Evaluating the Reproducibility and Regional Variation of Wall Shear Stress in Rat Model with the Use of Flow-Sensitive MRI

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Introduction:

With advantages of non-invasive, phase-contrast magnetic resonance imaging (PC-MRI) is valuable by providing information regarding the assessment of blood flow. The measurement of local flow profiles provide insights into the blood rheology, gaining the flow velocity and its derived parameters, such as wall shear stress (WSS) [1]. It has been proposed that exposure of the arterial wall to a relatively lower WSS will contribute to the development of atherosclerosis [2]. Rats with native hypertension (spontaneously hypertensive rat, SHR) are an excellent animal model to go further study on the atherosclerosis. However, WSS derived from PC-MRI in SHR model has not been fully discussed. This may be due partly to the fact that less numbers of image pixels covering the vessel lumen may contribute to errors in velocity estimation [3]. In this study, we concentrated on exploring the hemodynamic patterns of common carotid arteries (CCA) in the SHR model by measuring WSS with PC-MRI. The reproducibility of measured WSS was investigated to evaluate the errors resulted from limited numbers of pixels within the lumen of CCA. In addition, regional variations of WSS at each vascular segment were also computed to show the regional abnormal WSS in SHR model.

Materials and Methods:

Seven SHR (male, weight=310~350 g) and seven normotensive Wistar Kyoto (WKY) (male, weight=320~355 g) rats at ages of 16 weeks were anesthetized with 1.5% Isoflurane. All images were acquired in a 7T animal MRI scanner (Bruker ClinScan 70/30) with gradient strength of 630mT/m. PC-MRI was conducted by the prospective ECG triggering. A 2D single-slice time-resolved PC-MRI were performed as following parameters: TR/TE/θ=15.55msec/4.51msec/30°, matrix size=256×256, slice thickness=2 mm, number of average=10, and FOV=40×40mm. To evaluate spatial differences in WSS, the PC-MRI was performed at two levels, including middle (CCA_{mid}) and bifurcation (CCA_{bifur}). For investigating the intra-scan reproducibility, animals were scanned twice with identical localizer. WSS was calculated based on the following equation:

$$WSS = \eta \, dv/dr$$

where η is the viscosity of fluid, v is the velocity of fluid, and r is the vessel radius. Two parameters were extracted from each WSS function: temporal averaged WSS (WSS_{avg}) and systolic WSS (WSS_s). The WSS_{avg} was the average WSS over all cardiac cycle and WSS_s was the maximum WSS over the systolic phase. For assessing the intra-observer variability, the region of interest (ROI) outlining was repeated for each rat by the same operator on two different days. The velocity profile and WSS parameters were extracted by an analysis tool computed on Matlab [1].

Results:

The WSS parameters are compared in Fig. 1. For SHR, WSS_{avg} and WSS_s were significantly reduced in CCA_{bifur} when compared to those in CCA_{mid} (P<0.05). However, this phenomenon did not occur in WKY (normal control). With the hypertension as a risk for developments of atherosclerosis, SHR also exhibit the significantly lower WSS_{avg} and WSS_s in CCA_{bifur} when compared to WKY (P<0.05). The Bland-Altman plots demonstrating the reproducibility of WSS_{avg} for intra-observer variability and intra-scan variability are represented in Fig. 2(a) and 2(b), respectively. Both reproducibility measurements exhibited good agreements, and the corresponding intraclass correlation coefficients (ICCs) were 0.939 and 0.895, respectively. The results of the segmental WSS_{avg} analysis for WKY and SHR are displayed in Fig. 3(a) and 3(b), respectively. Figure 3(c) and 3(d) show the segmental WSS_s analysis for WKY and SHR, respectively. For WKY, WSS_{avg} and WSS_s were homogenous around the circumference of the vessels. For SHR, however, relative lower WSS_{avg} and WSS_s at the posterior of CCA_{bifur} were observed.

Discussion and Conclusions:

This study presents the feasibility and reproducibility of *in vivo* WSS measurements in SHR model by PC-MRI. With spatial resolution of 0.3 mm, high consistencies were demonstrated in the intra-observer and intra-scan analysis. This high reproducibility of WSS measurements could benefit the longitudinal studies of atherosclerosis in SHR model, which is a potential model for drug developments of atherosclerosis. For SHR, WSS_{avg} and WSS_s in CCA_{bifur} were significantly lower than those in $CCA_{mid.}$ Furthermore, SHR also exhibited significantly lower WSS_s and WSS_{avg} at CCA_{bifur} when compared with WKY. These findings imply the higher incidence of atherosclerosis for SHR at bifurcation sites. Regarding the regional changes of WSS, SHR model demonstrated relative lower WSS_{avg} and WSS_s than WKY model, especially at the posterior segments of CCA_{bifur} (Fig. 3). These suggest that prior to presence of atherosclerosis the regional decreased WSS may already provide useful information for the onset of atherosclerosis. In conclusion, noninvasive PC-MRI could be a potential technique for evaluating WSS in longitudinal studies of atherosclerosis in SHR model.

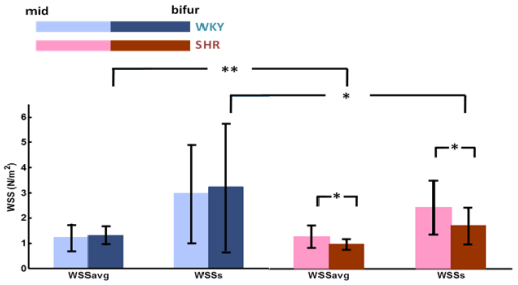

Figure 1. The WSS values for WKY (blue) and SHR (red). For SHR, WSS_{avg} and WSS_s in CCA_{bifur} were significantly lower than that in CCA_{mid}, implying the higher incidence of atherosclerosis at bifurcation sites. To compare with WKY, SHR exhibited significantly lower WSS_s and WSS_{avg} at CCA_{bifur}. (* indicated $P < 0.05$, ** indicated P<0.01)

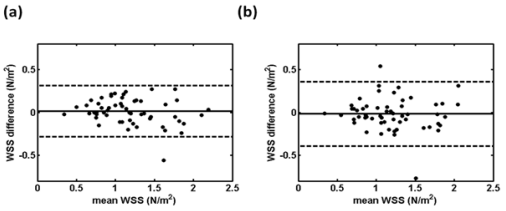

Figure 2. Bland-Altman plots demonstrated the reproducibility of WSS_{avg} for intra-observer (a) and intra-scan (b) variability. High reproducibility was shown with a limited number of pixels within CCA lumens.

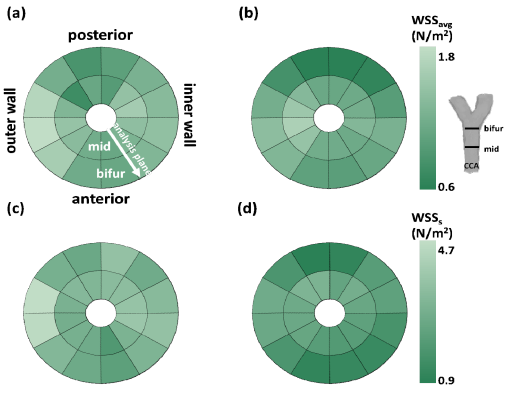

Figure 3. The regional distribution of WSS_{avg} and WSS_s at CCA_{mid} and CCA_{bifur} for WKY (a,c) and SHR (b,d) were shown. Relative lower WSS_{avg} and WSS_s in SHR at the posterior segments of CCA_{bifur} were observed.

References:

1. A.F. Stalder, et al. *Magn Reson Med* 2008; 60: 1218-1231. **2.** A.M. Shaaban, et al. *Am J Roentgenol* 2000; 174: 1657-1665. **3.** Tang et al. *J Magn Reson Imaging* 1993; 3: 377-385.