



Effective Health Care Program

Technical Brief
Number 7

Emerging MRI Technologies for Imaging Musculoskeletal Disorders Under Loading Stress



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Emerging MRI Technologies for Imaging Musculoskeletal Disorders Under Loading Stress

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

This EPC evidence report is a Technical Brief. A Technical Brief is a rapid report, typically on an emerging medical technology, strategy or intervention. It provides an overview of key issues related to the intervention—for example, current indications, relevant patient populations and subgroups of interest, outcomes measured, and contextual factors that may affect decisions regarding the intervention. Although 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 decision to request a Technical Brief is not solely based on the availability of clinical studies. The goals of the Technical Brief are to provide an early objective description of the state of the science, a potential framework for assessing the applications and implications of the intervention, a summary of ongoing research, and information on future research needs. In particular, through the Technical Brief, AHRQ hopes to gain insight on the appropriate conceptual framework and critical issues that will inform future comparative effectiveness research.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome comments on this Technical Brief. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to epc@ahrq.hhs.gov.

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Emerging MRI Technologies for Imaging Musculoskeletal Disorders Under Loading Stress

Structured Abstract

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

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

Findings. There exists a rapidly expanding array of MRI technologies designed to employ weight-bearing, stress-loading, or positioning protocols to more accurately diagnose musculoskeletal disorders. Often novel MRI devices have low magnetic field strength, which may adversely impact image quality. 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. Most importantly, 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 participant selection, outcomes investigated, and statistical analyses performed, to identify the imaging modalities and protocols with the highest clinical utility.

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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 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 health care resource utilization.³ Musculoskeletal complaints are some of the most common reasons for doctor visits⁴ and are significant sources 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) was 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

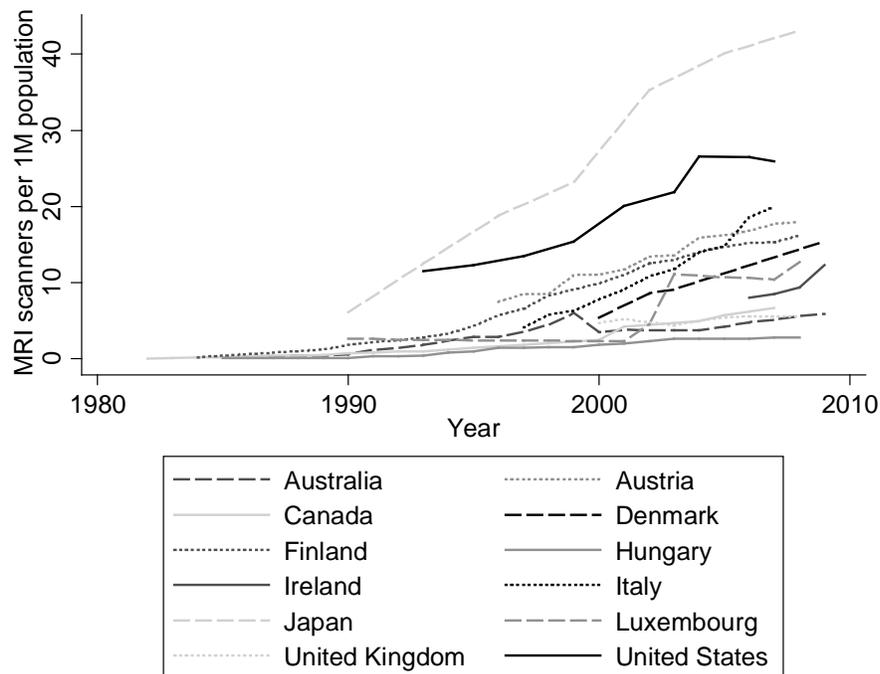
An MRI system consists of five major components: a magnet, a magnetic gradient system, a radio frequency (RF) coil system, a receiver, and a computer system. During MRI scanning, the patient is placed in a strong magnetic field. The strengths of the magnetic field employed in typical MRI machines range 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 antiparallel to the magnetic field. Parallel alignment is a low-energy state, while the antiparallel 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.

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 United States and worldwide) and in the number of scans performed. Based on data from the Organization for Economic Co-operation and Development (OECD), the United States is 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.

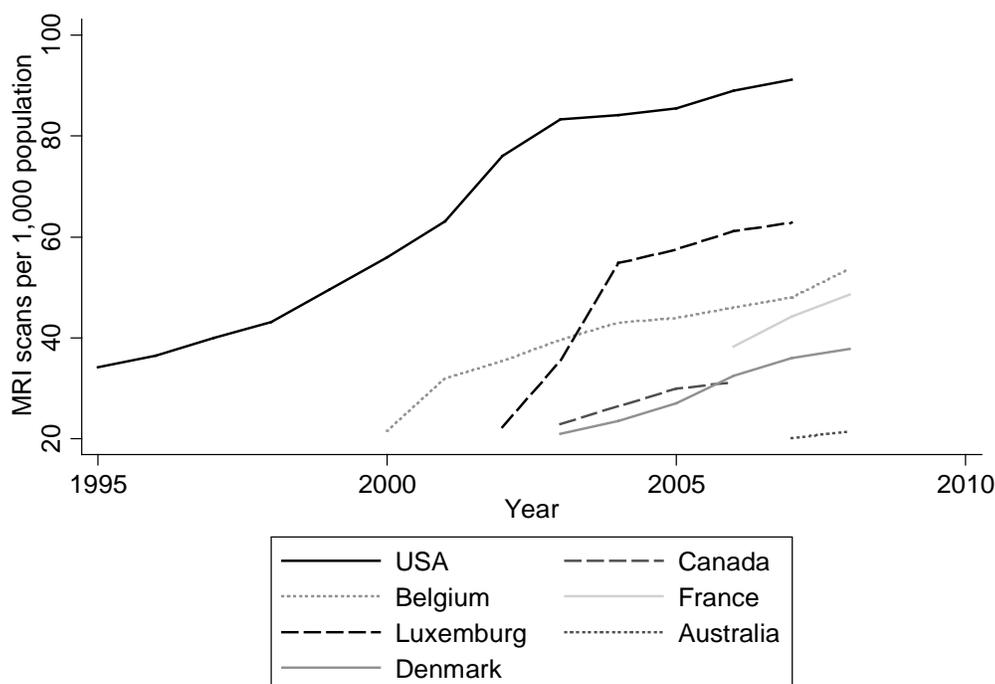
Figure 1. Growth patterns in the availability of MRI scanners in selected OECD countries



MRI scanners per million population in selected OECD countries with data available for at least 2 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 1,000 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 stress-loading imaging technologies, for spine imaging in particular.¹⁴⁻¹⁶ As discussed in the previous section, this appears to be a worldwide trend. In the United States, the increase in spine imaging has been accompanied by an increase in spinal surgery, which has also been documented by multiple studies. However, 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 percent 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.

One area of possible modification is the physiologic conditions under which the MRI scan is performed. 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 Furthermore, due to limited space in closed-bore MRI, it may not serve the needs of obese patients requiring less physiologically constraining imaging systems. 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. Open MRI systems have been designed to allow greater flexibility in patient positioning and may alleviate claustrophobia. 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. Devices have been developed 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. Other devices or placement techniques 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.

Despite the progress in developing new MRI techniques, considerable uncertainty remains as to the optimal imaging approach for most musculoskeletal conditions, the specific indications for MRI, and the relative benefits and harms of different MRI configurations (weight-bearing or not, open or closed, neutral positioning or flexion/extension). 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 the diagnostic validity or accuracy for upright, multipositional MRI (one specific type of stress-loading MRI technology). Additionally, the technology assessment could not determine whether technologies that allow positional imaging (for example, flexion and extension views) provide additional diagnostic information, despite the acquisition of non-neutral views being associated with additional costs.²⁴ Since then, other studies assessing the diagnostic utility of stress-loading MRI have been published, but no systematic evidence reviews have been published.²⁵⁻²⁸

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 health care 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 and input from Key Informants (KIs). The terminology used in the guiding questions to describe magnetic resonance imaging (MRI) technologies that were included in this Technical Brief was changed from “positional MRI” to current “stress-loading MRI” after the literature review determined that stress-loading MRI more accurately described the principle underlying the technologies of interest. 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?
- 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 United States? 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. Clinical 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 followup (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 literature review, KI interviews, grey literature, and evidence map (i.e., a systematic description of the characteristics of the published studies) to answer the guiding questions.

Identification of Key Informants and Interviews

In order to gain an understanding of the most important clinical uncertainties, patterns of use, and technical details about this new and rapidly evolving technology, we interviewed a selected number of 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 FDA Center for Devices and Radiological Health database to identify major MRI manufacturers and obtain FDA clearance status of relevant MRI devices. To identify potential harms of 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." Although the MAUDE database has several limitations because it collects information based on reporting from diverse sources, including clinicians, patients, user facilities or manufacturers, it can still provide useful data on rare or unexpected adverse events.³¹ 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. KIs provided additional relevant conference abstracts or book chapters, as well.

To assess the worldwide 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 1,000 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 nonexhaustive, methodology is employed to efficiently appraise the available evidence on a topic of interest as well as identify major knowledge gaps.³² The goal is 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. In contrast to systematic reviews, which are lengthy and labor intensive, 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.

Three reviewers jointly screened the first 300 citations to ensure that screening criteria were well understood and applied uniformly. Thereafter, the same investigators screened nonoverlapping 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 at least one reviewer considered potentially relevant. Three reviewers independently reviewed articles.

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, (2) the ability to perform imaging under stress-loading conditions; and (3) having an open or semi-open configuration. 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. A Venn diagram presenting our proposed operational classification is presented in Figure 3 (see the Findings section, Description of Stress-Loading MRI subsection.)

Although the focus of this report is stress-loading MRI, input from our KIs suggested that we expand our literature search to include studies of small bore, dedicated extremity MRI despite the absence of stress-loading applications, due to the technology's potential for rapid development and diffusion. We discovered a substantial literature available for dedicated extremity MRI, but because the technical features of these devices were determined to be distinct from those of the other technologies we considered, we were not able to integrate it meaningfully into the current report. However have presented our search results for dedicated extremity MRI in Appendix F and refer to these devices in the main text of the report for comparison purposes.

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, since stress loading is not a relevant approach for that joint. We did not consider studies of dynamic MRI (i.e., MRI while the joint is in movement), unless imaging was obtained under stress-loading conditions. 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, as defined in Findings (see the Description of Stress-Loading MRI subsection). Briefly, category A included open MRI scanners that allow obtaining views under different positions under stress loading; category B included devices that allow imaging under stress loading in different positions but have a closed bore configuration; category C included devices for stress loading under conventional (supine) positioning in a closed scanned; and category D included devices with an open configuration that allow imaging under stress loading in a conventional (supine position). Extracted data included: publication information (first author name, journal, and year of publication), study design, condition studied, study size and clinical 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 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)³³ 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 (Evidence Map). Based on the data items 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.³⁴ 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).

To determine whether particular findings or research groups are overrepresented 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 coauthors in common. Undirected graphs depicting groups of studies that were conducted by the same research team were generated.

Based on our overview of the literature and generally accepted statistical and epidemiological principles, we provide recommendations for improving study design and analyses in studies of novel imaging technologies.

Findings

Description of Stress-Loading MRI

This section addresses the operating principles and potential benefits and harms associated with stress-loading magnetic resonance imaging (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) database and Section 510(k) of the Food, Drug, and Cosmetic Act database.

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, (2) the ability to perform imaging under stress-loading conditions; and (3) having an open or semi-open configuration. 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.

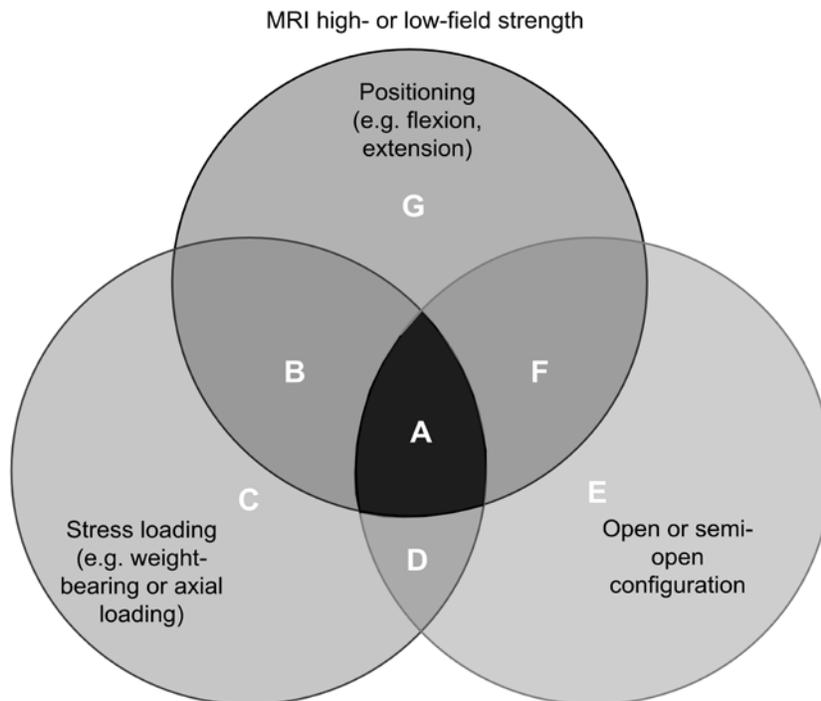
More specifically, the operational definitions for these three features are as follows:

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 falling

under areas A to D (stress loading). 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.). We excluded 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 because they do not provide information on stress-loading MRI and as such were considered outside the scope of this Technical Brief.^a

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



A = open MRI scanners that allow obtaining views under different positions under stress loading; B = devices that allow imaging under stress loading in different positions but have a closed-bore configuration; C = devices for stress loading under conventional (supine) positioning in a closed scanner; D = devices with an open configuration that allow imaging under stress loading in a conventional (supine position); E = open configuration MRI devices for imaging without stress loading, only in the supine (conventional position); F = devices with an open configuration that allow positional imaging, in the absence of stress loading. Please consult the text for details about devices considered in this Technical Brief.

All MRI is based on the same principles of physics to generate images. For stress-loading MRI devices, based on a review of the literature and 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.

^aAs discussed in the Methods section, a brief discussion of dedicated extremity MRI is included in Appendix F, due to the technology’s potential for rapid development and diffusion.

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 prerequisite for the use of MRI for clinical decisionmaking. 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. ³⁵⁻³⁷
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 supraphysiologic). 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 Tesla [T]), which is associated with lower image quality (also see the 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 total weight. The major disadvantage of axial-loading MRI is that it requires nonloaded 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 concern that some patients may not be able to complete weight-bearing, stress loading, or positional imaging due to the development of neurological symptoms, induced by the stress on the imaged joints during image acquisition.

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 the Evidence Map subsection of this section of the report, we describe in more detail the specific modifications of existing devices 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.³⁸ 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 decisionmaking, the most important feature is the ability to generate images of sufficiently high quality. All sources

agreed that magnetic field strength is generally the major determinant of image quality, although it should be noted that improved image quality may not directly translate to improved clinical or diagnostic utility of the scans.³⁹ 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. Among the factors that determine 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.³⁹ 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.⁴⁰ 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,⁴¹ the International Society for Magnetic Resonance in Medicine (available at: <http://www.ismrm.org/>), the FDA,⁴² and the ECRI Institute.⁴³

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 radio frequency

burns during scanning and instructs that the contacts be covered by the provided safety covers or bed cushion.^{44,45} 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.⁴⁶

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 “nonspecific 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. These are both well recognized problems in the literature and appears to affect both children and adults. 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.^{23,47-49} Some of the KIs suggested that scanning in open configuration scanners (including vertically open devices) may alleviate patient fears as well as accommodate larger patients.²³ Therefore, open MRI configurations, which have a wide gap between their magnets, may allow more patients to undergo needed 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, although they could in theory, and we found no published studies of such uses. There are, however, a significant number of studies of non-stress loading applications of extremity specific MRIs, which we have listed in Appendix F.

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.⁵⁰⁻⁵² Wide-bore MRI (sometimes referred to as “open-bore,” not to be confused with “open 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 devices 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

	<i>Theoretical advantages</i>	<i>Theoretical disadvantages</i>
Conventional closed-bore MRI	<p>Higher magnetic field strength compared with most other configurations may be associated with better image quality.</p> <p>Higher speed due to improved gradient systems may reduce scanning time and improve image quality.</p> <p>Most radiologists and technologists are familiar with such systems.</p>	<p>Imaging is obtained predominantly in the supine or prone position; findings that are only revealed under stress or in flexion/extension may be missed.</p> <p>Most scanners have narrow bores that may induce claustrophobia.</p> <p>Imaging of obese patients may not be possible due to limitations in bore diameter.</p>
Weight-bearing MRI	<p>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.</p> <p>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.</p>	<p>Magnetic field strength is typically much lower compared with conventional scanners, leading to reduced image quality.</p>
Axial-loading in open or closed-bore conventional scanners	<p>Technologies that simulate weight-bearing may provide advantages similar to those of weight-bearing imaging.</p> <p>Most axial-loading devices can be used in conventional scanners with high-field strengths (as well as open scanners).</p>	<p>Most commercial devices allow imaging limited to only the lumbar spine and only in the extended position.</p> <p>Requires nonloaded imaging to be obtained prior to the loaded scan to rule out pathologic conditions.</p> <p>Axial-loading equipment may induce or worsen pain or neurological symptoms.</p> <p>When performed in closed-bore scanners, has the same limitations as conventional devices, such as an inability to accommodate obese or claustrophobic patients.</p> <p>May not accurately replicate the effects of physiologic weight-bearing positions.</p>
Semi-open (small-bore) MRI	<p>Improved patient comfort and avoidance of anxiety-related reactions.</p> <p>Reduced noise during imaging.</p> <p>In newer devices, high strength magnetic fields result in improved image quality, possibly comparable to larger (whole body) MRI scanners.</p>	<p>Can only image the extremities (and in most cases not the shoulders or hip).</p> <p>Most systems have low-field strengths that may result in lower image quality.</p>

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

In searching studies for evidence map, we did not find any published data that addressed this question. However, 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.”⁵³ These policies probably reflect that stress loading MRI technologies are relatively at an early stage of the diagnostic test development process (see the Evidence Map subsection of this section and the Next Steps section of this report).

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 substantial divergence of opinion between the clinical experts (orthopedic surgeon and radiologist) and payers, our industry sources regarding how stress-loading MRI should be used in comparison to conventional MRI, when, and for whom. 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 triaging patients to other imaging modalities, as replacements of or add-ons to conventional MRI, varied greatly in clinical practice. In contrast, industry input suggested that the devices could be used as replacement tests for conventional MRI for imaging the cervical and lumbar spine.

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] All three devices were cleared by the FDA on a “substantially equivalent” basis with predicate MRI scanners.

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]. The former device was cleared by the FDA on a “substantially equivalent” basis for the indication for use stated as an accessory for axial compression of the lumbar spine in computerized tomography (CT) and MRI. The later device was considered as “substantially equivalent” to the DynaWell device.

Approximately how many and of what kind are facilities currently providing stress-loading MRI testing in the United States?

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 United States). This was according to a Fonar press release from late 2009.⁵⁴ 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 however external information indicated that the device is no longer marketed by GE Healthcare in the USA.

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 to 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.”⁵⁵

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 associated with different types of MRI devices, particularly with extremity and upright MRIs as compared to conventional MRIs. KIs

generally agreed that overall costs to health care facilities for obtaining and operating open, upright, and extremity-specific MRI scanners were lower compared with conventional MRI devices, as such devices have lower purchase and installation costs (e.g., costs for magnetic field shielding). KIs also added that, while health care 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 charge (to the patient or payer) for obtaining 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 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 \$1,200 based on information obtained from manufacturers.²⁴

Two additional issues concerning MRI imaging 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 decisionmaking (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 issue of image quality may also be important given that several attorneys appear to advocate the use of images obtained by MRI devices under stress loading (particularly upright weight-bearing MRI) for evidentiary purposes.^b

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 has the potential to 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.

^bThis issue was identified by one of the peer reviewers of this Technical Brief and is easily verifiable by simple Internet searches.

Evidence Map

As described in the Description section, we focused on three features of emerging MRI technologies and applications to define seven nonoverlapping categories (Figure 3) of MRI devices or techniques. Using this classification scheme, we defined four categories of stress-loading MRI technologies of interest for the evidence map (Table 3). These categories serve as operational definitions that we employed for the purpose of this report, and do not necessarily imply that the specific MRI technique has been utilized in the published studies. Indeed, our literature searches did not identify any studies investigating devices that would fall under category D.

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

Category (area in Figure 3)	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 an open MRI scanner.

^a 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. However, given this technology’s potential for rapid development and diffusion, we have summarized the available studies in Appendix F.

A = open MRI scanners that allow obtaining views under different positions under stress loading; B = devices that allow imaging under stress loading in different positions but have a closed bore configuration; C = devices for stress loading under conventional (supine) positioning in a closed scanner; D = devices with an open configuration that allow imaging under stress loading in a conventional (supine position); consult the Methods section for details about devices considered in this Technical Brief.

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.^{25-28,56-106} Of these, one paper reported data from two separate studies.²⁶ One additional paper was identified through hand searching of reference lists.¹⁰⁷ Thus a total of 57 studies (in 56 publications) were included in our evidence map.

We categorized these 57 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, 36 studies fell under category A (i.e., open, positional, and weight-bearing MRI),^{25-28,56-84,101,106,107} 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),^{86,103} and 19 studies fell under category C (i.e., use of specialized devices to “simulate” gravity [i.e., axial loading] in a conventional MRI).^{26,85,87-100,102,104,105} None of the qualifying studies fell under category D.

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). Twenty publications (36 percent of those reporting on eligible studies) were produced by four teams. One team that has published 6 manuscripts, corresponding to approximately 10 percent of all studies, includes the inventors of the DynaWell axial loading, Drs. Danielson and Willen, as co-authors.⁵⁵

Below, we present a summary of all 57 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 below in Comparative Studies That Reported Clinical Diagnostic or Patient Outcomes, and the characteristics of these studies and the outcomes they assessed are presented in Appendix E.

Characteristics of Eligible Studies

All of the studies were published between 1993 and 2010. The most commonly imaged body regions were the lumbar spine (33 studies) and knee (13 studies). Figure 4 presents the eligible studies stratified by study design and anatomic region assessed. Across all studies, the median of the mean/median age of patients with musculoskeletal diseases or conditions was 42.6 years (25th–75th percentile: 31.6, 50); the median mean/median age of controls (for case-control studies) was substantially lower at 29.9 years (25th–75th percentile: 28–34.4). Approximately 50 percent of the individuals included in the eligible studies were male (equally distributed in both patients and controls).

In general, studies were small; the median number of included cases was 26 (25th–75th percentile: 17, 45) and the median number of controls was 13 (25th–75th percentile: 12, 20; for case-control studies only). No randomized controlled study or nonrandomized comparative study of testing versus no testing was identified. The majority of studies were cross-sectional (37 studies), or had case-control designs (13 studies). Only five longitudinal studies and two studies obtaining imaging pre- and post-application (within minutes) of an orthopedic intervention or physical activity were included. The vast majority of studies did not systematically identify cases or controls (convenience sampling). Fifteen studies (27 percent) were comparative studies of two diagnostic tests and reported on clinical outcomes. Figure 5 presents the eligible studies stratified by study design and weight-bearing or stress-loading device used.

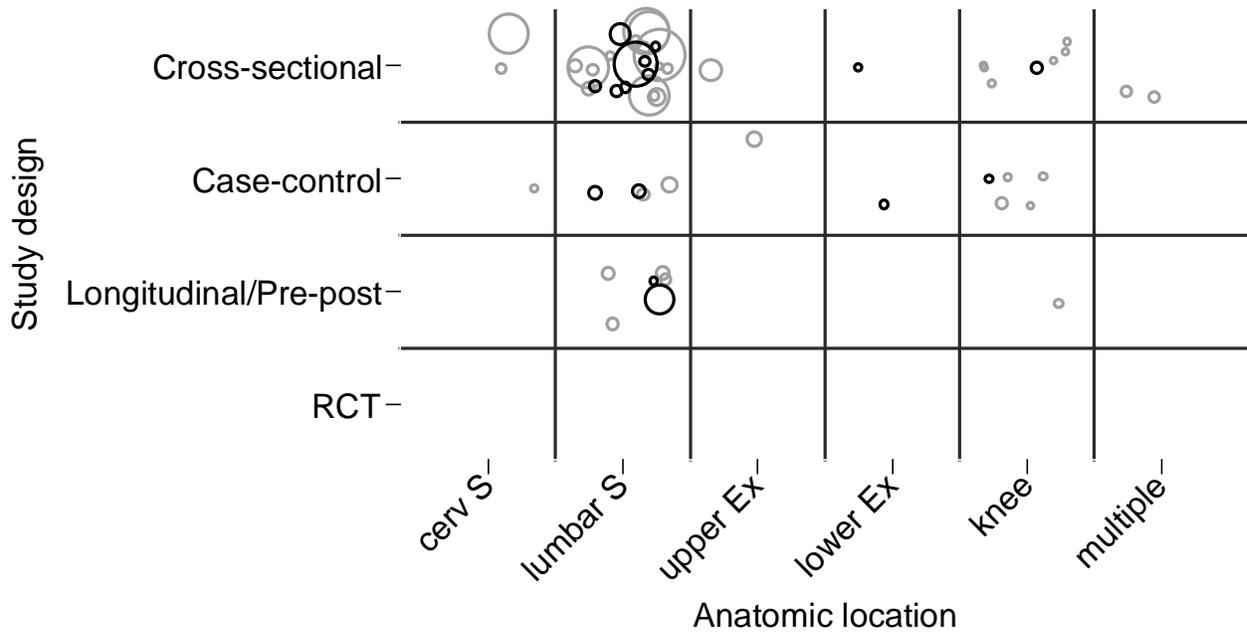
Patient-relevant outcomes were assessed infrequently (five studies). Most studies (27 studies, 47 percent) focused on the feasibility (defined as agreement in anatomic measurements between different imaging modalities as the outcome of interest) of imaging under weight-bearing or stress-loading conditions. Most studies (45 studies) exclusively enrolled symptomatic patients, 7 studies enrolled exclusively asymptomatic patients and 4 studies enrolled mixed populations (one study did not report this information). Only 14 studies assessed accuracy outcomes (we defined this broadly as a diagnosis of abnormality in symptomatic patients made based on weight-bearing or stress-loading MRI), 1 study addressed patient management or treatment planning, and 2 studies reported on disease monitoring.

Only 10 studies reported harms or adverse events associated with weight-bearing MRI testing (Table 4). In the studies that reported relevant information, most adverse events were new-onset

or worsening pain/neuropathy while the patients were placed under loading stress (weight-bearing or axial loading). Studies reported test interruption and incompleteness rates of 5 to 10 percent due to symptoms developing during stress loading; and one study reported amending its design (evaluating sitting instead of upright MRI) because patients could not stand still during the upright exam.⁷⁴

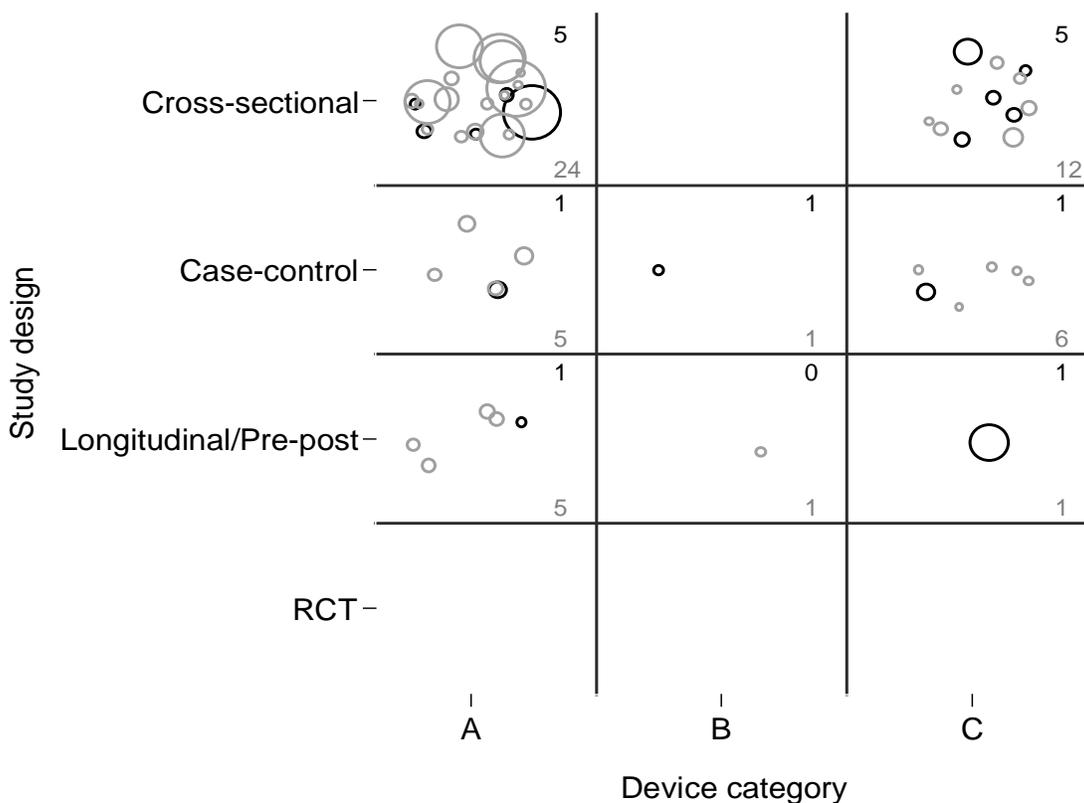
Most studies were conducted outside the United States (see also Appendix D). Funding information was often not reported; among studies that reported relevant information, frequently no funding source was identified (“no funding was received”). Given the lack of relevant information in a large number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

Figure 4. Studies stratified by design and anatomic region imaged



Studies are represented by black and gray circles of a size proportional to the number of enrolled patients. Two studies did not report their sample size and are not shown in the graph. Two studies with a pre/post-imaging design (monitoring changes within minutes of some intervention) are plotted along with longitudinal studies. Studies are classified into separate boxes based on the anatomic region and their study design. Placement of studies within each box is random. Studies depicted in black circles were comparative, that is, they directly compared different diagnostic methods and had clinical outcomes. Anatomic regions: cerv S = cervical spine; lumbar S = lumbar spine; upper Ex = upper extremity; lower Ex = lower extremity. Note that the majority of the studies pertained to the lumbar spine.

Figure 5. Studies stratified by design and device category



Studies are represented by black and gray circles of a size proportional to the number of enrolled patients. Two studies did not report their sample size and are not shown in the graph. Two studies with a pre/post-imaging design (monitoring changes within minutes of some intervention) are plotted along with longitudinal studies. 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 black circles were comparative, that is, they directly compared different diagnostic methods and had clinical outcomes. Within each box, the total number of studies is displayed in gray (lower right corner), and the number of comparative studies is displayed in black (upper right corner). Device categories (please also refer to Figure 3): A = weight-bearing MRI; B = specialized devices to obtain MRI imaging under weight-bearing conditions in a closed MRI scanner; C = stress-loading MRI in a conventional MRI scanner. No studies had a randomized design. RCT = randomized controlled trial.

Table 4. Studies of weight-bearing or stress-loading MRI that reported information regarding adverse events

Author, year	Patients enrolled	Imaging method	Adverse events/safety outcomes
Danielson, 1998	34	AL	Twenty (59%) patients experienced 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	AL	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	AL	Two (13%) patients did not complete the last scan due to discomfort.
Wang, 2008	27	AL	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	AL	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 AL and electrophysiological study revealed lumbosacral radiculopathy.
Ahn, 2009	51	AL	10% of patients did not complete the AL 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. Table 5 summarizes the characteristics of the patient populations or demographics, and Table 6 summarizes the study design characteristics of eligible studies.

Open, Positional, and Weight-Bearing MRI

Thirty six studies were classified as “open, positional, and weight bearing MRI” systems (category A). In general, studies were small; on average they included 101 cases (median = 30; 25th–75th percentile: 20, 50) and 20 controls (median = 13; 25th–75th percentile: 12, 20; for case-control studies only). The majority of studies were cross-sectional (24 studies), or had case-control designs (7 studies). Only four longitudinal studies were identified. Followup duration was less than a year (reported in three of the four studies). One study had a pre-post design, in which weight-bearing MRI was used to assess outcomes of spinal manipulation interventions (imaging was performed before and immediately after the intervention). The most commonly imaged body regions were the lumbar spine (20 studies) and knee (6 studies). Clinical outcomes were assessed infrequently; the majority of studies (25 studies) reported on anatomic measurements or rater agreement under weight-bearing or stress-loading conditions, 9 studies reported on accuracy outcomes, 2 studies reported on impact on diagnostic thinking, and no study reported on patient-centered outcomes.

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).^{86,103} 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 dynamic (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 Comparative Studies That Reported Clinical Diagnostic or Patient Outcomes.

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; 25th–75th percentile: 12, 34) and 20 controls (median = 14; 25th–75th percentile: 13, 18; for case-control studies only). The majority of studies were cross-sectional (13 studies), or had case-control designs (5 studies). One study had a longitudinal design but did not clearly report the duration of followup. 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); 13 studies reported on anatomic measurements/rater agreement, 4 studies reported on diagnostic accuracy, one study reported on the impact of the tests on diagnostic thinking, one study reported on the impact on treatment decisions, and no study reported on patient-centered outcomes.

Table 5. Summaries of descriptive characteristics of the studies considered eligible—patient characteristics or demographics^{a,b}

Study characteristic		All studies N=57	Open, positional, and weight-bearing MRI N=36	Specialized devices to “simulate” gravity in conventional MRI N = 19
Enrolled patients	Median number of patients [25th–75th percentile] (min-max)	26 [17-45] (8-553)	30 [20-50] (10-553)	24 [12-34] (8-250)
	Median number of controls [25th–75th percentile], y Only for case-control studies	13 [12-20] (5-50)	13 [12-20] (10-50)	14 [13-18] (10-43)
Sex	% male patients (median, 25th–75th percentile), y	51 [40-63]	54 [43-67]	45 [19-53]
	% male controls [median, 25th–75th percentile], y (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 [25th–75th percentile], y	42.6 [31.6-50]	41.9 [32-44.5]	48 [27.1-52]
	Patients >= 65 years of age, %	3 (5)	2 (6)	1 (6)
	Median of mean/median age of controls [25th–75th percentile], y	29.9 [28.0-34.4]	32.1 [26.8-34.4]	28.4 [28.1-36.3]
	Controls >= 65 years of age (only applicable to case-control studies) (n, %)	0	0	0
Symptomatic patients enrolled	Exclusively (n, %)	45 (79)	31 (86)	13 (68)
	Asymptomatic (n, %)	7 (12)	2 (6)	4 (21)
	Mixed/ NR (n, %)	5 (9)	3 (8)	2 (11)
Country	USA (n, %)	18 (32)	11 (31)	5 (26)
	Non-USA (n, %)	35 (61)	21 (58)	14 (74)
	Mixed (n, %)	4 (7)	4 (11)	0

^aNumbers represent studies (% total studies in category), unless otherwise stated. Percentages have been rounded to the nearest integer and may not sum to 100%.

^bAs 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

Table 6. Summaries of descriptive characteristics of the studies considered eligible—study design characteristics^{a,b}

Study characteristic		All studies N=57	Open, positional, and weight- bearing MRI, N=36	Specialized devices to “simulate” gravity in conventional MRI N = 19
Funding source reported	Yes (n, %)	36 (63)	20 (56)	14 (74)
	No (n, %)	21 (37)	16 (44)	5 (26)
Industry funding (only among studies that reported funding sources)	Yes (n, %)	11 (31)	3 (15)	6 (43)
	No ^c (n, %)	25 (69)	17 (85)	8 (57)
Study design	Cross-sectional (n, %)	37 (65)	24 (67)	13 (68)
	Case-control (n, %)	13 (23)	7 (19)	5 (26)
	Crossover (n, %)	0	0	0
	Longitudinal (n, %)	5 (9)	4 (11)	1 (5)
	Pre/post (n, %)	2 (4)	1 (3)	0
	NRCS (n, %)	0	0	0
Followup timing	Prospective (n, %)	5 (9)	5 (14)	0
	Retrospective (n, %)	1 (2)	0	1 (5)
	Not applicable (case-control or cross-sectional studies) (n, %)	48 (84)	30 (83)	16 (84)
	Unclear (n, %)	3 (5)	1 (3)	2 (11)
Number of participating centers	Multicenter (n, %)	4 (7)	3 (8)	1 (5)
	Single center (n, %)	39 (68)	22 (61)	15 (79)
	Not clear/ Not reported (n, %)	14 (25)	11 (31)	3 (16)
Clinical setting	Feasibility (n, %)	27 (47)	18 (50)	9 (47)
	Screening (n, %)	1 (2)	0	1 (5)
	Diagnosis (n, %)	15 (26)	9 (25)	6 (32)
	Prognosis/prediction (n, %)	1 (2)	0	0
	Patient management/ treatment planning (n, %)	1 (2)	0	1 (5)
	Monitoring (n, %)	2 (4)	2 (6)	0
	Multiple/ unclear (n, %)	10 (18)	7 (19)	2 (11)
Anatomic region	Cervical spine (n, %)	3 (5)	2 (6)	1 (5)
	Lumbar spine (n, %)	33 (58)	20 (56)	13 (68)
	Knee (n, %)	13 (23)	6 (17)	5 (26)
	Upper extremities (n, %)	2 (4)	2 (6)	0
	Lower extremities (other than knee) (n, %)	2 (4)	2 (6)	0
	Multiple regions (n, %)	4 (7)	4 (11)	0
	Reported adverse events	Yes (n, %)	10 (18)	5 (14)
	No (n, %)	47 (82)	31 (86)	14 (74)
Outcomes assessed	Accuracy outcomes (n, %)	14 (25)	9 (25)	4 (21)
	Impact on diagnostic thinking (n, %)	3 (5)	2 (6)	1 (5)
	Impact on treatment decisions (n, %)	1 (2)	0	1 (5)
	Impact on patients functional and clinical outcomes (n, %)	1 (2)	0	0
	Anatomic measurements/rater agreement/other/mixed (n, %)	38 (67)	25 (69)	13 (68)

NA= not applicable; NR=not reported; NRCS=nonrandomized comparative studies; y=years. Note that 2 studies belonging to category B are included in the “All studies” column but they were too few to tabulate separately.

^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%.

^b 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

^c The majority of these studies reported that “no funding was received.”

In summary, our evidence map showed that 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 many studies (approximately 50 percent) 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 percent) reported on clinically relevant outcomes. More details of these studies are described in following section.

Comparative Studies That Reported Clinical Diagnostic or Patient Outcomes

The most direct applicable study designs for clinical decisionmaking are studies that compare two or more diagnostic strategies, follow the patients through decision and treatment, and then report on patient outcomes. However, none of the comparative studies were in such design.

Of the 57 studies discussed above, 15 compared two diagnostic tests and reported either clinical diagnostic or patient outcomes.^{27,58,70,71,73,82,84-87,89,96,98,104,105} Of these, four compared open, positional, weight-bearing MRI in lumbar spine imaging with four different comparative tests^{27,70,82,84}; seven compared axially-loaded images of the lumbar spine with preloaded images in the same conventional MRI scanner;^{85,87,89,96,98,104,105} and four compared weight-bearing or stress-loading MRI with MRI without loading for diagnosis of extremity abnormalities.^{71,73,86} 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),^{82,87,89,98} and only one study reported changes in patient management based on additional information gained from axial loading MRI.¹⁰⁴ (Appendix E)

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 compared with conventional (non weight-bearing) MRI. However these studies did not report impact on treatment choice or patient outcomes.^{70,82,84} 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 myelography than during MRI and that more patients preferred MRI than myelography.⁸² However there was no data on whether diagnosis, treatment, or patient outcomes were affected.

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 that use of axially loaded MRI led to additional diagnoses or had impact on diagnostic thinking.^{85,87,89,96,98,104,105} One study also reported good surgical outcomes among patients whose hidden stenosis was disclosed by axial-loading MRI, but there was no control group for comparison.⁹⁸ 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.^{87,96,98,104,105} (see also Appendix D). At least two of the investigators in this group are the coinventors 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.^{71,73} 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.⁵⁸ The last, industry-funded, case-control study reported that loaded dynamic MRI produced significantly less missed diagnoses of patellofemoral joint abnormalities than did unloaded dynamic MRI.⁸⁶ However, no functional outcomes were reported to verify the importance of the imaging findings.

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 study's record on ClinicalTrials.gov indicates that data collection for the primary outcome measure was completed in February 2009, but we could not identify any related publication.

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, between 25 and 60 years old. 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 everyday activities in patients suffering from degenerative lumbar spinal stenosis after treatment using the Aperius PercLID device. The expected enrollment for this study is 163 subjects of both sexes older than age 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 ClinicalTrials.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.

Projected Uptake and Potential Growth

All KIs suggested that MRI under weight-bearing or stress-loading conditions is an actively growing research field. Several KIs indicated that this should be a key direction for future research for radiology in general. However, the majority of the studies conducted to date appear to be observational in design based on convenience samples of patients and healthy controls. Such studies are often not registered on ClinicalTrials.gov, and their results may not be generalizable to clinical settings. 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. The findings of our literature searches indicate that most studies of stress-loading MRI conducted to date pertain to the lumbar spine and the knee joint applications. 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), multipositional extremity MRI (mpExtremity MRI) that allows weight-bearing imaging of lower extremities in a standing position is being developed.¹⁰⁸ Our findings on dedicated extremity MRI scanners (summarized in Appendix F) indicate that this is a more mature imaging technology and suggest that a systematic review of the available literature may be feasible.

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 toward 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. We expand on these suggestions based on a proposed analytic framework in the Summary and Implications section of this report.

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 decisionmaking, 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.

Summary and Implications

Musculoskeletal disorders, particularly those of the back and knee, are a significant and growing source of pain and disability. The limitations of standard closed-bore magnetic resonance imaging (MRI) have created interest in combining stress-loading approaches with MRI technology to generate more clinically useful images. The set of possible features of emerging MRI technologies 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 technologies and summarized their theoretical advantages and disadvantages (Table 3).

Although the postulated advantages of stress-loading MRI seem promising, the diagnostic validity and clinical usefulness of stress-loading MRI in the management of musculoskeletal disorders is not clear. Clinician and insurance payer (both public and private) key informants (KIs) also expressed concerns regarding the clinical use of stress-loading MRI; current guidelines do not recommend the use of MRI under stress loading.¹¹² To date, only a few published studies compare stress-loading MRI with contemporary imaging alternatives, or report outcomes beyond anatomical changes (see the Evidence Map subsection of the Findings section of this report). 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.¹⁰⁹ 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 United States 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. Increasing use of conventional MRI has been associated with increased utilization of orthopedic surgical procedures, with unclear effects on patient outcomes. The apparent limited impact of MRI on patient outcomes may be due to the limited ability of MRI to discriminate between patients who require intervention and those who do not, as indicated by the high frequency of positive MRI exams on clinically asymptomatic patients.^{13,17,18,110-113} Currently, the published evidence on stress-loading MRI is inadequate to determine whether use of these devices will improve patient outcomes compared to conventional imaging techniques.

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 United States. However, according to KI feedback, stress-loading MRIs are rapidly evolving imaging modalities, and, given the rapid patterns of growth evident worldwide 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.^c

As shown in the Evidence Map subsection of the Findings section of this report, 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 unclear. We identified no randomized or nonrandomized 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 was identified by our literature searches. Box 1 summarizes the key decisionmaking uncertainties we identified regarding weight-bearing and stress-loading MRI.

Box 1. Key decisionmaking uncertainties for weight-bearing and stress-loading MRI

- ***Do the new features of emerging MRI technologies (such as stress loading, open configuration, and positioning) translate into improved diagnostic accuracy?***

The diagnostic accuracy of the available weight-bearing and stress-loading MRI methods has not been investigated in large, well-designed studies for any of the stress-loading devices we considered. Consequently, the validity of claims concerning the diagnostic superiority of stress loading over conventional MRI has not been tested.

- ***How do these technologies affect physicians’ diagnostic thinking or decisionmaking with regard to treatment, or patient outcomes?***

There is very little available evidence on how stress-loading MRI influences diagnostic or treatment decisions.

- ***Are there subgroups of patients (either in terms of disease or at a specific stage in the diagnostic process) for whom MRI under loading stress would be indicated?***

It is currently unclear if these technologies have higher diagnostic accuracy or improve outcomes among specific subgroups of patients.

- ***What is the clinical setting where such imaging would be most beneficial?***

Based on studies conducted to date, the clinical setting where stress-loading MRI would have maximal utility remains undefined.

- ***What are the consequences of false positive or negative findings?***

Given the absence of well-designed studies linking diagnostic testing with patient outcomes, it is difficult to estimate potential harms from over-treatment or missed diagnoses.

- ***What is the cost-effectiveness of these methods?***

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 and methodological limitations of existing studies. Modeling may be more informative after additional data on diagnostic validity become available.

^cFor example, see <http://www.fonar.com/news/072110.htm> and http://www.dynawell.biz/spinalinfo_conditions.htm (section on sciatica), both accessed on October 11, 2010)

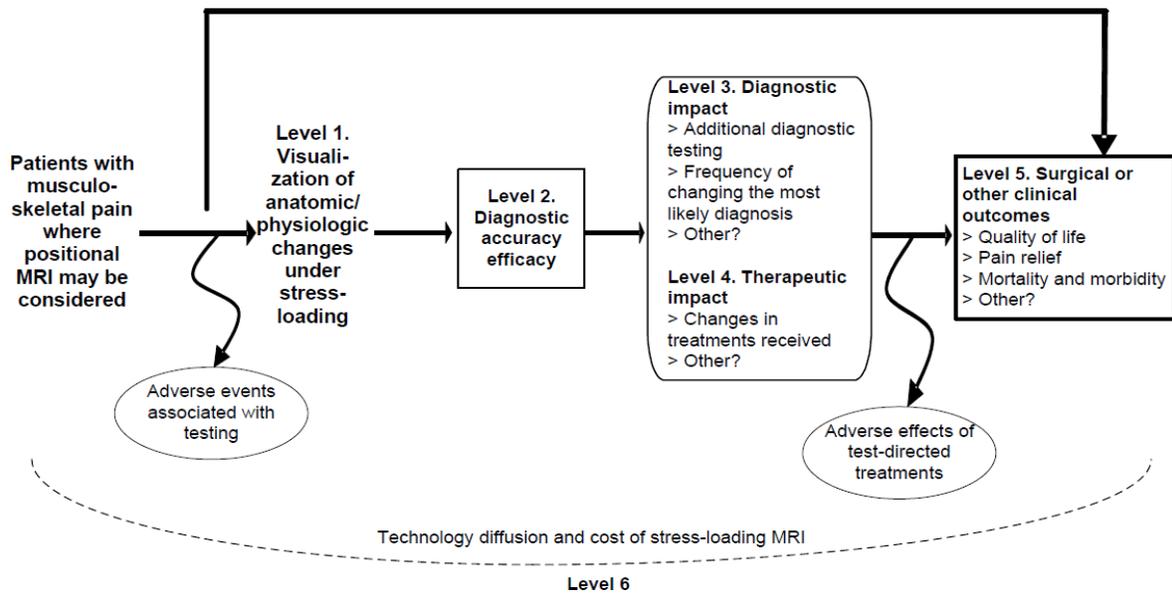
Next Steps

Conceptual Framework for Future Research and Policy

In this Technical Brief, we have organized emerging magnetic resonance imaging (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 the proposed classification scheme is based on three device features (open-bore design, patient positioning and imaging under loading stress), it should be noted that additional features, such as the ability to obtain dynamic/kinematic imaging or the device field strength, could 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 subclassify uses of simulated gravity.

Regardless of any special features of each specific diagnostic technology, the assessment of diagnostic tests typically follows a stepwise approach,¹¹⁴ 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 6). In the next section, we discuss specific approaches to future research, broadly following this scheme.

Figure 6. Application of the conceptual framework proposed by Fryback et al. for evaluating the efficacy of diagnostic imaging for researchers and policymakers³⁰



In this framework, patients undergoing MRI imaging with novel technologies may experience adverse events associated with the imaging process and (potentially) obtain additional diagnostic/prognostic/ monitoring information from the imaging performed under stress loading. This information may impact diagnostic or therapeutic thinking. Test-directed therapies impact patient outcomes directly, including pain and other clinical symptoms, quality of life, and clinical events. Overall, the impact of imaging under stress-loading on the healthcare system can be captured by assessing the cost-effectiveness of integrating these tests into clinical practice.

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

- Addressing the methodological issues in study design and analysis that are prevalent in the existing literature so that future studies can better evaluate the reliability and diagnostic accuracy of novel MRI technologies. (Fryback Levels 1 and 2).
- Assessing the impact on diagnostic thinking and therapeutic decision making of stress-loading MRI technologies using clinically relevant patient outcomes (Fryback Levels 3 and 4).
- Assessing impact of the most promising of these technologies on patient outcomes through prospective observational studies or RCTs. (Fryback Level 5).
- Creating special procedure codes for imaging using different MRI devices that will facilitate future research and policy decisions regarding these technologies.

These suggestions are expounded upon in further detail below.

Methodological Considerations for Future Studies of Diagnostic Accuracy

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 crosscutting 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 7). Adherence to these principles would facilitate the assessment of the reliability and clinical accuracy of the different imaging modalities.

Table 7. Common methodological issues and proposed solutions

Limitations in the existing evidence base	Proposed solutions
<i>Epidemiological issues</i>	
Case-control designs were often used to assess the ability of devices to identify differences between affected and unaffected individuals.	Although case-control designs are appropriate for identifying anatomic or physiologic differences between disease and healthy individuals, they have been shown to result in biased estimates of diagnostic accuracy. ¹¹⁵ Studies assessing diagnostic accuracy should instead aim to enroll patients representative of the spectrum of disease typically seen in clinical practice.
Detailed inclusion and exclusion criteria were not reported in the majority of studies. This was particularly evident regarding the selection of “healthy control individuals.”	When a case-control design is appropriate, 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. ¹¹⁶ Future studies should provide details about the study base and sampling methods employed to select cases and controls.
Details of the study design were often not reported.	General principles for the design of studies of imaging tests include the use of an appropriate reference standard, adequate description of the index and reference tests, blinded interpretation of test results, and independence of the index and reference standard tests. ¹¹⁷
Sample sizes were typically small (median number of cases: 26, 25th-75th percentile: 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. ¹¹⁶
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. ¹¹⁸
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. ^{117,119}
<i>Analytical aspects</i>	
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 or other correlated data-analysis methods, employed. ^{93,95}
Sample size determination was rarely based on prospective power calculations. ¹¹⁶	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.

Table 7. Common methodological issues and proposed solutions (continued)

Limitations in the existing evidence base	Proposed solutions
<p>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.¹²⁰⁻¹²³</p> <p>When comparing measurements or clinical findings obtained using different MRI devices, correlation or regression methods were often used to demonstrate “congruence” between technologies. Correlation and regression are inappropriate for assessing agreement between measurements.¹²⁴</p>	<p>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.¹²⁴⁻¹²⁶</p>
<p>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, that is, 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.</p>	<p>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.^{121,122,127,128}</p>

Assessing Impact on Diagnostic Thinking and Therapeutic Decisionmaking

Assessing the impact of imaging tests on diagnostic thinking and therapeutic decisionmaking is vital as this information allows direct inference on the effects of diagnostic tests on patient outcomes. Commonly used methods for assessing this impact are 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. More rigorous approaches are to assess the extent to which new information (from the diagnostic test) modifies the physician’s perception of a specific clinical case. For example, one can compare the diversity in the probability distribution of potential diagnoses before and after test information is obtained (i.e. quantify the change in entropy of the probability distribution of differential diagnoses induced by the test information). A good test allows clinicians to “narrow down” the diagnostic possibilities (i.e., reduce the diversity in the distribution of differential diagnoses).¹²⁹ 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.¹³⁰ 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.

Assessing Impact on Patient Outcomes in Observational Studies and RCTs

Ultimately, we need to know whether the use of a particular diagnostic test results in better outcomes for patients. The most internally valid evidence regarding the impact of a diagnostic test on patient outcomes 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, they may not be the best initial strategy in this case.¹³¹ A test affects patient outcomes mainly by influencing diagnostic thinking and therapeutic choices.¹³² 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).¹³² 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. However, a staged approach using observational studies to identify the best most promising technologies, may be possible.^{132,133} 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 (or comparing alternative tests) is necessary or whether the test can be implemented with no further study. This decision mainly depends on the relative accuracy of the diagnostic tests of interest and the availability of effective treatments for patients with an established disease diagnosis.¹³³ Lord et al. have proposed a framework for diagnostic test evaluation both by primary research studies and by systematic Technology Assessments.¹³² In addition to these methods, decision modeling methods can be used to evaluate the potential long-term impact of diagnostic tests on clinical outcomes.^{134,135}

With these considerations in mind, the most practical research strategy may be to explore the diagnostic accuracy (sensitivity and specificity) of different weight-bearing and stress-loading MRI approaches in well-designed cohort or case-control studies. An appropriate reference standard, such as surgical findings or myelography, may be available in some cases but require the patient to undergo invasive procedures. In other cases where a gold standard is lacking, specialized statistical methods can be used as described above. To be clinically useful and informative, observational studies should enroll patients representative of those seen in clinical practice, and limit verification and other biases.^{136,137} 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 only randomizing patients for whom conventional and emerging MRI technologies suggest different diagnoses (i.e., patients with discrepant imaging findings), should be considered.¹³⁶

Creating Separate Procedure Codes for Special MRI Procedures

Based on our searches of the grey literature and KI input, there appears to be no special procedure code for stress-loading MRI, and at least in some cases, stress-loading MRI may have been associated with increased health care costs (due to multiple billings for the same imaging

session). It is possible that separate procedure codes may increase transparency and allow better monitoring of the MRI examinations performed. Separate procedure codes would also facilitate future population-level research on the clinical use of stress-loading MRIs.

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Appendix A. Search Strategy

We present here our search strategy (appropriate for Ovid MEDLINE) for studies of MRI under stress loading. We used a composite search strategy combining methodological terms for studies of diagnostic tests, MRI imaging and the diseases of interest (musculoskeletal disorders).

1. exp Magnetic Resonance Imaging/
2. ("Magnetic Resonance Imaging" or "MRI").tw.
3. 1 or 2
4. ("dynamic" or "vertical" or "upright" or "stand*" or "seat*" or "open" or "position*" or "weight bearing").tw. or (("axial\$" and "load\$") or ("extremity specific" or "dedicated")).tw.
5. 3 and 4
6. limit 5 to yr="1975 -Current"
7. limit 6 to (english language and humans)
8. exp "sensitivity and specificity"/
9. exp Predictive Value of Tests/
10. exp ROC CURVE/
11. exp Mass Screening/
12. exp diagnosis/
13. exp REPRODUCIBILITY OF RESULTS/
14. exp false negative reactions/ or false positive reactions/
15. predictive value.tw.
16. (sensitivity or specificity).tw.
17. accuracy.tw.
18. screen\$.tw.
19. diagno\$.tw.
20. roc.tw.
21. reproducib\$.tw.
22. (false positive or false negative).tw.
23. likelihood ratio.tw.
24. di.fs.
25. or/8-24
26. (cf or bl or ra or ri or us or en).fs.
27. 25 or 26
28. 7 and 27
29. limit 28 to (addresses or bibliography or biography or case reports or comment or dictionary or directory or duplicate publication or editorial or guideline or in vitro or interview or lectures or legal cases or letter or news or newspaper article or "review")
30. 28 not 29
31. exp Cervical Vertebrae/
32. ("cervical myelopathy" or "cervical spine" or "cervical spondylotic myelopathy" or "Dural sac" or "Facet" or "Herniation" or "instability" or "intervertebral disc").tw.
33. exp Intervertebral Disk Displacement/
34. exp Intervertebral Disk/
35. ("kyphosis" or "lordosis" or "low* back").tw.
36. exp Low Back Pain/

37. ("lumbar" or "lumbar stenosis").tw.
38. exp Lumbar Vertebrae/
39. exp Neck Pain/
40. exp Neck/
41. ("neck" or "radicul*").tw.
42. exp Radiculopathy/
43. exp Sciatica/
44. sciatica.tw.
45. (scoliosis or spinal).tw.
46. exp Spinal Curvatures/
47. spinal osteophytosis/ or spinal stenosis/ or spondylolisthesis/ or thoracic vertebrae/ or whiplash injuries/
48. ("spinal stenosis" or "spine" or "spondylolisthesis" or "spondylosis").tw.
49. exp Joints/
50. ("foot" or "feet" or "knee*" or "hip\$" or "TMJ" or "temporomandibular" or "shoulder*" or "elbow" or "wrist*" or "hand\$").tw.
51. or/31-50
54. 30 and 51

Appendix B. Data Extraction Form

Data Extraction Form -- Positional MRI Technical Brief

Note: enter “-9 or -99” if no numeric data available; enter “nd” if no text data available

<IDNUM>

Extractor. _____

Author. (last name of the first author)

Year. ####

UI. ##### [Can be found in excel tracking sheet]

Reject. <Y> [Please make sure article fit our inclusion criteria BEFORE extraction]

rejectreason. _____ [Rejection reason]

Comments1.

Comments2.

Comments3.

Comments4.

Where was this study conducted?

US. US <Y>

NonUS. non-US <Y>

funding. Was funding source of the study reported? <Y> If no, skip the following question.

industryfund. Was any part of study funded by device industry? <Y>

Study Population?

StudyPop1. Suspected degenerative spondylolisthesis <Y>

StudyPop2. Suspected spinal stenosis: moderate or severe central stenosis <Y>
and lateral recess stenosis (displacing or compressing nerve root, disc extrusion)

StudyPop3. Radicular pain: moderate or severe central stenosis, lateral recess stenosis, <Y>
nerve root compression, and disc extrusion

StudyPop4. Non-specific spine pain: moderate or severe central stenosis, <Y>
lateral recess stenosis, nerve root compression, and disc extrusion

StudyPop5. Extra-spinal joint pain or function loss: e.g. narrowing <Y>
or musculoskeletal only

StudyPop6. Healthy volunteer <Y>

if other, described:

StudyPopOther. _____

Study population that may introduce bias (e.g. subject excluded based on: incomplete test results,

incomplete data, test unclear) describe reasons,

Populationbias1. _____

Populationbias2. _____

Populationbias3. _____

Populationbias4. _____

Study Design (Based on Dx test study purpose. Note that it may differ from original study design.)

RCT. parallel <Y>

NRCS. [Non Randomized Comparative Study] <Y>

Crossover. <Y>

CaseControl. <Y>

Longitudinal. <Y>

Crosssectional. <Y>

NoData. <Y>

FollowUPNA. Study design applicable for follow-up? <Y> [Note: cross-sectional and case-control design are not applicable for follow-up in Dx Test setting]

If yes, please enter the follow-up duration:

FollowUP. ### weeks - [calculation: (number of months * 30) / 7]

ProsandRetros. ##

1) Prospective

2) Retrospective

3) Not Applicable (e.g. cross-sectional or case-control)

-9) No data

Multicenter?. ##

1) Multicenter

2) Single center

-9) No data

Classification. [select one of these criteria] ##

1) Feasibility (no comparator - a group of patients get just one test)

2) Screening (use of the test to identify disease in the absence of clinical symptoms)

3) Diagnosis (use of the test to determine the presence and type of structural or functional abnormalities in the presence of clinical symptoms)

4) Prognosis/prediction (use of the test to predict response to treatment or natural course of the disease)

5) Patient management / treatment plan (use of the test to determine the management plan, including selection of treatment)

6) Monitoring (assessing response to treatment or relapse after therapy)

7) if unclear or multi-classifications were selected (please separate the selections with comma), describe:

ClassificationOther.

ExamLocation. reported (Joint or body part)? <Y>

Cervical. <Y>

Thoracic. <Y>

Lumbar. <Y>

Pelvic. (Coccyx or Sacral) <Y>

Knee. <Y>

Lowerextremities. (other than knees) <Y>

Upperextremities. <Y>

ExamLocOther. [other exam location] <Y> ExamLocSpec. [specify other exam location]

Adverse Events

AEreported.-- Are Adverse Events related to the test reported? <Y>

if YES specify:

AE1.

AE2.

AE3.

AE4.

Outcomes

Outcomes. ##

1) Diagnostic test performance (e.g., sensitivity and specificity, or accuracy), if selected please describe what was the “reference standard” used below:

RefStd.

[Note: a “reference standard” is what investigator considered to be the reference for a diagnosis

2) Impact on diagnostic thinking

3) Impact on treatment decisions

4) Impact on patients’ clinical and functional outcomes

5) Patient’s preference

6) If unclear or multi-outcomes were selected (please separate the selections with comma), describe:

OutcomeUnclear.

Except for feasibility studies, please describe briefly the comparisons (e.g. weight-bearing vs. not weight-bearing position in Upright MRI,

Upright MRI vs. axial loading in conventional MRI, ranges of motion before and after surgery evaluated by Upright MRI in weight-bearing position):

comparison1:

comparison2:

comparison3:

comparison4:

====The following section is for population characteristics=====

!!INSTRUCTION: If case-control study, enter cases' characteristics here in this section. The controls' characteristics should be entered in a duplicate section at the end of this data extraction form. For all other designs, enter the characteristics for TOTAL population here.

Male. (%) ###

Agemean. Mean age (yr) ###.# AgemeanSD. Age Mean SD ##.# [to convert SE to SD use the following formula:

$$SE=SD \text{ divided by square root of } N]$$

Agemedian. Median age (yr) ###

Agerangefrom. ### Agerangeto. ### [age range]

weightinfo. Were weight or BMI data reported? <Y>

if yes, please describe (report the mean BMI or just a description such as "obese" patients obese.

RaceReported. Was race/ethnicity of study population reported? <Y>

Hispanic. (%) ###

Caucasian. (%) ###

AfricanAmerican. (%) ###

Asian. (%) ###

NativeAmerican. (%) ###

Other. (%) ###

NKRefused. (%) ### [Don't know or refused]

PatientSymptoms. ## [Patient Symptoms Asymptomatic and Symptomatic as reported by the study author]

1) Asymptomatic.

2) Symptomatic.

3) BothSymp. [Note: if 'both symptoms' was selected, please report proportion of symptomatic subjects (%) below]

SymptomProportion. ##

-9) Nodata.

NEnrolled. ##### [Number of subjects enrolled]

AnalyzedSubjects. ##### AnalyzedLesion. ##### [Note: please report the number of subject/lesion at the last time point]

EnrollStartDate. (mm/yyyy) _____ EnrollEndDate. (mm/yyyy) _____ [Note: enter "nd" if no data]

====The following section is for test characteristics=====

!!IMPORTANT: Tests includes non-imaging tests, such as clinical examination or other chemical testing. Studies MUST have positional MRI test to be included.

CompareTests. Was the study comparing two Dx tests? <Y> [Definition: A study where diagnostic classification is

obtained using at least two different tests (one of which fulfils the definition of "weight bearing positional MRI") in the same physiological condition]

[Note: In this data extraction form, we are only collecting brief characteristics of positional MRI.

If a true comparative study, detailed technical specifications of the tests will be collected in a separate form.]

Following questions are positional MRI (i.e., weight bearing or simulating weight bearing MRI)

pMRIName. _____

[Note: name verbatim as reported by the researchers]

pMRIManufacture. _____ [Note: enter "nd" if no data]

pMRIdevicemodel. _____ [Note: enter "nd" if no data]

pMRIMagneticStrength. [Magnetic Field Strength] ##.# (T)

pMRIT1coil. [Coil used]

__ [Note: verbatim as reported by the researchers]

pMRI Position

pMRIstanding. <Y> (if YES specify: e=extension, f=flexion, n=neutral, r=rotation)

pMRIstandingSpec. _____ (Note: please separate the selections with a comma)

pMRISitting. <Y> (if YES specify: e=extension, f=flexion, n=neutral, r=rotation)

pMRISittingSpec. _____ (Note: please separate the selections with a comma)

pMRIAxialLoad. [Axial load] <Y> If yes, please describe the axial loading device below:

ALname.

__ [Note: name and manufacturer. If custom made device,
please verbatim as reported by the researchers]

ALforce. [Force of axial load]

__ [Note: usually reported as % body weight]

pMRIlength. [length of exam] ##### Minutes

pMRIcomment1.

__ [Comments on positional MRI test]

pMRIcomment2.

__ [Comments on positional MRI test]

=====
=====The following section is for controls' characteristics in case-control study=====

!!INSTRUCTION: Only use this section to enter controls' characteristics For all other designs, do not use this section.

ctrl. What was the control population?

ctrlselect. How was the controls selected?

[Note: enter "nd" if no data]

ctrlMale. (%) ### [for total population]

ctrlAgemean. Mean age (yr) ###.# ctrlAgemeanSD. Age Mean SD ##.# [to convert SE to SD use the following formula:

$$SD=SE \text{ divided by square root of } N]$$

ctrlAgedmedian. Median age (yr) ###

ctrlAgerangefrom. ### ctrlAgerangeto. ### [controls' age range]

ctrlweightinfo. Were weight or BMI data reported? <Y>

if yes, please describe (report the mean BMI or just a description such as "obese" patients
ctrlobese.

ctrlRaceReported. Was race/ethnicity of study population reported? <Y>

ctrlHispanic. (%) ### [Hispanic]

ctrlCaucasian. (%) ### [Caucasian]

ctrlAfricanAmerican. (%) ### [AfricanAmerican]

ctrlAsian. (%) ### [Asian]

ctrlNativeAmerican. (%) ### [NativeAmerican]

ctrlOther. (%) ### [Other race/ethnicity]

ctrlNKRefused. (%) ### [Don't know or refused]

ctrlPatientSymptoms. ## [Symptoms Asymptomatic and Symptomatic as reported by the study author]

1) Asymptomatic.

2) Symptomatic.

3) BothSymp. [Note: if 'both symptoms' was selected, please report proportion of symptomatic subjects (%) below]

ctrlSymptomProportion. ##

-9) Nodata.

ctrlNEnrolled. ##### [Number of controls enrolled]

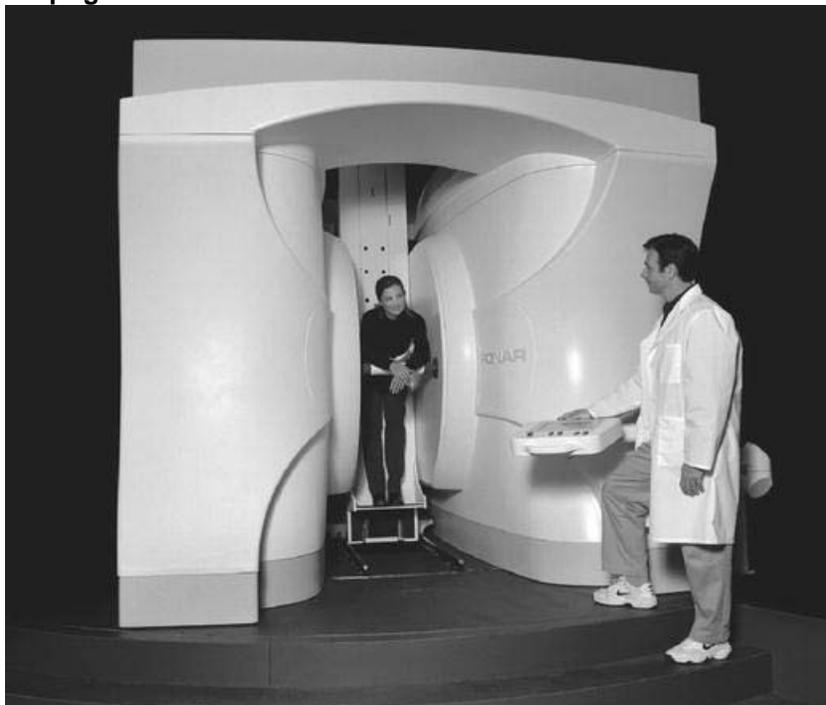
ctrlAnalyzedSubjects. ##### ctrlAnalyzedLesion. ##### [Note: please report the number of subject/lesion at the last time point]

ctrlEnrollStartDate. (mm/yyyy) _____ ctrlEnrollEndDate. (mm/yyyy) _____ [Note: enter "nd" if no data]

Appendix C. Examples of Commercially Available Devices That Allow MRI Under Weight-Bearing or Stress-Loading Conditions

Please note that permissions have been obtained to reproduce the following photographs. Sources for each photograph are listed in the respective figure legend.

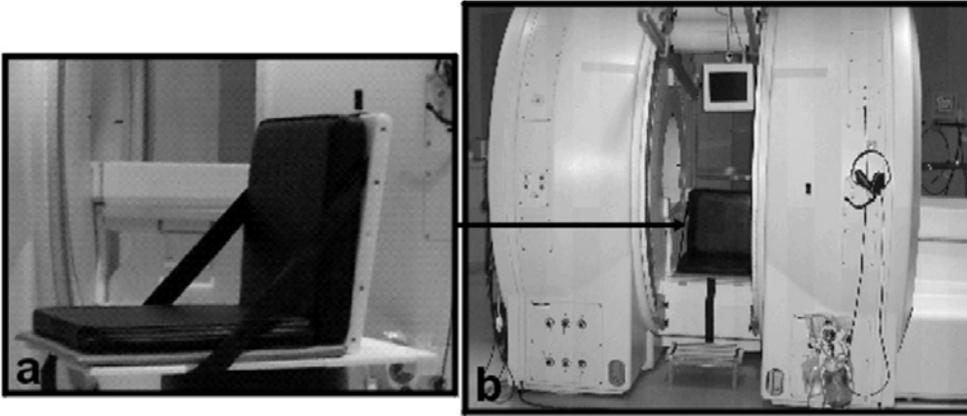
a. Upright® MRI



The FONAR Upright multipositional MRI allows positional (flexion, extension), weight-bearing (upright and sitting) imaging and has an open configuration (the patient does not enter a closed bore). The device has a 0.6 T horizontal field generated between two resistive magnets. A tilting table placed at right angles between these coils can be positioned at any angle from -20 to 90 degree (vertical), allowing supine and standing imaging. An MRI compatible seat can be added for imaging in a sitting position. Extension is achieved by positioning of a small cylindrical cushion just above the lumbrosacral junction. Flexion is achieved by leaning forward over a wedge-shaped cushion and supporting the hands on a horizontal bar (as shown in the photograph).

Source: Jinkins JR, Dworkin JS, Damadian RV. Upright, weight-bearing, dynamic-kinetic MRI of the spine: initial results. *Eur Radiol* 2005 Sep;15(9):1815-25. Epub 2005 May 20. Reproduced with permission from the publisher (Springer).

b. Signa SP/i



The Signa SP/i system was originally intended for use in interventional procedures as it allowed physician access to the patient while in the MRI field. The MRI system is characterized by two vertically oriented, doughnut-shaped superconducting magnetic coils. Several investigators have modified the scanner to allow imaging of the patient in different positions (flexion, extension), weight bearing (upright, sitting, or in other weight-bearing positions) and (because of the 56 cm vertical gap between the two magnet poles) can also be considered an open system. The photograph demonstrates the placement of an MRI-compatible chair (panel **a**) between the magnetic coils (arrow in panel **b**). Note: the device is no longer manufactured or sold by GE Healthcare in the US.

Source: Hébert LJ, Moffet H, Dufour M, Moisan C. Acromiohumeral distance in a seated position in persons with impingement syndrome. *J Magn Reson Imaging* 2003 Jul;18(1):72-9. Reproduced with permission from the publisher (John Wiley and Sons).

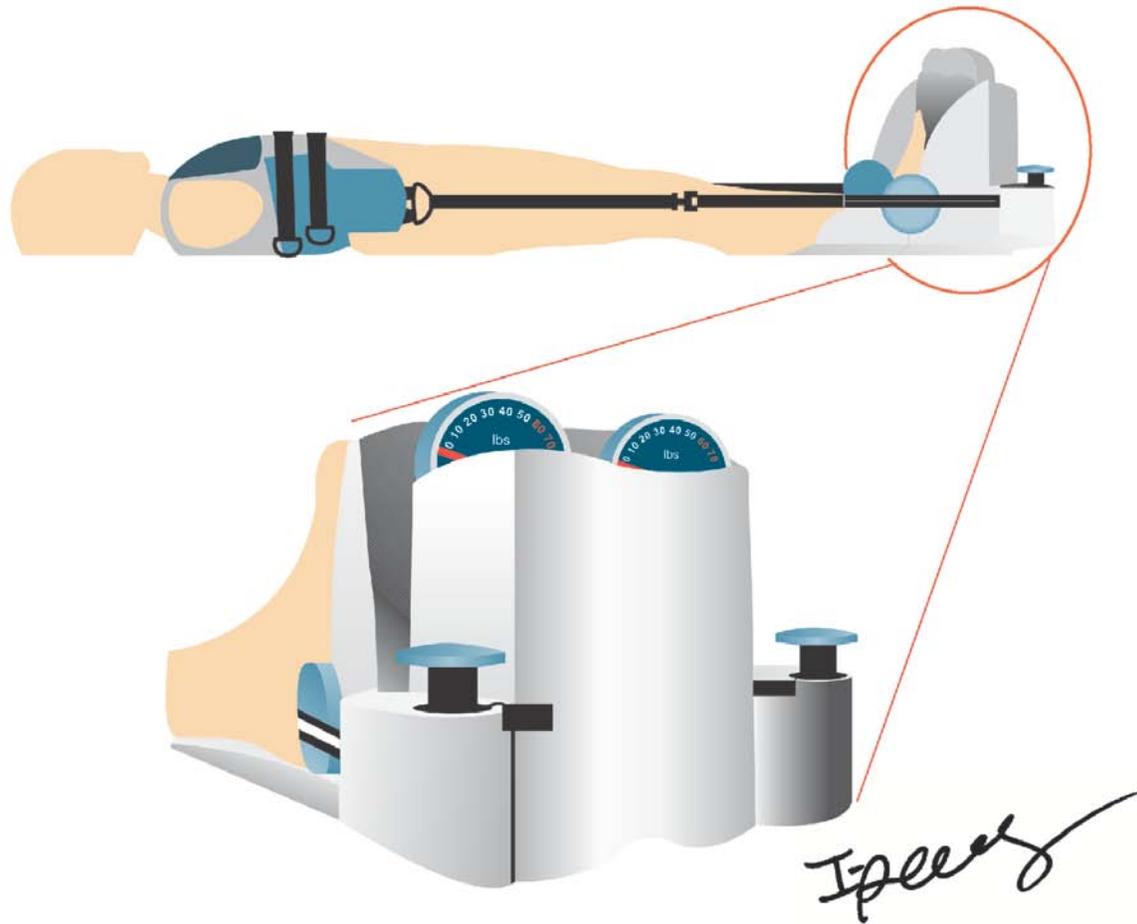
c. G-scan®



G-Scan (Esaote SpA, Genoa, Italy) has an open and tilting design and can perform scan in the supine position and in the upright weight-bearing position. Another unique feature is “Instant positioning.” Once the patient has been positioned on the table, just press the button of the joint under investigation which automatically moves the patient and coil in the isocenter. Note this device can image any body area (in this case, the feet).

Source: Sutura R, Iovane A, Sorrentino F, Candela F, Mularo V, La Tona G, Midiri M. Plantar fascia evaluation with a dedicated magnetic resonance scanner in weight-bearing position: our experience in patients with plantar fasciitis and in healthy volunteers. *Radiol Med* 2010 Mar;115(2):246-60. Epub 2010 Feb 22. Reproduced with permission from the publisher (Springer).

d. DynaWell L-spine



Simplified schematic modeled on the DynaWell L-spine device. The device consists of a harness attached to a nonmagnetic compression part by nylon straps which are tightened to axially load the lumbar spine. By tightening or loosening the adjustment knobs on the foot plates, the load can be regulated and equally distributed on the legs.

Overlap between author lists in included studies. Each publication is represented by an ellipse. Studies sharing at least one author are depicted as a group of ellipses linked amongst themselves with lines. Refer to the Methods Section for a description of how the graph was generated.

Appendix E. Comparative Studies of Diagnostic Tests

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/ range], yr (% male)	Weight-bearing MRI • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration	Comparator test	Outcomes	Main findings	Funding Comments
Lumbar spine imaging with open, positional MRI							
Vitzthum 2000 ¹ [10879759] Germany nd nd	50 (patients); 50 (healthy controls) Cases: Lumbar disc herniation (82%), lateral osteogenic recess stenosis (10%); degenerative spondylolithesis (8%) Controls: healthy volunteers Sampling not described.	Patients: 53 [34 to 71] (60) Controls: 24.5 [3.4] (56)	Open, interventional MRI • Open MRI • Signa SP (GE) • 0.5 T • nd • Sitting • Neutral, extension, flexion, rotation (dynamic) • Vertically open	Prior MRI finding: decompression of the lumbar nerve roots, which correlated with clinical symptoms	• Impact on diagnostic thinking • Functional patterns based on dynamic exam of flexion-extension, compared to results obtained in healthy controls	• In 32 (64%) patients dynamic exam of flexion-extension contributed important additional information to the preliminary diagnosis. • Patients had characteristics of a Type I functional pattern.	Nonindustry How controls were selected were not described
Weishaupt, 2000 ² [10751495] Switzerland Single nd	36 (30 analyzed) Recruited after MRI of lumbar spine. Low back pain or leg pain for >6 weeks, unresponsiveness to a trial of nonsurgical treatment, surgery not indicated or not urgent on the basis of clinical findings. Sampling not described.	38 [20 to 50] (57)	Open, interventional MRI • Positional MRI • Signa Advanced SP (GE) • 0.5 T • Flexible transmit-receive wraparound surface coil • Sitting • Extension, flexion (static) • Vertically open	cMRI • cMRI • Impact Expert (Seimen) • 1.0 T • Dedicated receive-only spinal coil • None • Supine neutral • Closed	• Diagnosis of disk abnormalities • Impact on diagnostic thinking • Pain assessment: a visual analogue scale was used for assessing pain intensity	• Diagnoses in supine position (cMRI) changed in 4 disks (5%) in seated flexion, and in 7 disks (9%) in seated extension. • Positional pain differences are related to position-dependent changes in foraminal size.	nd

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/ range], yr (% male)	Weight-bearing MRI <ul style="list-style-type: none"> • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration 	Comparator test	Outcomes	Main findings	Funding Comments
Wildermuth, 1998 ³ [9577486] Switzerland Single nd	30 Patients referred for lumbar myelography and agreeing to undergo MR imaging with an open system in another institute Consecutive	58 [27 to 84] (43)	Open, interventional MRI <ul style="list-style-type: none"> • Open MRI • Advantage SP (GE) • 0.5 T • Transmit-receive wraparound surface coil • Sitting • Extension, flexion (static) • Vertically open 	Lumbar myelography Radiographs were obtained with fluoroscopic guidance in the lateral decubitus, prone, and left and right posteroanterior oblique projections. Upright anteroposterior and lateral images were then obtained at flexion and extension.	<ul style="list-style-type: none"> • Patient preferences and anxiety during imaging • Correlation between MRI and myelographic measurements 	<ul style="list-style-type: none"> • More patients reported anxiety during myelography than during MRI, and more patients preferred MRI than myelography. • Myelography and positional MRI are comparable for quantitative assessment of sagittal dural sac diameters. 	Nonindustry 17% patients could not be contacted for preferences and anxiety outcomes.
Zou, 2008 ⁴ [18317181] US nd 2005 to 2006	533 Patients with symptomatic back pain with/without radiculopathy Selection criteria and sampling were not described.	46.2 [18 to 76] (42)	Kinetic, upright MRI in extension or flexion position <ul style="list-style-type: none"> • Upright multiposition MRI • Upright (Fonar) • 0.6 T • Quad channel planar coil • Standing • Extension, flexion (static) • Vertically open 	Kinetic, upright MRI in neutral position <ul style="list-style-type: none"> • Upright multiposition MRI • Upright (Fonar) • 0.6 T • Quad channel planar coil • Standing • Neutral • Vertically open 	Missed diagnosis of lumbar disc herniations, comparing flexion or extension to neutral position: the extent of lumbar disc bulges in neutral, flexed, and extended views were graded by 2 spine surgeons independently without knowing the patients' history and clinical findings.	19.4%, 13.3% 10.6%, and 9.1% missed diagnosis of a disc herniation in patients with grade 1 (0-3 mm), grade 2 (3-5 mm), grade 3 (5-7 mm), and grade 4 (7-9 mm) of lumbar disc bulges, respectively.	Nonindustry Missed diagnosis rates were calculated based on the number of lumbar discs

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/ range], yr (% male)	Weight-bearing MRI • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration	Comparator test	Outcomes	Main findings	Funding Comments
Lumbar spine imaging with axial-loading MRI							
Danielson, 1998 ⁵ [9817029] Sweden Single 1994 to 1996	34 Clinically suspected lumbar spinal canal narrowing which resulted in sciatica and/or neurogenic claudication Sampling was not described.	50 [25 to 71] (53)	cMRI with axial loading • cMRI with axial loading • Magnetom Impact (Siemens) • 1.0 T • Surface coil • Custom-made axial loading compression device ^a (300-400 Newtons or ~50% BW) • Axial loading of the lumbar spine in extension • Closed	Preloaded cMRI exam • cMRI (before axial loading) • Magnetom Impact (Siemens) • 1.0 T • Surface coil • None • PRP • Closed	• Diagnosis of recess and foraminal stenosis: a reduction in the space available to the nerve roots (recess <3 mm) in combination with loss of epidural fat • Pain during axial loading	• 7 patients (21%) had low back pain and 10 (29%) had leg pain in axial loading of the lumbar spine in extension (ACE) • 1 recess stenosis was found in 12 patients and a foraminal stenosis was seen in 1 patients. • 5 of the patients with leg pain in ACE had a disc herniation and 6 had a recess stenosis.	Industry Post hoc exclusion of patients from most of the analyses Based on the enrollment years and data presented in the table, patients were overlapped with Willen, 1997 and Willen, 2001

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/ range], yr (% male)	Weight-bearing MRI <ul style="list-style-type: none"> • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration 	Comparator test	Outcomes	Main findings	Funding Comments
Hiwatashi, 2004 ⁶ [14970014] Sweden Single nd	20 Patients with signs and symptoms of spinal stenosis; with detected appreciable difference in the caliber of the dural sac on the routine and the axially loaded MRI. Sampling was not described.	54 [32 to 75] (70)	cMRI with axial loading <ul style="list-style-type: none"> • cMRI with axial loading • nd • 1.0 T • Surface coil • DynaWell L-Spine: 50% BW • Axial loading of the lumbar spine in extension • Closed 	Preloaded cMRI exam <ul style="list-style-type: none"> • cMRI (before axial loading) • nd • 1.0 T • Surface coil • None • PRP • Closed 	<ul style="list-style-type: none"> • Additional information gained from the axially loaded images • Changes in treatment decisions based on preloaded cMRI, axial loading MRI, and patients' clinical history: decisions were made by 3 experienced neurosurgeons (who are also the coauthors of this paper) 	Additional information gained from axial loading during MRI of the lumbar portion of the spine changed neurosurgeons' treatment decision from conservative management to decompressive surgery for 5 (25%) patients.	nd Retrospective secondary database analyses. Selection of patients based on the MRI findings. Danielson was the 2 nd author.
Huang, 2009 ⁷ [19526378] Taiwan nd nd	32 (29 analyzed) Patients with diagnoses of degenerative L4-L5 spondylolisthesis, grade 1 or 2 slippage. Patients with degenerative scoliosis were excluded. Consecutive	nd (19)	cMRI with axial loading <ul style="list-style-type: none"> • cMRI with axial loading • Signa Cvi (Siemens) • 1.5 T • Phase array spinal coil • DynaWell: 50% BW • Supine in extension • Closed 	Preloaded cMRI exam <ul style="list-style-type: none"> • Preloaded MRI exam • Signa Cvi (Siemens) • 1.5 T • Phase array spinal coil • None • Supine • Closed 	<ul style="list-style-type: none"> • Disability: Oswestry Disability Index (ODI) • Physical functioning: Physical Function (PF) scale 	After adjustment for sex and age, significant associations were found between ODI, PF and the difference of segmental angulation, and the PF and the post-loaded lumbar lordotic angles (p=0.02)	Nonindustry Patients were excluded from the study after axial loading due to intolerable back pain, numbness or sciatica

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/ range], yr (% male)	Weight-bearing MRI <ul style="list-style-type: none"> • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration 	Comparator test	Outcomes	Main findings	Funding Comments
Manenti, 2003 ⁸ [14598603] Italy nd nd	50 (patients); 43 (healthy controls) Patients with a history of chronic lumbar pain and recurrent movement-induced painful blockages. Healthy controls were selected by matching weight, age, sex and job	Patients: 46 [19] (56) Controls: matching age and sex	cMRI with axial loading <ul style="list-style-type: none"> • Axial loading MRI • Gyroscan Intera (Phillips) • 1.5 T • Flexible surface coil • Axial compressor (MIKAI manufacturing, Genoa, Italy): 65% BW • Supine in extension • Closed 	Preloaded cMRI exam <ul style="list-style-type: none"> • Neutral unloaded routine MRI • Gyroscan Intera (Phillips) • 1.5 T • Flexible surface coil • None • PRP • Closed 	Diagnosis of discal degeneration or protrusion: 3 radiologists evaluated the mages through the compilation of an apposite questionnaire on the modifications occurring from the neutral to the loaded acquisitions.	Relative to the control group, 43 patients were studied for a total of 129 discal levels. 31 presented discal degeneration at 56 (43%) of the studied discal levels. Diagnosis of discal protrusion was made at 19 discal levels in 12 patients.	Nonindustry
Willen, 1997 ⁹ [9431634] Sweden Single 1994 to 1995	34 (80 sites) Patients selection criteria were not described. Sampling was not described.	53 [25 to 74] (53)	cMRI with axial loading <ul style="list-style-type: none"> • cMRI with axial loading • Magnetom Impact (Siemens) • 1.0 T • Surface coil • Custom-made axial loading harness^a (~50% BW) • Axial loading of the lumbar spine in extension • Closed 	Preloaded cMRI exam <ul style="list-style-type: none"> • cMRI (before axial loading) • Magnetom Impact (Siemens) • 1.0 T • Surface coil • None • PRP • Closed 	Diagnosis of disc abnormalities (e.g., disc herniation, lateral recess or foraminal stenosis, or a intraspinal synovial cyst at PRP changing to obvious manifestation at ACE)	<ul style="list-style-type: none"> • In 11 patients (16 sites), stenosis was found in one or two sites. • Narrowing of the lateral recess was noted in 13 sites. 	nd Post hoc exclusion of patients from most of the analyses Based on the enrollment years and data presented in the table, patients were overlapped with subsequent publications.

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/ range], yr (% male)	Weight-bearing MRI <ul style="list-style-type: none"> • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration 	Comparator test	Outcomes	Main findings	Funding Comments
Willen, 2001 ¹⁰ [11725243] Sweden Single 1994 to 1998	122 Patients were selected according to their symptoms (low back pain, sciatica, or neurogenic claudication). Sampling was not described.	50 [14 to 80] (52)	cMRI with axial loading <ul style="list-style-type: none"> • cMRI with axial loading • Magnetom Impact (Siemens) • 1.0 T • Surface coil • DynaWell L-Spine: 40% BW (never >50% BW) • Axial loading of the lumbar spine in extension • Closed 	Preloaded cMRI exam Protocol same as Willen, 1997	Impact on diagnostic thinking: AVI was defined as 1) a sig. reduction of the DCSA (>15 mm ²) to areas <75 mm ² (borderline value for canal stenosis) from PRP to ACE, or 2) a suspected disc herniation, lateral recess or foraminal stenosis, or a intraspinal synovial cyst at PRP changing to obvious manifestation at ACE	<ul style="list-style-type: none"> • AVI was found by the axially loaded MRI in 30% patients overall (in patients with sciatica or neurogenic claudication only). • No AVI was found in patients with low back pain. 	Industry Post hoc exclusion of patients from most of the analyses Based on the enrollment years and data presented in the table, patients were overlapped with the prior publication.

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/range], yr (% male)	Weight-bearing MRI • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration	Comparator test	Outcomes	Main findings	Funding Comments
Willen, 2008 ¹¹ [18277859] Sweden Single 1996 to 2002	250 Patients with clinical signs of neurogenic claudication and/or sciatica. Sampling was not described.	nd	cMRI with axial loading • cMRI with axial loading • nd • 1.0 T • Surface coil • DynaWell L-Spine: 40% BW (never >50% BW) • Axial loading of the lumbar supine in extension • Closed	Preloaded cMRI exam Protocol same as Willen, 1997 and Willen, 2001	• Impact on diagnostic thinking: AVI (same definition as Willen, 2001) • Patient outcomes after surgery	• In 24 patients, a hidden stenosis was disclosed in 1 to 3 disc levels, whereas no stenosis was detected at the unloaded exam. • At 1-6 year after surgery, majority of the 24 patients had much improved or improved leg or back pain, and subjective walking ability.	Industry Probably some overlaps with Willen, 2001 Outcome data were from the Swedish Spine Register 2005. Based on the enrollment years and data presented in the table, patients were overlapped with the prior publications

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/ range], yr (% male)	Weight-bearing MRI <ul style="list-style-type: none"> • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration 	Comparator test	Outcomes	Main findings	Funding Comments
Knee joints imaging							
Boxheimer 2006 ¹² [16373770] Switzerland Single 2002 to 2003	42 Patients suspected of having a meniscal tear; diagnosis of meniscal tears based on cMRI and confirmed by arthroscopy. Sampling was not described.	37 [18 to 60] (71)	Open, interventional MRI <ul style="list-style-type: none"> • kinematic MRI • Signa SP (GE) • 0.5 T • Flexible transmit-receive surface coil • Standing (allowing arms on a support frame) • Upright Vertically open	Supine position in open, interventional MRI <ul style="list-style-type: none"> • kinematic MRI • Signa SP (GE) • 0.5 T • Flexible transmit-receive surface coil • None • Supine, or supine 90° flexion with rotation Vertically open	<ul style="list-style-type: none"> • Diagnosis of meniscal displacement: a meniscal movement of 3 mm or more between weight-bearing and supine positions. Assessment of pain intensity: a visual analog scale was used.	<ul style="list-style-type: none"> • 58% menisci with tears did not reveal any displacement between the different knee positions. • Patients with displaceable meniscal tears reported significantly more pain in all three knee positions than did patients with nondisplaceable meniscal tear (P<0.05) 	

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/range], yr (% male)	Weight-bearing MRI • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration	Comparator test	Outcomes	Main findings	Funding Comments
Shellock, 1993 ¹³ [8327718] US Single nd	17 (patients); 5 (healthy controls) how controls were selected were not described	Patients: 31 [17 to 48] (39) Controls: nd	cMRI with kinetic resistance loading • 64 MHz MR imager • nd • 1.5 T • Transmit-and-receive quadrature body coil • Nonferromagnetic positioning device with a force of 30 ft-lb/sec (resistance) • Prone position with joints movement from ~45° to extension • Closed	cMRI without loading • 64 MHz MR imager • nd • 1.5 T • Transmit-and-receive quadrature body coil • Nonferromagnetic positioning device without load • Prone position with joints movement from ~45° to extension • Closed	Missed diagnosis of patellofemoral joint abnormalities in alignment and tracking (diagnosis was made by two radiologists in blinded fashion)	<ul style="list-style-type: none"> In symptomatic patients, the unloaded kinematic MRI showed 41% normal findings, while loaded kinematic MRI showed 5.9% normal findings. The severity of abnormalities was qualitatively the same with both techniques (9 cases) or greater with the loaded technique (7 cases) 	Industry

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/ range], yr (% male)	Weight-bearing MRI <ul style="list-style-type: none"> • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration 	Comparator test	Outcomes	Main findings	Funding Comments
Foot imaging							
Sutera, 2010 ¹⁴ [20177977] Italy Single 2009	20 (patients); 20 (healthy controls) Two groups of individuals underwent MRI with a dedicated system were included. Convenience sample	Patients: 36 [24 to 45] (80) Controls: 33 [20 to 41] (70)	Tilting MRI in upright position <ul style="list-style-type: none"> • Dedicated upright MRI • G scan (Esaote) • 0.25 T • Dedicated platform-shaped receiver coil • Standing (~82°) • Neutral • Laterally open 	Tilting MRI in supine position <ul style="list-style-type: none"> • Dedicated upright MRI • G scan (Esaote) • 0.25 T • Dedicated platform-shaped receiver coil • Conventional supine • Neutral • Laterally open 	Clinical diagnosis of plantar fasciitis: presence of perifascial oedema or both of fascia thickening and abnormal signal intensity (consensus by 3 radiologists blinded to patients' groups, history and clinical findings)	<ul style="list-style-type: none"> • Both supine and upright positions enabled identification of plantar fasciitis in 15/20 cases (75%) in patient group. • None of controls had a diagnosis of plantar fasciitis or abnormal MRI findings in either upright or supine position. 	Nonindustry

Author, year [UI] Country Center Enrollment year	N enrolled Inclusion criteria Sampling	Mean age [SD/ range], yr (% male)	Weight-bearing MRI <ul style="list-style-type: none"> • Device description • Model (manufacturers) • Field strength • Coil • Loading • Positioning • Configuration 	Comparator test	Outcomes	Main findings	Funding Comments
Weishaupt, 2003 ¹⁵ [12601213] Single 2000 to 2001	18 Patients suspected of having Morton's neuroma and underwent cMRI of their symptomatic forefoot in the prone position. Only those who had presence of >1 Morton's neuroma 5 mm or larger in its transverse diameter were included. Referred by foot surgeons or orthopedic foot surgeons	50 [25 to 72] (6)	Weight-bearing MRI <ul style="list-style-type: none"> • Weight-bearing MRI • Signa Advanced SP (GE) • 0.5 T • Flexible transmit-receive wraparound surface coil • Sitting • Extension, flexion (static) • Vertically open 	cMRI <ul style="list-style-type: none"> • cMRI • Impact Expert (Seimen) • 1.0 T • Send-receive extremity coil • None • Prone position • Closed Supine MRI in open scanner <ul style="list-style-type: none"> • Supine MRI • Signa Advanced SP (GE) • 0.5 T • Flexible transmit-receive wraparound surface coil • None • Supine • Vertically open 	Change in diagnosis of Morton's neuroma: <5 mm in transverse diameter, measurements were performed by 1 of the authors at a separate workstation using software	<ul style="list-style-type: none"> • No additional Morton's neuroma was found on any of the MR images. • Visibility of Morton's neuroma was significantly better in cMRI in the prone position compared with that in the supine position. 	nd Only included patients with successful imaging in all three Only included patients with a Morton's neuroma in the prone position.

ACE=axial loading of the lumbar spine in extension; AVI=additional valuable information; BW=body weight; cMRI=conventional MRI; CT=computed tomography; DCSA=dural sac cross-sectional area; PRP=psoas-relaxed position; SD=standard deviation

^aThis custom-made axial loading harness later became commercialized under the brand name of DynaWell L-Spine.

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Appendix F. Dedicated Extremity MRI Devices

Our literature searches as well as Key Informant (KI) feedback indicated that dedicated extremity magnetic resonance imaging (MRI) devices could 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 in the Description of Stress-Loading MRI subsection of the Findings section of the main report.

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.¹ As this study enrolled only healthy subjects, we did not include it in our evidence map. The literature on non-stress-loading 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-stress-loading dedicated extremity MRI. We present below 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.²⁻³⁷ 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; interquartile range [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 stress-loading 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 workup, 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 nonmedical expenses associated with the initial injury during the 6-month followup 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.³⁸ According to the KI affiliated with GE Healthcare, GE Healthcare is marketing two versions of a dedicated extremity MRI scanner (MSK Extreme 1.0T and the MSK Extreme 1.5T), and approximately 150 such devices are installed, 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 21, 2009, the MSK Extreme had an installed base of 175 scanners worldwide.³⁹ 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,” that is, 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 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 stress-loading applications; however, KIs suggested that this could be a promising area of future research. We identified extremely limited use of dedicated extremity MRI under stress loading. 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.

Summary and Implications

Due to their unique design (“semi-open” configuration) and the fact that they are not often utilized to take images under stress-loading conditions (at least in the currently available literature), we decided to assess dedicated extremity MRI scanners separately from other emerging technologies included in this report. We identified a large number of published studies, often comparative and assessing clinical outcomes, including a randomized controlled trial of

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

testing versus no-testing. It appears that these devices are commonly used in rheumatology (mostly for rheumatoid and other inflammatory arthritides) 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 utilization of such devices are expected. All considerations for future studies described in the Next Steps section of the main report apply equally to dedicated extremity MRI devices.

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 systematic review or technology assessment of their use for the diagnosis and monitoring of patients with rheumatoid arthritis and other inflammatory arthritides may be warranted.

Appendix Table. Studies of Dedicated Extremity MRI Devices

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Rheumatoid arthritis							
Xie, 2008 ⁴⁰ (Canada) [19032820] Case-control	39	Cases: RA	Cases: rheumatology clinics	OrthOne [ONI Medical Systems] (1.0T)	Cases vs. controls	MCP joints; wrist	Synovitis, bone edema, bone erosion (OMERACT RAMRIS scoring)
	41	Controls: no joint disease	Controls: community				
Savnik, 2001 ²⁸ (Denmark) [11419149] Cross- sectional	103	RA	NR	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	High-field MRI - Gyrosan ACS-NT [Philips, Best, Netherlands] (1.5T)	Wrist; MCP and IP joints	Synovial membrane volume, joint enhancement, joint effusion, bone edema, bone erosions (visual analysis)
Yoshioka, 2006 ⁴¹ (Japan) [16456819] Case-control	13	Cases: Suspected early RA, RA; soft- tissue swelling	NR	Compact MRI [originally developed by investigators] (0.21T)	Cases vs. controls Among cases only, also comparison to plain radiographs	Hand; wrist	Radiologists' routine reading
	13	Controls: no clinical symptom of arthritis					
²⁹ , 2000 (Germany) [10663314] Cross- sectional	10 ^a	Patients with ACL injuries who are able to hyperextend the uninjured knee.	NR	Artoscan [Esaote Biomedica, Genoa, Italy] (0.18T)	None.	Knee	Only anatomic measurements

^aThe study recruited 20 patients of whom 5 were excluded because of “lack of display of the ACL on parts of the image series.” Of the 15 patients analyzed, 5 were imaged with a 1.T superconducting magnet and were not included in our analyses.

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Duer-Jensen, 2008 ⁴² (Denmark) [17984195] Case-control	15 4	Cases: RA Controls: healthy individuals with no signs or symptoms of joint disease	Single academic hospital	2 E-MRI scanners were used: Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T) MagneVu MV1000 [MagneVu, Carlsbad, CA] (0.2T)	Plain radiographs. The Artoscan E-MRI results were considered as the gold standard and the MagneVu E- MRI and plain radiographs were treated as index tests to calculate diagnostic accuracy.	Hand ; wrist	Synovitis, bone edema, bone erosion (OMERACT RAMRIS scoring)
Cimmino, 2003 ⁴³ (Italy) [12746893] Case-control	36 5	Patients: RA Controls: healthy volunteers	10 outpatients in remission (per ACR criteria) and 26 patients with clinical involvement of at least one wrist either hospitalized in a university rheumatology clinic or as outpatients.	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	RA patients were classified into 3 groups based on disease severity. Imaging findings between the 3 disease groups and the controls were compared. Imaging parameters were also correlated with clinical outcomes and laboratory measurements.	Wrist	Association of imaging parameters with disease presence and severity. Correlation of imaging parameters with clinical and laboratory measurements. (clinical and laboratory findings were masked during image processing)

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Cimmino, 2005 ²⁴ (Italy) [15987474] Case-control	15	Cases: Psoriatic arthritis	Single academic rheumatology clinic, both inpatient wards and outpatient clinics	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Imaging findings between the 3 disease groups and the controls were compared.	Wrist	Association of imaging parameters with disease presence. Correlation of imaging parameters with clinical and laboratory measurements. (Image assessment was performed blind to the clinical and laboratory findings)
	49	Cases: RA, "consecutive"					
	30	Cases: RA, matched for age, disease duration and number of involved joints with the psoriatic arthritis group (9 patients overlapped with the group of consecutive RA patients)					
	8	Controls					
Duer-Jensen, 2009 ⁴⁴ (Denmark) [18718987] Case-control	20 5	Cases: RA Controls: healthy individuals	NR	2 E-MRI scanners were used: Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T) MagneVu MV1000 [MagneVu, Carlsbad, CA] (0.2T)	CT and plain radiographs All 4 tests were performed in cases and controls	Hand; wrist	Bone erosion detection (OMERACT RAMRIS scoring for MRI)

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Ejbjerg, 2005 ⁴⁵ (Denmark) [15650012] Case-control	37 28	Cases: RA Controls: healthy individuals	Single academic hospital	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	High-field MRI -Impact [Siemens] (1.0T) and plain radiographs All tests were performed on cases and controls; in 10 patients and 10 controls a preliminary study to determine the optimal imaging setting for the E-MRI was performed. Plain radiographs were only used for bone erosion detection.	Hand; wrist	Synovitis, bone edema, bone erosion (OMERACT RAMRIS definitions)
Freeston, 2007 ⁴⁶ (UK) [17666445] Cross- sectional	15	RA	NR	MagneVu MV1000 [MagneVu, Carlsbad, CA] (0.2T)	High-field MRI- Gyrosan ACS-NT [Philips, Best, Netherlands] (1.5T) and plain radiographs	Hand; wrist	Bone erosion detection (OMERACT definition of erosion)
Gaylis, 2007 ²⁰ (USA) [17694258] Retrospective longitudinal	48	Infliximab- treated RA	Single rheumatology practice	MagneVu 1000 [MagneVu, Carlsbad, CA] (0.2T)	Plain radiographs	Hand; wrist	Baseline bone erosion detection, monitoring of response to treatment (Two radiologists blinded to the patients' clinical status used a system to classify erosions as small, moderate or large. They also ascertained "regression" versus "stability" of the lesions)

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Tajiri, 1999 ⁴⁷ (Japan) [10406343] Case-control	8 5	Cases: RA with symptomatic subluxation of the distal ulna Controls: asymptomatic volunteers	NR	Artoscan [Esaote Biomedica, Genoa, Italy] (0.18T) using a custom-made positioning device to obtain scans of the upper extremity during rotation	Cases vs. controls regarding motion during rotation	Distal radioulnar joint	Images were analyzed with regard to rotation, distance between radius and ulna, and range of motion.
Roemer, 2005 ⁴⁸ (USA) [15633060]	23	Suspected or proven osteoarthritis of the knee	Participants in the MOST epidemiological study	OrthOne [ONI Medical Systems, Wilmington, MA] (1.0T)	Different imaging sequences	Knee	Grading of osteoarthritis (two musculoskeletal radiologists blinded to participant data read all MRI scans)
Schiff, 2007 ⁴⁹ (USA) [17519063] Cross- sectional	300 ^b	Clinical diagnosis of RA	Single community-based rheumatology practice	MagneVu MV1000 [MagneVu, Carlsbad, CA] (0.2T)	Comparison of clinical and laboratory findings and treatment-related data (change in therapeutic regimen) between “MRI positive” and “negative” patients. Multivariate modeling to identify predictors of a “positive” MRI scan.	Hand; wrist; feet	Marrow edema, subchondral cysts, erosions, joint space narrowing (four radiologists interpreted the exams, each scan was reviewed by a single rater)

^b Three hundred sixty patients were screened, 302 met the inclusion criteria and the first 300 were selected for the study.

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Segal, 2009 ⁵⁰ (USA) [19533741] Nested case- control	30 30	Cases: incident symptomatic knee osteoarthritis Controls: randomly selected individuals from the same cohort	Participants in the MOST epidemiological study	OrthOne [ONI Medical Systems, Wilmington, MA] (1.0T) ^c	Cases vs. controls (baseline MRI data were used to develop contact stress models to predict the development of incident osteoarthritis by 15 months of followup)	Knee	Prognosis of osteoarthritis development expressed as prognostic accuracy (computational stress analysis of the baseline MRI scan was used to predict the development of incident osteoarthritis)
Taouli, 2004 ⁵¹ (USA) [15039167] Cross- sectional	18	RA	Single academic rheumatology center	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	High-field MRI-Signa [General Electric medical Systems] (1.5T) and plain radiographs. Scores based on the different imaging methods were compared as continuous measurements.	Hand; wrist	Bone erosions, joint- space narrowing and synovitis. (Two independent reviewers assigned Genant-modified Sharp radiographic scores based on plain radiographs. A modification of the system was used for MRI)

^c The authors used the protocol described in Roemer, 2005.

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Lindegaard, 2001 ⁵² (Denmark) [11454641] Case-control	25 3	Cases: RA Controls: healthy individuals	Single academic rheumatology clinic Hospital staff	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Clinical examination and plain radiographs. Correlation of imaging scores with laboratory findings.	Hand; wrist	E-MRI: Detection of bone erosions (visual assessment), grading of synovitis (using a semi- quantitative system). Plain radiographs: presence and number of bony erosions (assessed by an independent investigator blinded to the clinical and E-MRI findings). Clinical exam: joint swelling and tenderness (assessed by a rheumatologist based on EULAR criteria).
Lindegaard, 2006 ⁵³ (Denmark) [16540550] Longitudinal study ^d	24 ^e	RA	Single academic clinic	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Plain radiographs. Radiographs and E- MRI assessments were performed at baseline, 6 and 12 months to assess disease course and response to treatment. Findings were correlated with clinical and laboratory results.	Hand; wrist	Monitoring of response to treatment based on number of erosions, bone edema, tenosynovitis (For E-MRI: OMERACT scoring by a radiologist blinded to clinical and radiographic findings; for radiographs: Larsen scores and presence of bone erosions)

^d It is not clear whether participant recruitment was prospective or retrospective.

^e Twenty-five patients were enrolled but one patient did not complete the required followup period of 1 year (withdrew due to “personal reasons”).

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Eshed, 2006 ⁵⁴ (Germany) [16882591] Cross-sectional	38	RA	Single center rheumatology outpatient clinic	C-scan [Esaote Biomedica, Genoa, Italy] (0.2T)	Image quality (contrast-to-noise and signal-to-noise ratios) and the presence of synovitis were compared between E-MRI using a single vs. a double dose of contrast-enhancing material.	Hand; wrist	Image quality parameters and synovitis scoring (OMERACT RAMRIS score)
Crues, 2004 ⁵⁵ (USA) [15088291]	132 of whom 125 were successfully imaged	Inflammatory arthritis (95% had RA and 5% had joint symptoms in the setting of psoriasis)	Single academic center	MagneVu MV1000 [MagneVu, Carlsbad, CA] (0.2T)	Plain radiographs	Hand; wrist	Erosions detected by each imaging modality and intra- and inter-rater agreement (two raters reviewed all scans)
Drapé, 1998 ⁵⁶ (France) [9646792] Cross-sectional	43	Knee osteoarthritis	Single center	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Arthroscopic evaluation	Knee	French Society of Arthroscopy scores and grades (qualitative and quantitative assessment by a single arthroscopist blind to the patient's identity and MRI findings; MRI assessment based on qualitative and quantitative assessment by two radiologists blind to the patient's identity and arthroscopic findings)

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Knee, shoulder, elbow, foot, ankle pathology							
Pessis, 2003 ⁵⁷ (France) [12744942] Prospective, longitudinal study	20	Symptomatic tibiofemoral osteoarthritis with indication for arthroscopic joint lavage	Single academic center	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Plain radiographs (weight-bearing fully extended and flexed knee) Arthroscopy performed immediately after the E- MRI All tests were repeated 1 year after the base- line examination.	Knee	For arthroscopy severity of cartilage breakdown, chondropathy. For E-MRI: articular cartilage lesions, bone marrow edema, subchondral bone abnormalities. (all tests were interpreted by a investigators unaware of the patient identity and the chronology of the investigations)
Zlatkin, 2004 ⁵⁸ (USA) [15112313] Cross- sectional	160	Suspected shoulder pathology	5 MRI facilities located within orthopedic practices	Artoscan [Esaote Biomedica, Genoa, Italy and GE Medical Systems/Lunar Corporation, Madison, WI] (0.2T)	Operative findings, ascertained from operative reports. The operative findings were considered as the reference test.	Shoulder	Diagnostic accuracy for rotator cuff disease or glenoid labrum lesions (two radiologists reviewed MRI images independently; MRI imaging reports were available to the surgeons at the time of surgery)
Pfahler, 1998 ¹⁵ (Germany) [9932184] Cross- sectional ^f	34	Lateral epicondylitis of the elbow resistant to treatment of at least 3 months	Single academic center	Dedicated system specially constructed for examination of the peripheral joints (0.2T)	Results from plain radiographs are presented (with no statistical comparison). Histopathological analysis of the extensor tendon was performed for 6 patients that underwent surgery.	Elbow	Diagnostic accuracy (number of positive MRI findings among symptomatic patients), comparison of findings in surgery (pathological examination of specimens obtained from 6 patients that underwent surgery)

^f Baseline data were reported on all 34 patients. During followup, six patients underwent surgery because they remained refractory to conservative treatment.

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Riel, 1999 ¹⁴ (Germany) [10024961] Cross-sectional	244	Patients with internal knee joint lesions	Single academic center	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Arthroscopy performed within "about" 48 hours of MRI.	Knee	Diagnostic accuracy (MRI scans were read by assessors blind to the orthopedic diagnosis and graded according to Reicher's classification. Arthroscopy was performed by a single surgeon)
Steinborn, 1999 ¹³ (Germany) [10460377] Case-control	23 7	Lateral epicondylitis of the elbow Healthy volunteers	Single academic center	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Comparison of radiologist-assigned grades obtained with different imaging sequences. For 11 of the 23 patients findings in the contralateral, unaffected elbow were compared with the affected one. Five patients underwent surgery within 6 weeks of the MRI examination and biopsy of the common extensor tendon was obtained. Intraoperative and histopathological findings were compared with MRI findings. Grading of MRI images using the same system as for patients w	Elbow	Grading of imaging findings in all patient groups using different imaging sequences. (two radiologists employed a common grading system)

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Verhoek, 1998 ⁵⁹ (Switzerland) [9626891] Cross- sectional	41 ^g	Consecutive patients referred for foot or ankle MRI	NR	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	High-field MRI-Impact [Siemens, Erlangen, Germany] (1.0T)	Foot; ankle	Image quality (qualitative and quantitative comparison of images obtained with the two devices in a blind manner) Patient preferences were assessed by questionnaire administered after both scans were completed.
Masciocchi, 1997 ⁶⁰ (Italy) [9481587]	58	"Painful syndrome" at the peritalar region	NR	"dedicated" system consisting of 0.2T and 0.5T equipment	Arthroscopy was performed in 22 cases and 36 patients were assigned to clinical follow-up. ^h	Ankle	Assignment of patients to diagnostic groups based on lesion site (visual assessment for E-MRI, surgical/arthroscopy findings or clinical follow- up findings).
Franklin, 1997 ⁶¹ (USA) [9167821] Cross- sectional	35	Acute or chronic knee pain that requiring arthroscopic evaluation	Single clinical practice	Artoscan [Lunar Corp., Madison, WI] (0.2T)	Arthroscopic evaluation	Knee	Diagnostic accuracy (EX MRI readings were considered as the index test and arthroscopic findings as the reference standard, assessors of each test were blind to the results of the other)

^g A total of 47 patients were asked to participate, and 6 refused or were unable.

^h Thirty-one patients had undergone conventional radiography and 18 had undergone CT. No results from these investigations were reported.

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Kersting- Sommerhoff, 1996 ³⁵ (Germany) [8798043] Cross- sectional	230	Acute and chronic lesions of the knee	Radiology department in a single academic center	Artoscan [Esaote Biomedica, Genoa, Italy] (0.18T)	Arthroscopic evaluation (for all patients) and high-field strength MRI (for 20 ⁱ patients)-ACS II [Philips, Eindhoven] (1.5T)	Knee	Diagnostic accuracy of EX-MRI compared to arthroscopic findings; image quality compared to high-field strength MRI; inter-rater agreement (3 raters) assessed in 20 patients (diagnostic accuracy was assessed at the lesion level and image quality was graded as “excellent”, “good”, “satisfactory”, or “non- diagnostic”)

ⁱ The study reported that comparative EX-MRI and high-field strength MRI examinations were done in “more than 50 patients,” 20 of whom were recruited “prospectively.” Data were reported only regarding the latter group.

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Fracture or other acute injury							
Bretlau, 1999 ⁶² (Denmark) [10622486] Prospective longitudinal study	52 of whom 47 were successfully imaged	Trauma patients with suspected scaphoid fracture.	NR	Artoscan [Esaote Biomedica, Genoa, Italy] (0.1T)	Plain radiographs (normal at the initial examination) were compared to E-MRI images (obtained within an average of 4 days after trauma). E-MRI scans were also obtained at an average of 11 days post trauma. Late plain radiographs (average 11 weeks after trauma) were used as the reference test. Late E-MRI scans were also performed.	Wrist	Presence of a scaphoid fracture (blind assessment by two radiologists in random order)
Raby, 2001 ⁶³ (UK) [11286584] Cross-sectional ^j	53	Patients at least 10 days post-injury with suspected scaphoid fracture	Review and fracture clinics of a single center	Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Management decisions based on radiological findings and clinical examination.	Wrist	Impact on treatment decisions (clinicians were asked to determine their treatment plan on the basis of clinical and radiological findings,

^j The main analyses in the study were based on changes in the management plan (comparison of the treatment plan before and after imaging results were reported to the clinician) engendered by MRI. There was an attempt to followup patients but the response rate was too low and the effort was abandoned.

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
	56	Patients with acute wrist injury and suspected scaphoid fracture attending the Accident and Emergency Department for the first time, usually at the day of injury	Accident and Emergency Department of a single center				before MRI had been obtain and they were also asked to revise the treatment plan after the MRI results were available) A rudimentary cost analysis is presented in the discussion section of the manuscript.
Nikken, 2005 ⁶⁴ (Netherlands) [16118171] RCT	500 [1:1 randomization]	Acute injury of the wrist, knee or ankle	Single university hospital	Plain radiographs followed by E-MRI with Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Plain radiographs only	Wrist; knee; ankle	Effectiveness (quality of life, time-to-completion of the diagnostic workup, number of additional diagnostic procedures during followup, number of days absent from work, number of days to convalescence) and costs (measures of medical and nonmedical costs associated with the initial injury during the 6-month followup period, societal perspective).

Author, year (Country) [PMID] Study Design	N enrolled	Patient population	Setting	E-MRI [Manufacture] (Field strength)	Comparison	MR Imaging location	Outcome (assessment)
Nikken, 2005 ⁶⁵ (Netherlands) [15618379] Retrospective analysis of RCT data to develop predictive ^k models	90 of whom 87 were randomized	Acute injury of the wrist	Single university hospital	Plain radiographs followed by E- MRI with Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Plain radiographs only	Wrist	Additional treatment after initial presentation (the outcome was assessed at followup visits and clinical or imaging findings were assessed as potential predictors in multivariable models).
Oei, 2005 ⁶⁶ (Netherlands) [15618380] ^l	189	Acute injury of the knee	Single university hospital	Plain radiographs followed by E- MRI with Artoscan [Esaote Biomedica, Genoa, Italy] (0.2T)	Plain radiographs only	Knee	Additional treatment after initial presentation (the outcome was assessed at followup visits and clinical or imaging findings were assessed as potential predictors in multivariable models).
Kühne, 1998 ⁶⁷ (Germany) [9474630] Cross- sectional ^m	28	ACL reconstruction within 3 to 5 years	Academic hospitals	Artoscan [Esaote Biomedica, Italy] (0.2T)	Correlation of imaging (MRI) and clinical (knee stability) outcomes in patients treated with two different methods of ACL reconstruction	Knee	MRI and clinical scores for knee stability (Clinical measurements using the KT-1000 arthrometer; MRI scores based on visual assessment)

ACL=anterior cruciate ligament; CT=computerized tomography; EULAR=European League Against Rheumatism; MCP=metacarpophalangeal; MOST=Multicenter Osteoarthritis Study; MRI=magnetic resonance imaging; NR=not reported; OMERACT=Outcomes of Rheumatoid Arthritis Clinical Trials; P=interphalangeal, RA=rheumatoid arthritis; RAMRIS=Rheumatoid Arthritis MRI Scoring System; RCT=randomized controlled trial.

^k This is a secondary analysis of data from the Nikken, 2005 RCT, listed on the above row.

^l This is a secondary analysis of data from the Nikken, 2005 RCT, listed two rows above.

^m A single MRI examination was performed at a mean followup time of 46 months following surgery. Only data at the followup visit are analyzed in the manuscript.

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