Clinical Safety of the Entovis **Pro**MRI® Pacing System

in Patients Undergoing MRI Scans

BIOTRONIK
excellence for life

ProMRI®

50 -70% of pacemaker patients will require an MRI during their lives.[1]

ProMRI® Study Background

Permanent cardiac pacemakers historically have been contraindicated for MRI scans.

Study Objective

Demonstrate the clinical safety of BIOTRONIK ProMRI® pacemaker systems under specific MRI conditions.

Systems Studied

- Entovis single-chamber pacemaker / Entovis dual-chamber pacemaker
- Setrox S 53 cm active fixation lead / Setrox S 60 cm active fixation lead

Study Design

- Prospective, single-arm, non-randomized, multi-center study
- Data pooled from ProMRI® (US)[2] and ProMRI® AFFIRM (Europe)[3]
- Investigational Device Exemption (IDE) study regulated by Food and Drug Administration
- 229 patients enrolled at 37 sites in the US and Europe
- Follow-up duration 3 months post-MRI

1. Kalin R and Stanton MS. Current clinical issues for MRI scanning of pacemakers and defibrillator patients. Pacing Clin Electrophysiology 2005;28: 326-328
2. Clinicaltrials.gov Registration NCT #01761162
3. Clinicaltrials.gov Registration NCT #01460992

100% free of MRI and pacing system related serious adverse events

Clinical Goal

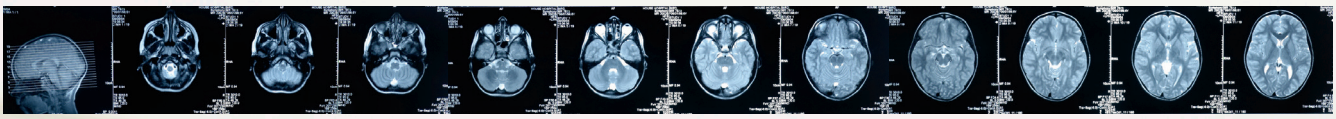
Evaluate the overall Serious Adverse Device Effect (SADE) free rate possibly related to the implanted system and the MRI procedure between pre-MRI and one-month follow-up.

Clinical Result

- No SADEs were adjudicated as related or possibly related to the implanted pacing system **and** the MRI procedure resulted in an SADE-free rate of 100.0% (229/229), $p < 0.001$, 95% CI: (98.4%, 100.0%)*

No MRI- and pacing-related adverse events.

*Compared to performance goal of 90%



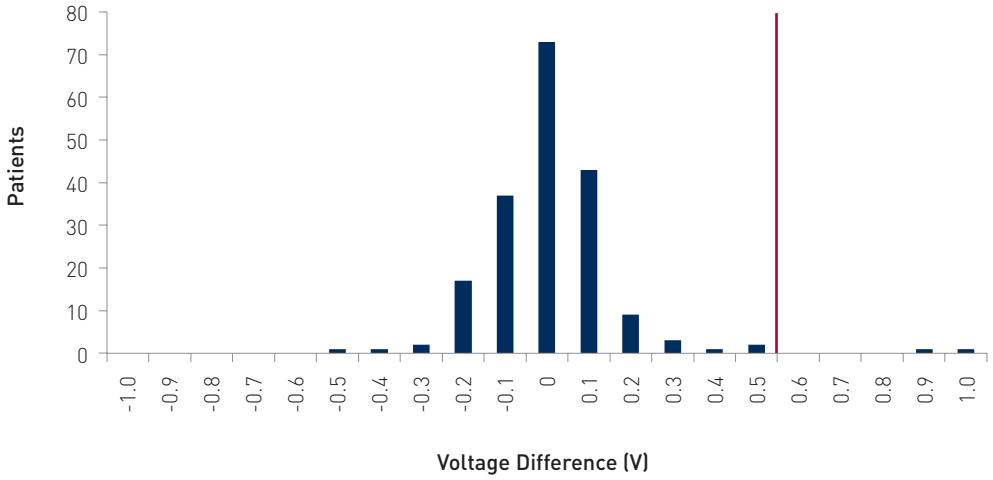
99% of patients experienced < 0.5 V atrial pacing threshold increase post-MRI

Clinical Goal

Evaluate atrial pacing threshold increase (defined as > 0.5 V between pre-MRI and one-month follow-up).

Clinical Result

Difference in R-Wave Sensing Amplitude (mV)	Results, n =191	P Value and CI*
Mean +/- SD	0.01 ± 0.16	
Range	-0.5 to 1.0	
Proportion of subjects with Atrial pacing threshold success	189 (99.9%)	p = 0.003, (96.3%, 99.9%)



Minimal changes in atrial pacing threshold

*Compared to performance goal of 95%

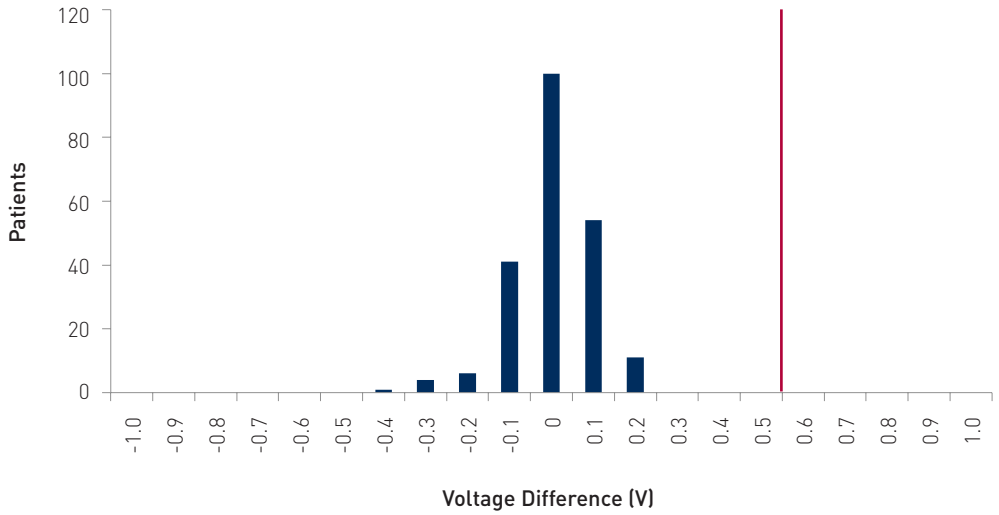
100% of patients experienced < 0.5 V ventricular pacing threshold increase post-MRI

Clinical Goal

Evaluate ventricular pacing threshold increase (defined as > 0.5 V between pre-MRI and one-month follow-up).

Clinical Result

Difference in Ventricular Pacing Threshold (V)	Results, n =217	P Value and CI*
Mean +/- SD	0.00 ± 0.10	
Range	-0.4 to 0.2	
Proportion of subjects with Ventricular Pacing threshold success	217 (100%)	p < 0.001, (98.3%, 100.0%)



Minimal changes in ventricular pacing threshold

*Compared to performance goal of 95%

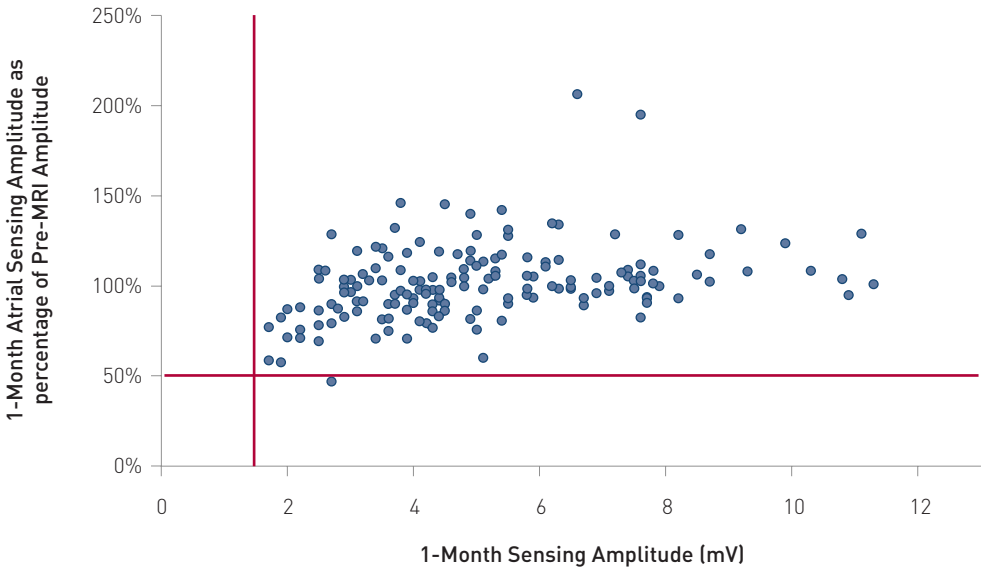
100% of patients experienced P-waves above 1.5 mV — 99.4% of patients experienced < 50% P-wave sensing attenuation

Clinical Goal

Evaluate P-wave sensing amplitude (defined as < 50% P-wave amplitude attenuation or < 1.5 mV at one-month follow-up).

Clinical Result

P-Wave Sensing Amplitude difference (mV)	Results, n =168	P Value and CI*
Mean +/- SD	0.04 ± 0.91	
Range	-3.4 to 3.7	
Subjects with Attenuation-free P-wave Sensing	167 (99.4%)	p < 0.001, (96.7%, 100.0%)



Stable atrial sensing post-MRI

*Compared to performance goal of 90%

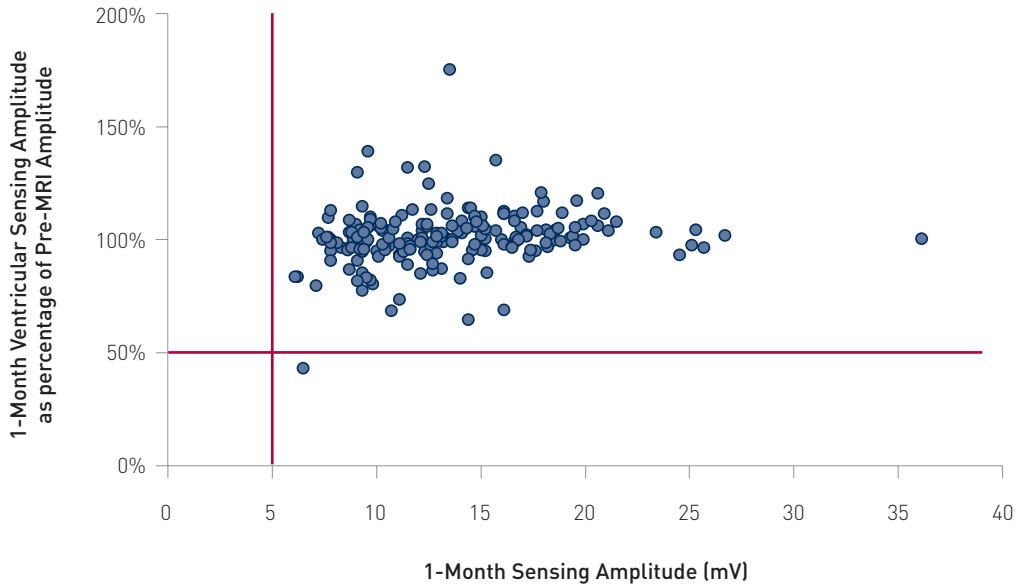
100% of patients experienced R-waves above 5 mV — 99.5% of patients experienced < 50% R-wave sensing attenuation

Clinical Goal

Evaluate R-wave sensing amplitude (defined as < 50% R-wave amplitude attenuation or < 5 mV at one-month follow-up).

Clinical Result

Difference in R-Wave Sensing Amplitude (mV)	Results, n =194	P Value and CI*
Mean +/- SD	-0.08 ± 1.65	
Range	-8.5 to 5.8	
Subjects with Attenuation-free R-wave Sensing	193 (99.5%)	p < 0.001, (97.2%, 100.0%)



Stable ventricular sensing post-MRI

*Compared to performance goal of 90%

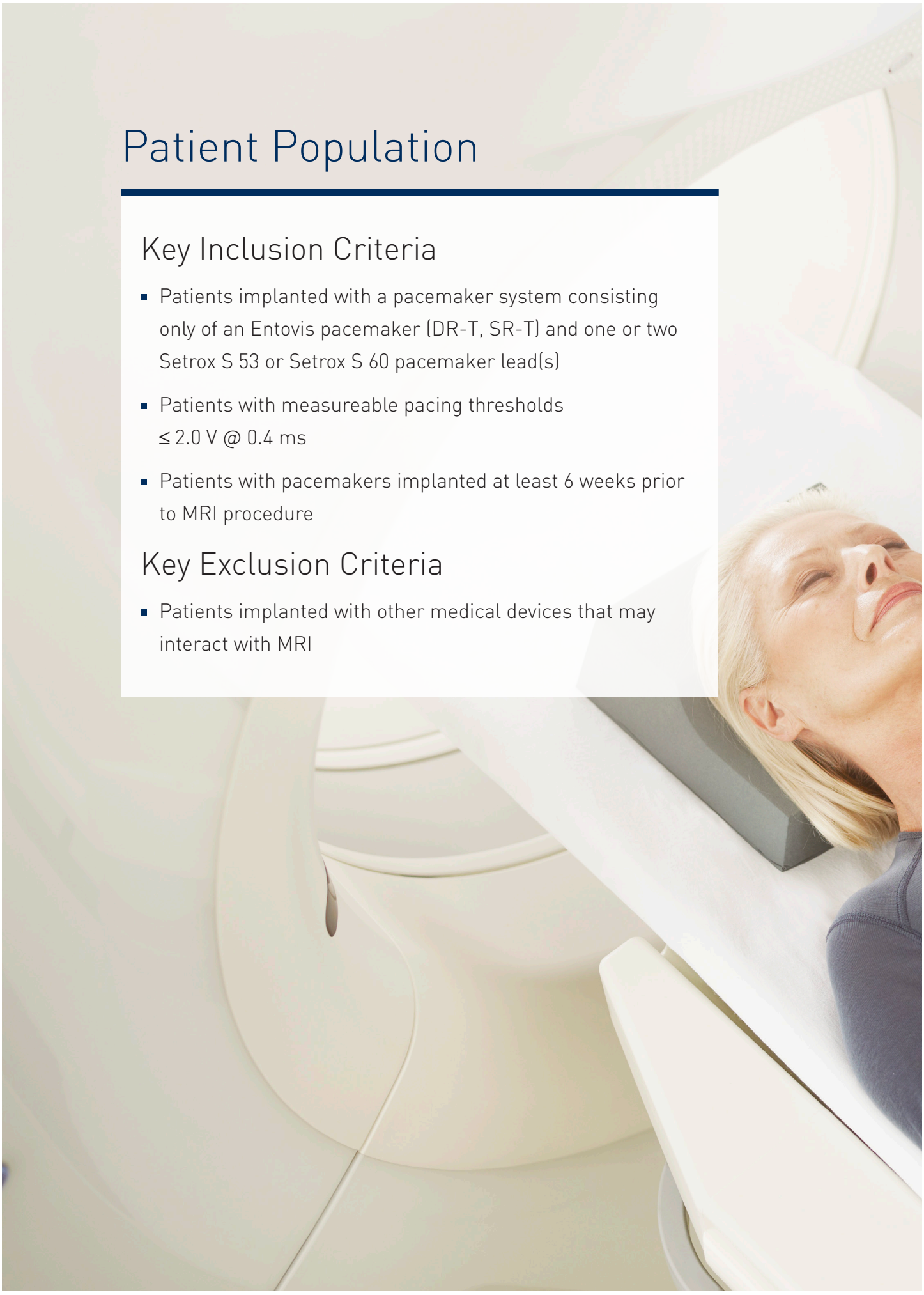
Patient Population

Key Inclusion Criteria

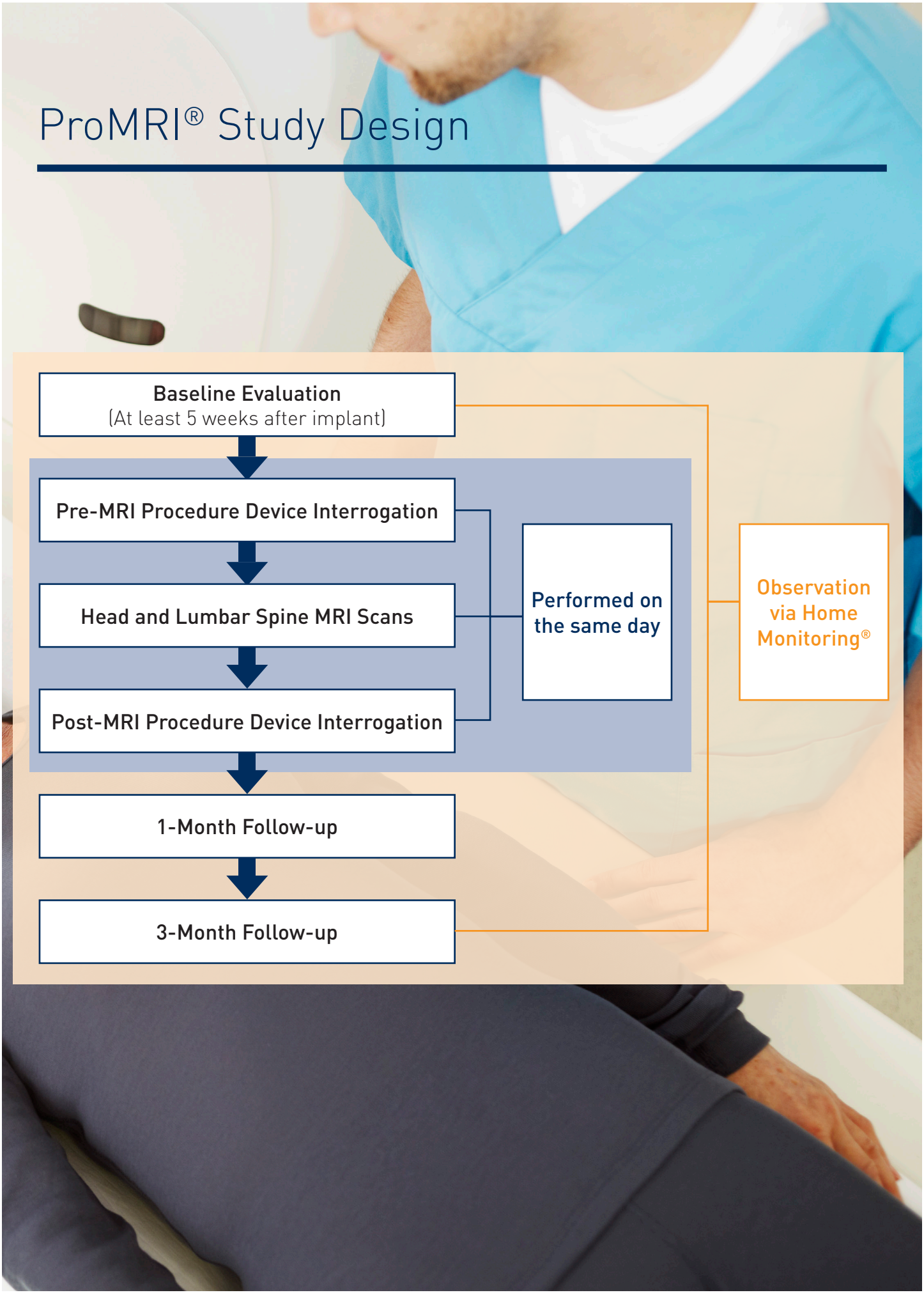
- Patients implanted with a pacemaker system consisting only of an Entovis pacemaker (DR-T, SR-T) and one or two Setrox S 53 or Setrox S 60 pacemaker lead(s)
- Patients with measureable pacing thresholds ≤ 2.0 V @ 0.4 ms
- Patients with pacemakers implanted at least 6 weeks prior to MRI procedure

Key Exclusion Criteria

- Patients implanted with other medical devices that may interact with MRI

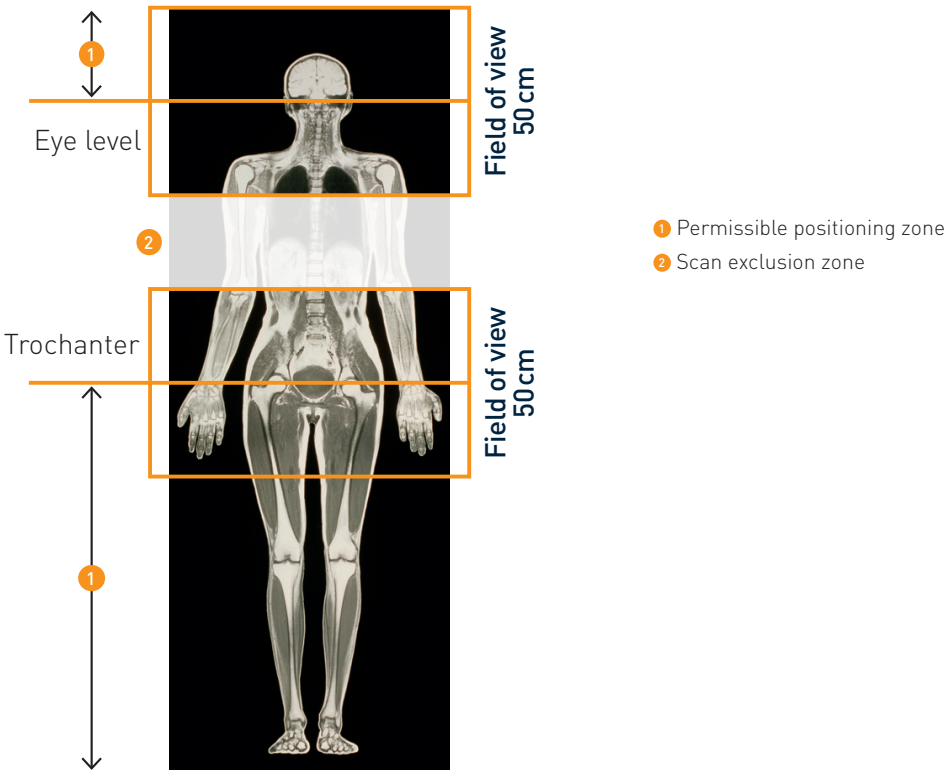


ProMRI® Study Design



ProMRI® Phase A Study MRI Isocenter Positioning Guidelines

- The study-defined scans consisted of both a head and lower lumbar MRI scans.
- Isocenter was set at the eyes and trochanter.
- MRI scanning systems configured with a closed tube, cylindrical magnets, and a static magnetic field strength of 1.5 tesla, manufactured by Philips, Siemens, or GE.

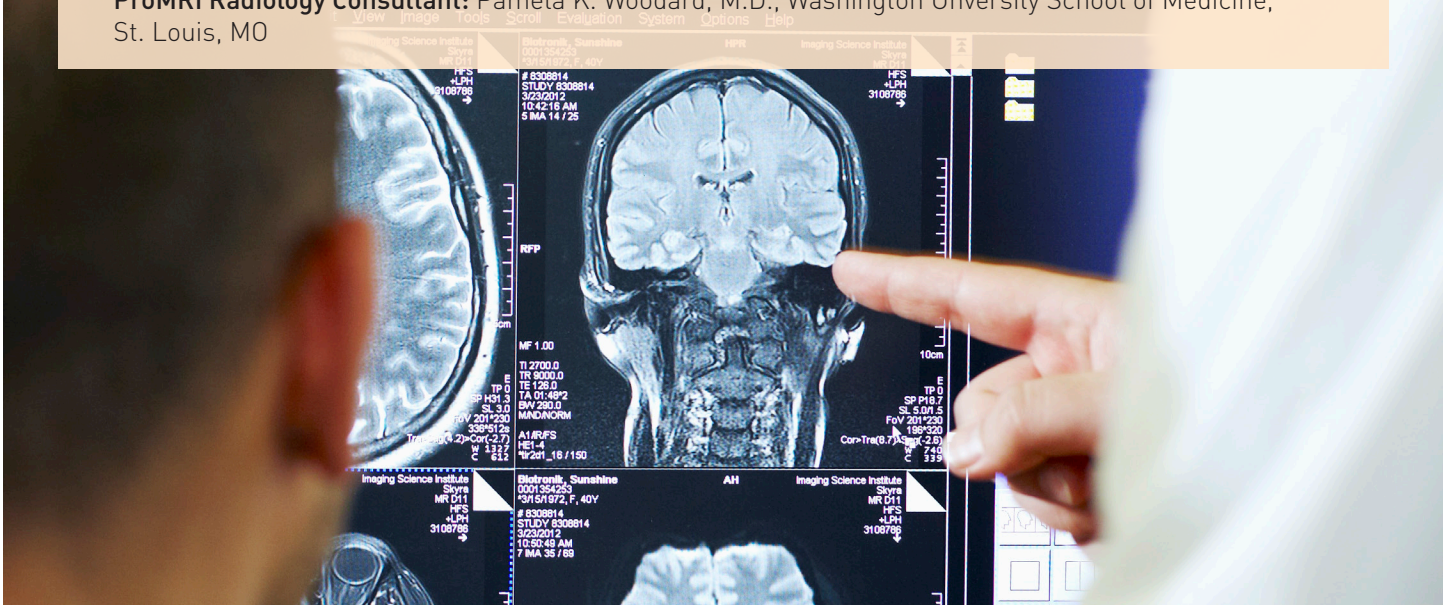


Special thanks to trial investigators:
ProMRI Investigators: William Bailey, M.D., Louisiana Heart Rhythm Specialists, Lafayette, LA; Lameh Fananapazir, M.D., Cumberland, M.D.; Leon Feldman, M.D., Eisenhower Desert Cardiology Center, Rancho Mirage, CA; Lawrence Rosenthal, M.D., UMass Memorial Medical Center, Worcester, MA; Alexander Mazur, M.D., University of Iowa Healthcare, Iowa City, IA; Carleton Nibley, M.D., John Muir Medical Center-Concord Campus, Concord, CA; Theofanie Mela, M.D., Massachusetts General Hospital, Boston, MA; Marye Gleva, M.D., Washington University, Saint Louis, MO; Harpeet Grewal, M.D., Bon Secours Memorial Regional Medical Center, Mechanicsville, VA; George Juang, M.D., New York Hospital Queens, Flushing, NY; Johan Aasbo, DO, NW Ohio Cardiology, Toledo, OH; Scott Kaufman, DO, Porter Health, Valparaiso, IN; William H. Stites, M.D., Research Medical Center, Kansas City, MO; Timothy Shinn, M.D., Michigan Heart, Ypsilanti, MI; Thomas Mattioni, M.D., Arizona Arrhythmia Consultants, Scottsdale, AZ; Anil Deshpande, M.D., St. Mary Medical Center, Langhorne, PA; Mark Marieb, M.D., Yale University, New Haven, CT; Craig McCotter, M.D., Upstate Cardiology, Greenville, SC; Zayd Eldadah, M.D., MedStar Washington Hospital Center, Washington, DC; Rick Henderson, M.D., Wake Forest Baptist Medical Center, Winston-Salem, NC; Michael Panutich, M.D., Newport Heart Hoag Memorial Hospital Presbyterian, Newport Beach, CA; Neil Bernstein, M.D., NYU Medical Center, New York, NY; G. Muqtada Chaudhry, M.D., Lahey Clinic, Burlington, MA

ProMRI Affirm Investigators: Alexander Kypta, OA Dr. Med., A.ö. Krankenhaus der Stadt Linz, Linz, Austria; Béla Merkely, Prof. Dr. Med., Semmelweis University Heart Center Budapest, Budapest, Hungary; Norbert Klein, Dr. Med., Universitätsklinikum Leipzig, Leipzig, Germany; Milos Taborsky, M.D., University Hospital Olomouc, Olomouc, Czech Republic; Johannes Brachmann, CA Prof. Dr., Klinikum Coburg gGmbH, Coburg, Germany; Rainer Zbinden, Dr. Med, Stadtspital Triemli, Zürich, Switzerland; Gerhard Lauck, CA Dr. Med., DRK Krankenhaus Neuwied, Neuwied, Germany; Wolfgang Haist, Dr. Med., St. Gertrauden Krankenhaus, Berlin, Germany; Klaus Amendt, Dr. Med., Diakoniekrankenhaus Mannheim, Mannheim, Germany; Sebastian Schellong, Prof. Dr., Städtisches Klinikum Dresden-Friedrichstadt, Dresden, Germany; Werner Jung, CA Prof. Dr., Schwarzwald Baar Klinikum, Villingen-Schwenningen, Germany; Christopher Aldo Rinaldi, M.D., St. Thomas, London, United Kingdom

ProMRI Data Monitoring Committee: Charles Henrickson, M.D., Oregon Health & Science University, Portland, OR; Jeffery Winderfield, M.D., Loyola University Medical Center, Maywood, IL; Sei Iwai, M.D., Westchester Medical Center, Valhalla, NY

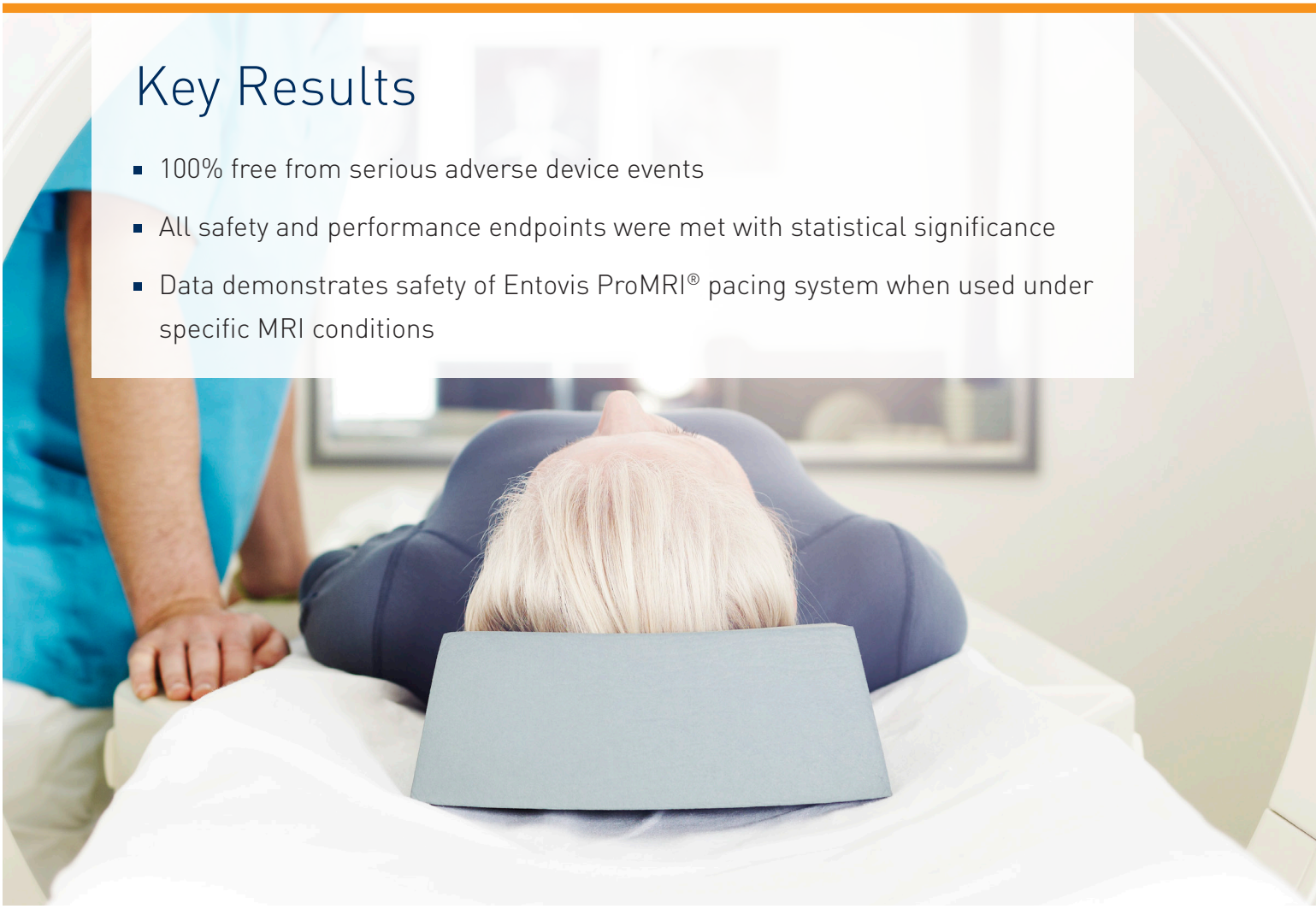
ProMRI Radiology Consultant: Pamela K. Woodard, M.D., Washington Unversity School of Medicine, St. Louis, MO



Clinical Safety of the Entovis **Pro**MRI® Pacing System in Patients Undergoing MRI Scans

Key Results

- 100% free from serious adverse device events
- All safety and performance endpoints were met with statistical significance
- Data demonstrates safety of Entovis ProMRI® pacing system when used under specific MRI conditions



BIOTRONIK, Inc.
6024 Jean Road
Lake Oswego, OR 97035-5369
(800) 547-0394 (24-hour)
(800) 291-0470 (fax)
www.biotronik.com

BR302 5/23/14

BIOTRONIK
excellence for life