Proposed Decision Memo for Magnetic Resonance Imaging (MRI) (CAG-00399R3)

Decision Summary

The Centers for Medicare & Medicaid Services (CMS) proposes that the evidence is adequate to conclude that magnetic resonance imaging (MRI) improves health outcomes for Medicare beneficiaries with implanted permanent pacemakers (PMs) when the PMs are used according to the FDA-approved labeling for use in an MRI environment. Therefore we propose that this use of MRI is reasonable and necessary under §1862(a)(1)(A) of the Social Security Act (the Act.)

We propose to change the language in section 220.2.C.1 of the NCD Manual to remove the contraindication for Medicare coverage of MRI in beneficiaries with implanted PMs when the PMs are used according to the FDA-approved labeling for use in an MRI environment. Other contraindications that may be present in any given beneficiary would continue to apply in patients with PMs.

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Proposed Decision Memo

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SUBJECT: Proposed Decision Memorandum on Magnetic Resonance Imaging
DATE: April 25, 2011

I. Proposed Decision:

The Centers for Medicare & Medicaid Services (CMS) proposes that the evidence is adequate to conclude that magnetic resonance imaging (MRI) improves health outcomes for Medicare beneficiaries with implanted permanent pacemakers (PMs) when the PMs are used according to the FDA-approved labeling for use in an MRI environment. Therefore we propose that this use of MRI is reasonable and necessary under §1862(a)(1)(A) of the Social Security Act (the Act.)

We propose to change the language in section 220.2.C.1 of the NCD Manual to remove the contraindication for Medicare coverage of MRI in beneficiaries with implanted PMs when the PMs are used according to the FDA-approved labeling for use in an MRI environment. Other contraindications that may be present in any given beneficiary would continue to apply in patients with PMs.

II. Background Information

The scope of this reconsideration is limited to Medicare coverage of MRI and does not include any coverage determination about the Medtronic RevoMRI SureScan Pacing System itself or any other pacemaker. In addition, we are not reconsidering coverage of MRI for any particular indication, i.e., for any specific disease(s) or condition(s).

As noted in prior NCAs on this topic, MRI "(formerly known as nuclear magnetic resonance imaging - NMRI) is a noninvasive method of graphically representing the distribution of water and other hydrogen-rich molecules in the human body." MRI is a diagnostic imaging modality that is capable of demonstrating a wide variety of soft-tissue lesions with contrast resolution equal or superior to computed tomography (CT) scanning in various parts of the body. Among its advantages are the absence of ionizing radiation and the ability to achieve high levels of tissue contrast resolution without injected iodinated radiological contrast agents.

However, MRI exposes the patient to strong magnetic fields which may cause the movement or heating of implanted medical devices that are ferromagnetic (e.g. surgical clips) or that have ferromagnetic components (e.g. pacemakers, prostheses.) The American College of Radiology's (ACR) guidance document on safe MR Practices (Kanal 2007) explicitly speaks to the need to address the possibility that the patient may have ferromagnetic foreign bodies or implants.

Authors have described the effects of intense and high-frequency magnetic fields on ferromagnetic or conducting objects. For example, a review of pacemaker malfunction (Hayes and Vlietstra, 1993) notes that "… exposure to MRI causes pacemakers to revert to an asynchronous mode (in which impulse generation by the pacemaker occurs at a fixed rate, independent of underlying cardiac activity). This effect can be avoided only in PMs in which the magnet response can be programmed 'off'." The review's authors suggested use of other techniques to allow safe MR scanning of non-PM-dependent patients. These authors also note that "… [i]f the body area to be imaged is in close proximity to the pacemaker site, the pacemaker-induced artifact on MRI may obscure the images."

A later review article (Schoenfeld, 2007) states that "…(p)otential interactions (of PMs) with MRI include pacing inhibition, inappropriate implantable cardioverter defibrillators (ICD) discharges, rapid pacing, mechanical pull and rotation of the device, and device reprogramming," and suggests strategies to improve safety of MR scanning for patients with PMs and ICDs: "…Certain strategies to minimize complications have been suggested, including the use of less powerful MRI machines; imaging limited to extremities (i.e., remote from the implanted device); careful reprogramming of the intracardiac device, including asynchronous modes and maximal pacing output; selection of appropriate spin sequences; limitation of MRI to patients who are not pacemaker dependent; and careful, continuous periprocedure monitoring."

III. History of Medicare Coverage

Section 220.2 of Chapter 1 of the Medicare National Coverage Determination (NCD) Manual provides coverage of MRI for a number of clinical indications. Coverage is limited to MRI instruments that have received FDA premarket approval, and such units must be operated within the parameters specified by the approval.

In addition, a MRI examination is not currently covered by Medicare if certain contraindications are present. These include patients with cardiac PMs subject to one exception (as indicated in the following section of the February 24, 2011 final decision memo).

CMS recently posted a final decision memorandum (CAG-00399R2) on February 24, 2011. That decision determined that CMS will cover MRI for beneficiaries with implanted PMs or ICDs through Coverage with Evidence Development (CED)/Coverage with Study Participation (CSP) in approved clinical studies of MRI. The decision memorandum emphasized that the studies would include certain safeguards to ensure that the exposure of the device to an MRI environment adversely affects neither the interpretation of the MRI results nor the proper functioning of the implanted device itself. In addition, the study must be designed to assess the utility and safety of MRI exposure in those patients with implanted PMs and ICDs. That decision memorandum is available at http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=246&ver=11&NcaName=Magnetic+Resonance+Imaging+(MRI)+(2nd+Recon)&bc=BEAAAAAAEAAA&).

A. Current Request for Reconsideration

CMS received a request letter dated February 25, 2011 from Mr. Bob Thompson, MS, MA, Senior Director, Reimbursement, Economics and Health Policy, Cardiac Rhythm Disease Management, Medtronic, Inc. The requester noted that the FDA approved Medtronic's RevoMRI SureScan Pacing System on February 8, 2011. The requester referenced a randomized controlled trial of 464 pacemaker patients demonstrating the safety of the device in the MR environment and provided CMS with a reference to the journal in which the study was published. The letter also included the February 8, 2011 FDA approval letter, which includes the FDA's post-approval study requirements and conditions for use.

The requester asked that CMS remove completely the contraindication in the MRI policy for patients with pacemaker devices that have been approved by the FDA for use in the MR environment. Specifically, Medtronic requested that CMS change the language in section 220.2.C.1 of the current policy to be replaced by the following:

“The MRI is not covered when the following patient-specific contraindications are present: It is not covered for patients with pacemakers that have not been approved by the FDA for use in the MR environment.”

B. Benefit Category

Medicare is a defined benefit program. An item or service must fall within a benefit category as a prerequisite to Medicare coverage §1812 (Scope of Part A); §1832 (Scope of Part B) and §1861(s) (Definition of Medical and Other Health Services) of the Act. Magnetic resonance imaging is considered to be within the following benefit category: other diagnostic tests §1861(s)(3).

Medicare regulations at 42 CFR 410.32(a) state in part, that "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary’s specific medical problem." Thus, except where other uses have been explicitly authorized by statute, Medicare does not cover MRI for routine screening or surveillance.

IV. Timeline of Recent Activities

March 3, 2011	CMS posts a tracking sheet and reopens a NCD for reconsideration based on a request from Medtronic to determine if there is sufficient evidence to change the policy. The initial 30-day public comment period begins.
April 2, 2011	Initial public comment period ended. CMS received a total of 15 comments.

V. FDA Status

FDA granted approval of the RevoMRI SureScan Pacing System, which was designed for use in the MR environment for certain MRI exams on February 8, 2011, based on an expedited review. The Medtronic RevoMRI SureScan Pacing System consists of a RevoMRI SureScan IPG implanted with two CapSure Fix MRI™ SureScan™ 5086MRI leads. On February 25, 2011, the FDA released copies of the FDA Approval Order, Summary of Safety and Effectiveness Data, and Labeling and Other Consumer Information. Specific information on labeling and other supporting documentation can be found on the FDA's website at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/pma/pma.cfm?num=P090013.

The FDA review was expedited "because: 1) pacemakers deliver therapy to treat a condition that is life threatening or irreversibly debilitating, 2) The Revo MRI SureScan Pacing System may offer patients a clinically meaningful advantage by allowing patients to undergo MRI procedures under certain conditions, and, 3) no legally marketed MR Conditional pacemaker is available." FDA expedited reviews do not refer to the time it takes to review a device; it raises the priority of the review because the device has the potential to impact public health. Therefore, an expedited FDA review might take longer than a normal review for new technologies such as the RevoMRI SureScan Pacing System.

In these documents, the FDA states that the RevoMRI SureScan Pacing System is a restricted device, as the label specifies that a health professional who has completed cardiology SureScan training must be present during the programming of the SureScan and a health professional who has completed radiology SureScan training must be present during the MRI scan. Continued approval is also contingent upon a post-market approval study that is designed to be global, non-randomized, and performed as a multi-center cohort study of patients undergoing implantation of the RevoMRI SureScan Pacing System. The study must include two arms: 1) the Chronic Lead Performance Arm and 2) the Multiple MRI Scan Arm. Progress reports to the FDA from Medtronic are due every six months.

In addition, the FDA stated that this device is MR-Conditional, meaning that certain criteria must be met for patients to get an MRI. These include: only scans from a 1.5 Tesla (T) scanner; no chest scans which lead to more heating; and limits on specific absorption rate (SAR), which limits the use of certain MRI sequences with higher power indications.

VI. General Methodological Principles

When making NCDs, CMS normally evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for beneficiaries. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

Public commenters sometimes cite the published clinical evidence and provide CMS with useful information. Public comments that provide information based on unpublished evidence, such as the results of individual practitioners or patients, are less rigorous and, therefore, less useful for making a coverage determination. CMS uses the initial comment period to inform the public of its proposed decision. CMS responds in detail to the public comments that were received in response to the proposed decision when it issues the final decision memorandum.

VII. Evidence

Below is a summary of the evidence we reviewed. CMS may consider published articles submitted by the requester either as sources of evidence, or for background and general information. Because we recently reconsidered MRI in February 2011, the underlying questions are similar in this reconsideration.

A. Introduction

We recently conducted an exhaustive review of the evidence for a clinical benefit of the MRI for patients with implanted pacemakers and implantable cardioverter defibrillators in the MRI reconsideration, which was posted in February 2011. A complete discussion of that review can be found at http://www.cms.gov/medicare-coverage-database/details/nca-details.aspx?NCAId=252&ver=3&NcaName=Magnetic+Resonance+Imaging+(MRI)+(3rd+Recon)&bc=BEAAAAAAAAAA&.[1]

New evidence about the use of MRI in patients with certain types of PMs has been brought to our attention by the requester. We opened this NCA reconsideration to review the evidence and obtain public comment. We were particularly interested in receiving comments on coverage in the context of FDA post approval requirements.

As noted earlier, this reconsideration is limited to MRI and does not include any coverage determination about the Medtronic RevoMRI SureScan Pacing System itself or any other pacemaker. In addition, this NCA does not re-evaluate existing coverage or non-coverage policies or other contraindications. We are still non-covering MRI for nationally non-covered indications in 220.2.C.2 of the NCD manual and if another existing contraindication applies.

We are providing an in depth analysis of relevant new evidence that has come to light since our last review.

B. Discussion of Evidence Reviewed

1. Questions

In assessing the evidence regarding this topic, CMS formulated two questions similar to those used in prior decisions relating to this topic area (for example, in the decision memorandum regarding the second reconsideration for MRI, CAG-00399R2 (February 2011)).

Q 1: Is there adequate evidence to conclude that MRI of Medicare beneficiaries with implanted pacemakers approved by the FDA for use in the MR environment improves health outcomes when conducted in accordance with FDA-approved labeling?

Q2. Is there adequate evidence to conclude that MRI of Medicare beneficiaries with implanted pacemakers approved by the FDA for use in the MR environment improves health outcomes when conducted outside of FDA-approved labeling?

We recognize that improvements in health outcomes may arise from changes in physician management of the patient's condition, brought about through thoughtful consideration of the results of diagnostic testing. We also searched for indications in qualifying clinical studies of safety concerns or adverse events in participants with implanted devices undergoing MRI. We considered this prudent in view of known adverse events to which subjects might be vulnerable.

As has been done in other decisions, CMS considered the evidence in the hierarchical framework of Fryback and Thornbury (1991) where Level 2 addresses diagnostic accuracy, sensitivity, and specificity of the test; Level 3 focuses on whether the information produces change in the physician's diagnostic thinking; Level 4 concerns the effect on the patient management plan and Level 5 measures the effect of the diagnostic information on patient outcomes.

2. External Technology Assessments

CMS did not request an external technology assessment (TA) on this issue.

3. Internal Technology Assessment

New evidence submitted by the requester is reviewed below:

Wilkoff BL, Bello D, Taborsky M, et al. Magnetic resonance imaging in patients with a pacemaker system designed for the magnetic resonance environment. *Heart Rhythm*. 2011 Jan;8(1):65-73. Epub 2010 Oct 7.

The aim of this randomized control trial (RCT) was to evaluate the safety and effectiveness of the EnRhythm MRI SureScan implantable pulse generator and CapSureFix MRI leads [model 5086 MRI leads] used in support of the RevoMRI SureScan Pacing System which was designed for safe use in MRI environment for bradycardia indicated patients. Compared to other pacemaker systems, the RevoMRI SureScan Pacing System had a number of design changes “to improve MRI compatibility [with pacemakers.]” These changes included (1) lead modification to reduce RF lead tip heating; (2) internal circuits changes to reduce the potential for cardiac stimulation; (3) a limited amount of ferromagnetic materials; (4) improvement of internal circuit protection to prevent disruption of the internal power supply; (5) the use of a Hall sensor, whose behavior in a static magnetic field is more predictable; and (6) the development of a dedicated programming care pathway to facilitate the choice between asynchronous versus nonstimulation modes, to increase the pacing output to 5.0 V/1.0 ms during MRI scanning, to prevent programming the MRI mode if the device failed any of the seven system integrity checks function, and to facilitate restoration of prescan program states and values.

Inclusion criteria included patients who met Class I or II of the dual-chamber pacemaker implant indications as specified in the ACC/AHA/HRS guidelines.[2] Over 84% of the primary indications were either AV block or sinus node detection in both the MRI and control groups. The 464 subjects who met the above criteria were enrolled in this RCT, and all were between 9 and 12 weeks post-implant. They were randomized to either undergo an MRI scan (MRI group, n = 258) or not to undergo MR-imaging (control group, n = 206). Initially patients were randomized 1:1, but later during the study the protocol was changed to 2:1 to meet the regulatory requirements that at least 200 subjects be MRI scanned patients. Participants were monitored for arrhythmias, symptoms, and pacemaker system function during 14 non-clinically indicated relevant brain and lumbar MR imaging sequences. Imaging was performed at 1.5 T on systems from GE, Philips and Siemens and included scans with high radiofrequency power deposition and/or high gradient dB/dt exposure. Position of the isocenter of the RF transmitter was above C1 or below T12. For both groups, protocol required that a clinical evaluation of the pacemaker system function be performed immediately before and after MR imaging, at 1 week and 1 month post-MRI. Total MRI time was approximately 60 minutes for magnetic field exposure and 30 minutes active MRI scanning. The primary endpoint for safety analyzed the MRI procedure complication-free rate. Primary endpoints used in evaluating pacemaker performance included comparisons of pacing capture threshold (PCT) at a pulse duration of 0.5 ms, sensed electrogram amplitude, and lead impedance between the two groups. An intent to treat analysis was proposed.

Technical observations and adverse events were evaluated, including sustained ventricular arrhythmias, pacemaker output inhibition, asystole, electrical reset, and pacemaker function during and after the MRI scan. Data stored within the pacemaker, rhythm strips during PCT testing, and case report forms were collected. Because heart rate and rhythm measured by electrocardiogram (ECG) were inaccurate due to MRI interference, pulse oximetry and oxygen saturation were used instead.

Data were analyzed using a one-sided binomial proportion test (>90%) for determination of the complication-free rate of MRI in both groups and a one-sided confidence interval (CI) of 97.5% was also calculated. In addition, the proportion of enrollees who had a change in PCT of ≤ 0.5V (before and after MRI) was compared using the same confidence limits. The proportion of patients who experienced a change in sensing amplitudes from before the MRI/control visit to the result at the 1-month post visit were tested for statistical equivalence between the two groups by two-sample, one-sided 97.5% CI. Success was achieved if the sensing amplitude decreased ≤ 50% and the amplitude remained above a clinically acceptable minimum of 1.5 mV in the atrium or 5.0 mV in the ventricle.

Adverse events were classified by an adverse events committee: by definition, in most cases, adverse events were classified according to their relationship to the implant procedure, to the MRI procedure, and to the pacing system. But in some cases adverse events were classified as having an unclear relationship to the implant procedure, the MRI procedure, or pacing system due to the inability to assign the component of the system or procedure as at fault. Adverse events were classified as either complications or observations. The operational definition of a complication was any adverse event that resulted in an invasive intervention or the termination of significant device function. The definition of an observation was any adverse event that was not a complication.

Of the 258 enrollees in the MRI group, 211 completed the protocol instructions and completed the 1-month post-MRI/control visit (no data on 1-week results for both the MRI group and the control group were reported). At this time interval of the study it was noted that 100% of the enrollees had no MRI-related complications (e.g., no documentation of sustained ventricular arrhythmias, pacemaker inhibition or output failures, electrical resets, or other pacemaker malfunctions). During this same time period 8 observations were classified as either MRI related or labeled as unclear in relationship to MRI. No complications were noted in the control group. And though 9 deaths occurred in the MRI group and 2 in the control group during the study period, deaths were reported as not to be related to exposure to MRI. The mean follow-up period was 11.2 ± 5.2 (range 0.1-21.5) months. Pacing capture threshold (PCT) events and sensed electrogram amplitude changes were reported as minimal and similar between both study groups. The proportions of patients in the MRI and control groups who experienced an increase in PCT ≤ 0.5 V from directly before the MRI/control visit to the 1-month post visit were clinically and statistically equivalent. In both groups the number of enrollees that experienced PCT changes was essentially none. When comparing MRI to control group there were no increases in PCT ≤ 0.5 V for MRI of atria (165/165 for MRI group, 164/164 in the control group), and increases in PCT ≤ 0.5 V for ventricular MRI numbered 190/190 in MRI group compared to 183/184 for the control group. Though study protocol mentioned intent to treat analysis, the PCT measurements comparing MRI to control group reported 200/200 (MRI atrial) did not have different before and after PCT measurements as compared to 177/177 (control) and similarly 224/225 (MRI ventricular) did not have different before and after PCT measurements as compared to 194/195 (control). The success rate for atrial sensing amplitude was 94.7% (124/131) in the MRI group and 92.8% (129/139) in the control group. The success rate for ventricular sensing amplitude was 97.0% (130/134) in the MRI group and 94.9% (129/136) in the control group. Sensing values below the 1.5 mV (atrial) or 5.0 mV (ventricle) at the 1-month post-MRI/control visit were the primary reasons for nonsuccess. The authors state that there were 226 persons that underwent MRI at any time during the study.

The authors do note a number of limitations which include 1) the use of MRI scanners on pacemaker patients was specifically limited to well-defined conditions in the trial, 2) safe use outside of these conditions has not been demonstrated, and 3) though this trial demonstrated the safety and efficacy of the device (MRI on persons with pacemakers), it was not sufficiently powered to look at more rare safety events. The authors concluded that this trial documented the ability of this pacemaker system to be exposed in a controlled fashion to MRI in a 1.5 T scanner without adverse impact on patient outcomes or pacemaker system function.

4. MEDCAC

A Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) meeting was not convened on this request.

5. Evidence-based guidelines

At www.guidelines.gov, the National Guideline Clearinghouse, a search for ‘magnetic resonance imaging’ provides more than 450 guidelines referring to MRI use in the diagnosis and management of a large variety of clinical situations. A large number of other guidelines are available through www.guidelines.gov covering MRI use in various oncologic, cardiovascular, neurodegenerative, traumatic and other diseases or conditions. In 12 guidelines, both ‘MRI’ and ‘pacemaker’ occur.

Recommendations from these guidelines generally contraindicate MRI use in patients with implanted PMs. Many of these guidelines are based not only on reviews of published literature, but also on consensus of experts.

An example of such a guideline was developed in the United Kingdom. The National Institute for Health and Clinical Excellence (NICE) 2008 guideline on MRI for diagnosis of patients with suspected stroke lists pacemakers among the contraindications to MRI use; however, the NICE recommendation is modified by its statement that " … the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering."

6. Professional Society Position Statements

In 2007, several professional societies suggested that the presence of an implanted PM or ICD should be considered as a relative contraindication[3] to MRI. The American Heart Association (AHA), the North American Society for Cardiac Imaging, and the Society for Cardiovascular Magnetic Resonance endorsed this document (Levine et al., 2007).

The ACR guidelines on MRI safety (Kanal et al., 2007) noted that adverse effects of MR scans on implanted cardiac devices can include " … [u]nexpected programming changes, inhibition of pacemaker output, failure to pace, transient asynchronous pacing, rapid cardiac pacing, the induction of VF, heating of the tissue adjacent to the pacing or ICD system, early battery depletion, and outright device failure requiring replacement may all occur during MRI of patients with pacemakers or ICDs. The ACR Blue Ribbon Panel on Magnetic Resonance Safety committee noted that multiple deaths have occurred under poorly and incompletely characterized circumstances when device patients underwent MRI. These deaths may have occurred as a result of pacemaker inhibition, failure to capture or device failure (resulting in prolonged asystole), and/or rapid cardiac pacing or asynchronous pacing (resulting in the initiation of ventricular tachycardia or fibrillation)." Nevertheless, the ACR panel suggested that "… It is recommended that **the presence of implanted cardiac pacemakers or implantable cardioverter defibrillators (ICDs) be considered a relative contraindication for MRI. MRI of patients with pacemakers and ICDs ('device patients') is *not* routine.** Should an MRI be considered, it should be done on a case-by-case and site-by-site basis, and only if the site is staffed with individuals with the appropriate radiology and cardiology knowledge and expertise on hand." (Note: Emphasis in bold font added by CMS.)

The ACR's Guidance Document for Safe MR Practices (Levine, 2007) recognizes the challenges of safe MR scanning in a patient with implanted electrically active cardiac devices and with ferromagnetic foreign bodies or implants, among others. This guidance document clarifies current terminology that may be used to identify safety levels for devices intended to provide safe pacing and MRI when used under specified conditions, and the terms such as "MR conditional" as defined below.

“MR safe”
An item that poses no known hazards in any MR environment. Using the new terminology, “MR safe” items include nonconducting, nonmetallic, nonmagnetic items, such as a plastic Petri dish.

“MR conditional”
An item that has been demonstrated to pose no known hazards in a specified MR imaging environment with specified conditions of use. Conditions that define the MR environment include static magnetic field strength, spatial magnetic gradient, dB/dt (time-varying magnetic fields), RF fields, and SAR. Additional conditions, including specific configurations of the item (e.g., the routing of leads used for a neurostimulation system), may be required.

“MR unsafe”
An item that is known to pose hazards in all MR environments. “MR unsafe” items include magnetic items such as a pair of ferromagnetic scissors.

Professional societies have not made any changes available to the public regarding the contraindication for the use of pacemakers in the MR environment since our last review in February 2011.

7. Expert Opinion

Except for the public comments summarized below, CMS did not receive expert opinion on the proposed decision.

8. Public Comments

A. Initial Comment Period 3/4/2011- 4/2/2011

During the initial public comment period, CMS received 15 public comments. One comment came from industry, three from medical device manufacturers, one from a physician group, four from medical centers, four from medical and diagnostic professional societies, one from an imaging center, and one from a national nonprofit organization. All comments agreed that CMS should cover MRI for patients with FDA-approved implanted pacemakers in accordance with FDA labeling, in order to give patients greater access to a beneficial diagnostic technology. One commenter noted that CMS should also develop a code modifier or create a new code to reimburse hospitals for the additional resources specific to monitoring these patients and for bedside device programming by clinicians. Several comments also mentioned the financial burden that will be put on pacemaker patients if CMS does not approve coverage of MRI. The commenters mentioned that the safety concerns for this population have been answered as a result of the FDA study and approval of a certain device for use in the MRI environment. They also stated that CMS should not delay coverage by requesting more data and they should expedite the nine month NCD process.

Several commenters expressed concern about using CED in conjunction with the FDA's post-market approval requirements. They wrote that with CED, CMS seems to be duplicating the FDA's mandate to "assure the safety, efficacy, and security of drugs, biological products, and devices." A second concern brought up by the commenters is that with CED, CMS will only cover MRI for patients with this device who are enrolled in clinical trials.

VIII. CMS Analysis

NCDs are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally by Medicare (§1862(l) of the Act). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." See §1862(a) (1) (A) of the Act.

We begin generally with an explanation of the basis for Medicare decisions about diagnostic tests such as MRI. The Medicare regulations at 42 CFR 410.32(a) state in part, "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem." Thus, in making or modifying an NCD on MRI, we look for evidence demonstrating how the treating physician uses the result of an MRI study to manage the further diagnostic or treatment strategy in Medicare beneficiaries with implanted PMs or ICDs. We believe that evidence of improved health outcomes is more persuasive than evidence of test characteristics.

We considered the evidence in the hierarchical framework of Fryback and Thornbury (1991).

In evaluating diagnostic tests, Mol and colleagues (2003) reported: “Whether or not patients are better off from undergoing a diagnostic test will depend on how test information is used to guide subsequent decisions on starting, stopping, or modifying treatment. Consequently, the practical value of a diagnostic test can only be assessed by taking into account subsequent health outcomes.” When a proven, well established association or pathway is available that demonstrates a virtually certain association between a well-defined, objectively assessed intermediate health outcome and one or more net beneficial patient outcomes of interest, intermediate health outcomes may also be considered. For example, if a particular diagnostic test result can be shown to change patient management and other evidence has demonstrated that those patient management changes improve health outcomes, then those separate sources of evidence may be sufficient to demonstrate positive health outcomes from the diagnostic test.

As a diagnostic test, an MRI study would not be expected to directly change health outcomes absent adverse effects of the MR scan itself. Rather, it would affect health outcomes through changes in disease management brought about by physician actions taken in response to test results. Such actions may include decisions to treat or withhold treatment, to choose one treatment modality over another, or to choose a different dose or duration of the same treatment. To some extent the usefulness of a test result is constrained by the available management alternatives. Ideally we would see evidence that the use of MRI changes outcomes for Medicare beneficiaries with implanted PMs, or at least leads treating physicians to change their diagnostic or treatment strategies in such a way that better outcomes are achieved.

In addition, CMS generally focuses on evidence that includes patients who are 65 years of age or older. The typical Medicare beneficiary is 65 years of age or older; however, a relatively small percentage of beneficiaries may be younger than 65 year old due to Medicare entitlement based on other factors such as end stage renal disease or disability. CMS favors evidence from studies in which the population reflects the affected Medicare beneficiary population.

As noted above, the requestor asked that the contraindication language in section 220.2.C.1 of the NCD Manual be replaced with the following:

> “The MRI is not covered when the following patient-specific contraindications are present: It is not covered for patients with pacemakers that have not been approved by the FDA for use in the MR environment.”

Medicare's existing contraindication to MRI coverage is based on the well established safety concerns about the effects of MRI exposure on implanted devices. On February 24, 2011, we made one exception to this policy to permit coverage in certain clinical studies. The requester's suggested language would require us to repeal the February 24, 2011 exception. The requestor did not submit evidence on MRI in patients with implanted legacy pacemakers. In light of our very recent review of this topic, we are not reconsidering this issue here. Therefore, we are not proposing to make this change.

The requestor based its request for an exception to the contraindication policy on the recent FDA approval, specifically on the demonstration of safety for its labeled use. In addition, the requestor furnished the clinical study evidence used to support its FDA approved label for the RevoMRI SureScan. It did not submit evidence that speaks to MRI use outside of the FDA label.

We extensively reviewed the additional evidence submitted by the requestor with regard to two questions:

Q 1: Is there adequate evidence to conclude that MRI of Medicare beneficiaries with implanted pacemakers approved by the FDA for use in the MR environment improves health outcomes when conducted in accordance with FDA-approved labeling?

The objective of the study was to evaluate the safety and effectiveness of a pacemaker designed for use in the MR environment. The authors performed a RCT that enrolled 464 subjects between MRI and control groups to compare non-complication rates. Dates of the study were not provided and as noted in the study, statistical analysis was performed by Medtronic. The authors concluded that MRI did not result in higher complication rates in persons who had a RevoMRI pacemaker compared to persons who were not exposed to MRI. As the authors reported, one limitation of the study was that it was not sufficiently powered to capture rare adverse events.

We note the following limitations were not discussed by the authors in their study report.

1. An intent to treat analysis was not followed. A large number of enrollees in both the intervention group and the control group were not accounted for in the final analysis.
2. The authors did not adjust for age groups or sex or race/ethnicity (the latter not reported in the paper), only using univariate analysis. Though it is reported that the average age is over 65 and less than 70, the data were not analyzed for the subgroup over 65 population nor are the numbers of enrollees demographically described other than by population means and ranges. We are unable to determine what effect these variables have on the results regarding Medicare beneficiaries.
3. The population studied consisted of persons with non-clinically indicated MRIs and we were unable to determine whether or not MRI this latter population is likely to have a problem/complication.

While the evidence reviewed in this decision memorandum is limited and does not directly speak to health outcomes, we are considering it in the larger context of the vast body of evidence on MRI that we have considered previously. MRI clearly leads treating physicians to change their diagnostic or treatment strategies in such a way that better outcomes are achieved for many conditions. In summary, we propose that the evidence is sufficient to determine that MRI of Medicare beneficiaries with implanted pacemakers approved by the FDA for use in the MR environment improves health outcomes when conducted in accordance with FDA-approved labeling.

Q2. Is there adequate evidence to conclude that MRI of Medicare beneficiaries with implanted pacemakers approved by the FDA for use in the MR environment improves health outcomes when conducted outside of FDA-approved labeling?

We find no evidence sufficient to address this question in a manner that would change current policy.

Healthcare Disparities

CMS is concerned about disparities in healthcare in the Medicare population, and when performing this assessment of the literature, there was little information addressing age, gender, race/ethnicity, socioeconomic status, or sexual orientation of study participants. While we are not aware *a priori* of factors that would meaningfully alter the conduct or interpretation of MRI in these subpopulations, we encourage the broad inclusion in clinical studies of patients who represent the breadth of the Medicare beneficiary population.

IX. Proposed Decision

The Centers for Medicare & Medicaid Services (CMS) proposes that the evidence is adequate to conclude that magnetic resonance imaging (MRI) improves health outcomes for Medicare beneficiaries with implanted permanent pacemakers (PMs) when the PMs are used according to the FDA-approved labeling for use in an MRI environment. Therefore we propose that this use of MRI is reasonable and necessary under §1862(a)(1)(A) of the Social Security Act (the Act.)

We propose to change the language in section 220.2.C.1 of the NCD Manual to remove the contraindication for Medicare coverage of MRI in beneficiaries with implanted PMs when the PMs are used according to the FDA-approved labeling for use in an MRI environment. Other contraindications that may be present in any given beneficiary would continue to apply in patients with PMs.

APPENDIX A
General Methodological Principles of Study Design
(Section VI of the Decision Memorandum)

When making NCDs, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the generalizability of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's potential risks and benefits.

The methodological principles described below represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has its unique methodological aspects.

Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias).
- Co-interventions or provision of care apart from the intervention under evaluation (performance bias).
- Differential assessment of outcome (detection bias).
- Occurrence and reporting of patients who do not complete the study (attrition bias).

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, in general, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The design, conduct and analysis of trials are important factors as well. For example, a well designed and conducted observational study with a large sample size may provide stronger evidence than a poorly designed and conducted randomized controlled trial with a small sample size. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

Randomized controlled trials
Non-randomized controlled trials
Prospective cohort studies
Retrospective case control studies
Cross-sectional studies
Surveillance studies (e.g., using registries or surveys)
Consecutive case series
Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess and consider the evidence.

Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage determinations for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation) and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations. One of the goals of our determination process is to assess health outcomes. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived. Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

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[1] A copy of the record of that decision will be incorporated in the record of this reconsideration.

[2] Epstein AE, Dimarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 Guidelines for device-based therapy of cardiac rhythm abnormalities. American College of Cardiology; American Heart Association Task Force on Practice Guidelines; American Association for Thoracic Surgery; Society of Thoracic Surgeons. Heart Rhythm. 2008 Jun;5(6):934-55. Epub 2008 May 19.

[3] "Relative contraindication" is a factor (in this case the presence of an implanted PM) that renders the carrying out of a medical procedure (here, an MRI) generally inadvisable due to potential adverse impact on the patient. However, the risk of harm due to a relative contra-indication to MRI may, in the physician's judgment about a particular patient, be outweighed by expected benefit of information gained from MRI.

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Bibliography

1. FDA News Release. U.S. Food and Drug Administration. FDA approves 1st pacemaker designed to work safely during some MRI exams. February 8, 2011. Accessed February 8,2011. Available from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm242651.htm.

2. Fryback DG, Thornbury JR. The efficacy of diagnostic imaging. Med Decis Making. 1991 Apr-Jun;11(2): 88-94.

3. Hayes DL, Vlietstra RE. Pacemaker malfunction. Ann Intern Med. 1993 Oct 15; 119(8): 828-35.

4. Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document for safe MR practices: 2007. *AJR* American Journal of Roentgenology. 2007; 188(6): 1447-1474.

5. Levine GN, Gomes AS, Arai AE, et al. Safety of magnetic resonance imaging in patients with cardiovascular devices: an American Heart Association scientific statement from the Committee on Diagnostic and Interventional Cardiac Catheterization, Council on Clinical Cardiology, and the Council on Cardiovascular Radiology and Intervention: endorsed by the American College of Cardiology Foundation, the North American Society for Cardiac Imaging, and the Society for Cardiovascular Magnetic Resonance. *Circulation.* 2007; 116(24): 2878-2891.

6. Mol BW, Lijmer JG, Evers JL, Bossuyt PM. Characteristics of good diagnostic studies. Semin Reprod Med 2003;21:17-25.

7. MRI reconsideration 2. Decision Memo for Magnetic Resonance Imaging (MRI) (CAG-00399R2). The Center for Medicare and Medicaid Services. Available from: http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=246&ver=11&NcaName=Magnetic+Resonance+Imaging+(MRI)+(2nd+Recon)&bc=BEAAAAAAEAAA&.

8. National Collaborating Centre for Chronic Conditions. Stroke. Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Jul. 37 p. (Clinical guideline; no. 68). (Cited as NICE 2008).

9. Revo MRI SureScan Pacing System- P090013. U.S. Food and Drug Administration. February 8, 2011. Accessed February 15, 2011. Available from: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/pma/pma.cfm?num=P090013.

10. Schoenfeld MH. Contemporary Pacemaker and Defibrillator Device Therapy: Challenges Confronting the General Cardiologist. Circulation 2007; 115: 638-53.

11. Wilkoff B, Bello D, Taborsky M, et al. Magnetic resonance imaging in patients with a pacemaker system designed for the magnetic resonance environment. *Heart Rhythm*, 2011; 8(1):65-73.

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