A comprehensive quantitative comparison of regional cardiac motion in mice and humans

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Introduction: Mouse models of cardiac defects such as infarction are often used to study the impact of myocardial pathologies on ventricular function. Such translational research is based on the assumption that normal cardiac function and its pathological alterations are similar in mice and humans. However, to date a detailed comparison of regional myocardial motion between mice and humans has not been performed. Tissue Phase Mapping (TPM) is a well-established technique to assess regional cardiac function in humans [1,2]. Two studies reported on the application of TPM in mice [3,4], none of which analysed the time course of the different myocardial velocity components (radial, rotational and longitudinal). Recently, a comparison between mice and humans of only global myocardial velocities was performed in a small number of subjects [5]. The aim of this work was to provide a more detailed analysis of regional myocardial wall motion in normal mice compared to three-directional velocity patterns in human hearts in a larger cohort.

Methods: TPM in humans was performed on a 1.5T Sonata MR-system (Siemens) and murine data were acquired on a 9.4T VNMRS DirectDrive MR-system (Varian Inc). For both experiments, a black blood Cine gradient echo sequence with prospective ECG-gating combined with navigator gating during free breathing (humans) or respiratory gating (mice) was applied. TPM was performed with three-directional velocity encoding with velocity sensitivities as specified below. Three slices in short axis view (basal, mid, apical) were acquired in 20 volunteers (29 ± 5 yrs) and 18 healthy C57/Bl6 mice (22.9 ± 0.6 g).

	Mice	Humans
Matrix size	128^2 (256^2 interp.)	256 x 96 (192 interp.)
Spatial resolution [mm]	0.1 x 0.1	1.3 x 1.3
Slice thickness [mm]	1	8
Temporal resolution [ms]	4.6	13.8
Venc in-/ through-plane [cm/s]	6 / 8	15 / 25

Table 1: Parameters for mice and human measurements.

Data post-processing was performed using customized software programmed in Matlab. The measured in-plane velocities (Vx,Vy) were transformed into radial (Vr) and circumferential (rotational, Vφ) velocities. To avoid temporal jitter, the time axis was normalized to the end-systolic time as defined by the first minimum peak during isovolumetric relaxation of the global radial velocities (see Fig. 2). Global and regional velocity time courses were calculated as the mean of myocardial pixels within the segmentation mask or within ROI according to the AHA 16-segment model. Peak systolic and diastolic velocities were determined for Vr and Vz as well as the change of Vφ during systole and the velocity twist between base and apex.

Results: The dynamics regional and global myocardial velocities were similar for radial and long-axis velocities (Fig. 2) but substantially different for LV rotation (Fig. 1). Additionally, clear differences of the myocardial motion pattern between mice and humans were observed, the most important itemized as follows:

- Different rotation during early systole (viewed from apex): clockwise rotation in mice, counter-clockwise in humans (all slices, see Fig. 1).
- Different rotation during mid-systole: only minor changes in velocities in mice after the velocity twist has developed (all slices, see Fig. 1).
- Different rotation during early diastole: initial clockwise rotation in all slices in humans, in mice only observable in apical slice (see Fig. 1).
- Ventricular filling in humans ends more abruptly compared to mice (steeper slope of diastolic deceleration in Vr and Vz) which is also clearly visible in regional plots of Vr and Vz in basal and midventricular locations (see arrows Fig. 2).
- Highest systolic long-axis velocities (Vz) were observed in the lateral wall for humans while mice showed highest velocities in septal regions (all slices).
- The change of rotational peak velocities between early and mid-systole (see arrows in Fig. 1) is higher in humans by a factor of ~6.5; the velocity twist (ΔVφ basal - mid - apex during mid-systole) by a factor of 5 (see table 2).
- Negative dip during isovolumetric relaxation (Vr) more pronounced in humans compared to mice (basal septal and anterior wall in humans; see circle Fig. 2).
- Peak velocities (table 2) were higher in humans by factors of ~3 / ~4.5 for radial / longitudinal velocities; differences are always more pronounced in basal slice.

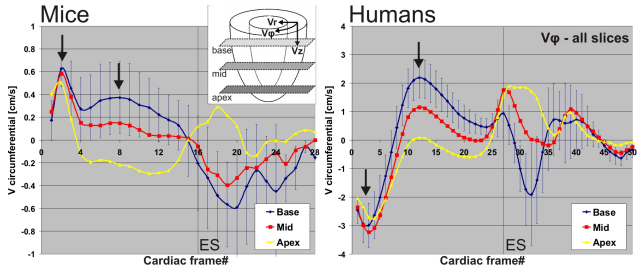

Fig.1: Global circumferential velocity time courses averaged over all mice and humans. The traces were normalized to (ES). Standard deviations indicating inter-subject variations of LV velocities are shown for the basal slice.

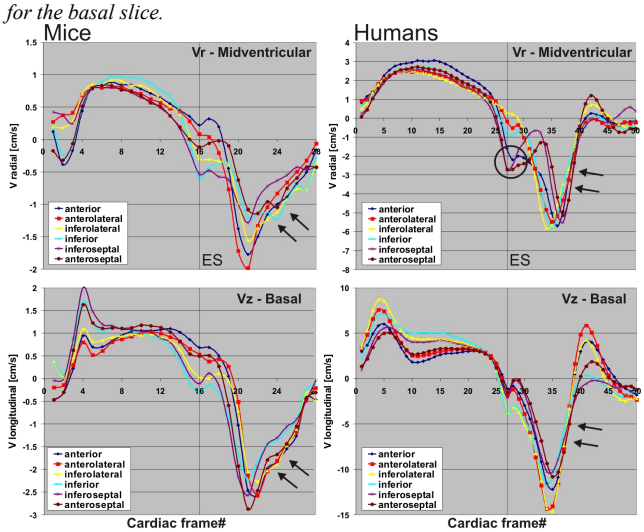

Fig.2: Regional velocity time courses exemplarily shown for the mid-ventricular radial component (upper graphs) and the basal longitudinal component (lower graphs).

Velocity component	Slice	Peak Systolic velocity [cm/s]		Peak Diastolic velocity [cm/s]	
		Humans	Mice	Humans	Mice
Vr	basal	2.9 ± 0.7	0.9 ± 0.2	-5.2 ± 1.4	-1.4 ± 0.3
	mid	2.7 ± 0.7	0.9 ± 0.2	-5.3 ± 1.5	-1.6 ± 0.5
	apical	2.3 ± 0.7	0.9 ± 0.2	-4.4 ± 1.8	-1.8 ± 0.4
Vz	basal	7.4 ± 1.5	1.4 ± 0.4	-12.7± 2.9	-2.7 ± 0.4
	mid	5.8 ± 1.5	1.2 ± 0.3	-8.7 ± 2.7	-2.3 ± 0.6
	apical	4.0 ± 1.4	0.9 ± 0.3	-4.3 ± 1.7	-1.1 ± 0.6
		Peak early-systole		Peak mid-systole	
Vφ	basal	-3.7 ±1.8	0.8 ± 0.4	2.6 ± 1.1	0.1 ± 0.2
	mid	-3.9 ±1.7	0.7 ± 0.3	1.5 ± 1.0	-0.1 ± 0.1
	apical	-3.3 ±1.4	0.7 ± 0.3	0.5 ± 0.8	-0.3 ± 0.2

Table 2: Global peak velocities in murine and human hearts.

Discussion: This work illustrates that the motion patterns of normal mouse hearts are similar to the human heart for radial and longitudinal, but inverted for tangential velocities. In addition, distinct differences in regional and global motion patterns were observed which should be taken into account when using mouse models for the analysis of LV function. About 20-30% of the murine cardiac cycle (in diastole) was not covered due to the black-blood module at the end of the cine train, and to allow for variations in heart rate. Therefore, together with the 8-10-fold higher heart rate in mice, the sampling density in murine experiments was only about 50% compared to humans despite the 3x higher temporal resolution. The motion pattern of mouse hearts is in agreement with previously published work, but velocities were found to be higher in our study [4].

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References: [1] Jung et al. JMRI 2006;1033. [2] Föll et al. Circ Cardiovasc Imaging 2010;3:54-64. [3] Streif et al. MRM 2003; 49:315. [4] Herold et al. MRM 2006; 55:1058-64. [5] Dall'Armellina et al. ISMRM 2009; p1811.