Pre-clinical functional Magnetic Resonance Imaging part II: The heart

Nadja M. Meßner[1], **Frank G. Zöllner**[*,1], **Raffi Kalayciyan, Lothar R. Schad**

Computer Assisted Clinical Medicine, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany

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Abstract

One third of all deaths worldwide in 2008 were caused by cardiovascular diseases (CVD), and the incidence of CVD related deaths rises ever more. Thus, improved imaging techniques and modalities are needed for the evaluation of cardiac morphology and function.
Cardiac magnetic resonance imaging (CMRI) is a minimally invasive technique that is increasingly important due to its high spatial and temporal resolution, its high soft tissue contrast and its ability of functional and quantitative imaging. It is widely accepted as the gold standard of cardiac functional analysis.
In the short period of small animal MRI, remarkable progress has been achieved concerning new, fast imaging schemes as well as purpose-built equipment. Dedicated small animal scanners allow for tapping the full potential of recently developed animal models of cardiac disease. In this paper, we review state-of-the-art cardiac magnetic resonance imaging techniques and applications in small animals at ultra-high fields (UHF).

Keywords: Small animal, cardiac disease, MRI, ultra-high field, functional imaging

Präklinische funktionelle Magnetresonanztomographie Teil 2: Herz

Zusammenfassung

Ein Drittel aller Todesfälle weltweit wurden 2008 durch kardiovaskuläre Krankheiten verursacht, und deren Inzidenz häuft sich mehr und mehr. Daher werden verbesserte Bildgebungstechniken und Modalitäten für die Auswertung kardialer Morphologie und Funktion benötigt. Die kardiale Magnetresonanztomographie (MRT) ist eine minimal-invasive Technik, die aufgrund ihrer hohen örtlichen und zeitlichen Auflösung, ihres hohen Weichteilkontrastes und ihrer Fähigkeit zur funktionellen und quantitativen Bildgebung immer wichtiger wird. Sie hat sich zu einem Goldstandard für die funktionelle Untersuchung von Herzkrankheiten entwickelt.
In der kurzen Zeitspanne der Kleintier-MRT wurden bemerkenswerte Fortschritte erzielt hinsichtlich neuer, schneller Bildgebungstechniken und speziell angefertigter Hardware. Dedizierte Kleintierscanner ermöglichen es, das Potenzial neu entwickelter Tiermodelle kardialer Krankheiten voll auszuschöpfen.
In diesem Review werden State-of-the-Art-MRT-Techniken und Anwendungen zur Untersuchung des Herzens an Kleintieren bei Ultrahochfeld vorgestellt.

Schlüsselwörter: Kleintier, Herzkrankheiten, MRT, Ultrahochfeld, funktionelle Bildgebung

[*] Corresponding author. Frank G. Zöllner, Computer Assisted Clinical Medicine, Medical Faculty Mannheim, Heidelberg University, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany. Tel.: +49(0)6213835117; fax: +49(0)6213835123.
E-mail: Frank.Zoellner@medma.uni-heidelberg.de (F.G. Zöllner).
[1] both authors contributed equally.

Introduction

Cardiovascular disease is the leading cause of death in the world [1]. The main causes of this disease are hypertension and atherosclerosis. Further risk factors for cardiovascular disease are manifold and arise from age, gender, high serum cholesterol levels, tobacco smoking, excessive alcohol consumption, sugar consumption, family history, obesity, lack of physical activity, psychosocial factors, diabetes mellitus, and even air pollution [2,3]. Though cardiovascular disease is attributed to the older population, the antecedents of cardiovascular disease, notably atherosclerosis, begin in early life [4,5]. Therefore, non-invasive tools to assess or prevent cardiovascular disease are needed.

Cardiac magnetic resonance imaging (CMRI) is such a modality that fulfills the requirements of spatial and temporal resolution and is seen as the gold standard of functional cardiac imaging [6]. CMRI in animals started in the mid-1980s with large animals such as dogs and basic applications like myocardial mass determination [7]. Other animal models and techniques were explored thereafter.

CMRI in mice has not been performed until the late 1990s, but as it is technically and economically favorable and as transgenic (TG) and knockout mice allow investigating the role of individual genes in tasks like myocardial infarction (MI) remodeling [8–10], it has become a field of intense research. Various different MR imaging techniques have been developed [11–13], amongst them cine imaging techniques for structural and functional information or contrast-enhancement techniques for infarct delineation [14]. In this paper, we review state-of-the-art CMRI techniques and applications at ultra-high fields (UHF). In contrast, the first part of this review focuses on pre-clinical kidney imaging [15].

Main Challenges in Small Animal Cardiac Imaging

The cardiovascular systems of large mammals like sheep, dogs and pigs are comparable to those of humans, but there are differences in position, size, and shape of the heart [16]. The conditions in rodents and rabbits are similar, too [17], although their hearts are obviously far smaller and beat faster (mouse: 400-600 bpm; rat: 320-370 bpm; rabbit: 150-250 bpm) than the human heart (60-100 bpm). Strong and fast movements of the heart and the in- and outflowing blood afford a high temporal resolution and turn CMRI in small animals into a challenging task. Small dimensions are yet another challenge, especially in the mouse, where the thickness of the left ventricular (LV) wall (1.5-1.8 mm) and right ventricular (RV) wall (0.5-0.6 mm) [17] demand for high spatial resolution in the sub-millimeter range. Image resolutions currently achievable by CMRI are summarized in Table 1.

Hardware

High field strengths bring along the advantages of high spectral resolution and signal-to-noise-ratio (SNR). Although there have been successful image acquisitions at 17.6 T [18,19], a range of 7-11.7 T seems to be the best compromise for murine CMRI to avoid high-field related problems such as susceptibility artifacts [12]. Furthermore, strong and fast switching gradients are needed to achieve short acquisition windows and prevent motion artifacts. The coils used for small animal MR can be classified as mid-range coils, as the product of the frequency and the coil diameter is in the range 2–30 MHz-m [20]. Most of them are linear volume coils, birdcage coils or surface coils. Volume coil excitation and surface coil reception are preferable [21]. The usage of cryogenically cooled coils (see Fig. 1) brings along the

Table 1
Examples of achievable spatial resolution in small animal cardiac MRI of different functional cardiac MRI techniques at various field strengths and MR systems.

Technique	System	Resolution [μm^3]	Animal Model	Reference
Cine gradient echo	11.7 T animal scanner	117 × 117 × 480	mouse	Subgang et al. [133]
	9.4 T animal scanner	150 × 150 × 1000	mouse	Sosnovik et al. [134]
	9.4 T animal scanner + cryogenic surface coil	43 × 138 × 300	mouse	Wagenhaus et al. [22]
	7 T animal scanner	156 × 195 × 1000	mouse	Protti et al. [52]
	1.5 T whole body scanner	352 × 440 × 2000	mouse	Voelkl et al. [135]
Sodium CSI	17.6 T animal scanner	1000 × 1000 × 1000	mouse	Neuberger et al. [99]
	9.4 T animal scanner	625 × 625 × 2000	mouse	Maguire et al. [100]
	7 T animal scanner	1000 × 1000 × 3500	rat	Jansen et al. [101]
Perfusion	9.4 T animal scanner	500 × 800 × 1500	mouse	Van Nierop et al. [94]
	7 T animal scanner	200 × 200 × 1000	mouse	Antkowiak et al. [91]
	3 T whole body scanner	200 × 200 × 1500	mouse	Makowski et al. [88]
Tagging	9.4 T animal scanner	150 × 150 × 1000	mouse	Sosnovik et al. [134]
	4.7 T whole body scanner	234 × 234 × 1000	mouse	Gilson et al. [58], Zhou et al. [59]
	1.5 T whole body scanner	625 × 313 × 2000	rat	Hyacinthe et al. [136]