Introduction: A number of studies have shown that the development of atherosclerosis in the carotid artery is also related to the geometry and local hemodynamic conditions [1,2]. Particularly, low absolute wall shear stress (WSS\textsubscript{mag}) and a high oscillatory shear index (OSI) predict the development of vulnerable plaques [3]. No comprehensive analysis of the segmental in-vivo topology of physiological WSS, its dependence on individual bifurcation geometry, and changes in wall parameter distribution associated with disease and treatment has been presented to date. In addition, the evaluation of the true magnitude and direction of regional WSS variations requires its assessment as a time-resolved vector quantity which was often not performed in previous studies.

To address these requirements we employed flow-sensitive 4D MRI with full bifurcation coverage and three-directional velocity encoding in combination with an optimized data quantification strategy [4-6]. The aim was to assess the normal in-vivo distribution of WSS\textsubscript{mag} and OSI (n=64) and to evaluate the dependence of critical wall parameters on individual bifurcation geometry. Further, the distribution of critical wall parameters was compared to patients with internal carotid artery stenosis (n=6) and after treatment (n=11).

Methods: Flow-sensitive 4D-MRI at 3T (Siemens Trio, flip angle=15°, TE/TR=3.1ms/5.7ms, venc=150cm/s, resolution=1.1x0.9x1.4mm\textsuperscript{3}, slab thickness = 50.4mm, 36 slices/slab) was used to assess time-resolved 3D blood flow in 64 normal carotid bifurcations (32 volunteers, 25.3 ± 3.4 years) and 17 patients with moderate ICA stenosis (n=6) and after surgical recanalization (endarterectomy, n=11). Inter-scan and inter-observer variability were analyzed in a subgroup of 10 volunteers. The resulting 4D MRI data was used for phase contrast angiography data calculation (PC-MRA, figure 1) and flow pattern visualization (EnSight, CEI, USA, figures 1 and 2). The distribution of wall parameters was evaluated in 7 analysis planes as shown figure 1. Wall parameter quantification was based on a direct interpolation of the local velocity derivative onto the segmented vessel contour, providing a WSS vector estimate which was characterized by its time-averaged magnitude (WSS\textsubscript{mag}) and inversion over the cardiac cycle (OSI) [4]. For volunteers, an individual ‘area at risk’ was quantified as the fraction of the posterior carotid bulb exposed to atherogenic low WSS\textsubscript{mag} and high OSI beyond group-defined 80% and 90% thresholds. Individual carotid geometry (d\textsubscript{ICA}/d\textsubscript{CCA} diameter ratio, bifurcation angle, tortuosity) was correlated (multiple regressions) with absolute wall parameters and area at risk to identify independent predictors and their relative contributions (standardized regression coefficients \(\beta\)) for atherosclerosis. To compare the topology of critical wall parameters between normal controls and patients, the incidence of individual lowest (highest) WSS\textsubscript{mag} (OSI) beyond a 15% threshold was mapped onto a multi-segment bifurcation model (figure 3).

Result: Repeated measurements and analysis of WSS\textsubscript{mag} and OSI demonstrated good inter-scan reproducibility (r=0.49 and 0.77, p<0.001) and low inter-observer variability (r=0.92 and 0.85, p<0.001).

Critical wall parameters were consistently concentrated in proximal bulb regions of the common and internal carotid artery (figure 3, right). However, the extent of the area at risk demonstrated a wide variation (0-90% of the bulb region) among the 64 normal carotid arteries. Multiple regressions revealed significant (p<0.01) relationships (|\(\beta\)|=0.44-0.48) between the area at risk and the d\textsubscript{ICA}/d\textsubscript{CCA} diameter ratio for all wall parameters. The size of regions exposed to high OSI demonstrated highly significant (p<0.01) relationships (|\(\beta\)|=0.47-0.59) with all analyzed geometry parameters (d\textsubscript{ICA}/d\textsubscript{CCA}, bifurcation angle, tortuosity). Consistently, the combination of tortuosity and d\textsubscript{ICA}/d\textsubscript{CCA} was a strong predictor (p<0.02, |\(\beta\)|=0.41-0.58) for disturbed absolute wall parameters in the bulb region as also exemplary illustrated in figure 2.

Discussion: Flow-sensitive MRI allows for the individual in-vivo quantification of wall parameter topology in the carotid artery. Bifurcation geometry was directly linked to exposure to critical wall parameters and may thus be a useful indicator for the individually increased risk for the development of flow-mediated atherosclerosis. The presence of ICA stenosis can alter wall parameter distributions, which may help to predict future growth of existing plaques or the risk for re-stenosis following treatment.

Fig. 1: Standardized evaluation of the wall parameter distribution in the carotid bifurcation. Based on the 3D PC-MRA geometry, 7 analysis planes were positioned in the common (CCA), internal (ICA), and external (ECA) carotid artery with an inter-slice distance of 4mm (left). Asymmetric flow profiles and reduced velocities in the posterior ICA bulb can result in considerably reduced WSS in this region (open arrows, right).

Fig. 2: Flow visualization in 2 volunteers of the study cohort illustrates the influence of bifurcation geometry on flow patterns and wall parameters. Increased ICA/CCA diameter ratio and bifurcation angle in volunteer 2 resulted in larger regions with low and recirculating flow (open arrows) generating increased exposure to low WSS indicating a higher risk of atherosclerosis.

Fig. 3: Distribution of critical wall parameters for n=64 normal carotid arteries, n=6 patients with moderate ICA stenoses and n=11 patients after therapy.

Acknowledgements: Deutsche Forschungsgemeinschaft (DFG), Grant # MA 2383/4-1, Bundesministerium für Bildung und Forschung (BMBF), Grant # 01EV0706.