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CLINICAL RESEARCH

Monocenter Investigation Micra® MRI study (MIMICRY): feasibility study of the magnetic resonance imaging compatibility of a leadless pacemaker system

Hermann Blessberger[1,2]*, Daniel Kiblboeck[1], Christian Reiter[1], Thomas Lambert[1], Joerg Kellermair[1,2], Pierre Schmit[3], Franz Fellner[3,4], Michael Lichtenauer[5], Alexander Kypta[1,5]†, Clemens Steinwender[1,2,5], and Juergen Kammler[1]

[1]Department of Cardiology, Med Campus III, Kepler University Hospital Linz, Medical Faculty of the Johannes Kepler University Linz, Krankenhausstr. 9, 4021 Linz, Austria; [2]Institute of Cardiovascular and Metabolic Research (ICMR), Medical Faculty of the Johannes Kepler University Linz, Linz, Austria; [3]Central Radiology Institute, Kepler University Hospital Linz, Medical Faculty of the Johannes Kepler University Linz, Linz, Austria; [4]Medical Faculty of the Friedrich Alexander University of Erlangen-Nuernberg, Erlangen, Germany; and [5]Department of Internal Medicine II, Paracelsus Medical University Salzburg, Salzburg, Austria

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Aims As *in vivo* real-life data are still scarce, we conducted a study to assess the safety and feasibility of cardiac magnetic resonance imaging (MRI) in patients with a leadless pacemaker system.

Methods and results In this prospective non-randomized interventional trial, we enrolled 15 patients with an MRI conditional Micra® leadless pacemaker system to undergo either a 1.5 T or 3.0 T cardiac MRI scan. Clinical adverse events as well as device parameters such as pacing threshold, sensing, impedance, and battery life were assessed at baseline as well as 1 and 3 months after the scan. Device parameter changes between different time points were tested for statistical significance and compared with pre-set cut-off values. Fourteen patients underwent the cardiac MRI scan according to the protocol as well as the scheduled follow-up visits. One participant was excluded from analysis, as the MRI scan was not possible because of severe claustrophobia. Other clinical events did not occur during the scan and the follow-up period. Device parameters stayed stable and changes during the observational period were statistically not significant (changes vs. baseline: pacing threshold: 0.01 ± 0.05 V, $P = 0.308$, 0.01 ± 0.07 V, $P = 0.419$, sensing: -0.15 ± 1.11 mV, $P = 0.658$, -0.19 ± 1.17 mV, $P = 0.800$, impedance: -7.86 ± 30.7 Ohm, $P = 0.447$, -7.86 ± 25.77 Ohm, $P = 0.183$, at 1 and 3 months follow-up, respectively). Parameter changes were not statistically different between patients who underwent imaging at 1.5 T ($n = 7$) or 3.0 T ($n = 7$).

Conclusion In our set of patients with a Micra® leadless pacemaker, cardiac magnetic resonance imaging at either 1.5 T or 3.0 T proved feasible and safe with no relevant changes in device parameters within 3 months of follow-up.

Keywords Leadless pacemaker • Magnetic resonance imaging • Safety assessment • Feasibility

Introduction

It is calculated that 2–3 out of four patients with a cardiac implanted device will have to undergo a magnetic resonance imaging (MRI) scan during their lifetime.[1,2] For them, safe access to MRI is crucial. The Micra® (Medtronic Inc., MN, USA) is a single chamber leadless pacemaker (LPM) system.[3–5] It consists of a small cylindrical capsule that contains a battery, an electronic control unit as well as a single tip electrode and is directly implanted into the right ventricle transvenously. As opposed to a conventional pacemaker system, the use of

* Corresponding author. Tel: +43 5 7680 83 6220; fax: +43 5 7680 83 6205. *E-mail address*: hermann.blessberger@kepleruniklinikum.at

† Deceased author.

What's new?

- Device parameters (pacing threshold, sensing, lead impedance, battery life) remained stable during a 3 month follow-up in patients with a leadless pacemaker system who had undergone a cardiac magnetic resonance imaging (MRI) scan at either 1.5 T or 3.0 T.
- Cardiac MRI was safe and feasible in our cohort of patients when performed at least 6 weeks after Micra® leadless pacemaker implantation.

LPMs eliminates potential complications such as pocket infections and fractures or dislocations of leads. Up to now, this system allows sensing and pacing in the right ventricle only, so that it is predominantly implanted in patients with atrial fibrillation with either slow atrioventricular conduction or complete heart block. The Micra® was labelled 'MRI conditional' on the grounds of experimental and animal studies and approved for both 1.5 T and 3.0 T scanners. However, there is still a paucity of real-life data corroborating these findings. MRI scanners produce strong static and graded magnetic and radiofrequency fields for image acquisition that can influence safety and function of implanted devices.[6] It has been shown for non-MRI conditional devices that lead dislocations, tissue heating with subsequent increases in pacing thresholds as well as over- or under-sensing of arrhythmias or hardware damages may occur. Magnetic fields may also interfere with different ferromagnetic components of LPMs.[7] As *in vivo* real-life data are still scarce, we conducted a study to assess the safety and feasibility of cardiac MRI in patients with this leadless pacemaker system.

Methods

Patient enrolment

We conducted a prospective, non-randomized, interventional single-centre study. The study protocol was approved by the local ethics committee. Written informed consent was obtained from each patient prior to enrolment. We pre-specified to recruit 15 participants for this feasibility and safety study. Patients were eligible if they were ≥18 years old and the Micra® LPM was implanted more than 6 weeks ago. This interval between implantation and study enrolment was chosen to allow initial ingrowth. Furthermore, pacing thresholds had to be stable and ≤2.0 V at 0.24 ms pulse width, pacing impedances had to be between 200 and 1500 Ohms and calculated battery life >8 years (=100%). We excluded patients with a life expectancy below 12 months, scheduled cardiac surgery within 3 months, glomerular filtration rate ≤30 mL/min/1.73 m^2, pregnancy, or other medical devices that may interact with the LPM.

Magnetic resonance imaging scans

Cardiac MRIs were performed using a long bore 1.5 T (Magnetom Avanto®, Siemens, Erlangen, Germany) or 3.0 T (Magnetom Skyra®, Siemens, Erlangen, Germany) magnet with standard cardiac surface receive coil without contrast. We performed the MRI examinations at either 1.5 T or 3.0 T in an alternating pattern (1:1 ratio). The maximum slew rate of the MRI scanner's gradient fields did not exceed 200 T/m/s per axis. Whole body specific absorption rate (SAR) was limited to ≤4 W/kg. Subjects underwent a heart scan according to standard scan protocols recommended by the Society of Cardiovascular Magnetic Resonance.[8] We obtained multiple slice transversal steady-state free precession images for anatomical orientation in the long axis and multiple short axis images of the left ventricle. Gradient echo cine imaging using a Fast Low Angle Shot (FLASH) sequence was performed of the four-chamber view of the left ventricle. T1- and T2-weighted Turbo Spin Echo (TSE) sequences were obtained of the four-chamber view and in the short axis. For detailed information about MRI sequences and scanner parameters, see Supplementary material online, *Table S1* and *S2*. Before undergoing the scan, the LPM was programmed to an MRI compatible mode (SureScan®) as described previously.[7] In brief, the device was set to a V00-mode, an asynchronous pacing mode without sensing and a default pacing rate well above the patient's intrinsic heart rate (usually 80 b.p.m.).[9] After the MRI procedure, the LPM system was checked and restored to previous settings. Two cardiologists and two radiologists went through all obtained MRI studies to look for possible pathologies. Relevant findings were discussed with the patient.

Endpoint definition and follow-up

Clinical adverse events as well as device parameters such as pacing threshold, sensing, impedance, and battery life were assessed at baseline as well as 1 and 3 months after the scan. Study endpoints were defined according to previously published literature[10–12]: The primary safety endpoint 1 evaluated MRI related SADEs (Serious Adverse Device Effects). For this endpoint calculation, only the number of probably or definitely MRI related events was taken into account. We considered clinically relevant arrhythmias due to device dysfunction as well as subclinical or overt technical damage of the LPM to be a SADE.[10,11] All other adverse events were also documented throughout the study but did not influence the specific SADE rate. The SADE free rate (%) was calculated by (1 - (number of SADEs/number of patients)) × 100. An expected SADE free rate of 90% and above was considered successful.[10,11] Changes in ventricular pacing threshold were defined as primary safety endpoint 2. Thereby, the cut-off was set to an increase of less than 0.5 V.[10,11] The secondary endpoint evaluated R-wave sensing attenuation and changes in impedance as well as battery life. Hereby, the cut-off was set to a drop in R-wave sensing of more than 50% or an absolute R-wave amplitude of less than 5.0 mV.[10,11] Impedance changes and battery life were observed descriptively.

Statistical analysis

Data were analysed with the software package Intercooled Stata 14 (Stata Corp. TX, USA). Discrete data are presented as counts and percentages, continuous variables as means with corresponding standard deviations. Device parameter changes between different time points were tested using the non-parametric Wilcoxon signed-rank test (paired difference test). An unpaired non-parametric Mann–Whitney *U* test or a χ^2 test with Fisher's exact modification were applied to compare baseline characteristics and device parameter changes between patients who underwent imaging at 1.5 T and 3.0 T, as appropriate. A two-sided *P*-value <0.05 was considered statistically significant.

Results

We prospectively enrolled 15 patients with an age range between 36 and 97 years (12 of them male, mean age 77.1 ± 14.2 years). Fourteen patients completed the MRI scan as well as the 1 and 3 month follow-up and were, therefore, included in the safety analysis. The one patient excluded from the analysis felt claustrophobic during MRI and was not able to finish the procedure as required by the protocol.

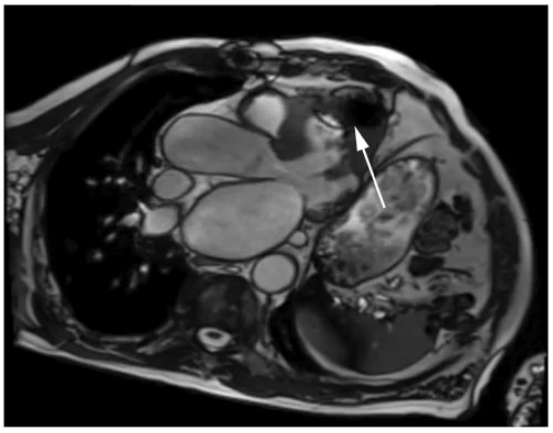

Figure 1 Left ventricular outflow tract view (TrueFISP steady state free precession sequence with a field strength of 3.0 T) with an arc-shaped artefact (white arrow) caused by the implanted leadless pacemaker system at the apex of the right ventricle.

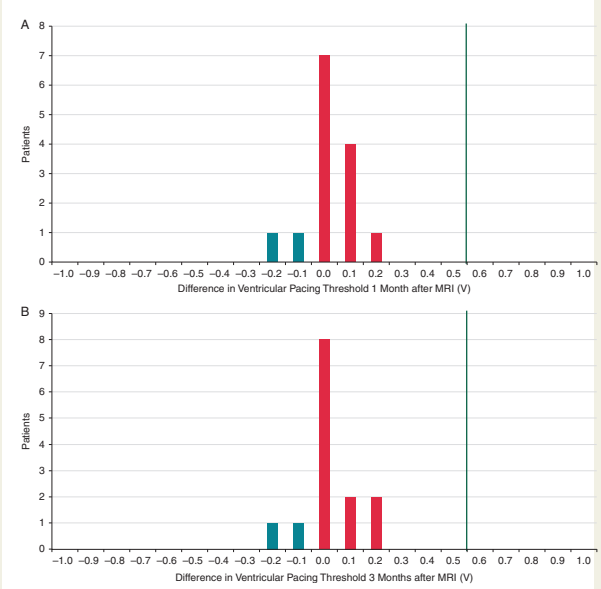

Figure 2 (*A* and *B*) Differences in ventricular pacing thresholds after 1 and 3 months. Vertical green line indicates pre-specified cut-off of 0.5 V.

Table 1 Baseline characteristics ($n = 14$)

	1.5 T scan ($n = 7$)	3.0 T scan ($n = 7$)	*P*-value
Coronary heart disease	3 (43%)	3 (43%)	1.000[a]
Arterial hypertension	5 (71%)	5 (71%)	1.000[a]
Diabetes mellitus type II	0 (0%)	3 (43%)	0.192[a]
COPD	0 (0%)	1 (14%)	1.000[a]
Left ventricular ejection fraction (%)	56 ± 9	56 ± 7	0.896[b]
Glomerular filtration rate (mL/min/1.73 m^2)	69 ± 9	54 ± 30	0.225[b]
Antiplatelet therapy	3 (43%)	0 (0%)	0.192[a]
Oral anticoagulation	5 (71%)	5 (71%)	1.000[a]
Indication for pacemaker therapy			
Atrial fibrillation with slow atrioventricular conduction	6 (86%)	4 (57%)	0.315[a]
Atrial fibrillation with complete atrioventricular block	0 (0%)	1 (14%)	
Sick sinus syndrome	1 (14%)	0 (0%)	
Sinus rhythm with intermittent complete atrioventricular block	0 (0%)	2 (29%)	

[a]$\chi 2$ test with Fisher's exact modification.
[b]Mann–Whitney *U* test.

Seven patients each underwent cardiac imaging at 1.5 T and 3.0 T. Baseline characteristics of enrolled patients are shown in *Table 1*. The time from LPM implantation to enrolment was 18.7 ± 9.7 months on average. The mean MRI active scanning time was 32 ± 7 min (range 22–45 min), whereas the average time in asynchronous MRI pacing mode (V00) was 108 ± 42 min (range 55–185 min). The LPM caused an arc-shaped artefact at the apex and adjacent ventricular walls (see *Figure 1*). Assessment of heart valves and left ventricular function was possible in all subjects. For the SARs in W/kg of all patients see Supplementary material online (*Table S3*).

Primary safety endpoint 1—SADE free rate

During the study period, no hospitalizations, deaths, or SADEs (SADE free rate of 100%) occurred. So, the primary safety endpoint 1 was met. One adverse event was encountered as one MRI scan had to be prematurely stopped due to claustrophobia. The participant had normal findings upon the LPM interrogation after the aborted scan.

Primary safety endpoint 2—pacing threshold

Ventricular pacing threshold remained stable during the study period and there was no clinically significant increase of ≥0.5 V in any of the 14 subjects (baseline: 0.59 ± 0.15 V, 1 month follow-up: 0.60 ± 0.18 V, $P = 0.308$, 3 month follow-up: 0.60 ± 0.16 V, $P = 0.419$, see *Figure 2A* and *B*). The results did not differ with respect to the field strength of the scanner used (see *Table 2*).

Secondary endpoint—R-wave sensing, impedance, and battery life

Ventricular sensing was stable throughout the follow-up period (baseline: 14.9 ± 4.7 mV, 1 month follow-up: 14.7 ± 4.7 mV, $P = 0.658$, 3 month follow-up: 14.7 ± 4.6 mV, $P = 0.800$, see *Figure 3A* and *B*). A clinically significant sensing attenuation of >50% as compared with baseline or absolute sensing values <5 mV were not observed in any patient after 1 and 3 months, respectively. The results did not differ with respect to the field strength of the scanner used (see *Table 2*).

Table 2 Change of device parameters after 1 and 3 months when compared with baseline values

	1 month (overall) $n = 14$	*P*-value[a] comparison vs. baseline	1 month (1.5 T) $n = 7$	1 month (3.0 T) $n = 7$	*P*-value[b] comparison 1.5 T vs. 3.0 T	3 months (overall) $n = 14$	*P*-value[a] comparison vs. baseline	3 months (1.5 T) $n = 7$	3 months (3.0 T) $n = 7$	*P*-value[b] comparison 1.5 T vs. 3.0 T
Pacing threshold (V)	0.01 ± 0.05 (-0.13 to 0.13)	0.308	0.03 ± 0.05 (-0.03 to 0.13)	-0.01 ± 0.05 (-0.13 to 0.03)	0.167	0.01 ± 0.07 (-0.12 to 0.15)	0.419	0.03 ± 0.05 (0 to 0.15)	-0.01 ± 0.08 (-0.12 to 0.13)	0.137
Sensing (mV)	-0.15 ± 1.11 (-2.30 to 2.0)	0.658	-0.49 ± 1.51 (-2.30 to 2.0)	0.18 ± 0.34 (-0.19 to 0.80)	0.178	-0.19 ± 1.17 (-3.0 to 1.5)	0.800	-0.43 ± 1.21 (-3.0 to 0.5)	0.03 ± 1.19 (-1.9 to 1.5)	0.949
Impedance (Ohm)	-7.86 ± 30.7 (-60 to 50)	0.447	-7.14 ± 17.99 (-30 to 20)	-8.57 ± 41.40 (-60 to 50)	0.898	-7.86 ± 25.77 (-70 to 40)	0.183	0 ± 20 (-20 to 40)	-15.71 ± 29.92 (-70 to 40)	0.191

Data are presented as means with corresponding standard deviations and ranges.
[a]Wilcoxon signed-rank test.
[b]Mann–Whitney *U* test.

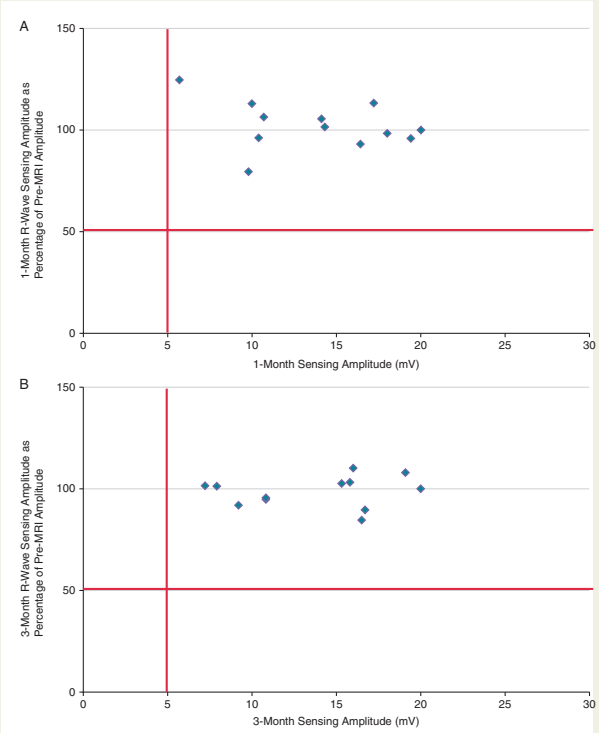

Figure 3 (*A* and *B*) Differences in sensing amplitudes after 1 and 3 months. Vertical and horizontal red lines represent pre-specified cut-offs of 5 mV and 50% attenuation when compared with baseline values, respectively.

Battery life remained above 8 years (=100%) in all patients during the whole follow-up. Furthermore, impedance did not change significantly when compared with baseline values (baseline: 527 ± 100 Ohm, 1 month follow-up: 519 ± 115 Ohm, $P = 0.447$, 3 month follow-up: 519 ± 94 Ohm, $P = 0.183$, see *Table 2*).

Discussion

Our study evaluated the feasibility and safety of an MRI conditional LPM system under 1.5 T and 3.0 T MRI scanning conditions. Magnetic and radiofrequency fields that change over time may dislocate the device, heat the tissue next to the LPM tip electrode or cause device dysfunction such as over- or under-sensing of arrhythmias or an electrical reset.[6,7] It has been shown for the Micra® in an *ex vivo* study that tissue heating at the tip electrode during an MRI scan indeed happened. In a non-perfused model of the right ventricle, the temperature rose less than 0.4°C at 1.5 T and less than 0.5°C at 3.0 T. These increases in temperature at the device–tissue interface were deemed negligible and safe and to be even lower in a real, blood perfused right ventricle.[7] *In vivo* data of patients who underwent an indicated MRI scan have not revealed any LPM related adverse events up to now.[3,7,13,14] However, these patients were not systematically assessed.

In our study, we did not detect any SADEs or relevant changes in device parameters during the study period. In addition, there was no

detectable difference between parameter changes or clinical courses of patients undergoing the scan at 1.5 T or 3.0 T.

Our results go in line with previously published data demonstrating the safety of MRI conditional pacemaker and ICD systems.[10,11,15–18] All our patients tolerated the V00 pacing mode during the MRI scan well, which is in contrast to a previous trial.[11] In this ICD trial, a patient with severely reduced left ventricular function experienced unbearable discomfort when the V00 mode was turned on before the MRI scan. We hypothesize that asynchronous V00 pacing above the intrinsic heart rate may have more clinical impact in individuals with severely reduced ejection fraction than in those with a virtually normal ejection fraction like in our investigation. None of our patients developed any rhythm disturbances during the MRI scan. Nevertheless, it is recommended to monitor patients with implantable devices during MRI scans, as V00 pacing may theoretically cause ventricular arrhythmias even if the asynchronous pacing rate is well above the intrinsic heart rate.[19]

Our study was limited by the following factors: our findings can only be applied to the leadless pacemaker under investigation and cannot be extended to other LPM systems. The limited number of patients restricted statistical power and precluded a balanced randomization between 1.5 T and 3.0 T. However, the number of patients who currently carry an LPM system is still small and their availability limited. Larger trials will be needed to confirm and corroborate our findings when patients become available.

Conclusion

In conclusion, in our set of patients with a Micra® leadless pacemaker implanted at least 6 weeks before the scan, magnetic resonance imaging of the heart at either 1.5 T or 3.0 T proved feasible and safe. No relevant changes in pacing thresholds, sensing, lead impedances or battery life were detected within 3 months of follow-up.

Supplementary material

Supplementary material is available at *Europace* online.

Conflict of interest: All authors take responsibility for all aspects of the reliability and freedom of bias of the data presented and their discussed interpretation. A.K. reported to be proctor for Medtronic Inc. All other authors declared no conflict of interest.

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