Cardiac function imaging in the axolotl using a new self-gating approach

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Target audience: Researchers in cardiac cine MRI on small animal models.

Purpose: The Mexican axolotl (*Ambystoma mexicanum*) is a widely applied amphibian model in regenerative medicine and biology due to its impressive regenerative properties (Davenport, 2005). This species is capable of regrowing complete limbs and regenerating damaged organs, such as the myocardium after induced infarction. Until now, quantitative evidence about the structural recovery concomitantly to the retrieval of functional capacity of the infarcted myocardium has been evaluated *in vitro*. In order to assess cardiac function in the regenerating heart of the axolotl *in vivo*, we have implemented a cardiac self-gating approach, as it turned out to be impossible to acquire ECG-signal during MR scanning. Self-gating was initially introduced by Larson et al. (2004), and various approaches for detecting the cardiac cycles in the raw data have later been proposed.

Methods: The images were acquired using a 1.5 T Philips Achieva scanner and a 23 mm single loop surface RF coil. Following high-resolution scout imaging, functional cine images of the heart were acquired using self-gating. Multi-slice 2D images were acquired using radial, partial echo k-space sampling. Sampling of each radial line was repeated 50 times consecutively to ensure covering at least one cardiac cycle for all k-lines. The FOV was 40x40 mm^2 and acquisition matrix was 160x160, providing a pixel size of 0.25x0.25 mm^2. Slice thickness was 0.5 mm, and TR/TE were 42/7.8 ms. Total scan time was 45 min. During post-processing, each temporal profile in spatial domain was subtracted from a profile averaged over all 50 repetitions. Accordingly, differences due to cardiac beating were enhanced. All subtracted profiles were visualized sequentially and the cardiac time intervals were determined by cross-correlation with a kernel consisting of slightly more than one heart period (Fig. 1). The automatically determined heart beat periods were subsequently corrected manually. Thereby, each acquired profile was ascribed to a cardiac time point, and this was used for the following retrospectively gated reconstruction into 25 heart frames.

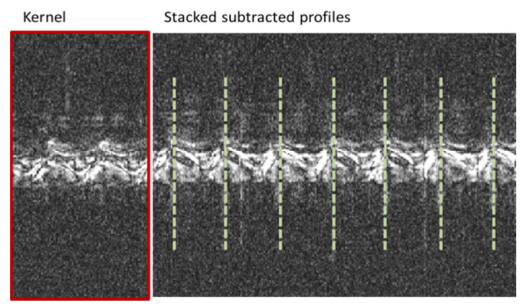

Fig. 1. The cardiac cycle periods were detected by cross-correlation of a kernel with the stacked profiles.

Results: Self-gated cardiac MRI facilitated reconstructions with sub-millimetre resolution of the beating minuscule axolotl heart with acceptable SNR (Fig. 2). This allowed for functional measurements of ejection fraction and cardiac output, which were 0.48 and 9.89 µL/s in a 12 cm axolotl at 22 °C.

Discussion: Cardiac MRI is a valuable complement to echocardiography in studies of cardiac function in small animal models. Though it is possible to apply ECG-gated cardiac MRI on rats, challenges arise on very small hearts, such as the axolotl heart, due to a weak ECG signal and RF interactions when ECG electrodes are placed in the very close proximity of the heart. Self-gated cardiac MRI offers great possibilities in these cases, and though the implemented technique requires post-processing of raw data, this step can be completed semi-automatically to reduce time. We propose to consider self-gating when encountering difficulties with ECG triggering, as this technique is already available on some preclinical systems, and it can be implemented readily on others.

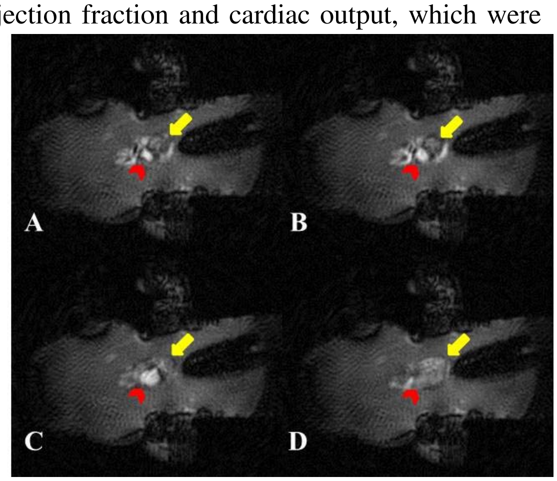

Fig. 2. The beating axolotl heart consisting of two atria (arrowhead) and one ventricle (arrow) in different phases. **A:** Atrial systole, **B:** ventricular systole, **C:** atrial diastole, **D:** ventricular diastole.

Conclusion: Self-gated cine cardiac MRI has proven useful in measuring functionality of the regenerating heart of the axolotl, and this method should be considered when encountering obstacles in traditional ECG gated cardiac MRI in small animal models.

References:

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Larson, A.C., White, R.D., Laub, G., McVeigh, E.R., Li, D. and Simonetti, O.P. 2004. Self-gated cardiac cine MRI. *Magnetic Resonance in Medicine* **51**: 93-102.