Evidence-based Practice Center Technical Brief Protocol

Project Title: *Technical Brief - Use and Safety of Positional MRI in the Management of Patients with Musculoskeletal Pain*

I. Background and Objectives for the Technical Brief

Magnetic resonance imaging (MRI) is an imaging tool that has found widespread use for the diagnosis and treatment of many disorders. It is typically used as a preferred imaging tool for rheumatologic, orthopedic and neurologic conditions, as it can better delineate soft tissue structures compared to plain X-rays or a computerized tomography (CT). Contrary to radiograms and CT, MRI does not use ionizing radiation to produce images but uses a strong magnetic field to exploit the magnetic properties of hydrogen atoms in the water content of the body.

Briefly, the images of the MRI are generated as follows: during MRI scanning, the patient is placed in a strong magnetic field. The magnetic field strengths employed in typical MRI machines range from 1.0 to 3.0 Tesla; for comparison, the earth's magnetic field has strength of 5×10^{-5} Tesla. Exposure to the field causes the magnetic moments of hydrogen atom nuclei (protons) in cellular water and lipid molecules to align with the magnetic field, much like a compass needle aligns with the earth's magnetic field. The alignment can be either parallel or anti-parallel to the magnetic field. Parallel alignment is a low-energy state and anti-parallel alignment is a high energy state; the energy difference between the two states being proportional to the strength of the magnetic field. Also, the higher the strength of the magnetic field, the greater number of protons acquires parallel alignment. Then, a radio frequency transmitter produces an electromagnetic pulse (RF) perpendicular to the magnetic field, with a frequency that causes the magnetic moments of the aligned protons to transition to the higher energy state. After the RF is turned off, the protons return to the low-energy state and the difference in energy between the two states is released as photons, producing the signal that the MRI scanner detects. The strength of the magnetic field determines the frequency of the emitted photons. Additional magnetic fields can be applied to generate gradients of magnetic field strength, in effect making the composite field strength different across points in the patient's body and allowing spatial localization. Also, because histologically different tissues (as well as healthy and pathologic forms of the same tissue) contain different concentrations of hydrogen atoms, their respective radiofrequency emissions are different. Finally, after appropriate transformation of the signals collected by the MRI scanner, diagnostically useful images are produced.[1,2,3]

The standard MRI scanner configuration includes a large, cylinder-shaped magnet. It requires that the patient be placed in a tube 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 MRI tube allows for limited movement and can induce claustrophobia or anxiety in some patients.

Open MRI systems, which allow greater flexibility and may preclude claustrophobia, have been designed to overcome some shortcomings of the traditional MRI machines. In open systems, the tube is open along the sides and/or is of shorter length so that only the part of the body that needs to be evaluated is surrounded by the magnet.

Some open MRI systems are open at the top and front with the magnets placed in such a way so as to allow an image to be taken in the upright, weight bearing positions (either when standing or in a seated position) as well as allowing for flexion and extension movements. The terms "Positional MRI" or "Upright MRI" have been used to describe MRI systems which are capable of these configurations. Its has been suggested that such systems may be useful for conditions that are challenging to diagnose with conventional or open MRI systems, such as cases where the pathology is only expressed in certain positions, or when loading/weight bearing is present.

Some of the conditions that have been evaluated with a positional MRI[4] include:

1. Suspected degenerative spondylolisthesis (>25% slip)

2. Suspected spinal stenosis: moderate/severe central stenosis (>1/3 canal) and lateral recess stenosis (displacing or compressing nerve root, disc extrusion)

3. Radicular pain: moderate/severe central stenosis, lateral recess stenosis, nerve root compression, and disc extrusion

4. Non-specific spine pain: moderate/severe central stenosis, lateral recess stenosis, nerve root compression, and disc extrusion

5. Extra-spinal joint pain/function loss: e.g. narrowing or musculoskeletal only

An evaluation of positional MRI against alternative diagnostic tools conducted by the state of Washington in 2007 did not reveal adequate data to determine diagnostic validity or accuracy.[4] Since then, other studies have been conducted to assess the diagnostic utility of positional MRI.[5,6,7]

An informal review of literature—guidelines, policies, and technology assessments—and interviews with a variety of stakeholders indicate that MRI for imaging of spinal conditions such as degenerative spondylolisthesis and spinal stenosis is commonly used and can be considered as an appropriate, noninvasive diagnostic test. However indications for use of non-recumbent, upright or positional MRI, lack consensus and need further evaluation.

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 $2048, respectively.[8] 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).

The objective of this technical brief is to describe the current state of use, enumerate the potential benefits and harms of positional MRI for the diagnosis, management, and treatment of patients with musculoskeletal disorders for whom this diagnostic test may

be considered, and describe the evidence available to date that supports these uses. We will achieve this objective through the engagement of topic experts and a literature scan. The Guiding Questions and methods of this technical brief are described herein.

II. Guiding Questions

Guiding question 1:

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

- a. What are the postulated advantages and disadvantages of positional MRI testing compared to contemporary imaging alternatives?
- b. To which populations and for what indications might they apply?
- c. Are they being proposed as replacement, triage, or add-on tests?
- d. What are the potential safety issues and harms of positional MRI technologies?

Guiding question 2:

What is the current availability and cost of positional MRI testing and what are there special requirements that positional MRI facilities have to fulfill?

- a. Who are the current (major) manufacturers of positional MRI machines? What is the current the Food and Drug Administration (FDA) clearance status of these positional MRI machines?
- b. Approximately how many facilities and of what kind are currently providing positional MRI testing in the U.S.? Do they use the technology mainly for routine work or for research purposes? What additional equipment or technical resources are needed in order to operate positional MRI, compared with standard MRI?
- c. What kinds of training, certification, and staffing are required to operate positional MRI or interpret its images?
- d. What is the cost of imaging with positional MRI as compared to other imaging alternatives?

Guiding question 3:

What published studies have reported on the diagnostic performance, efficacy/effectiveness or safety of positional MRI? Organize them according to the Fryback and Thornbury scheme,[9] and provide a synthesis of the following information as applicable:

- i   Groups of patients enrolled
- ii Type of positional MRI used
- iii Study design and size

iv   Role of the test in patient management

v   Setting where positional MRI testing was performed

vi   Outcomes assessed

vii   Adverse events, harms and safety issues reported

viii   Comparators used (applicable only to comparative studies)

ix   Length of follow-up (applicable only to longitudinal studies)

For our proposed operational definitions of these items, please see Box 3 in section III.

Guiding question 4:

What is the projected uptake of the positional MRI technology in the near future? What are 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 positional MRI technologies will be widely used in the near future?

b. What are possible areas of future research?

III. Methods

1. Data Collection:

A. Discussions with Key Informants

A representative panel of Key Informants has been identified through the previous Topic Refinement process. These individuals include medical experts/practitioners in radiology and orthopedics, public and private payers and medical directors, and a patient/consumer representative. The list of these individuals is in Appendix 1. Additional individuals may be added as necessary, according to information collected during the course of research.

Each Key Informant will be individually interviewed for their responses to Key Questions 1, 2 and 4. Through collaboration with Evidence-based Practice Center (EPC) staff experienced in qualitative research design, interview questions will be individualized to ensure that the unique perspective and expertise of each Key Informant is captured. Each interview will be recorded exclusively for the purpose of accurate transcription, and the recordings will be destroyed following the completion of this report. Additional information from the grey literature may be provided to Key Informants prior to their interview to facilitate these discussions.

Additionally, efforts are being made to obtain the separate input of positional MRI device manufacturers (who are also representative of the topic nominator).

B. Grey Literature search.

For Key Questions 1, 2 and 4, we will perform an Internet search for keywords to identify positional MRI technologies, including, but not limited to, "positional MRI", "upright MRI", and "weight bearing MRI". For these searches, unless otherwise advised, we intend to use the Google search engine and for each search string entered we will peruse the first 10 pages to identify relevant links. We note that open-ended searches of the Internet (including "Google searches") are challenging and not strictly reproducible. Using the exact same search string (search terms) on different dates will often return different pages among the top ranked ones. This is because of the algorithms used by search engines. For example, Google's PageRank™ algorithm "weights" each webpage based on the number and type of webpages that point to it (i.e., based on its incoming links). A given webpage is ranked higher when it receives many incoming links from high-ranking webpages. Because of the dynamics of the Internet, the top-ranking webpages can change over time. Second, by their very nature, algorithms such as PageRank™ will tend to give a lower rank to more recent webpages that have not yet accumulated enough incoming links from high-ranking sources, even if they are very relevant to the search string that was entered. This may result in

the paradox that recent information is not always prominent in a general search of the Internet. Consequently, manual perusal of a "manageable" number of results pages (e.g. the top 5-10 pages) can miss some important links. However, this is a limitation that we cannot address otherwise.

We will also search major MRI manufacturers' websites for information pertaining to positional MRI. To identify major MRI manufacturers and to obtain FDA clearance status of positional MRI, we will search the FDA Center for Devices and Radiological Health (CDRH) database using the FDA product code "LNH" and device name "MRI" to identify relevant positional MRI instrumentation. This search yields a total of 63 potentially relevant records (search date: 5/27/2010).

For potential harms with positional MRI instrumentation, we will query the FDA Manufacturer and User Facility Device Experience (MAUDE) database for any reported harms with positional MRI instrumentation.

C. Published Literature search.

Box 1 presents our proposed literature search strategy. This search will be conducted in Medline. We will supplement our literature search with hand searches based on references of a previous technology assessment[4] as well as review articles and manufacturers' documents. Box 2 summarizes our proposed eligibility criteria for selecting literature to be included in this technical brief. Both literature search strategy and eligibility criteria will be modified based on inputs from the Key Informants.

Data to be abstracted for answering Key Question 3 are described in section III.2.A. Additional data regarding the use and safety of positional MRI may be added based on the results of our calibration exercise (also see Data Organization and Presentation: A. Information Management) and inputs from Key Informants.

We do not foresee the need for updated literature searches, as this is a project that will be completed in a relatively short time frame (7 months or earlier).

Box 1. Proposed literature search strategy

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.
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

Box 2. Proposed eligibility criteria

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Population(s)

All patients with the following conditions:
- Suspected degenerative spondylolisthesis (>25% slip)
- Suspected spinal stenosis (moderate/severe central stenosis (>1/3 canal), lateral recess stenosis (displacing or compressing nerve root, disc extrusion)
- Radicular pain (moderate /severe central stenosis, lateral recess stenosis, nerve root compression, disc extrusion)
- Non-specific spine pain (moderate/severe central stenosis, lateral recess stenosis, nerve root compression, disc extrusion)
- Extra-spinal joint pain/function loss (e.g narrowing, musculoskeletal only)
- Chronic low back or vertebral skeletal pain of undiagnosed etiology (i.e. undiagnosed by conventional diagnostic imaging)

Interventions

- Positional MRI testing and positional MRI test-directed treatments

Outcomes

- Test performance of positional MRI
- Intermediate outcomes of patients:
  - Diagnostic impacts (i.e., effect on additional diagnostic testing, effect on limiting the differential diagnosis)
  - Therapeutic impacts (i.e., effect on treatments received, changes in planned treatment regimen)
- Clinical outcomes of patients:
  - Operative outcomes, including mortality and morbidity associated with surgery
  - Non-operativeoutcomes, including quality of life, pain relief, psychological outcomes

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2. Data Organization and Presentation:

A. Information Management, and Database Generation and Software

The Tufts EPC has developed specialized software (*Abstrackr* –beta) to facilitate abstract screening. The software will be used to provide a user interface that will allow the investigators to easily accept and reject abstracts on screen and track the selection process. The first few hundred (200-300) citations will be screened jointly by all investigators to ensure that screening criteria are well understood and applied uniformly. Thereafter, investigators will screen non-overlapping sets of the remaining citations.

For studies identified through the Literature Search, we will use Epidata version 3.1 (EpiData Association, Odense Denmark) to extract information on items of interest in electronic forms.[10] Box 3 presents the operational definitions that we propose to use; these definitions may change based on the content and structure of the papers that we will identify. The initial version of the data extraction form

will be piloted with 15 papers, and will be modified in an iterative process. A calibration exercise with 5 papers will be performed to ensure consistency and accuracy of data extraction across investigators. From studies considered relevant, we will extract data on the citation (first author name, journal and year of publication), study design, condition being studied, study size and setting, and patient selection criteria. We will also record details relevant to the technical specification of positional MRI. Moreover, we will record the outcomes being assessed in each study, including testing related harms, and classify them based on the Fryback and Thornbury scheme. For comparative studies of diagnostic tests, we will extract details on the comparators of positional MRI.

Specific, relevant input from Key Informant interviews will be integrated with information obtained through the published and grey literature sources. Key Informant responses to specific topics may be included by direct quote from recorded interviews for more accurate representation. All Key Informants will be informed beforehand of the audio recording process as described above.

B. Data Presentation

We will generate tables summarizing items relevant to Key Question 3. Based on the data items that we will extract (see section III.2.A) we will calculate 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.[11]

Qualitative synthesis of information will be facilitated by the use of tables and graphs in order to effectively summarize the evidence provided by the relevant studies. We will explore graphical presentation of data including histograms or weighted scatter plots. For example, provided that relevant data are available, we will generate scatter plots of study designs over settings of test use, where the each study will be represented by a circle proportional to the study size. Such a graph can simultaneously convey the amount of evidence (studies and patients) available along with important clinical information (study setting) and study design information. Alternative graphs depicting study designs, medical conditions where positional MRI is utilized, sample sizes enrolled, and the specific outcomes investigated, will be generated. Statistical analyses will be conducted using Stata version 11.1/SE (Stata Corp., College Station, TX).

Box 3. Operational definitions for the data extraction and analysis.

i   Types of patients/patient selection criteria: inclusion and exclusion criteria, characteristics of enrolled patients (demographics, disease spectrum).

ii   Type of positional MRI used (if applicable): technical specifications of MRI machines, including magnetic field strength.

iii   Study design (randomized or observational; prospective or retrospective; cross-sectional, case-control or longitudinal; single center or multicenter) and study sample size.

iv   Proposed use of the test: replacement test (e.g. instead of conventional MRI), triage test (e.g. use of positional MRI todecide whether a myelogram is needed), or add-on/confirmatory test (e.g. use of positional MRI in addition to CT or conventional MR).

v   Setting for positional MRI; studies will be classified as investigating

    a. Screening: use of the test to identify disease in the absence of clinical symptoms.

    b. Diagnosis: use of the test to determine the presence and type of structural or functional abnormalities in the presence of clinical symptoms.

    c. Prognosis/ prediction: use of the test to predict response to treatment or natural course of the disease.

    d. Patient management or treatment planning: use of the test to determine the management plan, including selection of treatment.

    e. Monitoring: assessing response to treatment or relapse after therapy.

vi   Outcomes measured

    a. diagnostic test performance

    b. impact on diagnostic thinking

    c. impact on treatment decisions

    d. impact on clinical and functional outcomes

vii   Adverse events, harms and safety issues: all unintended consequences of the testing process *per se*.

viii   Comparator used (applicable only to comparative studies)

ix   Length of follow-up (applicable only to longitudinal studies)

IV. References

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V. Definition of Terms

Not applicable.