In Vivo Transit Time MR-Measurements of Pulse Wave Velocity in the Murine Aorta at 17.6 Tesla

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INTRODUCTION

Aortic stiffness increases in an early state of arteriosclerosis, assessable by pulse wave velocity (PWV) MR-measurements [1,2]. Up to now only studies in larger animals and humans have been reported in literature. A convenient model to study arteriosclerosis is the Apolipoprotein E-deficient transgenic mouse (ApoE-/-) [3]. As part of a comprehensive measuring protocol to examine vessel morphology and function in the mouse two non-invasive MR-imaging techniques measuring the transit time of the pulse wave in the murine aorta were developed. Because pulse wave and flow velocities are similar to velocities in humans, but dimensions are about 20-times smaller, the challenges in these projects were especially the high temporal and spatial resolutions needed (temporal resolution: 1ms, spatial resolution: ≤100µm).

METHOD

Because the pulse wave correlates with changes in cross sectional area of the vessel, the MR-technique measures cross sectional areas of the murine aorta at high temporal rates in two different positions simultaneously (Fig.1). The technique is a transit time method based on a high-resolution CINE-sequence [4], with incorporated flow compensation in three spatial directions (TR: 5.0ms, TE: 1.6ms, in plane resolution: 80x80µm^2, slice thickness: 1mm). To obtain time intervals between movie frames of 1ms, the CINE-sequence is segmented (Fig.2). The total acquisition time is below 30min with threefold averaging. The time course of the vessel cross sectional areas is determined by custom-built post-processing software running under Matlab (MathWorks, Inc., USA). PWVs are calculated by: $PWV = d/\Delta t_{pw}$ (Eq.1), with d being the distance between descending and abdominal aorta (Fig.1), and Δt_{pw} the delay between the onsets of the pulse waves at the two locations (Fig.3). All measurements are performed on a Bruker AVANCE 750 spectrometer (17.6 T, 750MHz, vertical bore) equipped with an actively shielded gradient system (1T/m), a home-built 27mm TEM-resonator. The heart and breath trigger are acquired using a pressure balloon affixed to the mouse's chest and a home-built heart-triggering/breath-gating unit. Heating or cooling the gradient system to keep the body temperature of the mouse constant is of vital importance for the measurement, because the heart rate depends on body temperature. In an enhancement of the transit time method additional bipolar flow encoding gradients in the slice direction are inserted into the MR-technique. Thus, the sequence acquires the time course of blood flow velocities in two different positions. The PWV is calculated according to Eq.1, in this case Δt_{pw} is the delay between the onsets of the pulse waves in the flow velocity curves.

RESULTS

First in vivo measurements of the PWV without flow encoding on two 12-month-old mice (C57Bl/6, body weight ca. 40g) showed PWVs of approximately 5.5m/s. The images of the descending aorta show a nearly elliptical cross section and contain acceleration artifacts. Is the body weight below 36g the cross section of the descending aorta appears almost circular and acceleration artifacts are not noticeable. In vivo measurements with implemented flow encoding indicated PWVs of 3.5m/s to 5 m/s. With flow encoding acceleration artifacts in the magnitude image did not vitiate the measurement of PWV, however in some experiments the heart rate was not constant, which affected the accuracy of the PWVs measured.

DISCUSSION

Literature states PWVs of 3m/s for 12-month-old C57Bl/6 mice, measured using Doppler ultrasound and pressure catheters [3,5]. In mice with a body weight above 36g we measured higher PWVs and noted acceleration artifacts and deformed cross sections. An explanation for these effects might be that heavier mice are corseted in the resonator. The change in temperature during the measurements with flow encoding is due to a different heat dissipation compared to the sequence without flow encoding.

CONCLUSION

Our preliminary results demonstrate that in vivo MR-measurements of PWV are feasible at a magnetic field strength of 17.6 Tesla in mice. Further validation is necessary.

PERSPECTIVE

At present Doppler ultrasound measurements to verify the PWV measurements are conducted. Studies to validate the transit time technique are performed on smaller mice to avoid the corseting in the resonator. Studies investigating the effect of age and existence of arteriosclerosis on the PWV are in progress. The tempering protocol is adapted for the flow encoding sequence. Studies on the progression of arteriosclerosis and regression upon therapy in ApoE-/- mice are pending.

REFERENCES

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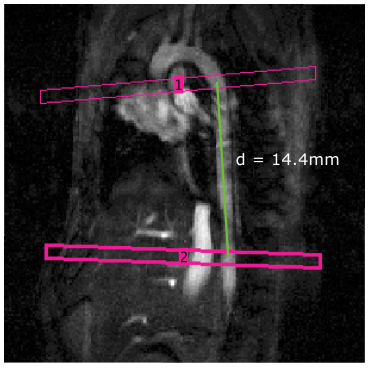

Fig.1: reference scan with imaging slices

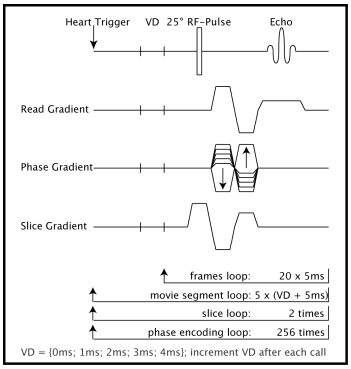

Fig.2: schematic diagram of the MR-sequence; VD is a variable delay list

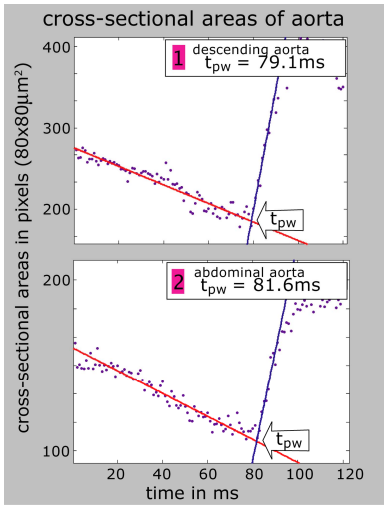

Fig.3: cross sectional area curves and linear fits to determine onset of pulse waves (t_{pw}); Δt_{pw} = t_{pw} (abdominal aorta) - t_{pw} (descending aorta)