interesting topic.

Future aspects of transcranial sonoperfusion will include the replacement of the established bolus kinetic methods by more rapid perfusion techniques. The transportation of these techniques in a clinical setting with a bilateral approach will be a challenge. Also the development of new ultrasound probes with the possibility of a three-dimensional perfusion acquisition is an exciting outlook.

Selected papers:

- Niesen WD, Burkhardt D, Hoeltje J, Rosenkranz M, Weiller C, Sliwka U. Related Articles, Links Transcranial grey-scale sonography of subdural haematoma in adults. *Ultraschall Med.* 2006;27:251-5.
- Niesen WD, Rosenkranz M, Eckert B, Meissner M, Weiller C, Sliwka U. Hemodynamic changes of the cerebral circulation after stent-protected carotid angioplasty *AJNR Am J Neuroradiol.* 2004;25:1162-7.
- Niesen WD, Weiller C, Sliwka U. Unstable cerebral hemodynamics in carotid artery occlusion and large hemispheric stroke: a cerebral blood flow volume study. *J Neuroimaging.* 2004;14:246-50

Matthias Reinhard: Dynamic cerebral autoregulation in neurovascular disease

Assessment of the protective mechanism of cerebral autoregulation may be the most natural measure for hemodynamic integrity of cerebral circulation. Apart from studies in acute ischemic stroke and intracranial hemorrhage, a main field of research pertains to obstructive carotid artery disease, in which a predictive value of dysautoregulation for ischemic events could recently be confirmed. Further current pathophysiological studies aim to analyze cerebellar autoregulation dynamics by transcranial PICA monitoring. This may be of particular interest in migraine which is associated with an increased rate of vascular borderzone cerebellar lesions. Methodological advances include the urgent technical simplification of dynamic autoregulation testing obviating the use of a continuous blood pressure monitor and extending dynamic autoregulation testing to BOLD magnetic resonance imaging.

Selected papers:

- Reinhard M, Roth M, Guschlbauer B, Harloff A, Timmer J, Czosnyka M, Hetzel A. Dynamic cerebral autoregulation in acute ischemic stroke assessed from spontaneous blood pressure fluctuations. *Stroke.* 2005;36:1684-9

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- Reinhard M, Muller T, Guschlbauer B, Timmer J, Hetzel A. Dynamic cerebral autoregulation and collateral flow patterns in patients with severe carotid stenosis or occlusion. *Ultrasound Med Biol*. 2003;29:1105-13.
- Reinhard M, Roth M, Muller T, Czosnyka M, Timmer J, Hetzel A. Cerebral autoregulation in carotid artery occlusive disease assessed from spontaneous blood pressure fluctuations by the correlation coefficient index. *Stroke*. 2003;34:2138-4

Andreas Harloff: Multimodality imaging in atherosclerosis and stroke.

The diagnostic impact of transesophageal echo-cardiography (TEE) and recommendations for the use of TEE in the diagnostic workup of stroke patients in clinical routine were derived from our detailed findings in 500 patients. However, due to the semi-invasiveness and limited diagnostic accuracy of TEE for the detection of aortic plaques we also evaluated alternative diagnostics: normal intima-media thickness as measured by high-resolution Duplex sonography was found to exclude complex aortic plaques (≥ 4 mm or thrombi) in acute stroke patients with a high level of confidence. Furthermore, predictive accuracy was even increased by combining carotid IMT with the less popular parameter carotid distensibility (DC). Furthermore, by use of a novel 3D MRI protocol at 3Tesla and its improved visualization of the aortic arch we detected additional aortic embolic high-risk sources in 30% of patients classified as cryptogenic stroke despite extensive routine diagnostics including TEE. Additionally, the visualization of 3D blood flow characteristics in MRI in such patients showed individual retrograde flow channels originating from complex plaques in the descending aorta into the brain-supplying arteries. Thus, the exact role of plaques in the descending aorta as a frequent but novel high-risk source for embolic stroke in larger cohorts will be the aim of our future studies.

Selected papers:

- Markl M, Harloff A, Bley TA, Zaitsev M, Jung B, Weigang E, Langer M, Hennig J, Frydrychowicz A. Time-resolved 3D MR velocity mapping at 3T: improved navigator-gated assessment of vascular anatomy and blood flow. *J Magn Reson Imaging*. 2007;25:824-831.
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Andreas Hetzel and Matthias Reinhard: Ultrasound imaging in giant cell arteritis

Temporal or giant-cell arteritis is the most common form of vasculitis in older Caucasians. Over the last years, color-coded (duplex) sonography has attracted increasing interest as a noninvasive diagnostic tool for patients suspected of having temporal arteritis. This approach has evolved with the development of high frequency high-resolution ultrasound scanners. As a main sign, a dark (hypochoic) so-called "halo" around the vessel wall was found as pathognomonic for acute arteritis. Because of its high positive predictive value in typical cases ultrasound represents an elegant bed-side

method for rapid diagnosis of giant cell arteritis. It also allows to detect less common but clinically equally important manifestations e.g. in the vertebral arteries. Current projects aim to assess the value of ultrasound in comparison with magnetic resonance imaging, which evolved as another noninvasive but costly imaging option for giant cell arteritis.

Selected papers:

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The Freiburg's Favourites of Recent Literature

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- Martini SR, Hill MD, Alexandrov AV, Molina CA, Kent TA. Outcome in hyperglycemic stroke with ultrasound-augmented thrombolytic therapy. *Neurology.* 2006;67:700-2.
- Poppert H, Sadikovic S, Sander K, Wolf O, Sander D. Embolic signals in unselected stroke patients: prevalence and diagnostic benefit. *Stroke.* 2006;37:2039-43.



Freiburg group: Dr. Hetzel (center) and his team.