

Ultrasound Biomicroscopic Study of Arteries in Detection of Doxorubicin-induced Disorders*Shi J. Liu**Department of Pharmaceutical Sciences, University of Arkansas for Medical Sciences, Little Rock, Arkansas 27705, USA*

Ultrasound biomicroscopy (UBM) has been a valuable, non-invasive technique in monitoring cardiac function such as echocardiography. However, UBM is not commonly used in vascular research, especially in small animals. In addition, the use of doxorubicin (DOX), an anti-cancer drug, in treatment for malignancies is limited because of its cardiotoxicity. Whether DOX causes vascular disorders is unknown. Objectives: this study aimed to use UBM to monitor function of major arteries in response to DOX treatment. Methods: Mice were injected intrapleurally with a single dose of DOX (20 mg/kg body weight) or an equivalent volume of saline. The kinetics of blood flow through ascending aorta (AAo), pulmonary artery trunk (PAT), and left coronary artery (LCA) were monitored with Doppler UBM before and after DOX treatment using Vevo®2100 and VisualSonics® software. Results: While abnormal cardiac function was usually observed 3 days after DOX treatment, mean velocity and mean pressure gradient of time-integral AAo blood flow were reduced by 30% and 49%, respectively (n=6). The blood flow of LCA was reduced about 40% (n=5) accompanied by an increased resistive index. The reduction in peak velocity of LCA blood flow during systole was greater than that during diastole. In contrast, the peak velocity of blood flow in PAT was reduced by 10% (n=7), which worsened by 22% with a 40% decrease of mean pressure gradient at 7 days after DOX treatment. Meanwhile, no significant change in these arteries was observed in control group. The reduction in AAo blood flow could result from DOX-induced cardiotoxicity, while reduction of LCA blood flow could cause cardiac dysfunction. The change in PAT could be due to the effect of increased oxidative stress by DOX. Conclusion: UBM could effectively detect hemodynamic changes in major arteries induced by DOX, and thus enhance its application in preclinical research and drug discovery.