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Emerging MRI Technologies for Imaging Musculoskeletal Disorders under Loading Stress

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Acknowledgments

Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about healthcare. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and healthcare services to meet the needs of Medicare, Medicaid, and the State Children's Health Insurance Program (SCHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments and Comparative Effectiveness Reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care. Technical Briefs are the most recent addition to this body of knowledge.

A Technical Brief provides an overview of key issues related to a clinical intervention or health care service—for example, current indications for the intervention, relevant patient population and subgroups of interest, outcomes measured, and contextual factors that may affect decisions regarding the intervention. Technical Briefs generally focus on interventions for which there are limited published data and too few completed protocol-driven studies to support definitive conclusions. The emphasis, therefore, is on providing an early objective description of the state of science, a potential framework for assessing the applications and implications of the new interventions, a summary of ongoing research, and information on future research needs. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an e-mail list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly, while Technical Briefs will serve to inform new research development efforts.

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Executive Summary

Background: Musculoskeletal conditions are the most common cause of disability in the United States. The differential diagnosis of nonspecific musculoskeletal complaints is challenging, and the use of imaging modalities, such as magnetic resonance imaging (MRI), is often required to establish a diagnosis, determine treatment, or monitor disease progression. Although MRI is widely used in medicine today, there remains considerable uncertainty as to the optimal imaging approach for most musculoskeletal conditions.

Purpose: To describe the current state of application, and enumerate the potential benefits and harms of emerging MRI technologies under loading stress (for example, under weight-bearing or simulated weight-bearing conditions) for the diagnosis and management of patients with musculoskeletal disorders, and to summarize the state of current research.

Methods: Interviews with selected Key Informant (KI), a structured review of grey literature, and an evidence map (i.e., a systematic description of the characteristics of the published literature) of MEDLINE®-indexed original research publications (last search: September, 2010).

Findings: There exist a rapidly expanding array of MRI technologies designed to employ weight-bearing, stress-loading, or positioning protocols to more accurately diagnose musculoskeletal disorders. However, the diagnostic accuracy of the available technologies has not been investigated in well designed studies; thus, considerable uncertainty remains regarding the impact of these techniques and technologies on physicians' diagnostic thinking and decision making with regards to treatment. Furthermore, potential subgroups of patients that may particularly benefit from loading stress MRI cannot be identified with certainty. There are as yet no trials that compare the impact of these technologies on patient outcomes with conventional MRI. Therefore, the relative benefits and harms of different imaging technologies remain unclear. Future studies should address the prevalent methodological limitations in the existing literature, regarding patient (and control) selection, outcomes investigated, and statistical analyses performed, to identify the imaging modalities and protocols with the highest clinical validity. Comparative studies of diagnostic tests should also be performed to identify the loading stress MRI technologies that have high diagnostic accuracy and may be candidates for further assessment in randomized studies of testing versus no-testing strategies.

Background

Musculoskeletal conditions are the most common causes of disability in the United States.[1] Among these, arthritis (osteoarthritis and rheumatoid arthritis) and back or spinal problems are the first and second (respectively) leading causes of disability among adults.[2] As the U.S. adult population ages, the prevalence of these conditions appears to be increasing, resulting in concomitant increases in healthcare resource utilization.[3] Musculoskeletal complaints are some of the most common reasons for doctor visits,[4] and are significant source of lost productivity. According to the American Productivity Audit, pain of musculoskeletal origin (including back-pain, arthritis-related pain, and pain due to other musculoskeletal conditions) were reported by 7.2 percent of the workforce as having occurred over the previous two weeks.[5,6] In the same cross-sectional study, back pain was the second most common cause of missed days at work (after headache). Importantly, pain of musculoskeletal origin was also a leading cause of total lost productive time, a measurement that takes into account the pain-related reduction in productivity while at the workplace. Similar patterns are observed in other industrialized countries.[7]

Clinically, the differential diagnosis of nonspecific musculoskeletal complaints is challenging, and the use of imaging modalities is often required to establish a diagnosis, guide treatment, or monitor disease progression. Magnetic resonance imaging (MRI) is a widely used medical technology, and is often employed as the preferred imaging tool for disorders of the musculoskeletal system (rheumatologic and orthopedic) and neurologic conditions, as it can better delineate soft tissue structures than either plain X-rays or computerized tomography (CT). Although more costly and with a longer procedural time compared with CT, MRI has emerged as the imaging modality of choice for complex musculoskeletal disorders.[8] Unlike radiographs and CT, MRI uses no ionizing radiation to produce images. Rather, this imaging technique employs a strong magnetic field to exploit the magnetic properties of hydrogen atoms in the water and lipid content of the body.

How MRI Images are Generated

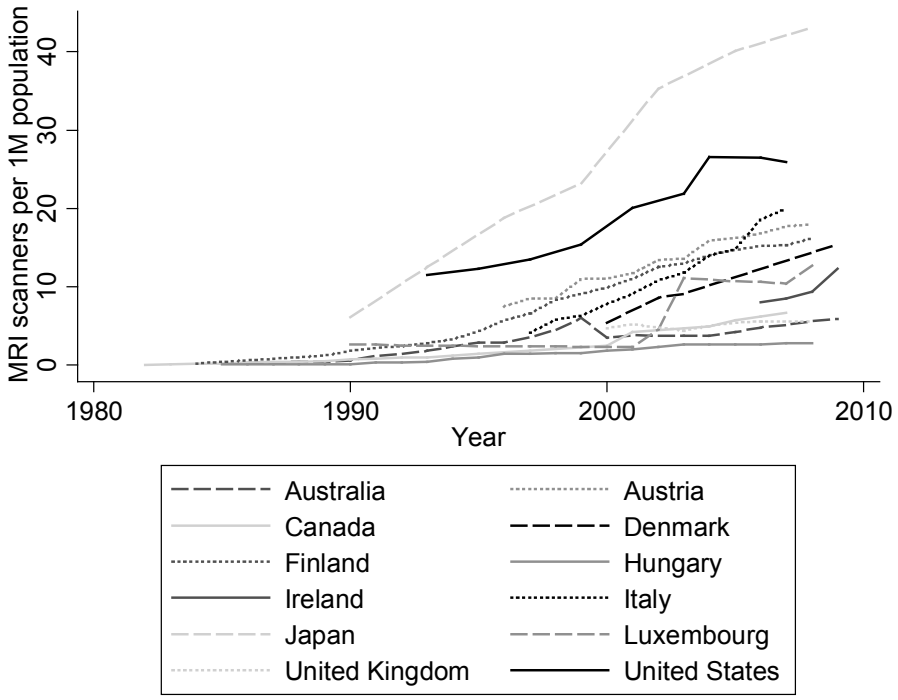
An MRI system consists of five major components: a magnet, a magnetic gradient system, a radio frequency (RF) coil system, a receiver, and a computer system. During MRI scanning, the patient is placed in a strong magnetic field. The strengths of the magnetic field employed in typical MRI machines range from 1.0 to 3.0 Tesla (T). (In comparison, the strength of the Earth's magnetic field is 5×10^{-5} T.) Exposure to the field causes the magnetic moments of hydrogen atom nuclei (protons) in water and lipid molecules in the body to snap into alignment with the magnetic field (much like a compass needle aligns with the Earth's magnetic field). The alignment can be either parallel or anti-parallel to the magnetic field. Parallel alignment is a low-energy state, while the anti-parallel alignment is a high energy state; the distribution of protons among these two energy states is proportional to the strength of the magnetic field (the higher the strength of the magnetic field, the greater the number of protons that acquire parallel alignment). During an MRI scan, an RF transmitter produces an electromagnetic pulse perpendicular to the magnetic field, with a frequency that causes the magnetic moments of the aligned protons to transition to the higher energy state. As the RF transmitter pulses off, the protons return to the low-energy state, radiating the difference in energy between the two states as photons. These photons comprise the signal that the MRI scanner detects (the strength of the magnetic field determines the frequency of the emitted photons).

Additional magnetic fields can be applied to generate gradients of magnetic field strength, in effect varying the composite field strength across the patient's body and thus allowing for spatial localization. In addition, as histologically distinct tissues (as well as healthy and pathologic forms of the same tissue) contain different concentrations of hydrogen atoms, their respective radiofrequency emissions are unique. In combination, these effects, following appropriate transformation of their signals as collected by the MRI scanner, allow for the production of diagnostically useful images.[9-11]

Growth patterns of MRI technology

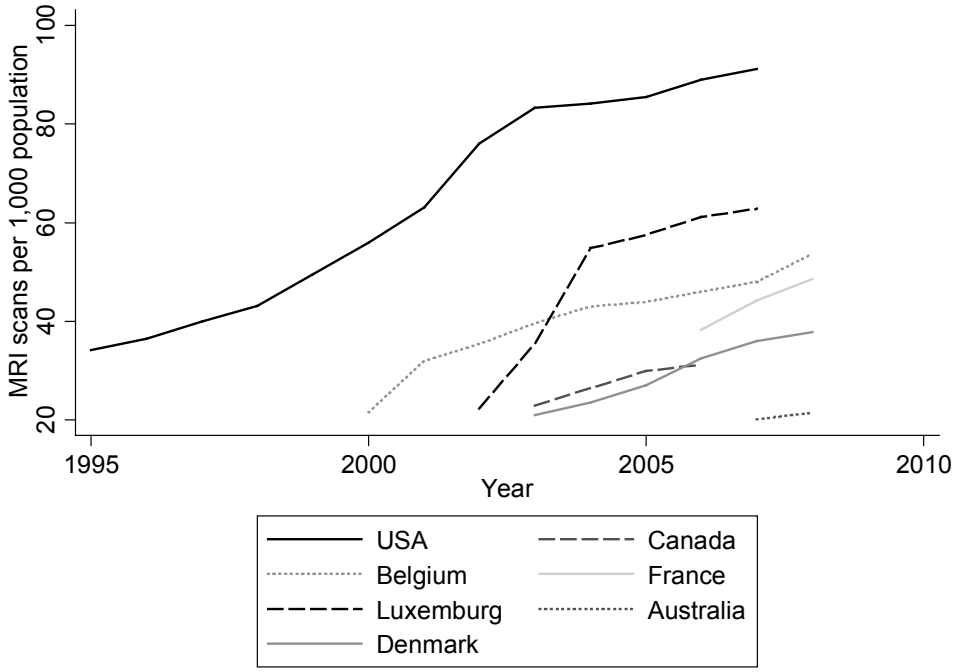
MRI diagnostic technologies represent a rapidly growing field, with continuous increases both in the number of installed scanners (in the U.S. and world-wide), as well as in the number of scans performed. Based on data from the Organization for Economic Co-operation and Development (OECD), the U.S. is currently a world leader both in the availability (number of scanners per million population; second only to Japan) and utilization (number of MRI scans per year per 1,000 population; highest in the world) of MRI scans.[12] **Figure 1** demonstrates the annual growth in the number of MRI units per million population and **Figure 2** the growth in MRI exams performed per 1,000 population for all OECD countries that have reported data for at least two time points (U.S. data are the oldest and most frequently updated). Unfortunately, similar estimates are not available by type of scanner; however, available data can be considered indicative of an increasing trend.

Figure 1: Growth patterns in the availability of MRI scanners in selected OECD countries



MRI scanners per million population in selected OECD countries with data available for at least two separate years. The graph was generated by the authors based on OECD Health Data 2010. OECD, Organization for Economic Co-operation and Development.

Figure 2: Growth patterns in the use of MRI in selected OECD countries



MRI scans per 1000 population in hospitals and ambulatory care (total) for selected OECD countries with data available for at least two separate years. The graph was generated by the authors based on OECD Health Data 2010. OECD, Organization for Economic Co-operation and Development.

Emerging Stress-Loading MRI technologies

Due to the high disease burden, the development of imaging technologies to facilitate the diagnosis and management of musculoskeletal conditions is an active area of research. Often, new technologies are adopted early in their development in the hopes of improving patient outcomes, and, therefore, sometimes have not yet been rigorously evaluated.[13,14] Multiple studies have identified rapid increases in the use of advanced imaging technologies, and for spine imaging in particular.[14-16] As discussed in the previous section, this appears to be a worldwide trend. In the USA, the increase in spine imaging has been accompanied by an increase in spinal surgery, which has also been documented by multiple studies. It is not certain whether increased utilization of advanced imaging and surgical interventions have improved patient outcomes. This may be due to the limited ability of MRI to discriminate between patients who require intervention and those that do not, or the limited therapeutic effect of the available interventions.[13,17] An additional concern stems from the high frequency of positive MRI exams on clinically asymptomatic patients, which has been reported to exceed 50% in some studies.[18-22] These limitations, along with the relatively high cost of obtaining MRI scans, have spurred research to modify existing devices and develop novel technologies to improve diagnostic accuracy with an aim to improving patient-relevant outcomes.

Although all MRI devices in clinical use are based on the same principles (outlined in the "Growth patterns of MRI technology" section), there are many possible configurations of MRI devices, and further mechanical modifications of existing devices are often implemented to obtain imaging under conditions that are believed to generate more clinically relevant findings.

The standard clinical MRI scanner configuration includes a large, cylindrical magnet, in which the patient is placed lying flat, either prone or supine. The patient is required to remain motionless during the imaging period, which can range from a few seconds to several minutes, depending on the exam. The typical closed-bore MRI allows for limited movement and can induce claustrophobia or anxiety in some patients.[23]

Open MRI systems, which allow greater flexibility in patient positioning and may preclude claustrophobia, have been designed to overcome some of the shortcomings of conventional MRI machines. In such systems, the bore is open, typically laterally, and may be of shorter length so that only the body part of interest is placed under the magnet.

Some open MRI systems are oriented vertically, with the magnets placed in such a way as to allow an image to be taken in weight-bearing positions, either upright or while sitting. In addition, such a configuration can allow for flexion and extension views to be obtained. The terms "(multi-) positional MRI" or "upright MRI" have been used to describe MRI systems that are capable of these configurations. It has been suggested that such systems may be useful for conditions that are challenging to diagnose with conventional or open MRI systems, such as cases where the symptoms only manifest in certain positions, or when the joint or body part of interest is stress-loaded or bearing weight. Some of the conditions that have been evaluated with a positional, upright MRI include suspected degenerative spondylolisthesis, suspected spinal stenosis, radicular pain, nonspecific back pain, and extra-spinal joint pain or loss of function.[24]

In response to the limitations of conventional MRI in imaging musculoskeletal conditions, engineers and scientists have attempted to develop new MRI techniques that better mimic actual physiologic conditions, such as weight-bearing, upright, or other physiologic positions, on the theory that images taken under more natural conditions would be better at capturing pathology and therefore result in more accurate diagnoses and better patient outcomes. However, there remains considerable uncertainty as to the optimal imaging approach for most musculoskeletal conditions, and, even when MRI is clearly indicated, the relative benefits and harms of different MRI configurations (weight-bearing or not, open or closed, neutral positioning or flexion/extension) are not clearly established. Specific indications for the use of weight-bearing or stress-loading MRI lack consensus and need further evaluation. A technology assessment conducted on behalf of the State of Washington in 2007 did not reveal adequate data to determine diagnostic validity or accuracy for upright, multi-positional MRI (one specific type of stress-loading MRI technology).[24] Since then, other studies assessing the diagnostic utility of stress-loading MRI have been published.[25-28] The present Technical Brief is designed to evaluate all stress-loading MRI modalities and assess the state of the literature concerning their clinical utility.

Systematic assessment of the available imaging modalities is also necessitated by their substantial cost. A 2005 study of Florida hospitals analyzing financial data from fiscal year 2002 found the mean operating expense and charge per procedure for MRI was $165 and $2,048, respectively.[29] However, costs and charges associated with MRI can vary depending on type of MRI used (e.g., standard vs. open), the anatomic localization of the medical condition (e.g., knee vs. spine) or location of the MRI facility (e.g., city, state, country), and it is unclear how positional MRI technologies may affect the overall healthcare cost-burden.

The objectives of this Technical Brief are to describe the current state of use of stress-loading MRI technologies, enumerate their potential benefits and harms for the diagnosis and management of patients with musculoskeletal disorders for whom this diagnostic test may be considered, and to describe the evidence available to date that supports these applications.

Methods

Guiding Questions

This Technical Brief aims to answer the following guiding questions that were developed in collaboration with the Agency for Healthcare Research and Quality (AHRQ) and input from Key Informants. The terminology used in the guiding questions to describe MRI technologies that were included in this Technical Brief has changed from "positional MRI" to current "stress-loading MRI" due to expansion in scope during literature review for the evidence map. Throughout the report, we use "stress-loading MRI" or "MRI technologies under loading stress" to cover all MRI modalities and applications that allow imaging under stress-loading or weight-bearing conditions, which include positional or upright MRI devices.

Guiding question 1:

What are the operating principles of stress-loading MRI, and what are the potential benefits and harms associated with its use?

a. What are the postulated advantages and disadvantages of stress-loading MRI testing compared to contemporary imaging alternatives?

b. To which populations and for what indications might such testing apply apply?

c. Is stress-loading MRI being proposed as a replacement, triage, or add-on test?

d. What are the potential safety issues and harms of stress-loading MRI technologies?

Guiding question 2:

What is the current availability and cost of stress-loading MRI testing, and what are the special requirements that stress-loading MRI facilities have to fulfill?

a. Who are the current (major) manufacturers of stress-loading MRI machines? What is the current Food and Drug Administration (FDA) clearance status of these stress-loading MRI machines?

b. Approximately how many and of what kind are facilities currently providing stress-loading MRI testing in the U.S.? Do they use the technology mainly for routine work or for research purposes? What additional equipment or technical resources are needed in order to operate stress-loading MRI, compared with standard MRI?

c. What kinds of training, certification, and staffing are required to operate stress-loading MRI or interpret its images?

d. What is the cost of imaging with stress-loading MRI technology as compared to other imaging alternatives?

Guiding question 3:

What published studies have reported on the diagnostic performance, efficacy/effectiveness, or safety of stress-loading MRI? Organize them according to the Fryback and Thornbury scheme,[30] and provide a synthesis of the following information as applicable:

1. Groups of patients enrolled
2. Type of stress-loading MRI used

3. Study design and size
4. Role of the test in patient management
5. Setting where stress-loading MRI testing was performed
6. Outcomes assessed
7. Adverse events, harms and safety issues reported
8. Comparators used (applicable only to comparative studies)
9. Length of follow-up (applicable only to longitudinal studies)

Guiding question 4:

What is the projected uptake of stress-loading MRI technology in the near future? What are the potential areas for future research that are most meaningful given the current state of the evidence and the projected uptake of the technology?

a. Are there indications that stress-loading MRI technologies will be widely used in the near future?

b. What are possible areas of future research?

To address these questions we used a combination of Key Informant interviews, grey literature, and evidence map (i.e., a systematic description of the characteristics of the published literature) to answer the guiding questions.

Identification of Key Informants and Interviews

In order to gain an understanding of the most important questions, patterns of use, and technical details about this new and rapidly evolving technology for which the available information is rapidly evolving, we interviewed a selected number of Key Informants (KIs). When identifying KIs, we aimed for a diverse and representative group that was likely to generate a broad range of perspectives on MRI technology. Eight KIs were chosen, consisting of a director of a public Health Technology Assessment program (public payer), a Medical Director of a private insurance payer, a neuro-radiologist, an orthopedic surgeon, a radiologist whose clinical expertise and research are focused on the use of stress-loading positional MRI, two business managers with research backgrounds in MRI currently employed by two different MRI device manufacturers, and a patient with chronic low-back pain. We did not use a formal method to identify KIs, such as random sampling from a large pool of candidates for reasons of timeliness and feasibility.

At the beginning of the project, two group KI calls were conducted that included all KIs except for the two industry business managers due to conflicts of interest. These two calls helped us to finalize our literature search strategy and guiding questions. To better understand the context and application of the MRI technologies, we then performed one-on-one interviews with each KI (with the exception of the patient), and tailored our interview questions to the expertise and unique perspective of each KI (e.g., public or private insurance payer, clinicians, or MRI device manufacturers). Recordings were made of each interview for the purpose of accurate transcription, and then destroyed following the composition of interview summaries. Interview summaries were sent to each respective KI to confirm their accuracy. We did not obtain further input from the patient representative as we did not have additional patient-specific questions.

Grey Literature Search

We performed an Internet search for keywords to identify relevant MRI devices and their manufacturers. Search terms included, but were not limited to, "positional MRI," "upright MRI," "stand up MRI," "weight bearing MRI," and "axial loading MRI." We also searched MRI manufacturers' Web sites for additional information. These searches yielded background information (primarily in the form of company brochures), and helped us formulate interview questions for KIs. Additionally, we searched the Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) database to identify major MRI manufacturers and to obtain FDA clearance status of relevant MRI devices. To identify potential harms with regards to relevant MRI devices, we queried the FDA Manufacturer and User Facility Device Experience (MAUDE) database using specific device brand names, manufacturers, or the product code "LNH." We also searched for private insurance (e.g., Blue Cross Blue Shield, Aetna, and Anthem) reimbursement policies for positional (weight-bearing) MRI, and ClinicalTrials.gov for relevant ongoing studies using the same terms as our primary Internet search. Key informants provided additional relevant conference abstracts or book chapters, as well.

To assess the world-wide patterns of growth in MRI availability and utilization, we used the latest version of health data from the Organization for Economic Co-Operation and Development (OECD) to obtain estimates of the number of MRI scanners per million population in OECD countries and the number of MRI scans conducted per 1000 population annually.[12]

Building an Evidence Map

An evidence map aims to summarize the extent and distribution of evidence in a broad clinical area. A systematic and replicable, but non-exhaustive, methodology is employed to allow for an efficient appraisal of the available evidence on a topic of interest as well as the identification of major knowledge gaps.[31] Such an approach can be used to direct limited resources to potentially more fruitful areas for systematic review as well as to complement comprehensive systematic reviews on specific key questions. It aims to provide investigators with information about the type and amount of research available, the characteristics of that research, and the topics where a sufficient amount of evidence has accumulated for synthesis.

Individual systematic reviews are labor intensive activities and might require the evaluation of hundreds of articles before identifying a handful of studies meeting the predetermined eligibility criteria. An evidence map that provides a "bird's-eye" view requires only a fraction of the resources needed to produce a full systematic review, allowing users to appreciate the depth, breadth, and characteristics of research in a particular area before investing valuable resources in a full systematic review. Evidence mapping is a cost-effective method to inform users of the current state of research findings that could be used to generate hypotheses, inform ongoing research, and identify research gaps.

Published Literature Search

Our search strategy employed the National Library of Medicine's Medical Subject Headings (MeSH) keyword nomenclature developed for MEDLINE®. We searched for studies that used MRI with weight-bearing or stress-loading protocols in patients with musculoskeletal conditions, published from 1975 to September 2010. We combined MeSH or search terms for MRI, terms relevant to weight-bearing or loading devices and techniques (e.g., dynamic, vertical, upright, stand*, seat*, open, position*, weight bearing, axial$ or load$), and terms relevant to patient populations (e.g., spinal osteophytosis, intervertebral disk displacement, spinal stenosis, spondylolisthesis, thoracic vertebrae, or whiplash injuries). We expanded our search to include

dedicated extremity MRI research by adding the terms "extremity specific" or "dedicated." The details of our search strategies are listed in Appendix A. Our KIs provided additional relevant citations.

The first 300 citations were screened jointly by three reviewers to ensure that screening criteria were well understood and applied uniformly. Thereafter, the same investigators screened non-overlapping sets of the remaining citations. Citations not considered relevant by a single investigator were screened independently by a second investigator to increase the sensitivity of the screening process. We retrieved full-text articles for all citations considered potentially relevant by at least one reviewer. Articles were reviewed independently by three reviewers.

Definitions and Study Eligibility Criteria

Based on preliminary searches and KI input, we identified several configuration or imaging acquisition features that we considered relevant to produce an accurate description of the capabilities and limitations of the diverse MRI imaging systems designed to improve accuracy by imaging joints under physiologic conditions. We focused on three distinct features of these emerging MRI technologies and applications: (1) the ability to choose alternative positioning (black circle), (2) the ability to perform imaging under stress-loading conditions (red circle); and (3) having an open or semi-open configuration (blue circle). Specific devices may incorporate one or more of these features. In the “Findings” section we describe the classification scheme that we developed based on these features to categorize the different MRI devices that we reviewed, and the operational definitions that we employed for this purpose.

Although we originally intended to only consider stress-loading applications of these semi-open systems (small-bore, dedicated extremity MRIs), based on input from our KIs, we expanded our scope to include all studies of such devices, regardless of the use of positioning or stress-loading, due to the technology’s potential for rapid development and diffusion.

We included published studies of any design with primary data on the application of eligible MRI imaging methods in at least 10 patients (or a total of 10 cases and controls for case-control studies) with any musculoskeletal condition except those affecting the temporomandibular joint. Studies exclusively recruiting healthy individuals were excluded. We did not consider narrative reviews, editorials, letters to the editor, or other publications not reporting primary research findings. We did not consider studies published only in abstract form.

Data Extraction

Data were extracted from studies considered relevant in categories A through D. Extracted data included: publication information (first author name, journal, and year of publication), study design, condition studied, study size and setting, patient selection criteria and outcomes assessed. We also recorded data relevant to the specific weight-bearing or loading technique as well as the technical specifications of the respective MRI device.

For studies considered relevant in category E, we extracted only data concerning PICOD (Population, Intervention, Comparator, Outcome, and study Design).

For all comparative studies of two diagnostic tests (one of which must have involved weight-bearing or stress-loading MRI), we extracted additional information on the comparators, outcomes, and key findings.

We used Epidata version 3.1 (EpiData Association, Odense Denmark)[32] to extract information on items of interest in an electronic form (Appendix B). When possible, we gave examples or definitions for items of interests in the data extraction form to minimize the

variation in interpretation. Prior to extraction, we performed a series of calibration exercises to ensure consistency and accuracy of data extraction across investigators.

Data Presentation and Analysis

Our findings are presented in the order of guiding questions. We summarized findings from grey literature searches and KI interviews qualitatively. We generated tables and graphs to summarize information relevant to Guiding Question 3. Based on the data items that we extracted (see Data Extraction section, above), we calculated summary descriptive statistics over the eligible studies, such as proportions (e.g., of studies with a specific characteristic), or medians and interquartile range (e.g., for study sample sizes), as applicable.[33] We graphically presented quantitative data using line-graphs (for growth curves) and weighted scatter plots (to summarize the sample sizes, study designs and specific MRI devices investigated in the studies we reviewed). Statistical analyses and graphs were generated using Stata version 11.1/SE (Stata Corp., College Station, TX).

In an effort to explore if particular findings or research groups are over represented in the literature, we identified studies that had any overlap in author lists by cross-checking author names and institutions across the studies we reviewed. Studies defined as "conducted by the same research teams" were those that had any co-authors in common. Undirected graphs depicting groups of studies that were conducted by the same research team were generated.

Findings

I. Description of stress-loading MRI

This section addresses the operating principles and potential benefits and harms associated with stress-loading MRI. In addition, we discuss the availability and cost of the relevant imaging technologies and the requirements for their use. Findings are based on multiple data sources, including one-to-one discussions with Key Informants (KIs), our review of the literature (including grey literature sources), a review of device manufacturers' and health insurance companies' Web sites, and searches of the Food and Drug Administration's (FDA) Manufacturer and User Facility Device Experience (MAUDE) and Section 510(k) of the Food, Drug, and Cosmetic Act databases.

What are the operating principles of stress-loading MRI, and what are the potential benefits and harms associated with its use?

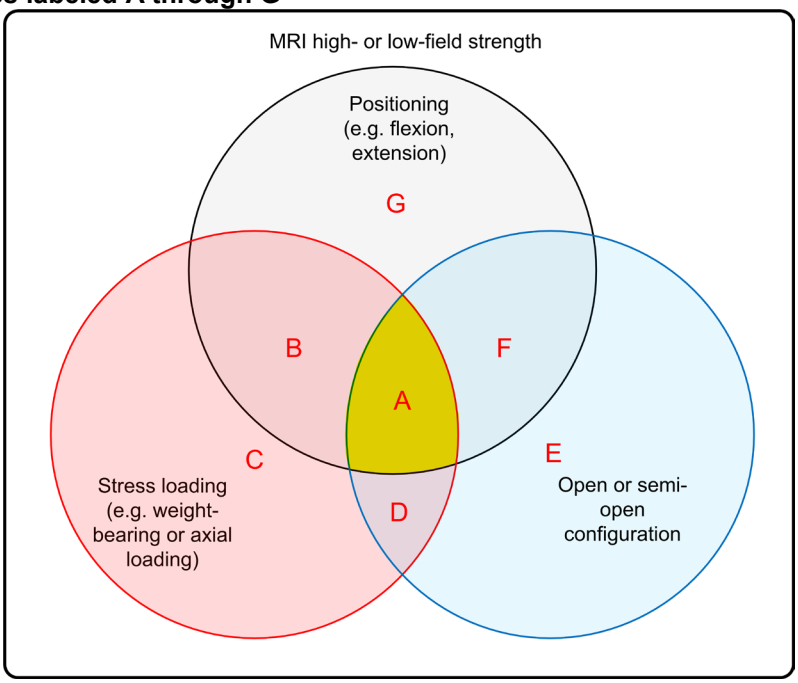
We identified several configuration or imaging acquisition features that we considered relevant to produce an accurate description of the capabilities and limitations of the diverse MRI imaging systems designed to improve accuracy by imaging joints under physiologic conditions. We focused on three distinct features of these emerging MRI technologies and applications (see **Figure 3**): (1) the ability to choose alternative positioning (black circle), (2) the ability to perform imaging under stress-loading conditions (red circle); and (3) having an open or semi-open configuration (blue circle). Specific devices may incorporate one or more of these features. **Figure 3** details the possible combinations of these features among different devices in a Venn diagram. Given the multitude of device configurations in the studies we reviewed, it is likely that the diagram is not comprehensive. However, it is sufficient to categorize the MRI machines that were used in the reviewed studies, and was therefore helpful in organizing studies and comparisons across device categories. Theoretically, all three features could appear in both high- and low-field strength MRI scanners; however, open MRI scanners have typically been of low magnetic field strengths.

More specifically, the operational definitions for these three features are as follows:

1. **Positioning**: Special devices or placement techniques that allow imaging of the patient in postures other than the typical supine position, such as placing the spine or joint in the position of pain or anatomic abnormality through flexion or extension. Positional image acquisition can be either static or dynamic (during movement between different positions), or conducted under weight-bearing or non weight-bearing conditions.
2. **Stress-loading**: Devices that enable imaging in weight-bearing positions or simulate gravity (for example through axial loading, a technique that compresses the body along the joint of interest) in open, semi-open, or conventional scanners.
3. **Open or semi-open configuration**: Any MRI scanner that does not require the patient's body to be placed in a closed (typically cylindrical) bore. With appropriate mechanical modifications, such devices can be used to obtain images under stress-loading or weight-bearing conditions, or positions of pain or anatomic abnormality through flexion or extension.

Seven categories, as defined by the seven distinct regions of the three overlapping feature circles, are labeled A through G. In the present Technical Brief, we include all studies captured by the red circle (stress-loading, areas A to D). Given the diversity of available technologies and the large number of potential modifications to existing systems, it is infeasible to review all studies of open MRI devices or all studies where non-supine patient positioning was attempted in a closed scanner (via restraints or voluntary flexion/ extension, etc.). Semi-open, extremity dedicated scanners are typically not used in conjunction with stress-loading. As discussd in the "Methods" section, although we originally intended to only consider stress-loading applications of these semi-open systems, we expanded our scope to include all studies of such devices, regardless of the use of positioning or stress-loading, due to the technology's potential for rapid development and diffusion. We excluded all studies that used open MRIs without using positioning or stress-loading (area E), and studies that used devices or protocols falling under areas F and G. Devices that fall in the excluded areas (E, F, and G) do not provide information on stress-loading MRI and as such were considered outside the scope of this Technical Brief.

Figure 3. Three features of emerging MRI technologies and applications, covering seven non-overlapping categories labeled A through G



All MRI is based on the same principles of physics to generate images. With regards to stress-loading MRI devices, based on KI input, we compiled a list of features relevant for comparison in evaluating patients with musculoskeletal symptoms (**Table 1**). We discuss these features of emerging MRI technologies as follows.

Table 1. Features for stress-loading MRI

Feature	*Description*
Ability to image the joint under stress	The ability to reproduce physiologic stresses via weight-bearing or simulated weight-bearing may increase the ability to diagnose pathologic conditions that anatomically manifest only under stress (physiologic or supra-physiologic).
Ability to image joints in symptomatic positions (static or dynamic)	The ability to obtain MRI imaging at joint positions physiologically similar to those examined during the clinical examination, such as placing the spine or joint in the position of pain or anatomic abnormality through flexion or extension. Image acquisition during movement may be useful for investigating changes that occur in joints or muscles during active motion.
Field strength	High image quality is a pre-requisite for the use of MRI for clinical decision-making. Magnetic field strength is a major determinant of image quality with higher strength resulting in better image quality.
Speed	The ability to obtain images faster may increase image quality (by reducing motion artifacts) and patient comfort (by reducing acquisition times). Patient comfort is important both for increasing patient satisfaction and because pain during the exam may induce motion artifacts or preclude the completion of the test. KIs and the literature suggested that the particular gradient coil system is an important determinant of imaging speed.[34-36]
Safety	There are no established harms associated with the use of magnetic resonance to obtain medical images *per se*. Standard limitations associated with the use of strong magnetic fields, such as the inability to scan patients with certain metallic implants or pacemakers, as well as the potential for toxicity from paramagnetic contrast agents, apply to all MRI devices. For devices that allow patient movement or devices with rotating parts, appropriate safety precautions are necessary to avoid falls or other causes of mechanical injury.
Bore configuration	Most stress-loading MRI systems have an open configuration. We defined an open MRI system as any MRI scanner that did not require the patient's body to be placed in a closed (typically cylindrical) bore. With appropriate mechanical modifications, such devices can be used to obtain images under stress-loading conditions or positions of pain, or anatomic abnormality through flexion or extension. Open MRI devices also serve the needs of obese and claustrophobic patients requiring less physiologically constraining imaging systems.

KI = Key Informant(s), MRI = magnetic resonance imaging

Imaging under stress-loading and in symptomatic positions (static or dynamic)

The ability to reproduce physiologic stresses via weight-bearing or simulated weight-bearing may increase the ability to diagnose pathologic conditions that anatomically manifest only under stress (physiologic or supra-physiologic). In theory, imaging acquisition in stress-loading conditions can be performed in either high- or low-field strength MRI systems with open, semi-open, or closed configurations. In practice, techniques to obtain stress-loading images are more limited in a closed-bore MRI scanner due to the lack of space. Thus, stress-loading imaging in conventional scanners is usually obtained via the use of axial-loading devices to "simulate" gravity in the supine position. In contrast, there is a diversity of technologies available, as well as a large number of potential modifications that can be made, to existing open or semi-open scanners to obtain stress-loading images.

Open scanners provide extra (patient- and working-) space that allows for the acquisition of images under physiologic stress. Most of these systems are open laterally, and patients are typically placed in a supine (non-weight-bearing) position. We identified one open scanner device, with a tilting design, that can perform scans both in the supine position and in the upright weight-bearing position, and two vertically open (upright) scanners that allow positional (flexion, extension), weight-bearing (upright and sitting) imaging. Vertically open (upright) scanners allow the acquisition of scans in several different positions, including flexion and extension views of the cervical and lumbar spine, the knees, or the shoulders. The ability to

obtain MRI imaging at joint positions physiologically similar to those examined during the clinical examination, such as placing the spine or joint in the position of pain or anatomic abnormality through flexion or extension, may reveal additional abnormalities. For those scanners which allow for dynamic imaging, special software is required.

The primary disadvantage of open, weight-bearing MRIs is their low field strength (existing systems have a maximum field strength of 0.6 T), which is associated with inadequate image quality (also see "*Field strength and image quality"* section).

Another approach used to obtain imaging under stress is through the use of specialized devices that exert force on specific joints while the patient is positioned in a conventional (closed-bore) MRI scanner. Most commonly, commercially available or custom-made devices are used to obtain MRI images of the spine under simulated gravity, but imaging of other joints, such as the knee, is also possible. For spinal imaging, gravity is typically simulated using a compressive system comprised of a vest worn by the patient over the shoulders and upper chest attached to a footplate (via cables or other means) against which the patient's feet are braced. The axial force, in theory, reproduces the effects of upright posture. The force applied is usually 50 percent or less of that produced by the patient's weight. The major disadvantage of axial-loading MRI is that it requires non-loaded imaging to be obtained prior to the loaded scan to rule out certain pathologic conditions that would render the scan unsafe, and the axial-loading equipment may induce or worsen pain or neurological symptoms. Some of the KIs expressed their concern that some patients may not be able to undergo weight-bearing, stress loading, or positional imaging due to neurological symptoms induced by the stress on the imaged joints. Based on this input, we recorded relevant information from all studies we identified through the MEDLINE® literature search that were considered eligible for data extraction (see section II). Some of the studies we reviewed (see Section III, "Evidence Map") reported stress loading-related adverse events.

Positional imaging is not possible in the commercially available axial-loading devices, as they require the patient to maintain an extended position in order for the compressive force to be transferred to the spine. However, we did identify descriptions of weight-bearing imaging where compression was applied while the knees were flexed (in most cases, to obtain images of the knee joints under physiologic conditions).

A KI suggested that imaging of the joints in desired positions may be obtained virtually with any imaging device, provided appropriate mechanical modifications or "ingenuity" in patient placement. In Section II (Evidence Map) of this report, we describe in more detail the specific modifications of existing devices that we encountered in the published literature. Indeed, our literature search identified many studies where commercially available MRI devices were mechanically modified to obtain imaging under stress loading conditions that were considered desirable.

Field strength and image quality

While no professional society defines "low-field strength," the scientific literature indicates that the commonly used cutoff point for low-field strength is below 0.5 T, 0.5 to 1.0 T for mid-field strength, and greater than 1.0 T for high-field strength.[37] We found that, in the studies we reviewed, open MRI scanners typically had field strengths less than 1.0 T and that open, weight-bearing MRI devices had a maximum field strength of 0.6 T.

There was agreement among all KIs and external information sources (medical physics literature, internet Web sites) that for MRI to be effectively used for clinical decision making, the

most important feature is the ability to generate images of sufficiently high quality. All sources agreed that high magnetic field strength is generally the major determinant of image quality. It should be noted that improved image quality may not directly translate to improved clinical or diagnostic utility of the scans.[38] Both clinicians as well as payer representatives expressed concerns about the image quality of all devices with low magnetic field strength and questioned whether these scanners produce images of adequate quality to be used for diagnostic purposes. Within the theoretical constraints of image quality, signal-to-noise ratio, contrast-to-noise ratio, and artifacts are three characteristics that are clearly influenced by field strength. However, which of these parameters has the most relevance to clinical diagnosis remains unanswered.[38] Information from manufacturers' materials stated that since all available scanners have achieved the minimum regulatory technical requirements for image quality, therefore each device's technical specifications should be considered adequate for clinical use. An industry KI stated that the use of specialized receiver coils can compensate for the low field strength limitation in terms of image quality. We found that a variety of receiver coils were used based on the configuration of the MRI device but did not find supporting information on this claim in the literature.

Image acquisition speed

Gradient coils that can generate high gradient strengths and slew rates are required to produce high imaging speeds and improved image quality.[39] The ability to obtain images faster may increase image quality (by reducing motion artifacts) and patient comfort (by reducing acquisition times). Patient comfort may influence patient preferences for the choice of a specific diagnostic modality. Furthermore, position or loading stress-related discomfort may influence the quality of the diagnostic information obtained from an MRI scan as patients may not be able to maintain a stable position during image acquisition (because of pain or other neurological symptoms) and thus create motion artifacts.

Patient safety

Of particular concern for emerging technologies is whether their use is associated with risks to patients. Based on KI interviews and our review of the literature, there appear to be no additional serious safety issues associated with stress-loading MRI *per se* as compared with conventional MRI technologies. However, the standard limitations that apply to MRI in conventional scanners apply to open and stress-loading MRIs as well: patients with metal implants, including those with surgical implants, intracranial aneurysm clips or pacemakers may not be able to be scanned; there is a potential for adverse events from the use of paramagnetic contrast agents; and hearing protection while undergoing MRI is required. Information related to MRI safety issues and guidance on best practices for ensuring patient and provider safety are provided by the American College of Radiology,[40] the International Society for Magnetic Resonance in Medicine (http://www.ismrm.org/), the FDA,[41] and the ECRI Institute.[42]

We searched the FDA MAUDE database for reported adverse events associated with the use of any of the specific stress-loading MRI devices we identified through KI input and our MEDLINE® and grey literature searches. We identified two MAUDE Product Problem Report documents (dated July 2006, October 2007; May 2009) regarding patients' safety associated with the Fonar UPRIGHT® Multi-Position™ MRI device. These two reports discussed the occurrence of skin burns due to electrical contacts on the patient's bed, but indicated that these were cases of operator error and not a defect in the device. The device contains caution labels on the bed and instructions in the user manual indicating that contact with the skin may induce RF burns during scanning and instructs that the contacts be covered by the provided safety covers or

bed cushion.[43,44] Another report discussed a solder joint failure in the motion control computer power supply of the device. That report led to action on the part of the company in order to replace the power supply and its harness with components that had been modified to correct the problem for all devices on the market.[45]

As previously mentioned, axial-loading devices apply a compressive force to the spine and are indicated for those patients in whom a diagnosis may not have yet been established (for example patients with "non-specific spine pain" referred for MRI imaging). It is important that alternative imaging methods are used in these patients prior to capture of the axially-loaded image to rule out fracture or neoplastic disease, as the additional force may cause spinal cord compression.

Bore configuration

The majority of KIs mentioned that a substantial proportion of patients may avoid undergoing an MRI scan due to claustrophobia, and that some obese patients may not be able to undergo conventional MRI. This is indeed a well recognized problem in the literature and appears to affect both children and adults.[23,46-48] Some of the KIs estimated that such fear is present in approximately 5 percent of patients, and that scanning in open configuration scanners (including the vertically open devices we considered in detail) may alleviate such concerns as well as accommodate larger patients. There is evidence that 4 to 30 percent of patients experience anxiety-related reactions while undergoing MRI.[23] Furthermore, due to the global rise in obesity, the need for wider-bore MRI systems may increase. Open MRI configurations, which have a wide gap between their magnets, may allow more patients to undergo necessary imaging exams.

Other open MRI configurations include semi-open, extremity-specific MRI systems (that is, systems that image specific joints such as the knee, elbow, or wrist). Such systems are rarely used in stress-loading applications; in such cases mechanical changes to the scanner configuration allow for applying stress to the joint of interest. Because of this, we discuss these devices in a separate section (see section IV).

KIs also mentioned that a new, more expansive MRI system, called wide-bore MRI, was recently introduced, and serves the needs of obese and claustrophobic patients requiring larger imaging systems.[49-51] Wide-bore MRI is similar in configuration and strength (1.5 or 3T) to that of a conventional MRI but with a larger space in the cylindrical bore. However, we did not find research employing wide-bore MRI devises in stress-loading applications.

We summarize the aforementioned theoretical advantages and disadvantages of competing MRI technologies in **Table 2**.

Table 2. Theoretical advantages and disadvantages of conventional and emerging MRI technologies

	Theoretical advantages	*Theoretical disadvantages*
Conventional closed-bore MRI	Higher magnetic field strength compared with most other configurations may be associated with better image quality. Higher speed due to improved gradient systems may reduce scanning time and improve image quality. Most radiologists and technologists are familiar with such systems.	Imaging is obtained predominantly in the supine or prone position; findings that are only revealed under stress or in flexion/extension may be missed. Most scanners have narrow bores that may induce claustrophobia. Imaging of obese patients may not be possible due to limitations in bore diameter.

Weight-bearing MRI	Imaging in weight-bearing positions (standing or sitting) may reproduce the physiologic conditions under which symptoms develop or are most prominent, possibly improving the diagnostic yield. Imaging in flexion or extension is also possible in upright scanners and may reproduce the physiologic conditions under which symptoms develop or are most prominent.	Magnetic field strength is typically much lower compared with conventional scanners, leading to reduced image quality.
Axial- loading in open or closed-bore conventional scanners	Technologies that simulate weight-bearing may provide advantages similar to those of weight-bearing imaging. Most axial-loading devices can be used in conventional scanners with high-field strengths (as well as open scanners).	Most commercial devices allow imaging limited to only the lumbar spine and only in the extended position. Requires non-loaded imaging to be obtained prior to the loaded scan to rule out pathologic conditions. Axial-loading equipment may induce or worsen pain or neurological symptoms. When performed in closed-bore scanners, has the same limitations as conventional devices, such as an inability to accommodate obese or claustrophobic patients. May not accurately replicate the effects of physiologic weight-bearing positions.
Semi-open (small-bore) MRI	Improved patient comfort and avoidance of anxiety-related reactions. Reduced noise during imaging. In newer devices, high strength magnetic fields result in improved image quality, possibly comparable to larger (whole body) MRI scanners.	Can only image the extremities (and in most cases not the shoulders or hip). Most systems have low-field strengths that may result in lower image quality.

Are stress-loading MRIs used for routine clinical assessments or for research purposes?

The general consensus of the clinical KIs was that stress-loaded MRIs are not commonly used for the diagnosis or management of musculoskeletal disorders, and should still be considered experimental. In agreement with this, most insurers' policies that we reviewed consider stress-loading MRI as investigational and not medically necessary for any indication. Many insurers' policies were based on literature reviews and referenced the systematic Health Technology assessment of positional MRI conducted on behalf of the State of Washington.[24] Frequently, insurers reported conducting regularly updated literature searches to support their policy decisions, and, in the vast majority of cases, the evidence was considered as insufficient to demonstrate clinical utility beyond that of conventional MRI. We identified only one insurer that considered "open MRI units of any configuration, including MRI units that allow imaging when standing (Stand-Up MRI) or when sitting, to be an acceptable alternative to standard closed MRI units". However, this insurer also considered "repeat MRI scans in different positions (such as flexion, extension, rotation and lateral bending) and when done with and without weight-bearing to be experimental and investigational."[52] These policies probably reflect that stress loading MRI technologies are relatively at an early stage of the diagnostic test development process (see sections III. Evidence Map and "Next steps")

To which populations and for what indications might stress-loading MRI apply? Is stress-loading MRI being proposed as a replacement, triage, or add-on test?

There was a substantial divergence of opinion between the clinical experts (orthopedic surgeon and radiologist) and our industry sources regarding the clinical utility of stress-loading MRI. In general, Clinical KIs indicated that there was not enough evidence to answer these questions, and that, in their (clinician and payer KIs') experience, whether these devices were used for triage, substitutions, or add-ons for conventional MRI varied greatly in clinical practice. In contrast, industry input suggested that the devices can be used as replacement tests for conventional MRI for imaging the cervical and lumbar spine.

With axial-loading devices, both conventional (unloaded) and stressed (axially loaded) images must be obtained. As noted earlier, conventional imaging must be conducted prior to applying simulated loads to rule out pathologic conditions that would render the scan unsafe. As such, applications of axially-loaded tests are *de facto* "add-on tests," and studies of axial-loading devices tend to be comparative in design (i.e., comparing preloaded MRI with loaded MRI images). The FDA 510(k) document of the axially-loaded MRI devices states, "Ideally, the examination is performed directly after the basic unloaded investigation and thus decided by the radiologist."

Who are the current (major) manufacturers of stress-loading MRI devices? What is the current FDA clearance status of these MRI devices?

We identified the following three manufacturers of weight-bearing MRI devices (listed chronologically by FDA clearance date): 1) Signa SP/2 (General Electric Medical Systems) [510(k) # K893509], 2) Indomitable MRI Scanner (Fonar Corporation) [510(k) # K002490] (later brand name Upright™ MRI); and 3) Esaote S.p.A G-SCAN [510(k) # K042236]

We identified the following two commercially available axial-loading devices, commonly referred to as medical compression devices (listed chronologically by FDA clearance date): 1) DynaWell L-spine compression device [510(k) # K992120]; and 2) Choy Compression Frame (Choy Medical Technologies) [510(k) # K070968].

All five devices were cleared by the FDA on a "substantially equivalent" basis.

Approximately how many and of what kind are facilities currently providing stress-loading MRI testing in the U.S.?

According to the KI affiliated with Fonar, there are about 70 American College of Radiology accredited MRI providers equipped with the Upright™ MRI, and approximately 140 Upright™ MRI scanners are currently installed worldwide (mostly in the U.S.). This was in accordance to a Fonar press release from late 2009.[53] We could not obtain estimates for the number of Signa SP/2 devices available.

The Signa device was marketed as an interventional and intraoperative magnetic MRI (with a 56-cm-wide vertical gap, allowing access to the patient and permitting the execution of MRI-guided interventional procedures). Many investigators had modified this device and used it to provide weight-bearing MRI testing. Our KI affiliated with GE Healthcare indicated that, to the best of his knowledge, the Signa SP/2 was still on the market. We, however, cannot verify this information.

What kinds of training, certification, and staffing are required to operate stress-loading MRI or to interpret its images?

There is no specific mandatory accreditation for the operation of any of the stress-loading MRI devices, including, open, upright, and extremity MRIs. Specialized personnel would have to become proficient with the operational software and in the patient positioning platforms. One KI affiliated with a weight-bearing MRI manufacturer indicated that the manufacturer provided training for positioning patients and scanning protocols with the installation of a new scanner.

In most cases, a board certified radiologist is required to interpret MRI images. KIs indicated that images generated by low field strength systems may require more "experienced" readers compared with those from high field strength systems (e.g., 1.5T systems, which are currently the norm) It should be noted that reader experience is difficult to define and measure and that the interaction of "experience" with specific devices would be hard to substantiate.

What additional equipment or technical resources are needed in order to operate stress-loading MRI compared with standard MRI?

A KI affiliated with a weight-bearing MRI manufacturer indicated that weight-bearing MRI systems have similar installation ("sitting") requirements as conventional MRI devices.

Commercially available axial-loading devices appear to have no additional requirements compared with the use of the same MRI devices in unloaded conditions; based on information available on the Web site of the manufacturers of the DynaWell axial compression system, the device can be used in "all known CT and MRI scanners on the market."[54]

Dedicated extremity MRI devices appear to have significantly reduced technical requirements for installation and operation. Specifically, they have a smaller size (allowing them to be installed in relatively small spaces), do not require shielding of the room in which they are installed (because they include a small Faraday cage that provides shielding), and do not require a special power supply or air conditioning.

What is the cost of imaging with stress-loading MRI as compared with other imaging alternatives?

We attempted to collect information on the costs of imaging with different types of MRI devices, particularly with extremity and upright MRIs as compared to conventional MRIs. KIs generally agreed that overall costs were lower with open, upright, and extremity-specific MRI scanners compared with conventional MRI devices, as they have lower purchase and installation costs (e.g., costs for magnetic field shielding). KIs also added that, while healthcare facilities may be able to reduce costs by using this group of devices, the cost savings are typically not reflected in patients' billing charges. We did not identify additional information on the cost of obtaining specific MRI devices.

Perusal of insurance company Web sites indicated that most policies assign two billing codes for MRI imaging, one for images generated by devices with low magnetic field strengths (< 1.0 T), and the other for images generated by devices with high magnetic field strength (> 1.0 T). We could find no separate billing code that differentiated between weight-bearing and non-weight-bearing imaging, or imaging obtained in different positions (e.g., flexion/extension). Based on input from our KIs, insurance companies typically reimburse patients for one image per visit. All stakeholders confirmed this assertion. None of our stakeholders had knowledge of

the exact cost of an MRI image by billing code, or what the difference in cost between the two billing codes might be. A 2007 Technology Assessment of upright MRI commissioned by the Washington State Health Care Authority did not report an independent cost analysis of this imaging modality; however, based on information obtained from manufacturers, the authors did report an estimated cost of $1,450 for a single image from an upright MRI, and costs for obtaining additional views ranging from $350 to $1200.[24]

Two additional issues concerning MRI costs emerged during our interviews with stakeholders: (1) the potential for technically inadequate MRI images requiring a second exam with a conventional MRI, and (2) the potential for emerging MRI devices to generate multiple images in a single exam, leading to multiple billing and increased costs. The first issue concerned the marketing of emerging MRI devices with lower strength magnets by private clinics directly to consumers. Clinician KIs recounted examples where patients had decided to obtain upright MRI scans (with the implication that it was without their doctor's recommendation) only to receive poor quality images that were insufficient for clinical decision-making (particularly regarding surgical planning). These patients were often required to obtain additional MRI imaging in conventional scanners. The KIs noted that, in such cases, patients may be required to pay out-of-pocket for the second MRI examination.

The second issue, put forth by the public payer KI, was that, as of the time of the interview, no specific billing code was available for the upright/positional MRI and that, due to the ability of the Fonar Corporation's positional MRI to generate multiple "views" during one imaging session, each "view" was billed separately. The KI indicated that, on average, this has resulted in the number of scans being billed per patient visit at the positional MRI facilities in Washington State to be 2.5 times higher compared with that of conventional MRI facilities.

In summary, the emergence of new technologies and the diversification of MRI devices further magnify the problem of cost and raise a new set of concerns regarding the relative quality and cost effectiveness of imaging using different types of devices, as well as who should bear the increased cost-burden.

II. Evidence Map

As described in the Description section, we focused on three features of emerging MRI technologies and applications to define seven non-overlapping categories (**Figure 3**) of MRI devices or techniques. Using this classification scheme, we defined stress-loading MRI technologies of interest for the evidence map (**Table 3**).

Table 3. Definitions and examples for the MRI device or technique groups considered

Category (area in Figure 1)	Definition	Examples[a]
A (center intersection)	Open, positional, and weight-bearing MRI	Upright® MRI (Fonar), [modified] Signa SP (GE), and G-scan (Esaote)
B	Use of specialized devices or placement methods to obtain MRI imaging under weight-bearing conditions in a closed MRI scanner	Weight-bearing and dynamic (e.g., flexion, extension, or rotation) postures in a conventional closed-MRI scanner
C	Use of specialized devices to "simulate" gravity (i.e., axial loading) in conventional MRI.	The DynaWell® L-spine compression device or the Choy compression frame in a conventional closed-MRI scanner in the typical supine position, or weight-bearing (static) postures in a conventional closed-MRI scanner.
D	Use of specialized devices to "simulate" gravity (i.e., axial loading) in open MRI scanners while the patient is in the typical supine position.	The DynaWell® L-spine compression device or the Choy compression frame in an open MRI scanner, or weight-bearing (static) postures in a conventional closed-MRI scanner.
E (partially, expanded scope)[b]	"Semi-open" MRI scanners without weight-bearing or loading.	MSK Extreme (GE, 1.0 or 1.5 T), Artoscan Extremities MRI (0.2 T)

[a] Please see Appendix C for more detailed descriptions of the commercially available devices listed in this table.
[b] Semi-open, extremity dedicated scanners are typically not used in conjunction with stress-loading. We expanded our scope to include all studies of such devices, regardless of the use of positioning or stress-loading, due to the technology's potential for rapid development and diffusion. These studies are not included in the evidence map and are summarized in a separate section (see IV. Dedicated extremity MRI devices)

a. Evidence Map of All Eligible Studies

Our Medline search yielded 5,984 citations, 326 of which were retrieved in full text. Full-text articles were screened based on study eligibility criteria, yielding 55 publications that used MRI with weight-bearing or stress-loading protocols in patients with musculoskeletal conditions.[25-28,55-105] Of these, one paper reported data from two separate studies.[26] Thus a total of 56 studies were included in our evidence map.

We categorized these 56 studies according to our definitions for emerging MRI technologies under weight-bearing or loading stress as specified in **Figure 3** (areas A to D). Based on these definitions, 35 studies fell under category A (i.e., open, positional, and weight-bearing MRI),[25-28,55-83,100,105] two studies fell under category B (i.e., use of specialized devices to obtain MRI imaging under weight-bearing conditions in a closed MRI scanner),[85,102] and 19 studies fell under category C (i.e., use of specialized devices to "simulate" gravity [i.e., axial loading] in a conventional MRI).[26,84,86-99,101,103,104]

It should be noted that multiple studies originated from the same research centers and it is often not possible to ascertain whether patients or controls were shared between studies conducted by the same investigators. Patient population overlap creates the impression that more studies are available on a given clinical question than may be the case. In an effort to explore

whether particular findings or research groups were over-represented in the literature, we generated a graph to depict groups of studies that had overlapping author lists (Appendix D). One team that has published 6 manuscripts, corresponding to approximately 10% of all studies we considered eligible, includes as co-authors Drs. Danielson and Willen, inventors of the DynaWell axial loading device (Drs. Danielson and Willen are identified as inventors of the device on the company's website [54]). We caution that the graph in Appendix D does not necessarily imply overlap of patient populations, and should rather be regarded as a method to identify the most active research groups in the field.

Below, we present a summary of all 56 studies followed by a more detailed presentation of the characteristics of studies falling under each device category. Although these analyses include the comparative studies we identified (i.e., studies that applied at least two diagnostic tests on the same patient population and investigated clinical outcomes), these studies are also further discussed in section II.b.

A detailed summary of study characteristics is presented in **Table 4**.

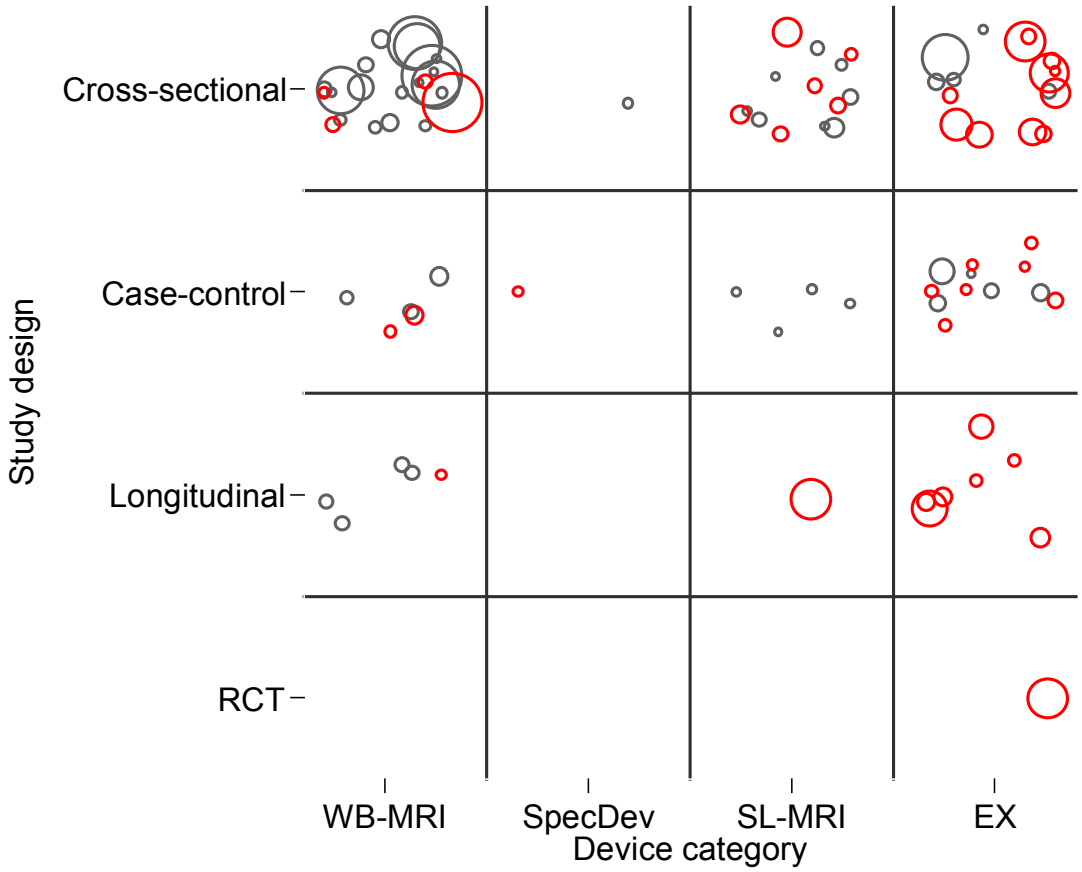
Characteristics of eligible studies

Eligible studies were published between 1993 and 2010. In general, studies were small; on average they included 73 cases (median = 26; IQR = 17, 42) and 18 controls (median = 13; IQR = 12, 20; for case-control studies only). The majority of studies were cross-sectional (39 studies), or had case-control designs (11 studies). Only six longitudinal studies were included. The most commonly imaged body regions were the lumbar spine (32 studies) and knee (13 studies). The vast majority of studies did not systematically identify cases or controls (convenience sampling). Clinical or patient-relevant outcomes were assessed infrequently (5 studies). Most studies (28 studies, 50%) focused on the feasibility (defined as agreement in anatomic measurements between different imaging modalities as the outcome of interest) of imaging under weight-bearing or stress-loading conditions. Only 12 studies assessed diagnostic accuracy (we defined this broadly as a diagnosis of abnormality in symptomatic patients made based on weight-bearing or stress-loading MRI). No randomized controlled study or non-randomized comparative study of testing versus no testing was identified.

Most studies were conducted outside the U.S. (see also Appendix D). Funding information was often not reported; among studies that reported relevant information, frequently, no funding source was identified ("no funding was received"). Given the lack of relevant information in a large number of studies and the potential influence of different editorial policies on reporting financial support, it is difficult to interpret this finding.

Fifteen studies (27%) were comparative studies of two diagnostic tests. **Table 6** in section II.b. presents the characteristics of these studies and the outcomes they assessed. **Figure 4** presents the eligible studies stratified by study design and weight-bearing or stress-loading method used. Only 10 studies reported harms or adverse events associated with weight-bearing MRI testing.

Figure 4: Study designs and comparisons reported in eligible studies. For comparison, we have also included data from studies of dedicated extremity MRI (see section IV).



Studies are represented by circles of a size proportional to the number of enrolled patients. Studies are classified into separate boxes based on the device investigated and their study design. Placement of studies within each box is random. Studies depicted in red were comparative, i.e., they directly compared different diagnostic methods and had clinical outcomes. Device categories (please also refer to Figure 3): WB-MRI indicates weight-bearing MRI (category A); SpecDev indicates specialized devices to obtain MRI imaging under weight bearing conditions in a closed MRI scanner (category B); SL-MRI indicates stress-loading MRI in a conventional MRI scanner (category C); EX indicates dedicated extremity MRI. For this analysis, the studies by Nikken 2005[106] and Oei 2005[107], which reported on predictive models built using an RCT dataset (see Nikken 2005[108]), were considered as "longitudinal studies."

Table 4. Studies of weight-bearing or stress-loading MRI reporting on adverse events. Studies are included here provided they reported on the incidence of adverse events (including reporting of "no adverse event")

Author, year	Patients enrolled	Imaging method	Adverse event reported
Danielson, 1998	34	Axial loading	Twenty (59%) patients had pain. Of those 7 (21%) had LBP and 10 (29%) had leg pain. Two (6%) patients had LBP both in PRP and AL, one (3%) of whom had leg pain in AL. One (3%) patient had no LBP but had sensory disturbance.
Weishaupt, 2000	36	Weight-bearing MRI	MRI could not be completed due to severe pain in 6 (17%) patients
Hebert, 2003	41	Weight-bearing MRI	None.
Kimura, 2005	12	Axial loading	One (6%) control did not undergo imaging because AL led to radicular pain
Karadimas, 2006	30	Weight-bearing MRI	Attempted to obtain upright MRI but patients had difficulty standing still. All imaging was obtained in a neutral sitting position
Madsen, 2008	16	Axial loading	Two (13%) patients did not complete the last scan due to discomfort.
Wang, 2008	27	Axial loading	Two (7%) patients did not complete the loaded test because of pain induced by loading.
Morishita, 2008	NR	Weight-bearing MRI	"Some" patients needed pain control prior to MRI because of severe discogenic or radicular pain in upright, weight-bearing positions. The position was difficult to maintain for more than 30 minutes.
Huang, 2009	32	Axial loading	Three (9%) patients could not complete the axially loaded exam due to pain (n=1) or sciatica and numbness (n=2). In one (3%) patient, sciatica and numbness were persistent after axial loading and electrophysiologic study revealed lumbosacral radiculopathy.
Ahn, 2009	51	Axial loading	10% of patients did not complete the axial loading imaging due to back pain or sciatic pain.

AL, axial loading; LBP, low back pain; NR, not reported; PRP, psoas-relaxed position.

Provided below is a qualitative summary of the findings regarding the populations studied, outcomes assessed, and reporting completeness in the eligible studies, arranged by categories of MRI device.

Open, positional, and weight-bearing MRI

Thirty five studies were classified as "open, positional, and weight bearing MRI" systems (category A). In general, studies were small; on average they included 95 cases (median = 28; IQR = 20, 45) and 20 controls (median = 13; IQR = 12, 20; for case-control studies only). The majority of studies were cross-sectional (24 studies), or had case-control designs (6 studies). Only five longitudinal studies were identified. The most commonly imaged body regions were the lumbar spine (19 studies) and knee (6 studies). It was infrequent that clinical outcomes were assessed; the majority of studies focused on the feasibility of imaging under weight-bearing or stress-loading conditions (19 studies).

MRI imaging under weight-bearing conditions in a closed MRI scanner

Only two studies (both with the same first author) assessed MRI imaging under weight-bearing conditions in a closed MRI scanner (category B).[85,102] The investigators used a positioning device with a section cut out to permit uninhibited movement of the patellofemoral

joints in a conventional MRI (prone position) for capturing kinematic images under loaded or unloaded conditions.

The first study was conducted in 1993 among 19 patients with a clinical diagnosis of abnormal patellar alignment and tracking. The authors reported that the positioning device "will soon be commercially available for use with Signa MR imaging systems (GE Medical Systems) and can be easily modified for use with other MRI systems." The main findings of this study are described later in this report in section II.b.

Subsequently, the same positioning device and kinematic MRI protocol were used to evaluate the effect of applying a stabilizing brace to 15 patients who had hallmark signs and symptoms of patellar malalignment. This study was published in 2000 and reported that the positioning device had become commercially available.

"Simulated" gravity in conventional MRI scanners

Nineteen studies used an axial-loading device to "simulate" gravity in conventional MRI scanners (category C). In general, studies were small; on average they included 40 cases (median = 24; IQR = 12, 34) and 20 controls (median = 14; IQR = 13, 18; for case-control studies only). The majority of studies were crossectional (14 studies), or had case-control designs (4 studies). The most commonly imaged body regions were the lumbar spine (13 studies) and the knee (5 studies). It was infrequent that clinical outcomes were assessed; most studies focused on the feasibility of imaging under weight-bearing or stress-loading conditions (9 studies).

Table 5. Summaries of descriptive characteristics of the studies considered eligible. As only two studies assessed MRI imaging under weight-bearing conditions in a closed MRI scanner (category B), we did not include a separate column for this group of studies[a]

Study characteristic		All studies N=56	Open, positional, and weight-bearing MRI N=35	MRI imaging under weight-bearing conditions in a closed MRI scanner N = 19
Enrolled patients	Median number of patients[IQR] (min-max)	26 [17-42] (8-553)	29 [20-45] (10-553)	24 [12-34] (8-250)
	Median number of controls [IQR] Only for case-control studies	13 [12-20] (5-50)	13 [12-20] (10-50)	14 [13-18] (10-43)
Sex	% male patients (median, IQR)	50 [40-63]	53 [43-67]	45 [19-53]
	% male controls [median, IQR] (only applicable to case-control studies)	53 [20-65]	58 [40-70]	NA (only 2 studies provided information)
Mean or median age (only among studies that reported relevant information)	Median of mean/median age of patients [IQR]	42.7 [31.6-50] y	41.7 [32-44.5] y	48 [27.1-52]
	Patients >= 65 years of age	3 (5)	2 (6)	1 (6)
	Median of mean/median age of controls [IQR]	29.9y [28y-34.4y]	32.1y [26.8y-34.4y]	28.4y [28.1y-36.3y]
	Controls >= 65 years of age (only applicable to case-control studies)	0	0	0

Study characteristic		All studies N=56	Open, positional, and weight-bearing MRI N=35	MRI imaging under weight-bearing conditions in a closed MRI scanner N = 19
Symptomatic patients enrolled	Exclusively	43 (80)	30 (86)	11 (69)
	Asymptomatic	7 (13)	2 (6)	4 (25)
	Mixed	4 (7)	3 (9)	1 (6)
Country	USA	18 (32)	11 (31)	5 (26)
	Non-USA	35 (63)	21 (60)	14 (74)
	Mixed	3 (5)	3 (9)	0
Funding source reported	Yes	35 (63)	19 (56)	14 (74)
	No	21 (37)	16 (46)	5 (26)
Industry funding (only among studies that reported funding sources)	Yes	11 (31)	3 (16)	6 (43)
	No[b]	24 (69)	16 (84)	8 (57)
Study design	Cross-sectional	39 (70)	24 (69)	14 (74)
	Case-control	11 (20)	6 (17)	4 (21)
	Crossover	0	0	0
	Longitudinal	6 (11)	5 (14)	1 (5)
	NRCS	0	0	0
Follow-up timing	Prospective	1 (2)	0	0
	Retrospective	5 (9)	5 (15)	1 (5)
	Not applicable (case-control or cross-sectional studies)	47 (84)	29 (83)	16 (84)
	Unclear	3 (5)	1 (3)	2 (11)
Number of participating centers	Multicenter	4 (7)	3 (9)	1 (5)
	Single center	39 (70)	22 (63)	15 (79)
	Not clear/ Not reported	13 (23)	10 (29)	3 (16)
Study setting	Feasibility	28 (50)	19 (54)	9 (47)
	Screening	1 (2)	0	1 (5)
	Diagnosis	12 (21)	6 (17)	6 (32)
	Prognosis/prediction	1 (2)	0	0
	Patient management/ treatment planning	2 (4)	1 (3)	1 (5)
	Monitoring	2 (4)	2 (6)	0
	Multiple/ unclear	10 (18)	7 (20)	2 (11)
Exam location	Cervical spine	2 (4)	2 (6)	0
	Lumbar spine	32 (57)	19 (54)	17 (100)
	Knee	13 (23)	6 (17)	0
	Upper extremities	2 (4)	2 (6)	0
	Lower extremities (other than knee)	2 (4)	1 (3)	0
	Multiple regions	5 (9)	4 (11)	0
Reported adverse events	Yes	10 (18)	5 (14)	5 (31)
	No	46 (82)	30 (86)	14 (74)
Outcomes assessed	Diagnostic accuracy	14 (25)	9 (26)	4 (21)
	Impact on diagnostic thinking	3 (5)	2 (6)	1 (5)

Study characteristic		All studies N=56	Open, positional, and weight-bearing MRI N=35	MRI imaging under weight-bearing conditions in a closed MRI scanner N = 19
	Impact on treatment decisions	1 (2)	0	1 (5)
	Impact on patients functional and clinical outcomes	1 (2)	0	0
	Anatomic measurements/rater agreement/other/mixed	37 (66)	24 (69)	13 (68)

IQR, inter-quartile range; NA, not applicable; NRCS, nonrandomized comparative studies; y, years.
[a] Numbers represent studies (% total studies in category), unless otherwise stated. Percentages have been rounded to the nearest integer and may not sum to 100. Studies belonging in category B were too few to be tabulated separately.
[b] The majority of these studies reported that "no funding was received."

The evidence map shows that, in general, studies of stress-loading MRI are small in sample size and employ study designs of relatively low internal validity. Outcomes are also not immediately clinically applicable, with most studies (65%) focusing on the feasibility of imaging under weight-bearing or stress-loading conditions (for example, agreement in anatomic measurements between different imaging modalities was a common outcome). Very few studies (12%) reported on clinically relevant outcomes.

Ongoing studies in ClinicalTrials.gov

Our search for ongoing clinical trials utilizing weight-bearing or stress-loading MRI identified three ongoing studies: NCT00665548, NCT00706459, and NCT00887744.

Briefly, the first study is a collaborative case-control study currently being conducted by the University of California, San Francisco and Pfizer. The study aims to enroll a total of 33 female subjects older than 40 years of age. Cases will be osteoarthritis patients, while controls will be healthy volunteers. The goal of the study is to compare two modalities (X-ray and MRI) for imaging the knee joint under both weight-bearing and non-weight-bearing conditions. A 3.0T scanner will be used to obtain all MRI scans.

The second study is also being conducted by investigators at the University of California, San Francisco, with funding from the National Institutes of Health. Also a case-control study, the total enrollment target is 105 subjects of both sexes, aged between 25 and 60 years. Cases will be patients with lumbar back pain scheduled for back surgery, patients with degenerative disease without classic discogenic back pain, and patients who have undergone discectomy for herniated discs. Controls will be age-matched volunteers without back pain. All study subjects will undergo lumbar spine imaging using a 3.0T MRI scanner (including axially loaded scanning) to assess whether this method can be used to identify painful degenerated discs in patients with chronic back pain. The investigators indicated that this study would serve as a pilot for a larger trial.

The third study is an interventional, multicenter, single arm, post-marketing, clinical followup study. The primary purpose of the study is to measure the change in severity of symptoms and ability to function in every day activities in patients suffering from degenerative lumbar spinal stenosis after treatment using the AperiusTM PercLID™ device. The expected enrollment for this study is 163 subjects of both sexes over the age of 21. A secondary outcome

of the study involves positional MRI scanning to measure the changes in spinal canal, foramina, and disc, immediately post-operatively and after 12 months of followup.

Enrollment for all three studies was completed in 2009; however, their results are not yet available on the ClinicalTrial.gov Web site and we could not identify any corresponding publications in MEDLINE®. Thus we are not certain the motivation or purpose of including the stress-loading MRI in these studies. It should be noted that these three studies are small in sample size and conducted in three different patient populations, so it is unlikely that their results, once published, would change the conclusion of our evidence map.

b. Comparative studies that reported clinical diagnostic or patient outcomes

Of the 56 eligible studies, 15 compared two diagnostic tests.[27,57,69,70,72,81,83-86,88,95,97,103,104] Of these, four compared open, positional, weight-bearing MRI in lumbar spine imaging, using four different comparative tests [27,69,81,83]; seven compared axially-loaded images of the lumbar spine with preloaded images in the same conventional MRI scanner;[84,86,88,95,97,103,104] and four compared weight-bearing or stress-loading MRI with MRI without loading for diagnosis of extremity abnormalities.[70,72,85] None of these studies used a "gold standard" (e.g., surgical findings) for their diagnoses, only four studies reported patient outcomes (pain, anxiety, testing preference, or physical function),[81,86,88,97] and only one study reported changes in patient management based on additional information gained from axial loading MRI.[103] (Appendix F)

Of the four studies of lumbar spine imaging comparing open, positional, weight-bearing MRI, two small studies (enrolling ≤50 patients) reported that open, positional, weight-bearing MRI contributed additional information to diagnoses, based on comparisons with the studies' conventional (non weight-bearing) MRI findings.[69,81,83] Another study assessed patient preferences and anxiety during open, positional MRI and during lumbar myelography in 30 subjects, and reported that more patients were anxious during myolography than during MRI and that more patients preferred MRI than myelography.[81]

The fourth study compared diagnosis of lumbar abnormalities based on upright MRI in the extension or flexion positions to diagnosis based on upright MRI in the neutral position. [27] Subjects were 533 patients with different grades of disc herniation. All positions (extension, flexion, or neutral) were performed while patients were standing (thus all were weight-bearing positions). A range of "missed diagnoses" by upright MRI in the neutral position as compared to upright MRI in the extension or flexion positions was reported. It should be noted that the reported "missed diagnoses" assumed upright MRI was the reference standard and no functional outcomes were reported.

All seven studies of lumbar spine imaging comparing axially-loaded images with preloaded images in the same conventional MRI scanner reported favorable findings for axially-loaded MRI in terms of additional diagnoses or impact on diagnostic thinking.[84,86,88,95,97,103,104] One study also reported good surgical outcomes among patients whose hidden stenosis was disclosed by axial-loading MRI. [97] However, it should be noted that five of the seven studies came from the same group of investigators in Sweden, and that there were obvious overlaps in patients reported in the five studies.[86,95,97,103,104] (see also Appendix D). At least two of the investigators in this group are the co-inventors of an axial-loading device, DynaWell L-Spine, which is currently commercially available. All seven studies suffered from potential selection and/or verification biases.

Two of the four studies comparing weight-bearing MRI with MRI in the supine position (not weight-bearing) found that the two techniques were comparable and that weight-bearing MRI did not provide additional information for the diagnosis of plantar fasciitis or Morton's neuroma.[70,72] Another study included only patients who had a prior diagnosis of meniscal tears by conventional MRI and confirmed by arthroscopy; weight-bearing MRI was not used to provide additional information for the diagnoses. This study reported that patients with displaceable meniscal tears (diagnosed by weight-bearing MRI) had significantly more pain than patient with nondisplaceable meniscal tears.[57] The last, industry-funded, case-control study reported that loaded kinematic MRI produced significantly less missed diagnoses of patellofemoral joint abnormalities than did unloaded kinematic MRI.[85] However, no functional outcomes were reported.

III. Projected Uptake and Potential Growth

In this section, we summarize potential directions of future research based on input from Key Informants (KIs) and our literature searches. Our own suggestions for potential avenues of future research are discussed in the section "Future Steps."

KI suggestions for future research

All KIs suggested that MRI under weight-bearing or stress-loading conditions is a growing research field. Several KIs indicated that this should be a key direction for future research for radiology in general. Industry sources also suggested that future developments in MRI equipment are likely to focus on imaging specific joints or organ systems in physiologic conditions, instead of the current practice of using whole-body, conventional MRI systems for all diagnostic purposes. Our industry KIs did not disclose specific projections for future uptake of their respective technologies; however, based on information from Fonar Corporation's official Web site, a new open, in-office (small-bore), multi-positional extremity MRI (mpExtremity MRI™) that allows weight-bearing imaging of lower extremities in a standing position is currently being developed.[109]

Clinically oriented KIs suggested that a stepwise approach to the further development of weight-bearing or stress-loading imaging would be preferable. Initially, studies would be conducted to standardize diagnostic methods across centers and ensure that images of adequate quality could be obtained. Specifically, clinicians contended that research efforts ought to be bent towards developing imaging protocols that mimic orthopedic clinical examination, such as imaging in flexion/extension or under stress-loading. After these initial steps, larger validation studies should be undertaken, followed by appropriately controlled studies to assess the impact of using weight-bearing MRI on clinical or patient outcomes.

Regarding the selection of outcomes for future studies, KIs agreed that diagnostic tests should be judged by the amount of additional information they offer as compared to other imaging methods. Clinicians and stakeholders suggested that studies should look beyond diagnostic accuracy and investigate the impact on diagnostic decision making, clinical treatment decisions, and patient outcomes. Additionally, both clinician and payer KIs mentioned costs as an important aspect of diagnostic decision making and suggested that the cost-effectiveness of MRI technologies should be established by further research. Industry KIs suggested that the cost-effectiveness of their respective products was evident.

We expand on these suggestions and explore future research approaches in "Future Steps."

IV. Dedicated extremity MRI devices

Our literature searches as well as Key Informant (KI) feedback indicated that dedicated extremity MRI devices should be considered as part of the Technical Brief due to a number of possible advantages over conventional MRI devices, such as not requiring the patient's body to be placed in the scanner's bore. The theoretical benefits and drawbacks of these "semi-open" devices are discussed earlier in section I.

Based on our review of the published literature, it became apparent that extremity dedicated scanners are typically not used to obtain imaging under weight-bearing or stress-loading conditions. Specifically, out of a total of 38 relevant studies using a dedicated MRI scanner (including 2 studies enrolling healthy subjects only), only one used mechanical modifications to obtain images under loading conditions among healthy subjects.[110] As this study enrolled only healthy subjects, we did not include it in our evidence map. The literature on non-weight bearing applications of dedicated extremity MRI studies appears to be rather extensive and includes several comparative studies and a randomized controlled trial; therefore, we decided to present a summary of the relevant studies. Here, we briefly summarize the clinical settings, diseases, and comparisons reported in the 36 published applications of non-weight-bearing dedicated extremity MRI. Appendix D presents a table of detailed information regarding the populations, specific extremity MRI devices, comparators, and outcomes assessed in each study.

Summary of study characteristics

Overall, we identified 36 relevant studies that examined dedicated extremity MRI devices.[106-108,111-143] Reviewed studies were conducted among a variety of patient populations; the most common conditions evaluated were rheumatoid arthritis (15 studies), extremity injuries (5 studies) and osteoarthritis (4 studies). Twelve studies had a case-control design, 16 were cross-sectional, and 7 were longitudinal studies. Three studies reported on primary (efficacy and cost) or secondary (predictive modeling) analyses based on a randomized controlled trial comparing a testing versus no testing strategy in patients with acute extremity injuries. Twenty six studies directly (in the same patients) compared two or more diagnostic modalities. Sample sizes were generally small, with an average of 80 cases (median = 38; IQR: 23, 97) and 14 controls (median = 7; IQR: 5, 12; only for case-control studies). The majority of studies used low-field strength scanners manufactured by Esaote Biomedica (Genoa, Italy) or MagneVu (Carlsbad, CA).

In general, the literature on dedicated extremity MRI appeared to be more developed as compared to weight-bearing MRI studies, as our search returned multiple comparative studies assessing clinical outcomes and studies with more rigorous designs, including a randomized trial of imaging with MRI in addition to plain radiograph versus radiographs alone (discussed below).

Randomized controlled trial of dedicated extremity MRI

We identified one randomized trial comparing plain radiographs followed by dedicated extremity MRI imaging versus plain radiographs alone for the diagnosis of acute extremity injuries. The study was conducted in a single academic center and enrolled 500 patients with acute injuries of the wrist, knee, or ankle, randomized 1:1 to the two diagnostic interventions. The dedicated extremity scanner used was the Artoscan [Esaote Biomedica, Genoa, Italy] MRI device, which has a magnetic field strength of 0.2T. The primary analysis of the trial reported on clinical effectiveness (assessed based on quality of life measurements, time-to-completion of the diagnostic work-up, number of additional diagnostic procedures during follow-up, number of

days absent from work, and number of days to convalescence) and costs (measures of medical and non-medical expenses associated with the initial injury during the 6-month follow-up period, as well as societal costs). Secondary analyses based on data obtained from the same clinical trial population were published separately and reported on the development of models for predicting the need for additional treatment after initial presentation.

Current availability of dedicated extremity MRI

In late 2009, GE entered into an agreement to purchase certain assets of ONI Medical Systems, Inc., a privately held company headquartered in Wilmington, Massachusetts, USA.[144] According to the KI affiliated with GE Healthcare, currently GE Healthcare is marketing two versions of this scanner (MSK Extreme™ 1.0T and the MSK Extreme™ 1.5T), and there are approximately 150 dedicated extremity MRI devices with field strengths of 1.0 to 1.5 T. Based on a press release concerning the ONI MSK Extreme® (GE Healthcare), as of October 21st, 2009, the MSK Extreme® had an installed base of 175 scanners worldwide.[145] The availability of lower field strength dedicated extremity MRI scanners is estimated to be larger given that they have been on the market for a longer time. Generally, because of their relatively low installation requirements, dedicated extremity MRI scanners are marketed to private orthopedic or rheumatology physician practices. Multiple manufacturing company Web sites, in addition to KI input, have suggested that these devices are also commonly used as "capacity enhancers," i.e., they are installed in facilities that already have several whole-body conventional scanners to increase the total volume of MRI scans these facilities can offer. To the best of our knowledge, the MagneVu 1000 device, a dedicated extremity MRI device, is not currently available commercially (the manufacturer appears to have filed for bankruptcy);[a] however, there exists an installed base of somewhat less than 100 devices.

Possible future research

Dedicated extremity MRI scanners are typically not used in weight-bearing applications; however, KIs suggested that this could be a promising area of future research. We only identified two studies of stress loading extremity MRI. These two studies were conducted in healthy people so did not meet our inclusion criteria for evidence map. However, the availability of high-field strength systems makes this an interesting area for future research. In addition, the availability of low- and high-field strength devices would allow for opportunities to directly compare the diagnostic accuracy of low- and high-field strength systems.

[a] Available at: http://www.auntminnie.com/index.asp?sec=ser&sub=def&pag=dis&ItemID=77843, last accessed October 10th, 2010. The company's Web site is no longer available (www.magnevu.com, last attempt to access: October 10th, 2010).

Summary and Implications

The set of possible features of emerging MRI technology for evaluating patients with musculoskeletal symptoms under loading stress includes: high image quality and speed, ability to image the joint under stress, ability to image joints in symptomatic positions, ability to obtain dynamic imaging, and patient comfort and safety. We compared these features between competing emerging MRI technologies and summarized their theoretical advantages and disadvantages (**Table 3**). Although the postulated advantages of stress-loading MRI seem promising, the clinical usefulness of stress-loading MRI in the management of musculoskeletal disorders is not clear. To date, only a few published studies compare stress-loading MRI with contemporary imaging alternatives, or report outcomes beyond anatomical changes (see section II). Moreover, specific indications and clinical settings where stress-loading MRI should be obtained have not been fully elucidated or evaluated, and most of the existing studies appear to have serious methodological limitations (see section II). Clinician and insurance payer (both public and private) Key Informants (KIs) also expressed concerns regarding the clinical use of stress-loading MRI. A key issue was the impact of low-field strength on the image quality of stress-loading MRI devices. This was compounded by the inadequate evidence-basis supporting the superiority (or even equivalence) of stress-loading MRI to conventional imaging alternatives.

Our findings emphasize the existing clinical need for improving the diagnostic performance of MRI examinations but also highlight the risks of bringing to clinical use imaging modalities with uncertain clinical utility. A combined assessment of past trends in the growth of MRI imaging in the U.S. and the interest in the field expressed by clinicians, researchers, and device manufacturers suggests that further increases in the use of stress-loading MRI may be expected in the future. Yet, the majority of published evidence on stress-loading MRI does not provide data on either clinical or patient outcomes.

The number of deployed stress-loading MRI scanners appears to be relatively low; the device types for which we were able to obtain specific estimates of the number of installed scanners appear to have an installed base of only a few hundred units in the US. However, according to KI feedback, stress-loading MRIs are rapidly evolving imaging modalities, and, given the rapid patterns of growth evident world-wide for MRI availability and utilization, it is expected that their use will continue to grow. Manufacturers of these devices are actively marketing their devices for clinical use, and some radiology practices are directly marketing stress-loading MRI to consumers. The diversity of existing stress-loading applications and the emergence of new technologies are a cause of concern among health professionals and policy-makers, particularly regarding their imaging quality and cost effectiveness.

Although all commercially available stress-loading MRIs we reviewed are considered as "substantially equivalent" (to conventional MRI) by the FDA, given the potential implications of an incorrect diagnosis, we argue that further validation of the diagnostic accuracy and clinical utility of these devices is necessary. Both false positive and false negative results may have serious consequences, such as suggesting (when not necessary) or delaying (when needed) surgical or other treatments for musculoskeletal conditions. In addition, MRI may be used as part of the investigation of worker compensation claims or for evidentiary purposes and should therefore be thoroughly vetted as valid means of establishing injury.[b]

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[b] For example, see http://www.fonar.com/news/072110.htm and http://www.dynawell.biz/spinalinfo_conditions.htm (section on sciatica), both accessed on October 11th, 2010)

As shown in the evidence map, the published evidence on stress-loading MRI is of poor methodological quality and the majority of studies reviewed did not report clinical outcomes. As such, the clinical utility of these imaging devices is currently unclear. We identified no randomized or non-randomized comparative studies of testing strategies for stress-loading MRI. Comparative studies of diagnostic tests applied to the same individuals were few, had small sample sizes, and reported on heterogeneous, typically surrogate outcomes. There was little or no evidence regarding the impact of these tests on physician's diagnostic thinking or decision-making with regards to treatment. The relative costs and benefits of these technologies are unclear; no formal quantitative assessment has been performed. **Box 1** summarizes the key decision-making uncertainties we identified regarding weight-bearing and stress-loading MRI.

Box 1: Key decision-making uncertainties for weight-bearing and stress-loading MRI

- The diagnostic accuracy of the available weight-bearing and stress-loading MRI methods has not been investigated in large, well-designed studies in any of the stress-loading devices that we considered. Consequently, the validity of claims concerning the diagnostic superiority of stress loading over conventional MRI has not been definitively tested.
- The impact of these technologies on physicians' diagnostic thinking or decision-making with regards to treatment, or patient outcomes is uncertain.
- Patient subgroups where MRI under loading stress would be indicated, or the setting where such imaging would be most beneficial, are not well defined.
- Potential harms from missed diagnoses or over-treatment in cases of false positive findings may be substantial.
- The cost-effectiveness of these methods has not been established. Although modeling of cost-effectiveness would be possible given the available data, it is likely that there would be considerable uncertainty regarding the optimal diagnostic strategy given the small sample sizes of existing studies.

Dedicated extremity MRI scanners

Due to their unique design ("semi-open" configuration) and the fact that they are not often utilized to take images under stress-loading conditions (in published literature), dedicated extremity MRI scanners were assessed separately from other emerging technologies. We identified a large number of published studies, often comparative and assessing clinical outcomes, including a randomized controlled trial of testing versus no-testing. It appears that these devices are commonly used in rheumatology (mostly for rheumatoid arthritis and other inflammatory arthritis) as well as the initial evaluation of acute extremity (wrist, knee, and ankle) trauma. Given the relatively recent availability of higher-field strength dedicated extremity MRI scanners, further increases in the availability of such devices are expected. All considerations for future studies described in the "Next Step" section apply equally to dedicated extremity MRI devices.

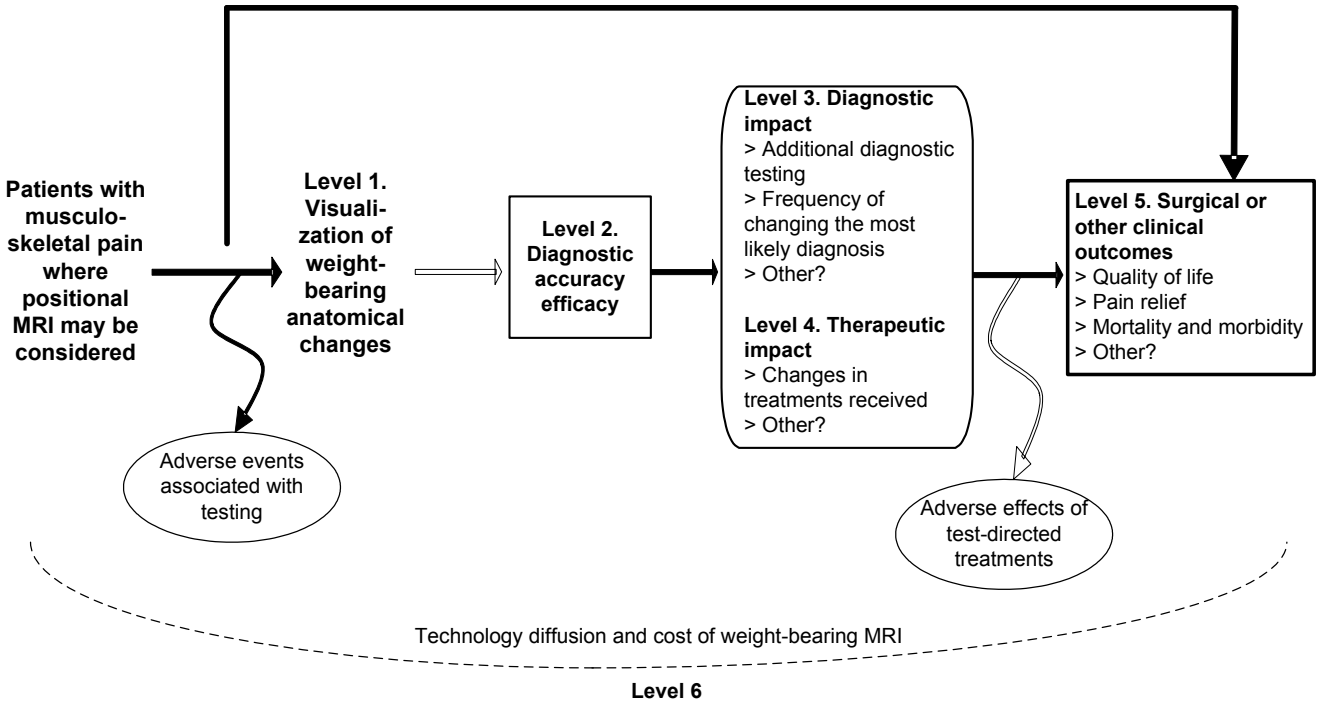
Next Steps

Conceptual framework for future research and policy

In this Technical Brief, we have organized emerging MRI devices into categories based on technical features such as stress-loading, positional imaging, and the configuration of the scanner bore. Although it is likely that our scheme may not anticipate all possible modifications of existing devices or future technical advances, we feel that, currently, it provides a practical way of categorizing a diverse group of imaging technologies. Although we proposed a classification scheme based on three device features (open bore design, patient positioning and imaging under loading stress), it should be noted that additional aspects, such as the ability to obtain dynamic imaging or the device field strength, should also be considered as part of this classification scheme. For example, imaging under stress loading using axial loading devices can be performed both in conventional (high field strength) and open (typically, low field strength).MRI scanners; thus, field strength can be used to further sub-classify uses of simulated gravity.

Despite the special features of each diagnostic technology, the assessment of diagnostic tests typically follows a stepwise approach,[146] progressing from the establishment of technical and clinical validity, to the assessment of the impact of the test on physicians' diagnostic thinking and therapeutic decision making, as well as clinical outcomes. Finally, a global assessment of the test from a societal perspective can be performed. This stepwise assessment approach, as described by Fryback and Thornbury,[30] is also applicable to stress-loading MRI (**Figure 5**). In the next section, we discuss specific approaches to future research, broadly following this scheme.

Figure 5. Application of the conceptual framework proposed by Fryback et. al. for evaluating the efficacy of diagnostic imaging for researchers and policymakers[30]



Based on this conceptual framework, findings from the evidence map, and input from Key Informants, we suggest that future research and policy on emerging MRI technologies under loading stress include the following:

- Assessing the impact on diagnostic thinking and therapeutic decision making of stress-loading MRI technologies using clinically relevant patient outcomes.
- Addressing the methodological issues in study design and analysis that appear to be prevalent in the existing literature.
- Creating special billing codes for special MRI procedures that will facilitate future research and policy decisions regarding these technologies.
- Assessing impact of the most promising of these technologies on patient outcomes through prospective observational studies or RCTs.

These suggestions are expounded upon in further detail below.

Assessing impact on diagnostic thinking and therapeutic decision making

Assessing the impact of imaging tests on diagnostic thinking and therapeutic decision making is vital as diagnostic tests influence patient outcomes mainly via these routes. Available methods are typically based on questionnaire evaluation of the proportion of cases in a patient cohort for whom the imaging test was considered "helpful" for diagnosis or treatment choice, quantification of the change in entropy of the probability distribution of differential diagnoses, the change in clinicians' subjectively estimated diagnosis probabilities pre- and post-test, or the (subjective) log-likelihood ratio for test positive and negative results.[147] However, there is an inherent subjectivity in these approaches, most available methods do not take into account diagnostic accuracy (since the "true" diagnosis typically remains unknown after the test is performed, and this is most often ignored in the above mentioned calculations), and impact on physician's thinking does not necessarily translate to impact on clinical outcomes.[148] If they are to be informative, studies of impact on diagnostic and therapeutic thinking need to be conducted in representative patient populations and diagnostic/treatment settings, preferably after the diagnostic accuracy of the tests of interest has been established.

Methodological considerations for future studies

Based on our review of the study designs and methods utilized in the published studies (across diverse clinical applications, and different MRI technologies and configurations), here we briefly discuss several cross-cutting methodological issues that we have identified. Although some issues are unique to each device and clinical application, several apply more generally and have been summarized below (**Table 6**).

Table 6. Common methodological issues and proposed solutions

Limitations in the existing evidence base	Proposed solutions
Epidemiological issues	
Detailed inclusion and exclusion criteria were not reported in the majority of studies. This was particularly evident regarding the selection of "healthy control individuals."	For case-control studies, the selection of control participants representative of the study base is crucial. Serious bias can arise if the control group is not representative of the population that gave rise to the cases.[149] Future studies should provide details about the study base and sampling methods employed to select cases and controls.

Sample sizes were typically small (median number of cases: 26, IQR: 17, 41). Because statistical power to test hypotheses depends on sample size, existing studies do not allow accurate conclusions to be drawn.	Future studies should be larger, ideally designed based on power calculations, to be able to reliably detect plausible effect sizes and provide precise estimates of diagnostic accuracy.[149]
For studies of diagnostic accuracy, outcome definitions were often unclear, as were the means of ascertaining them.	Future studies should report the definitions of outcomes and ascertainment methods. For subjective outcomes it is best to obtain outcome assessment by multiple raters, report their expertise, and perform a formal test of rater agreement.[150]
For studies assessing clinical outcomes, blinding to test results was frequently not reported or not performed.	Since the interpretation of imaging tests is frequently subjective, assessments should preferably be performed in a blinded fashion to avoid bias.[151,152]
Analytical aspects	
Multiple anatomic regions or pathologic lesions were present in each patient. For example, in studies of rheumatoid arthritis, multiple erosions could be present in multiple bones in a single patient. Similarly, in studies of lumbar spine imaging, multiple spinal levels might be assessed. Typically, analyses ignored the natural "clustering" of multiple observations within individuals.	Methods that ignore "clustering" can result in biased and spuriously precise estimates of sensitivity and specificity. Future studies should use methods that account for within patient clustering. Only rarely were more appropriate methods, such as multilevel modeling, employed.[92,94]
Sample size determination was rarely based on prospective power calculations.[149]	Power calculations would ensure that studies enroll enough patients to be able to reliably test their hypotheses. For simple statistical tests, such as the comparison of two means or proportions, power calculations are easy to implement in most commercial statistical packages. For more complicated designs expert input may be required.
In most cases the analytic validity of imaging tests was unclear or not established. This was particularly evident for studies of stress-loading MRI, where a reference test was often not available.[153-156] When comparing measurements or clinical findings obtained using different MRI devices, correlation or regression methods were often used to demonstrate "congruence" between technologies. It is known that correlation and regression are inappropriate for assessing agreement between measurements.	Future studies should use standardized and replicable procedures for stress-loading MRI, and assess the test agreement between stress-loading MRI and an independent imaging modality. Studies should use appropriate methods for assessing agreement, both for continuous and categorical outcomes.[157-159]
In comparative studies of imaging tests, in the absence of a gold standard, authors frequently and arbitrarily selected one of the tests as a "reference" and proceeded to calculate sensitivity and specificity for the other test, i.e., treating it as the "index test." It was common that the "reference test" in one study was considered as the "index test" in another. It is well appreciated that sensitivity and specificity estimates are biased when the gold standard is tarnished.	When no gold standard test is available, it is preferable to use methods that account for its absence (i.e., treat the prevalence as an additional parameter to be estimated). Such methods are available under both frequentist and Bayesian frameworks.[154,155,160,161]

Creating separate billing codes for special MRI procedures

Based on our searches of the grey literature and Key Informant input there appears to be no special billing code for stress-loading MRI, and at least in some cases, stress-loading MRI may have been associated with increased healthcare costs (due to multiple billings for the same imaging session). It is possible that separate billing codes may increase transparency and allow better monitoring of the MRI examinations performed. Separate billing codes would also facilitate future population-level research on the clinical use of stress-loading MRIs.

Assessing impact on patient outcomes in observational studies and RCTs

Ideally, the most internally valid evidence regarding a diagnostic test can be obtained from randomized controlled trials (RCTs) of alternative testing strategies. Several randomized designs have been proposed for diagnostic, prognostic, and predictive tests and can be applied to weight-bearing or stress-loading MRI. Although RCTs can produce robust evidence on the impact of diagnostic tests on clinical outcomes and costs, to a large extent, effects of medical tests are indirect in nature.[162] A test affects patient outcomes mainly by influencing diagnostic thinking and therapeutic choices.[163] In addition, an imaging test can be used as a replacement test (e.g., weight-bearing MRI instead of conventional MRI), an add-on test (e.g., axially-loaded MRI following conventional MRI) or a triage test (e.g., weight bearing or axially loaded MRI to determine if myelography is necessary).[163] In each case, a different threshold for test positivity can be used. Each permutation of different tests, test combinations, and test thresholds represents a candidate test-and-treat strategy. It is often infeasible or inefficient to assess all potential strategies in RCTs.[163,164] Instead, diagnostic accuracy can be assessed in the clinical context of interest using observational designs, and then, based on the performance of the tests, a decision can be made on whether an RCT of testing versus no testing is necessary or whether the test can be implemented with no further study. Lord et al. have proposed a framework for diagnostic test evaluation both by primary research studies and by systematic Technology Assessments.[163] In addition to these methods, decision modeling methods can be used to evaluate the potential long-term impact of diagnostic tests on clinical outcomes.[165,166]

With these considerations in mind, the most practical research strategy may be to explore the predictive accuracy (sensitivity and specificity) of different weight-bearing and stress-loading MRI approaches in well-designed cohort or case-control studies. Such studies should probably take precedence over conducting RCTs at this stage of the development of these technologies. To be clinically useful and informative, they should enroll patients representative of those seen in clinical practice, and limit verification and other biases.[167,168] Such studies should be relatively feasible, given the high prevalence of the conditions of interest (musculoskeletal disease), the familiarity of clinicians and patients with MRI, and the lack of known harms related to MRI imaging. When RCTs are contemplated, strategies to increase efficiency, such as randomizing to different therapeutic strategies only those patients for whom conventional and weight-bearing or stress-loading MRI suggest different diagnoses (i.e. patients with discrepant imaging findings), should be considered.[167]

Future steps for assessing dedicated extremity MRI scanners

The literature on dedicated extremity MRI scanners appears to be fairly extensive and more mature compared to the other technologies discussed herein. Given the recent availability of high-field strength dedicated extremity scanners, we believe that a technology assessment of their use for the diagnosis and monitoring of patients with rheumatoid arthritis and other inflammatory arthritis may be warranted.

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