UTE-based Reflection Point analysis for early diagnosis of infected cardiac valves in mice

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Target audience: Physicists, cardiologists and radiologists with interest in cardiovascular MRI and infective endocarditis.

Purpose: Infective endocarditis is a chronic bacterial infection, often leading to severe or life-threatening conditions (1). It is characterized by the presence of septic vegetations on the surface of the endocardium and the valves (2). According to the Duke criteria infective endocarditis is mainly diagnosed based on positive blood cultures and echocardiogram abnormalities (1). Typical echo-Doppler measurements can detect the site of infection, the extent of valvular damage as well as the cardiac function. However, for definite diagnosis repeated and combined transthoracic and transesophageal echocardiography have to be performed (1) and negative findings occur regularly (3), delaying adequate antibiotic therapy. Due to its excellent spatial resolution and tissue contrast MRI is also a powerful tool for non-invasive diagnosis of diseases, but its low temporal resolution, compared to echocardiography, and its susceptibility to flow artifacts in the images have delayed the progression in MR imaging of the cardiac valves. Recent developments of self-gated radial acquisition techniques such as self-gated UTE afforded better visualization of the valves. Flow artifacts were significantly reduced and allowed for the observation of the cardiac valves during the full cardiac cycle, making MRI an interesting alternative imaging tool for infective endocarditis (4). Here, we developed a novel MRI tool kit for the detection of infective endocarditis in mice, allowing for early diagnosis and detailed characterization of morphological and functional changes of infected cardiac valves.

Methods: *Mouse model of chronic endocarditis*: Experiments were performed on male and female CD1 wild-type mice. In the mouse model, a 32-G polyurethane catheter was placed at the aortic root via left carotid artery of the mouse, to induce a mechanical trauma of the endothelial layer of the aortic valves. Either 10^4, 10^5 or 10^6 colony forming units (CFU) of *S. aureus* bacteria were injected i.v. 24 h after catheter placement. A control group received the catheter only. *MRI protocols*: 2D self-gated cine UTE (slice thickness: 1mm, TE/TR=314 µs/5 ms, flip angle: 15°, field of view: 32x32 mm^2, resolution: 125x125 µm^2, number of projection: 246) sequence was acquired at 9.4 T on a Bruker BioSpec94/20 using a 35 mm volume coil. For visualization of the structure and thickening of infected and non-infected cardiac valves in mice Reflection Point analysis was performed. *Reflection Point visualization technique*: The technique was implemented within the IntraGate tool. In the reconstructed image Reflection Points (R) are defined by one deliberately chosen signal intensity value - usually the tissue of interest. Thus, all pixels with this chosen intensity value are defined as Reflection Points. Pixel intensities of the original image (X_i) are subsequently weighted according to the distance to the Reflection Point. The displayed pixel intensity (X_i') is calculated by: $X_i'=R-X_i$. The smaller the distance, the brighter the pixels are pictured. Signal intensity of the Reflection Points is the brightest. As a consequence, tissue interfaces are enhanced and partial volume effects preserved. *Analysis:* 4 to 6 mice per group were measured by MRI. Aortic valves were scored according to (1) valve thickening, (2) functional defects leading to changes in the flow and (3) additional structures, such as vegetations and abscesses. Morphological and functional features were rated in a blinded fashion using a 6-level scale from zero to five (0=not conspicuous, 5=most conspicuous) by two MRI specialists independently. Artifacts were assessed by scores ranking from 0 (no artifacts) to 5 (pronounced artifacts).

Fig. 1: Scoring of artifacts in self-gated UTE images and images post-processed by Reflection Point analysis.

Results and Discussion: In a mouse model of chronic endocarditis induced by *S. aureus* bacteria, aortic valves were characterized by self-gated UTE. High quality images of the cardiac valves allowed for detailed observation of the valvular structure and function during the full cardiac cycle. In contrast to standard reconstruction significantly reduced artifacts and sharp delineation of the valvular structures was achieved by post-processing Reflection Point analysis (Fig. 2 A and B). Scores from artifact assessment showed a significant improvement in image quality (p=0.01) when Reflection Point analysis was applied allowing for accurate morphological evaluation (Fig. 1). Using this post-processing analysis tool, infective valves revealed valve thickening in correspondence to the bacterial load (Fig. 2 C). Compared to the control group which obtained the surgery only, substantially thicker valves were already observed for 10^4 bacteria. Blood agar cultures confirmed increased bacterial vegetations on the valves when higher bacterial concentrations were applied.
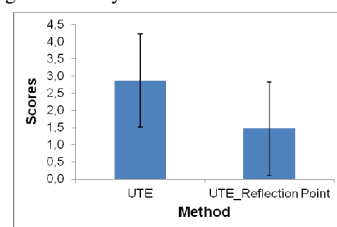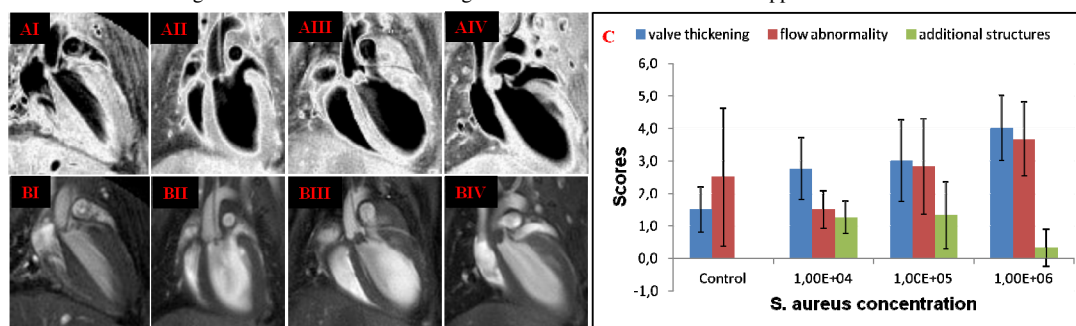

Fig. 2: (A) and (B) UTE-based Reflection Point analysis and UTE images of (I) non-infective and (II-IV) infective valves induced by *S. aureus* using either (II) 10^4, (III) 10^5 and (IV) 10^6 CFUs. Significant valve thickening was observed for infected valves. (C) Scores regarding the visualization of valve thickening, flow abnormalities and additional structures such as vegetations and abscesses.

Conclusion: Self-gated cine UTE allows for detailed visualization of the cardiac valves during the full cardiac cycle but images often suffer from partial volume artifacts. High lightening the valvular structures by Reflection Point analysis rescales image intensities and corrects for pixel wise signal gradients caused by small structures and surface coils. In our study we could show that UTE-based Reflection Point analysis is a powerful tool for early diagnosis of infective endocarditis.

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