A Single Institution Registry Trial Evaluating the Safety of MRI for Patients with Non-MRI Conditional Pacemakers and ICD

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Background

Millions of people in the United States and around the world have an implanted cardiac device. Between 1993 and 2009, overall pacemaker use increased by 50%, with 2.9 million permanent pacemakers implanted (Ferreira, et al, 2014). As of 2003, an estimated three million people met implant criteria for an implantable cardiac defibrillator (ICD) for either primary or secondary prevention (Nazarian, et al, 2006). It is further estimated that up to 75% of patients with a pacemaker or ICD will need medical magnetic resonance imaging (MRI) at some point following device implant (Nazarian, et al, 2006). Patients over 65 years of age comprise the majority of patients with implanted pacemakers or ICDs, and thus are extremely likely to require a MRI at some point after device implant.

MRIs provide excellent spatial resolution and multi-plane 3-D analysis. MRI is particularly good for soft tissue imaging and is the preferred imaging method for many neurological and musculoskeletal conditions (Mollerus, Albin, Lipinski, & Lucca, 2008). In addition to its superior imaging characteristics, MRI does not expose patients to ionizing radiation.

Pacemakers and ICDs have long been considered an absolute contraindication MRI due to concerns of the potential interactions between MRI and implantable cardiac devices including:

- Tissue heating, especially at the lead tip/myocardial interface
- Induction of ventricular arrhythmias such as ventricular tachycardia/fibrillation
- Pacemaker reset
- Reed switch closure, resulting in suspension of tachyarrhythmia detection/therapies
- Inhibition of pacing
- Increased pacing threshold/failure to capture
- Damage to circuitry

In recent years, however, several studies have concluded that MRI can be safe for patients with non-MRI conditional pacemakers and/or ICDs (Nazarian, et al, 2006, 2011). In these studies, investigators limited the MRI scans to magnets generating a field of 1.5 Tesla. Initially, the specific absorption rate (SAR) was limited to $\leq$ 2.0 W/kg, but as investigators found no association between SAR and the device variables studied, that restriction was later removed (Nazaraian, 2011). In 2011 Nazarian, et al published the results of their study of patients with pacemakers (237) or ICDs (201) who underwent medically indicated MRI. The study indicated that MRI is safe for pacemaker and ICD patients when appropriate screening protocols are in place and followed, with no immediate or long-term events requiring lead or system revision or reprogramming (Nazarian, et al., 2011). A 2008 study determined that MRI scanning did not cause sufficient damage to the myocardium to produce a significant rise in troponin-I levels (Mollerus, Albin, Lipinski, & Lucca, 2008). In 2009, Mollerus et al also determined that device patients undergoing MRI did not have any increase in arrhythmic activity during the scan (Molerus, Albin, Lipinski, & Lucca, 2009).

Registry Purpose

This registry is a prospective single institution study of MRI examinations in patients with pacemakers or ICD's who will undergo an MRI that is ordered for routine clinical care. The purpose of the registry is to

accumulate pre-and post-scan device interrogation data for the purpose of determining the risk of MRI for patients with implantable devices.

Registry data will add to existing data on the safety of MRI scans for patients with pacemakers and ICDs. This safety data may impact physicians' diagnostic choices for this patient population. Patients with conditions for whom MRI is the best diagnostic modality but who have not been able to undergo MRI scanning may be able to do so through registry participation. The diagnostic information obtained from the scan may assist physicians' treatment decisions and may ultimately affect patient outcomes.

In addition, to our knowledge, previous registries of MRI's in non-conditional cardiac devices have been limited to academic centers. This registry would be among the first to demonstrate the feasibility and safety of this approach in a community hospital setting.

Study Methods

The registry research involves acquiring and analyzing the data of device function and adverse events related to the MRI scan.

The need for MRI will be determined on a case-by-case basis based on the patient's medical history and treatment plan/goals, independent of the registry and research purposes. Only patients with implanted devices with orders for clinically indicated MRI scans will be considered for registry inclusion. Clinical review will be performed and the patient considered after determination that no other imaging modality would be appropriate.

The appropriateness of the MRI study must be discussed, in person or via phone call, between a cardiac radiologist, as determined by Paul Leslie, M.D., and the requesting physician. The discussion should include consideration of alternative imaging modalities and diagnostic quality of MRI imaging of requested body region given implanted device(s). The requesting physician is then responsible for discussing with the patient and/or their medical proxy the reasoning for the determination, based on the final decision made by a radiologist.

All patients will be screened prior to enrollment. Any patient with any commercially available pacemaker or ICD system implanted after 2001 who meet all of the inclusion criteria and none of the exclusion criteria, and who require a medically-indicated MRI as described above will be eligible to enroll in the study. The presence/absence of capped/abandoned/epicardial leads/subcutaneous coil will be confirmed and documented by review of the most recent chest x-ray obtained. The x-ray must post-date the most recent device/lead intervention, as determined by a review of the patient's medical record.

If an MRI procedure is deemed absolutely necessary, the MRI will be performed at the Lancaster General Hospital Lime Street MRI facility. MRI scan sequences, field intensity and field(s) of exposure will be selected to minimize risk to the patient while gaining needed diagnostic information for diagnosis or therapy management.

The MRI will be performed with a 1.5 T scanner utilizing institutional protocols and the following settings:

- Normal operating mode
- SAR ≤ 2.0 W/kg per patient.

Prior to the procedure, a pacemaker technologist or manufacturer clinical representative will interrogate the pacemaker or ICD and record the following parameters:

- Patient's underlying rhythm
- Atrial and right/left ventricular pacing thresholds
- P-wave and R-wave amplitude

- Lead impedance (atrial, ventricular, high voltage)
- Battery voltage
- Arrhythmia history
- Tachyarrhythmia therapy

The following pacemaker/ICD parameters will be deactivated for the duration of the MRI:

- Magnet response (ICD)
- Rate response
- PVC response
- Noise reversion response
- Ventricular sense response
- Mode switching
- Tachycardia detection/therapies (ICD)
- EGM triggers

Patients who are not pacemaker dependent will have their pacemaker/ICD programmed to AAI/VVI/DDI at 40 beats per minute for the duration of the MRI. Patients who are pacemaker dependent (pacing at programmed lower rate during the pre-scan interrogation) will have their pacemaker/ICD programmed to AOO/VOO/DOO at the programmed lower rate for the duration of the MRI. Emergency equipment, including a MRI compatible defibrillator and transcutaneous pacemaker, will be available throughout the procedure in the event of an adverse clinical event. In addition to radiology staff, a pacemaker technologist or manufacturer clinical representative and an EP tech/RN with current ACLS will be present for the duration of the procedure. An EP physician/advanced practice provider (APP) must be immediately available (i.e., in the hospital) to provide medical intervention, such as placement of a temporary external pacemaker if required. In the event that a code is called by the MRI staff, hospital protocol indicates that ER staff will respond to the code.

Radiology staff and the electrophysiology (EP) technologist or nurse with current ACLS certification will monitor the following patient parameters at least every 5 minutes throughout the MRI scan:

- Heart rate
- Heart rhythm
- Non-invasive blood pressure
- Oxygen saturation
- Symptoms

If any of the following adverse symptoms/events occur during the scan, the test will be immediately terminated:

- Burning/pulling sensation in device pocket/chest during MRI
- Potentially lethal/previously non-diagnosed arrhythmias during MRI
- Spontaneous and unanticipated pacing rate change
- SOB
- Chest pain
- Feeling of heat/pulling in the chest or device pocket

The patient will be removed from the scanner to the holding area and the device interrogated and reprogrammed to original parameters or as indicated by interrogation. If needed, emergency treatment will be provided as per ACLS protocols or at the discretion of the monitoring physician. The following parameters will be compared to the pre-MRI results:

- Patient's underlying rhythm

- Atrial and right/left ventricular pacing thresholds
- P-wave and R-wave amplitude
- Lead impedance (atrial, ventricular, high voltage)
- Battery voltage

All device-related adverse events/symptoms will be documented on the data collection form and reported to the IRB. The patient will remain in the MRI suite holding area until medically stable. The need for further treatment will be at the discretion of the monitoring physician.

The EP physician/APP will review and compare the pre/post MRI device data prior to the patient's discharge from the MRI suite. Following testing, the pacemaker or ICD will be reprogrammed to the pre-procedure parameters. The need for device reprogramming related to the MRI scan will be based on the clinical judgment of the attending electrophysiologist.

Follow-up

Patients who do not experience a device-related adverse event will continue with their routine pacemaker/ICD follow-up.

Patients who experience one or more device-related adverse events during the MRI will return 1-7 days post-MRI for follow-up pacemaker/ICD testing to confirm appropriate function. At a minimum, device interrogation/testing will include:

- Atrial and right/left ventricular pacing thresholds
- P-wave and R-wave amplitude
- Lead impedance (atrial, ventricular, high voltage)
- Battery voltage

The need for further follow-up will be determined by the physician based on testing results and clinical need.

The results of the follow-up device interrogation, including whether MRI-related adverse events have resolved, will be documented and kept in the device chart and recorded in the Registry database.

If the insurance provider does not cover the MRI and device checks, those costs may be the full responsibility of the patient. The patient will be informed of the status of the pre-authorization before scheduling the MRI.

Inclusion Criteria

1. Patient has a non-MRI conditional permanently implanted pacemaker or ICD implanted after 2001
2. Patient has a strong clinical indication for MRI where MRI is the diagnostic modality of choice for specific disease state without acceptable alternative imaging technologies as determined by the ordering physician and a radiologist
3. Patient is at least 18 years of age
4. Patient is willing and able to sign study informed consent and HIPAA authorization

Exclusion Criteria

1. Non-device related contraindication for MRI (such as implanted metallic objects, claustrophobia, morbid obesity)
2. Presence of capped/abandoned/epicardial leads or subcutaneous coil
3. Pregnancy
4. Device generator at elective replacement interval
5. Abdominal device implant

Adverse Events

For purposes of this registry, the following will be considered adverse events and will be reported to the IRB:

- Burning/pulling sensation in device pocket/chest during MRI
- Potentially lethal/previously non-diagnosed arrhythmias during MRI
- Spontaneous and unanticipated pacing rate change
- Power on reset
- Immediately post-MRI device parameter changes
    - Greater than 50 ohm change in atrial or ventricular (RV and/or LV) lead impedance
    - Greater than 5 ohm change in high voltage lead impedance
    - Greater than 50% decrease in atrial or ventricular (RV and/or LV) sensing threshold
    - Greater than or equal to a 1 volt increase in atrial or ventricular (RV and/or LV) pacing threshold
- MRI related device malfunction/failure
- Serious injury/death related to MRI device malfunction/failure

Changes in vital signs or termination of the scan not related to the presence of a pacemaker or ICD (i.e., anxiety-related increase in heart rate/blood pressure, tachypnea/SOB, etc) will not be considered adverse events and will not be reported.

All adverse events will be reported to the IRB in writing within 10 days of discovery. Any death of a patient will be reported to the IRB within 24 hours of discovery by research staff.

Sample Size

All patients who meet all the inclusion criteria and none of the exclusion criteria and who are willing sign the Registry consent/HIPAA Authorization will be enrolled in this registry at Lancaster General Hospital. Registry enrollment will continue indefinitely and/or until CMS approval of the procedure.

Any patient who signs the registry informed consent/HIPAA form but does not have an MRI will not be considered a registry participant (consented not enrolled). Patients who sign the research consent form and enter the MRI environment are considered enrolled, even if they do not successfully complete the scan.

Qualifications of Site Investigator:

Site investigators must be a board certified cardiac electrophysiologist or radiologist. The supervising physician/APP must be able to place and use a temporary external cardiac pacemaker. The facility must have the appropriate physicians and staff available for the insertion of an emergency temporary transvenous cardiac pacemaker if needed.

Data Collection

Each patient's pre procedure and post procedure device data, vital signs, and adverse events as described in the protocol will be reviewed by one of the study investigator cardiac electrophysiologists. Registry data will be entered into a secure research database (RedCap). Access to the registry data and patient information will be restricted to Lancaster Heart & Vascular Institute (LHVI) cardiology research staff and physicians. Hard copy data and source documents (data collection forms, informed consent and HIPAA authorization, device interrogation data) will be stored in secure files at the LHVI research office.

Registry data will be reviewed and analyzed at least quarterly and after the first 25 patients have been scanned. Our data may ultimately expand the routine use of MRI to include this patient population. We will track the incidence of adverse events (as defined in this protocol), look for data trends (patient types that experience AEs, devices that are adversely affected and how, etc.) using the appropriate statistical testing and tools.

We will also collect data on what alternative testing the ordering physician would have used, if any, instead of MRI, and how the use or non-use of MRI affected patient management.

Data Monitoring Safety Plan

The Internal Safety Committee for this Registry will be comprised of three individuals who work at LGH, and will include a statistician, a radiologist specializing in MRI procedures, and an EP cardiologist or other technical staff familiar with cardiac device parameters and programming. Neither Paul Leslie, M.D. or Sandeep Bansal, M.D. will be a member of the Safety Committee.

The Safety Committee will meet every 6 months to review study data and all adverse events as described in the Registry protocol. If the committee identifies a safety issue, enrollment may be suspended until the issue has been satisfactorily resolved.

Consent Process

Potential registry participants will be identified as described in the protocol. All registry participants must meet all of the inclusion criteria and none of the exclusion criteria. Informed consent will be obtained by one of the investigators or his/her designee from the study team. A copy of the signed informed consent and HIPAA Authorization will be scanned into the patient's permanent medical record in EPIC.

Risks of Study Participation

There are no known significant risks associated the exposure to electromagnetic fields from MRI scans. However, patients may be unable to tolerate the confined space of the MRI unit. This can lead to:

- Claustrophobia (fear of enclosed spaces)
- Mild diaphoresis (sweating)
- Hearing impairment (difficulty hearing)
- Sensation of bodily warmth
- Body stiffness related to immobility

Pacemakers and ICDs have historically been a contraindication for MRI, due to the potential for tissue heating where the lead is in contact with the heart tissue, the effect of electromagnetic fields on device

function (change of pacing mode or not sensing or treating abnormal rhythms), and the potential for mechanical malfunction. However, several recent large clinical trials have demonstrated that MRI can be safe for patients with non-MRI conditional pacemakers or ICDs when protocols are in place and adhered to.

The potential risks associated with the use of MRI with a non-MRI conditional pacemaker or ICD include, but may not be limited to, the following:

- Movement and or vibration of the device generator and/or leads
- Lead electrode (the metal end of the lead) heating with heart muscle damage resulting in loss of sensing or capture or both
- Device heating resulting in discomfort and/or tissue damage
- Life-threatening arrhythmias (ventricular tachycardia, ventricular fibrillation) T
- Other arrhythmias (atrial fibrillation, atrial flutter, bradycardia, SVT)
- Failure of the device to pace the heart
- Change in pacemaker or ICD function, including changes in mode, rate or output
- Inability to detect or treat abnormal heart rhythms
- Delivery of ICD therapy when it is not needed
- Need for device reprogramming)
- Need for a new device

There may be additional risks associated with study participation that are unknown at this time.

Benefits of Study Participation

There may be benefit from study participation due to the use of a standardized MRI protocol designed to minimize the risks associated with MRI use in the presence of a non-MRI conditional pacemaker or ICD. This may include the diagnostic benefit of the MRI itself, which is the diagnostic exam of choice for several disease entities. Study participation may also lead to a generally accepted protocol for MRI for patients with a non-MRI conditional pacemaker or ICD. Alternatively, there may be no benefit of study participation.

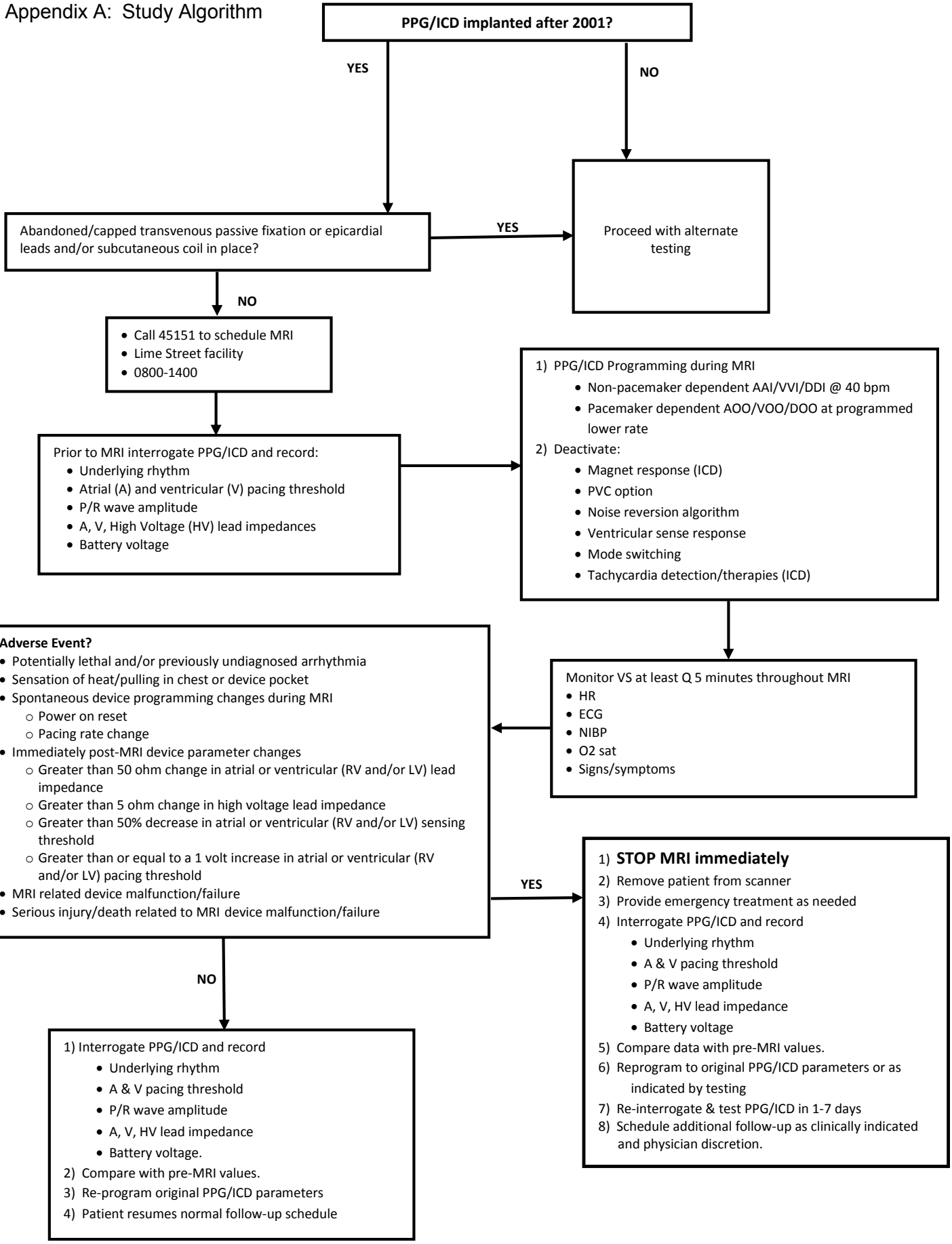
Study Results

The study investigators and research staff will analyze data at least quarterly. Results will be reported to the IRB at least every six months and to CMS quarterly. At a minimum, the reports will include:

- The number of patients screened
- The number of patients scanned
- The device models scanned
- Incidence and description of adverse events (as described above). Adverse events will also be reported to the IRB as they occur (see above)
- Patient outcomes

Registry results will be submitted for publication to one or more peer reviewed journals and may also be presented internally to physicians and other stakeholders who care for the defined study population. Results will also be reported on the ClinicalTrials.gov website on at least an annual basis.

Appendix A: Study Algorithm



References

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Johns Hopkins Research Participant Informed Consent and Privacy Authorization Form for the clinical trial Safety and Clinically Indicated Magnetic Resonance Imaging in Patients with Permanent Pacemakers (PPM) and Implanted Cardioverter Defibrillators (ICDs). Courtesy of Henry Halperin, MD, MA. Johns Hopkins Hospital, Baltimore, MD.

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