Clinical safety of the ProMRI pacemaker system in patients subjected to thoracic spine and cardiac 1.5-T magnetic resonance imaging scanning conditions

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BACKGROUND Permanent cardiac pacemakers have historically been considered a contraindication to magnetic resonance imaging (MRI).

OBJECTIVE The purpose of the ProMRI Phase B Study, a multicenter, prospective, single-arm, nonrandomized study, was to evaluate the clinical safety of the Biotronik ProMRI pacemaker system in patients undergoing thoracic spine and cardiac MRI.

METHODS The ProMRI Phase B study enrolled 245 patients with stable baseline pacing indices implanted with an Entovis pacemaker (DR-T or SR-T) and Setrox 53-cm and/or 60-cm lead(s). Device interrogation was performed at enrollment, pre- and post-MRI scan, and 1 and 3 months post-MRI. End-points were (1) freedom from MRI- and pacing system–related serious adverse device effects through 1 month post-MRI; (2) freedom from atrial and ventricular MRI-induced pacing threshold increase (>0.5 V); and (3) freedom from P- and R-wave amplitude attenuation ($<50\%$), or P wave <1.5 mV, or R wave <5.0 mV at 1 month post-MRI.

RESULTS In total, 216 patients completed the MRI and 1-month post-MRI follow-up. One adverse event possibly related to the implanted system and the MRI procedure occurred, resulting in a serious adverse device effect–free rate of 99.6% (220/221; $P < .0001$. Freedom from atrial and ventricular pacing threshold increase was 100% (194/194, $P < .001$) and 100% (206/206, $P < .001$) respectively. Freedom from P- and R-wave amplitude attenuation was 98.2% (167/170, $P < .001$) and 100% (188/188, $P < .001$) respectively.

CONCLUSION The results of the ProMRI Phase B study demonstrate the clinical safety and efficacy of the ProMRI pacemaker system in patients subjected to thoracic spine and cardiac MRI conditions.

KEYWORDS Bradycardia pacing; Clinical trial; ENTOVIS; Magnetic resonance imaging; Pacemaker; Safety; ProMRI

ABBREVIATIONS **CI** = confidence interval; **FDA** = Food and Drug Administration; **MR** = magnetic resonance; **MRI** = magnetic resonance imaging; **SADE** = serious adverse device effect; **SAR** = whole-body specific absorption rate

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Introduction

Permanent cardiac pacemakers have historically been considered a contraindication to magnetic resonance imaging (MRI). An estimated 50% to 75% of pacemaker patients will require MRI during their lives.[1] MRI is the reference standard and imaging modality of choice in many fields of medicine. Strong static, gradient, and radiofrequency fields used to create the magnetic resonance (MR) images can be detrimental to pacemaker function and lead function, and can potentially cause harm to patients. Studies have shown that MRI may be hazardous in patients with older generations of implanted pacemakers.[2–5] Although routine MRI scans with conventional pacemakers and implantable cardioverter-defibrillator usually are

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discouraged unless the diagnostic benefits outweigh the risks, pacemakers specifically designed for the MRI environment have recently been shown to be safe under certain conditions and to maintain image quality.[6–13] Currently, the US Food and Drug Administration (FDA) has given approval to Biotronik and Medtronic MR-conditional pacemaker systems for full body scanning.[14,15]

The ProMRI Phase B study is a prospective, single-arm, nonrandomized, multicenter study designed to demonstrate the clinical safety of the ProMRI pacemaker system (Entovis SR-T and DR-T with Setrox S 53-cm/60-cm leads, Biotronik, Berlin, Germany) when used in patients undergoing thoracic spine or cardiac 1.5-T MRI scanning (ClinicalTrial.gov Identifier: NCT02009696). Thoracic spine or cardiac scanning places the pacemaker and leads within the MRI at the imaging landmark, where power deposition and, therefore, heat deposition risk remain the highest.[16]

Methods

Study design

Patients with a single- or dual-chamber Entovis pacemaker and Setrox S 53-cm and/or 60-cm leads were eligible for enrollment 5 weeks postimplant. Pacemakers were implanted in the pectoral chest region according to published guidelines.[17] A total of 245 patients were enrolled based on the statistical requirements of a 96% success rate, the ratio of dual-chamber vs ventricular devices, and estimated attrition rates.

The study was approved by the institutional review board/ethics committees at each site, and patients gave written informed consent before enrollment.

Inclusion criteria were (1) age $\geq$18 years, informed consent, and ability to complete the MRI studies and required follow-up, including ability to be followed remotely by Cardio Messenger Home Monitoring; (2) stable lead position and pacemaker indices for 5 weeks before the study; (3) pacing threshold(s) $\leq$2.0 V at 0.4ms; (4) pacing impedance(s) between 200 and 1500 Ω; (5) spontaneous rhythm allowing measurement of atrial and ventricular sensing indices; (6) battery capacity $>$30%; and (7) absence of phrenic nerve stimulation at 4.8 V at 1.0 ms.

Exclusion criteria were (1) persistent atrial arrhythmia ($>$7 days) or permanent atrial arrhythmia with an atrial lead; (2) planned cardiac surgery within 3 months of enrollment; (3) pregnancy; (4) life expectancy $<$3 months; and (5) implanted medical device or metallic item that might complicate MRI studies.

Study follow-up and procedures are summarized in Figure 1. Pacemakers were interrogated at all study visits: baseline, pre-/post-MRI, 1 month post-MRI, and 3 months post-MRI for changes in system parameters (sensing, threshold, impedance, system status). All patients were remotely monitored using Home Monitoring to collect daily sensing amplitudes, pacing capture thresholds, and impedance data.

Study-defined MRI scans consisting of thoracic spine or cardiac MRI were conducted 7 days to 2 months after enrollment. Patients were excluded from MRI scan if they had pre-MRI threshold(s) $>$2.0 V at 0.4 ms, lead impedance $<$200 or $>$1500 Ω, phrenic nerve stimulation at 4.8 V at 1.0 ms, or threshold variation exceeding ±0.5 V from baseline. All patients underwent pre-MRI screening at each institution.

An independent Data Monitoring Committee comprising 3 physicians not participating in the trial and blinded to investigational sites adjudicated all pacing system and MRI procedure adverse events, as well as hospitalizations and deaths, to determine any end-point relevance or relation to the MRI procedure.

Magnetic resonance imaging

Study MRI, purely for research purposes, was performed with scanners manufactured by Philips, Siemens, or GE

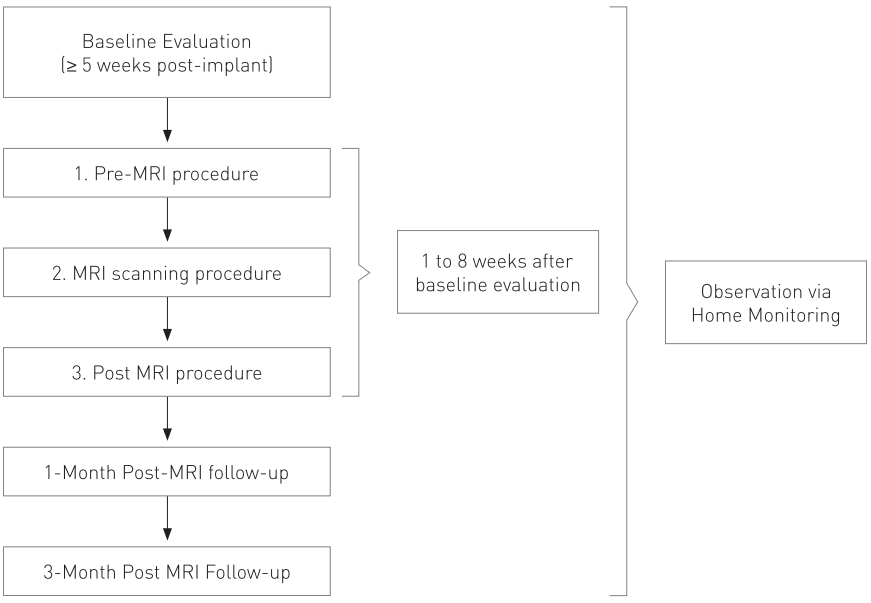

Figure 1 Flowchart of study. MRI = magnetic resonance imaging.