Upright magnetic resonance imaging (uMRI)

Assessing signals for update

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Upright MRI

Effectiveness of upright MRI for evaluation of patients with suspected spinal or extra-spinal joint dysfunction

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Presented by:

SPECTRUM RESEARCH

Effectiveness of upright MRI for evaluation of patients with suspected spinal or extra-spinal joint dysfunction

1. Introduction

A Comparative Effectiveness Review (CER) titled: *Effectiveness of upright MRI for evaluation of patients with suspected spinal or extra-spinal joint dysfunction*, was originally released in May 2007 by the Health Technology Clinical Committee.

<u>HTCC Coverage Determination</u>

Upright and positional MRI is **not a covered benefit** due to insufficient evidence to conclude that the health technology is safe, efficacious, and cost-effective.

<u>Health Technology Background</u>

Upright and positional MRI (uMRI) is a magnetic resonance imaging test designed to be preformed with patients in weight bearing or different positions, (e.g. upright, sitting, standing, flexed or extended). Current alterative imaging tests used to diagnose spinal and other joint conditions are a regular MRI (lying down), Computerized Tomography (CT) myelogram, regular or flexion and extension radiographs (x-rays), and discography.

The potential advantage of a uMRI is that the weight bearing or positional images may capture additional findings. Also, the open MRI equipment may improve patient compliance by combating the claustrophobia of traditional MRI scanners and enhance patient comfort. Potential disadvantages are that weight bearing and different positions can cause patient pain and result in an inability to complete the test; and the magnet strength, which determines image quality, of a uMRI is lower (o.6T for uMRI compared to a standard MRI range of 1.0T to 3.0T).

The potential impact on the health system is unknown. Potential benefits may include: more accurate findings, reduced reliance on other tests, and more appropriate treatments and better health outcomes. Potential risks are that lower quality images, less accurate findings, or more findings without an understanding of clinical significance lead to additional or unnecessary tests, inappropriate treatment, and poorer health outcomes.

<u>Committee Findings</u>

The HTCC reviewed and considered the upright and positional MRI technology assessment report, information provided by the Administrator, and invited public and agency comments.

Committee members were confident that scientific evidence confirms that the technology is safe because the technology is comparable to other MRI tests and administration of the test is unlikely to case a significant adverse health effect.

Committee members found that there was insufficient scientific evidence to make any conclusions about uMRI's effectiveness, including whether uMRI: accurately identifies an appropriate diagnosis; can safely and effectively replace other tests; or results in equivalent or better diagnostic or therapeutic outcomes.

Taking safety and effectiveness data together, the committee found that there was insufficient evidence to conclude whether the use of uMRI would result in less, equivalent, or more health benefit. Most compelling evidence cited by committee members included:

- Technology is ten years old, but no accuracy studies and very few reliability studies
- Of the studies available, most were poor quality and sample sizes were very small
- Image quality is lower and some evidence of higher percentage of individuals not being able to complete the test due to pain from positioning
- Other tests are currently available for diagnosing same conditions, even though it was noted that those tests might also have limitations
- One study that was of higher quality raised the possibility that uMRI might be less beneficial due to decreased findings
- Most other payers do not cover, though one payer does
- There was no National Medicare Coverage Decision
- There are no evidence based clinical guidelines addressing appropriate uMRI usage

Committee members found that there were no independent cost analysis, but the cost of use of the uMRI would be higher based on manufacturer reported costs of $1450 for a single image with additional images costs ranging from $350 to $1200.

After 5 years the original CER was due for a surveillance assessment in June 2012.

2. Methods

2.1 Literature Searches

We conducted a limited literature search for the years 2007-2012 using the identical search strategy used for the original report. This search included three main databases: PubMed, Cochrane Library, and EMBASE. Appendix A includes the search methodology for this topic.

2.2 Study Selection

In general we used the same inclusion and exclusion criteria as the original CER.

2.3 Expert Opinion

We shared the conclusions of the original report with X# experts in the field (including the original project leader, suggested field experts, original technical expert panel (TEP) members) for their assessment of the need to update the report and their recommendations of any relevant new studies. Appendix B shows the questionnaire matrix that was sent to the experts.

2.4 Check for Signals for Re-review

Since this CER did not contain meta-analyses, all signals are qualitative.

2.5 Compilation of Findings and Conclusions

For this assessment we abstracted the data from the included studies and constructed demographic and results tables, Appendix C and D. We also constructed a summary table that included the key questions, the original conclusions, and the findings of the new literature search, the expert assessments, and any FDA reports that pertained to each key question, Table 1. To assess the conclusions in terms of the evidence that they might need updating, we used a 4-category scheme:

- Original conclusion is still valid and this portion of the CER does not need updating
- Original conclusion is possibly out of date and this portion of the CER may need updating
- Original conclusion is probably out of date and this portion of the CER may need updating
- Original conclusion is out of date

In making the decision to classify a CER conclusion into one category or another, we used the following factors when making our assessments:

- If we found no new evidence or only confirmatory evidence and all responding experts assessed the CER conclusion as still valid, we classified the CER conclusion as still valid.
- If we found some new evidence that might change the CER conclusion, and/or a minority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as possibly out of date.
- If we found substantial new evidence that might change the CER conclusion, and/or a majority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as probably out of date.
- If we found new evidence that rendered the CER conclusion out of date or no longer applicable, we classified the CER conclusion as out of date. Recognizing that our literature searches were limited, we reserved this category only for situations where a limited search would produce prima facie evidence that a conclusion was out of date, such as the withdrawal of a drug or surgical device from the market, a black box warning from FDA, etc.

2.6 Determining Priority for Updating

We used the following two criteria in making our final conclusion for this CER:

- How much of the CER is possibly, probably, or certainly out of date?
- How out of date is that portion of the CER? For example, would the potential changes to the conclusions involve refinement of original estimates or do the potential changes mean some therapies are no longer favored or may not exist? Is the portion of the CER that is probably or certainly out of date an issue of safety (a drug withdrawn from the market, a black box warning) or the availability of a new drug within class (the latter being less of a signal to update than the former)?

3. Results

3.1 Search

A systematic review was undertaken for articles published between January 2007 and May 2012. We used two search strategies to identify articles from MEDLINE, EMBASE and the Cochrane Library. We used key words to detect articles that used the term “upright,” “positional,” or “weight-bearing” in combination with “magnetic resonance imaging” or “MRI.” Among the articles describing upright or positional MRI, we evaluated the full text to determine if the studies met our inclusion criteria. Full text of potential articles meeting the inclusion criteria by both methods were reviewed by two independent investigators to obtain the final collection of included studies, Figure 1.

The literature search identified 122 titles. After title and abstract review, we further reviewed the full text of 27 journal articles. The remaining 95 titles were rejected because they were case reports, commentary, or did not include topics of interest. Among the 27 articles that went on to full text review, 25 were rejected because subjects did not meet the inclusion criteria and/or did not include a comparison of interest, Table 2. Of the two articles that were further reviewed, both were abstracted into an evidence table (Appendix C).

3.2 Identifying Signals for Re-review

Table 1 summarizes the original key questions, the conclusions of the original report, the results of the literature and FDA searches, the experts' assessments, and the recommendations of Spectrum Research, Inc. (SRI) regarding the need for update.

Table 1. uMRI Summary Table

<table>
<tr><th>Conclusions from CER Executive Summary</th><th>Literature Search</th><th>FDA</th><th>Expert Opinion</th><th>Conclusion from SRI</th></tr>
<tr><td colspan="5">Key Question 1: What is the evidence to describe the concordance (i.e., ability to detect clinically important findings associated with known conditions) of upright MRI compared with currently available diagnostic testing (e.g., standard MRI ± loading, CT myelogram ± upright, plain films [flexion and extension], discography, operative findings) in patients (including appropriate sub-populations) with conditions 1-5*?

If a reference standard is available for any of these conditions, what are the test characteristics, PPV (positive predictive value), NPV (negative predictive value), sensitivity and specificity, of upright MRI compared with standard diagnostic testing?</td></tr>
<tr><td colspan="5">Spinal Conditions:</td></tr>
<tr><td>-Disc pathology

Three retrospective cohort studies [1,5,8] with the lowest quality of evidence (LoE IV) found similar agreement comparing rMRI with uMRI in identifying disc pathology in both the cervical and lumbosacral spine.

In the cervical spine, rMRI detected 61% of posterior disc herniations compared with 70% in uMRI [1].

In the lumbosacral spine, rMRI detected 31% of posterior disc herniations compared with 45% in uMRI [1].

Complete agreement was found when comparing rMRI with uMRI in the seated neutral position in the qualitative determination of posterior disc bulge (100% agreement) [8].

Seated flexion had a 95% agreement and seated extension had a 91% agreement with supine neutral in the diagnosis of disc form (normal, bulging, protrusion, or sequestration) [5].</td><td>One prospective cohort study with low quality of evidence (LoE III) found no difference between uMRI and rMRI concerning mean disc height [3].

rMRI had a mean cumulative disc height of 174.8mm compared with uMRI mean of 172.2mm (no significant difference) in patients with lumbar spinal stensosis [3].</td><td rowspan="2">Two additional uMRI systems have received FDA clearance (in addition to the GE Signa™ SP/i system and the FONAR Upright™ MRI system): the Paramed Srl MrOpen 05 and the Esaote G-scan.

The Paramed Srl MrOpen 05 product was approved in 2010 via the 510(K) and is indicated for use as a diagnostic total body imaging device with the following limitation: no angiography, no cardiac imaging, no breast imaging.

The Esaote G-scan was originally approved in</td><td></td><td>Conclusion is still valid and this portion of the HTA does not need updating.</td></tr>
<tr><td>-Foraminal stenosis

There is limited evidence (three retrospective cohort studies [5,7,8] each with LoE IV) to suggest that uMRI provides similar diagnostic information compared with rMRI with respect to foraminal stenosis.</td><td>No new data</td><td></td><td>Conclusion is still valid and this portion of the HTA does not need updating.</td></tr>
</table>

Conclusions from CER Executive Summary	Literature Search	FDA	Expert Opinion	Conclusion from SRI
Seated neutral position had complete agreement (100%) with rMRI in determining foraminal size [8]. Seated flexion had 84% and seated extension had 86% agreement compared with supine neutral position of evaluating the degree of foraminal stensosis [5]. Agreement was also seen in the score of foraminal stenosis in supine neutral, extension and flexion position comparing uMRI to myelography (94% and 92% agreement, respectively) [7].		2004 via the 510(K), and again in 2011 after modifications were made for improved safety and performance. The G-scan is intended for use on the limbs, joints, and spinal column, including upper limb (hand, wrist, forearm, elbow, arm, and shoulder), lower limb (foot, ankle, calf, knee, thigh, and hip), and imaging portions of the spinal column (cervical, thoracic, and lumbo-sacral sections)		
-Nerve root compromise The evidence for concordance between rMRI and uMRI is very low (two LoE IV retrospective cohort studies [5,7]) with respect to lumbar nerve root compromise. Comparing seated flexion and extension with supine neutral positions provided 74% and 77% agreement, respectively [5]. Comparing uMRI with myelography, there was substantial concordance (93%) in mean sagittal diameter of the dural sac within each position (supine neutral, extension, and flexion) at five separate intervertebral spaces [7].	One prospective cohort study [3] with low quality of evidence (LoE III) found no difference between uMRI and rMRI concerning mean dural sac cross-sectional area (DCSA) values. No significant differences were found between the mean DCSA values of uMRI and rMRI at any of the five lumbar levels [3].			Conclusion is still valid and this portion of the HTA does not need updating.
-Spondylolisthesis The evidence for concordance between rMRI and uMRI is very low (one LoE IV retrospective cohort study [1]) with respect to spondylolisthesis. rMRI identified spondylolistheis seven times (15%) compared with uMRI 11 times (24%). Percent agreement between the two was 91% [1].	No new data			Conclusion is still valid and this portion of the HTA does not need updating.

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Conclusions from CER Executive Summary	**Literature Search**	**FDA**	**Expert Opinion**	**Conclusion from SRI**
-Juxtafacet cysts (JFC) No data	There is insufficient evidence (one retrospective cohort study with the lowest level of evidence (LoE IV)) to suggest that uMRI provides additional diagnostic information compared with rMRI with respect to JFC [4]. MRI in the standing (extension) position had a detection rate of 97%, supine had a rate of 89%, and sitting had a rate of 78% [4]. The size (mm) of the JFCs was significantly bigger in the standing position, compared to supine and sitting (6.7±2.3 vs. 5.5±2.9 vs. 4.6±3.0, respectively) [4].			There is insufficient evidence to update the HTA with respect to JFC
Extra-spinal conditions				
-Morton neuroma One LoE III prospective study [6] provided no evidence to suggest uMRI images contribute towards the identification of Morton neuroma compared with existing diagnostic tests.	No new data			Conclusion is still valid and this portion of the HTA does not need updating.

Conclusions from CER Executive Summary	Literature Search	FDA	Expert Opinion	Conclusion from SRI
Prone position was judged best, followed by supine, then upright weight-bearing position last [6].				
-Glenohumeral instability One prospective LoE II study [2] provided no evidence to suggest uMRI images add to the identification of glenohumeral instability. uMRI underestimated instability in 70% of the cases compared to clinical exam under anesthesia [2].	No new data			Conclusion is still valid and this portion of the HTA does not need updating..
Key Question 2: What is the evidence to describe the reliability (i.e., test-retest, intra-reader, inter-reader performance) of upright MRI and how does this reliability compare with available diagnostic testing in patients with 1-5*?				
One retrospective LoE II cohort study [7] provides limited evidence that lumbar foraminal stenosis may be determined reliably between radiologists using seated uMRI in patients whose symptoms are severe enough to warrant a myelogram. The kappa statistic calculated and reported was 0.62 (substantial agreement) between two observers independently determining the grade of foraminal stenosis [7].	No new data			Conclusion is still valid and this portion of the HTA does not need updating.
Key Question 3: What is the evidence to describe the diagnostic impact (i.e., effect on additional diagnostic testing, effect on limiting the differential diagnosis) of upright MRI compared with available diagnosis testing in patients with conditions 1-5*?				
No data	No new data			Conclusion is still valid and this portion of the HTA does not need updating.

Conclusions from CER Executive Summary	Literature Search	FDA	Expert Opinion	Conclusion from SRI
Key Question 4: What is the evidence to describe the therapeutic and patient impact (i.e., effect on treatments received, efficiency of moving from diagnostic testing to treatment, outcomes [pain, function, adverse events] of test-directed treatment [operative and non-operative]) of upright MRI compared with available diagnostic testing in patients with conditions 1-5* (e.g., what is the likelihood that positive upright MRI findings accurately predicts favorable outcome following test-directed treatment)?				
No data	No new data			Conclusion is still valid and this portion of the HTA does not need updating.
Key Question 5: What is the evidence that upright MRI in the acute setting is more effective (diagnostic and therapeutic impact) than available diagnostic testing in the sub-acute/delayed setting in patients with conditions 1-5*?				
No data	No new data			Conclusion is still valid and this portion of the HTA does not need updating.

*Inclusion criteria for subject abnormalities/conditions:

1) Suspected degenerative spondylolisthesis (>25% slip)

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

3) Radicular pain (moderate/severe central stenosis, lateral recess stenosis, nerve root compression, disc extrusion)

4) Non-specific spine pain (moderate/severe central stenosis, lateral recess stenosis, nerve root compression, disc extrusion)

5) Extra-spinal joint pain/function loss (e.g. narrowing, musculoskeletal only)

4. Conclusions

4.1 Key Question 1: What is the evidence to describe the concordance (i.e., ability to detect clinically important findings associated with known conditions) of upright MRI compared with currently available diagnostic testing (e.g., standard MRI ± loading, CT myelogram ± upright, plain films [flexion and extension], discography, operative findings) in patients (including appropriate sub-populations) with conditions 1-5*?

If a reference standard is available for any of these conditions, what are the test characteristics, PPV (positive predictive value), NPV (negative predictive value), sensitivity and specificity, of upright MRI compared with standard diagnostic testing?

4.1a Disc pathology

Conclusion is still valid and this portion of the CER does not need updating.

4.1b Foraminal stenosis

Conclusion is still valid and this portion of the CER does not need updating.

4.1c Nerve root compromise

Conclusion is still valid and this portion of the CER does not need updating.

4.1d Spondylolisthesis

Conclusion is still valid and this portion of the CER does not need updating.

4.1e Juxtafacet cysts (JFC)

There is inconclusive evidence to add a conclusion concerning JFC, therefore this portion of the CER does not need updating.

4.1f Morton neuroma

Conclusion is still valid and this portion of the CER does not need updating.

4.1g Glenohumeral instability

Conclusion is still valid and this portion of the CER does not need updating.

4.2 Key Question 2*:* What is the evidence to describe the reliability (i.e., test-retest, intra-reader, inter-reader performance) of upright MRI and how does this reliability compare with available diagnostic testing in patients with 1-5*?

Conclusion is still valid and this portion of the CER does not need updating.

4.*3 Key Question 3:* What is the evidence to describe the diagnostic impact (i.e., effect on additional diagnostic testing, effect on limiting the differential diagnosis) of upright MRI compared with available diagnosis testing in patients with conditions 1-5*?

Conclusion is still valid and this portion of the CER does not need updating.

4.4 Key Question 4: What is the evidence to describe the therapeutic and patient impact (i.e., effect on treatments received, efficiency of moving from diagnostic testing to treatment, outcomes [pain, function, adverse events] of test-directed treatment [operative and non-operative]) of upright MRI compared with available diagnostic testing in patients with conditions 1-5* (e.g., what is the likelihood that positive upright MRI findings accurately predicts favorable outcome following test-directed treatment)?

Conclusion is still valid and this portion of the CER does not need updating.

4.5 Key Question 5: What is the evidence that upright MRI in the acute setting is more effective (diagnostic and therapeutic impact) than available diagnostic testing in the sub-acute/delayed setting in patients with conditions 1-5*?

Conclusion is still valid and this portion of the CER does not need updating.

*Inclusion criteria for subject abnormalities/conditions:

1) Suspected degenerative spondylolisthesis (>25% slip)
2) Suspected spinal stenosis (moderate/severe central stenosis (>1/3 canal)), lateral recess stenosis (displacing or compressing nerve root, disc extrusion)
3) Radicular pain (moderate/severe central stenosis, lateral recess stenosis, nerve root compression, disc extrusion)
4) Non-specific spine pain (moderate/severe central stenosis, lateral recess stenosis, nerve root compression, disc extrusion)
5) Extra-spinal joint pain/function loss (e.g. narrowing, musculoskeletal only)

References:

[1] Ferreiro Perez A, Garcia Isidro M, Ayerbe E, Castedo J, Jinkins JR. Evaluation of intervertebral disc herniation and hypermobile intersegmental instability in symptomatic adult patients undergoing recumbent and upright MRI of the cervical or lumbosacral spines. *Eur J Radiol.* 2007;12(47):27.

[2] Hodge DK, Beaulieu CF, Thabit GH, 3rd, et al. Dynamic MR imaging and stress testing in glenohumeral instability: comparison with normal shoulders and clinical/surgical findings. *J Magn Reson Imaging.* 2001;13(5):748-756.

[3] Madsen, R., T. S. Jensen, et al. (2008). "The effect of body position and axial load on spinal canal morphology: an MRI study of central spinal stenosis." Spine (Phila Pa 1976) **33**(1): 61-67.

[4] Niggemann, P., J. Kuchta, et al. (2012). "Juxtafacet cysts of the lumbar spine: a positional MRI study." Skeletal Radiol **41**(3): 313-320.

[5] Weishaupt D, Schmid MR, Zanetti M, et al. Positional MR imaging of the lumbar spine: does it demonstrate nerve root compromise not visible at conventional MR imaging? *Radiology.* Apr 2000;215(1):247-253.

[6] Weishaupt D, Treiber K, Kundert HP, et al. Morton neuroma: MR imaging in prone, supine, and upright weight-bearing body positions. *Radiology.* Mar 2003;226(3):849-856.

[7] Wildermuth S, Zanetti M, Duewell S, et al. Lumbar spine: quantitative and qualitative assessment of positional (upright flexion and extension) MR imaging and myelography. *Radiology.* May 1998;207(2):391-398.

[8] Zamani AA, Moriarty T, Hsu L, et al. Functional MRI of the lumbar spine in erect position in a superconducting open-configuration MR system: preliminary results. *J Magn Reson Imaging.* Nov-Dec 1998;8(6):1329-1333.

Figure 1. Flow chart showing results of literature search

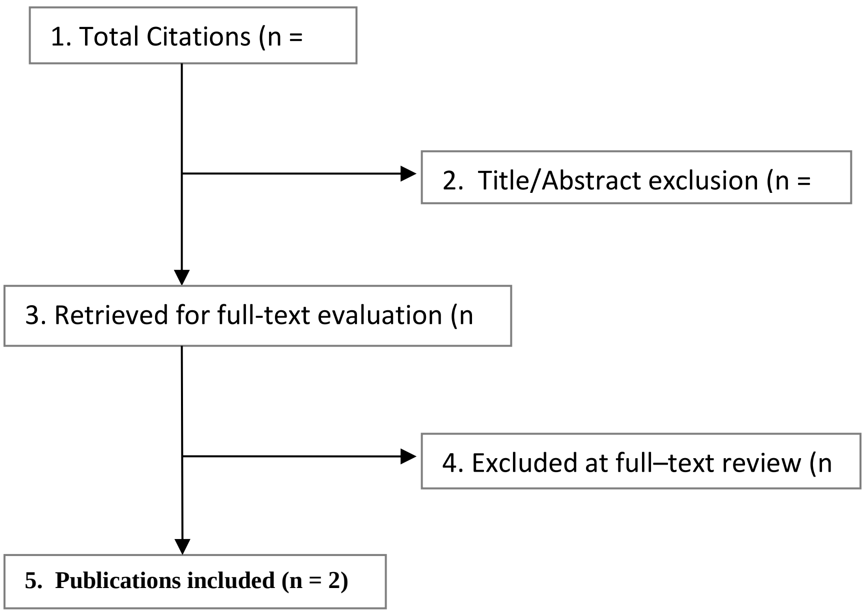

Table 2. List of excluded articles after full-text review

Study	**Reason for Exclusion:**
Alyas, F., D. Connell, et al. (2008). "Upright positional MRI of the lumbar spine." Clin Radiol **63**(9): 1035-1048.	Review paper
Alyas, F., J. Sutcliffe, et al. (2010). "Morphological change and development of high-intensity zones in the lumbar spine from neutral to extension positioning during upright MRI." Clin Radiol **65**(2): 176-180.	Case report
Castinel, B. H., P. Adam, et al. (2010). "Epidemiology of cervical spine abnormalities in asymptomatic adult professional rugby union players using static and dynamic MRI protocols: 2002 to 2006." Br J Sports Med **44**(3): 194-199.	Dynamic, not uMRI
Dragoo, J. L., C. Phillips, et al. (2010). "Mechanics of the anterior interval of the knee using open dynamic MRI." Clin Biomech (Bristol, Avon) **25**(5): 433-437.	Subjects don't meet inclusion criteria
Draper, C. E., J. M. Santos, et al. (2008). "Feasibility of using real-time MRI to measure joint kinematics in 1.5T and open-bore 0.5T systems." J Magn Reson Imaging **28**(1): 158-166.	Dynamic, not uMRI
Gedroyc, W. M. (2008). "Upright positional MRI of the lumbar spine." Clin Radiol **63**(9): 1049-1050.	Commentary
Gilbert, J. W., J. C. Martin, et al. (2011). "Lumbar stenosis rates in symptomatic patients using weight-bearing and recumbent magnetic resonance imaging." J Manipulative Physiol Ther **34**(8): 557-561.	Not a specific uMRI study; no comparison
Harada, T., Y. Tsuji, et al. (2010). "The clinical usefulness of preoperative dynamic MRI to select decompression levels for cervical spondylotic myelopathy." Magn Reson Imaging **28**(6): 820-825.	Dynamic, not uMRI
Keorochana, G., C. E. Taghavi, et al. (2011). "Effect of sagittal alignment on kinematic changes and degree of disc degeneration in the lumbar spine: an analysis using positional MRI." Spine (Phila Pa 1976) **36**(11): 893-898.	Not a specific uMRI study; no comparison
Lindgren, K. A., J. A. Kettunen, et al. (2009). "Dynamic kine magnetic resonance imaging in whiplash patients and in age- and sex-matched controls." Pain Res Manag **14**(6): 427-432.	Dynamic, not uMRI
Liodakis, E., M. Kenawey, et al. (2011). "Upright MRI measurement of mechanical axis and frontal plane alignment as a new technique: a comparative study with weight bearing full length radiographs." Skeletal Radiol **40**(7): 885-889.	Subjects don't meet inclusion criteria
Mauch, F., C. Jung, et al. (2010). "Changes in the lumbar spine of athletes from supine to the true-standing position in magnetic resonance imaging." Spine (Phila Pa 1976) **35**(9): 1002-1007.	Subjects don't meet inclusion criteria

Study	**Reason for Exclusion:**
Michael, J. W., H. P. Springorum, et al. (2008). "Upright MRI of the shoulder demonstrates labrum dynamics." Int J Sports Med **29**(12): 999-1002.	Subjects don't meet inclusion criteria
Miura, J., M. Doita, et al. (2009). "Dynamic evaluation of the spinal cord in patients with cervical spondylotic myelopathy using a kinematic magnetic resonance imaging technique." J Spinal Disord Tech **22**(1): 8-13.	Dynamic, not uMRI
Nath, R. K., M. Paizi, et al. (2007). "Upright MRI of glenohumeral dysplasia following obstetric brachial plexus injury." Magn Reson Imaging **25**(9): 1277-1282.	Not a specific uMRI study; no comparison
Neuschwander, T. B., J. Cutrone, et al. (2010). "The effect of backpacks on the lumbar spine in children: a standing magnetic resonance imaging study." Spine (Phila Pa 1976) **35**(1): 83-88.	Subjects don't meet inclusion criteria
Nicholson, J. A., A. G. Sutherland, et al. (2011). "Single bundle anterior cruciate reconstruction does not restore normal knee kinematics at six months: an upright MRI study." J Bone Joint Surg Br **93**(10): 1334-1340.	Not a specific uMRI study; no comparison
Nicholson, J. A., A. G. Sutherland, et al. (2012). "Upright MRI in kinematic assessment of the ACL-deficient knee." Knee **19**(1): 41-48.	Subjects don't meet inclusion criteria
Rabin, A., P. C. Gerszten, et al. (2007). "The sensitivity of the seated straight-leg raise test compared with the supine straight-leg raise test in patients presenting with magnetic resonance imaging evidence of lumbar nerve root compression." Arch Phys Med Rehabil **88**(7): 840-843.	Dynamic, not uMRI
Sahara, W., K. Sugamoto, et al. (2007). "Three-dimensional clavicular and acromioclavicular rotations during arm abduction using vertically open MRI." J Orthop Res **25**(9): 1243-1249.	Dynamic, not uMRI
Schlamann, M., L. Reischke, et al. (2007). "Dynamic magnetic resonance imaging of the cervical spine using the NeuroSwing System." Spine (Phila Pa 1976) **32**(21): 2398-2401.	Dynamic, not uMRI
Stemper, B. D., J. L. Baisden, et al. (2010). "Determination of normative neck muscle morphometry using upright MRI with comparison to supine data." Aviat Space Environ Med **81**(9): 878-882.	Subjects don't meet inclusion criteria
Stemper, B. D., S. J. Tang, et al. (2011). "Upright magnetic resonance imaging measurement of prevertebral soft tissue in the cervical spine of normal volunteers." Spine J **11**(5): 412-415.	Subjects don't meet inclusion criteria
Wei, F., J. Wang, et al. (2010). "Effect of lumbar angular motion on central canal diameter: positional MRI study in 491 cases." Chin Med J (Engl) **123**(11): 1422-1425.	Not a specific uMRI study; no comparison

Study	**Reason for Exclusion:**
Yan, J., Y. Wang, et al. (2010). "Vertical weight-bearing MRI provides an innovative method for standardizing Spurling test." Med Hypotheses **75**(6): 538-540.	Not a specific uMRI study; no comparison

Appendix A.

The detailed strategy below is presented in PubMed syntax. Parallel strategies were used to search the Cochrane Library and EMBASE. Keyword searches were conducted in the other listed resources.

PubMed Search Strategy
(2007 – May 2012)
Limited to English language, human population

Search Strategy for Key Questions 1 and 2

#1	Search (dynamic [TI] OR vertical [TI] OR upright [TI] OR stand-up [TI] OR standing [TI] OR seated [TI] OR open [TI] OR position* [TI] OR weight bearing [TI])
#2	Search ("Magnetic Resonance Imaging"[TI] OR MRI [TI])
#3	Search #1 AND #2
#4	Search "dynamic MRI" [TI] OR "dynamic magnetic resonance imaging" [TI] OR "vertical MRI" [TI] OR "vertical magnetic resonance imaging" [TI] OR "upright MRI" [TI] OR "upright magnetic resonance imaging" [TI] OR "stand-up MRI" [TI] OR "stand-up magnetic resonance imaging" [TI] OR "standing MRI" [TI] OR "standing magnetic resonance imaging" [TI] OR "seated MRI" [TI] OR "seated magnetic resonance imaging" [TI] OR "open MRI" [TI] OR "open magnetic resonance imaging" [TI] OR "position* MRI" [TI] OR "position magnetic resonance imaging" [TI] OR "weight bearing MRI" [TI] OR "weight bearing magnetic resonance imaging" [TI]
#5	Search "Low Back Pain"[MeSH] OR "Intervertebral Disk Displacement"[MeSH] OR "Sciatica"[MeSH] OR "Radiculopathy"[MeSH] OR "Spondylolisthesis"[MeSH] OR "Spinal Stenosis"[MeSH] OR "Intervertebral Disk"[MeSH] OR "Lumbar Vertebrae"[MeSH] OR spine[TI] OR dural sac[TI] OR facet[TI] OR "low back"[TI] OR "intervertebral disc"[TI] OR sciatica[TI] OR radicul*[TI] OR spondylolisthesis[TI] OR "spinal stenosis"[TI] OR lumbar [TI] OR "cervical vertebrae"[MeSH] OR "neck"[MeSH] OR "neck pain"[MeSH] OR "cervical myelopathy" OR "cervical spondylotic myelopathy" OR "radiculopathy"[MeSH] OR "thoracic vertebrae"[MeSH] OR "spinal curvatures"[MeSH] OR neck[TI] OR "cervical spine" [TI] OR scoliosis[TI] OR kyphosis[TI] OR lordosis[TI] OR "spinal osteophytosis"[MeSH] OR spondylosis [TI] OR "Whiplash Injuries"[MeSH]
#6	Search #3 AND #5
#7	Search #4 AND #5
#8	Search #6 OR #7
#9	Search ("Reproducibility of Results"[MeSH] OR "Validation Studies"[Publication Type])
#10	**#8 AND #9**
#11	Search ("Joints"[MeSH] OR foot OR feet OR knee* OR hip OR hips OR tmj OR temporomandibular OR shoulder* OR elbow OR wrist* OR hand OR hands)

#12	Search #3 AND #11
#13	Search #4 AND #11
#14	Search #12 OR #13
#15	#9 AND #14
#16	**Limit: NOT (letter OR editorial)**

Search Strategy for Key Questions 1, 3, 4 and 5

#1	Search (dynamic [TI] OR vertical [TI] OR upright [TI] OR stand-up [TI] OR standing [TI] OR seated [TI] OR open [TI] OR position* [TI] OR weight bearing [TI])
#2	Search ("Magnetic Resonance Imaging"[TI] OR MRI [TI])
#3	Search #1 AND #2
#4	Search "dynamic MRI" [TI] OR "dynamic magnetic resonance imaging" [TI] OR "vertical MRI" [TI] OR "vertical magnetic resonance imaging" [TI] OR "upright MRI" [TI] OR "upright magnetic resonance imaging" [TI] OR "stand-up MRI" [TI] OR "stand-up magnetic resonance imaging" [TI] OR "standing MRI" [TI] OR "standing magnetic resonance imaging" [TI] OR "seated MRI" [TI] OR "seated magnetic resonance imaging" [TI] OR "open MRI" [TI] OR "open magnetic resonance imaging" [TI] OR "position* MRI" [TI] OR "position magnetic resonance imaging" [TI] OR "weight bearing MRI" [TI] OR "weight bearing magnetic resonance imaging" [TI]
#5	Search "Low Back Pain"[MeSH] OR "Intervertebral Disk Displacement"[MeSH] OR "Sciatica"[MeSH] OR "Radiculopathy"[MeSH] OR "Spondylolisthesis"[MeSH] OR "Spinal Stenosis"[MeSH] OR "Intervertebral Disk"[MeSH] OR "Lumbar Vertebrae"[MeSH] OR spine[TI] OR dural sac[TI] OR facet[TI] OR "low back"[TI] OR "intervertebral disc"[TI] OR sciatica[TI] OR radicul*[TI] OR spondylolisthesis[TI] OR "spinal stenosis"[TI] OR lumbar [TI] OR "cervical vertebrae"[MeSH] OR "neck"[MeSH] OR "neck pain"[MeSH] OR "cervical myelopathy" OR "cervical spondylotic myelopathy" OR "radiculopathy"[MeSH] OR "thoracic vertebrae"[MeSH] OR "spinal curvatures"[MeSH] OR neck[TI] OR "cervical spine" [TI] OR scoliosis[TI] OR kyphosis[TI] OR lordosis[TI] OR "spinal osteophytosis"[MeSH] OR spondylosis [TI] OR "Whiplash Injuries"[MeSH]
#6	Search #3 AND #5
#7	Search #4 AND #5
#8	Search #6 OR #7
#9	**Limit: NOT (letter OR editorial)**
#10	Search ("Joints"[MeSH] OR foot OR feet OR knee* OR hip OR hips OR tmj OR shoulder* OR elbow OR wrist* OR hand OR hands)
#11	Search #3 AND #10
#12	Search #4 AND #10
#13	Search #11 OR #12
#14	Search "Arthritis, Experimental"[MeSH] OR "Arthritis, Infectious"[MeSH] OR "Spondylarthritis"[MeSH] OR "Arthritis, Rheumatoid"[MeSH]
#15	**Search #13 NOT #14**

Search Strategy for Economic or Cost Evaluation

#1	Search ("Magnetic Resonance Imaging"[TI] OR MRI [TI])
#2	Search #1 AND "Economics" [MeSH]
#3	Search (DYNAMIC [TI] OR VERTICAL [TI] OR UPRIGHT [TI] OR STAND-UP [TI] OR STANDING [TI] OR SEATED [TI] OR OPEN [TI] OR POSITION [TI] OR WEIGHT BEARING [TI])
#4	Search #2 AND #3
#5	Search "dynamic MRI" [TI] OR "dynamic magnetic resonance imaging" [TI] OR "vertical MRI" [TI] OR "vertical magnetic resonance imaging" [TI] OR "upright MRI" [TI] OR "upright magnetic resonance imaging" [TI] OR "stand-up MRI" [TI] OR "stand-up magnetic resonance imaging" [TI] OR "standing MRI" [TI] OR "standing magnetic resonance imaging" [TI] OR "seated MRI" [TI] OR "seated magnetic resonance imaging" [TI] OR "open MRI" [TI] OR "open magnetic resonance imaging" [TI] OR "position* MRI" [TI] OR "position magnetic resonance imaging" [TI] OR "weight bearing MRI" [TI] OR "weight bearing magnetic resonance imaging" [TI]
#6	#5 AND "Economics" [MeSH]
#7	Search "Costs and Cost Analysis"[MeSH] AND "Low Back Pain"[MeSH]
#8	Search "Costs and Cost Analysis"[MeSH] AND "Magnetic Resonance Imaging"[MeSH] AND "Low Back Pain"[MeSH]

Appendix B.

Questionnaire for experts

Appendix C. Demographic table

Table 3. Description of concordance and reliability studies of the spine comparing upright MRI to other imaging modalities

Author (Year)	LoE	Study design	Demographics	Patients	uMRI	rMRI	Protocol	Diagnostic criteria	Methods concerns
Madsen (2008)	**III**	Prospective Cohort Concordance	N = 16 Mean age: 53 years (18-80) Male: 44% Race: NR	Neurogenic claudication mainly manifested during walking or in an erect position; suspected discogenic pain caused by instability due to early disc degeneration or a minor degenerative spondylolisthesis mainly manifested in an erect position	n = 16 Specs: Fonar Upright MRI, 0.6 T, axial T1 weighted and sagittal T2 weighted images (256x256, ST = 4-5 mm)	n = 16 Specs: Fonar Upright MRI, 0.6 T, axial T1 weighted and sagittal T2 weighted images (256x256, ST = 4-5 mm)	Each patient had 4 MRI scans in different positions: 1. **uMRI**: vertical V 2. **rMRI**: horizontal with axial compression of 40% of their body weight (H40) 3. **rMRI**: horizontal with no applied load (H0) 4. **rMRI**: horizontal with axial compression of 50% of their body weight (H50) **Assessed:** Quantitative: disc height, lumbar lordosis, dural sac	**Disc height:** Centroid method- significant reduction: ≥ 3.5 mm **Lumbar lordosis:** Cobb's mehod **DCSA:** Significant reduction: > 35 mm^2 Borderlines for: **Absolute spinal stenosis:** 75 mm^2 **Relative stenosis:** 100 mm^2	2 patients did not complete the last scan (H50) because of discomfort

Author (Year)	LoE	Study design	Demographics	Patients	uMRI	rMRI	Protocol	Diagnostic criteria	Methods concerns
							cross-sectional area (DCSA), stenosis **Interpretation:** all measurements were made by a single observer **Blinding:** single observer blinded to any clinical information and patient data		
Niggemann (2012)	**IV**	Retrospective Cohort Concordance	N = 50 Mean age: 62.3 ± 10.1 years Male: 52% Race: NR	Low back pain, sciatica, and/or spinal claudication	n = 50 Specs: FONAR Upright MRI, 0.6-T open magnet, sagittal T2- and T1-weighted scan (640x640, ST = 4.5 mm) and axial T2-weighted sequence (576x576, ST = 4.5 mm)	n = 32 Specs: FONAR Upright MRI, 0.6-T, sagittal T2-weighted scan (512x512, ST = 4.5 mm); axial T2-weighted sequence (512x512, ST = 4.5 mm)	uMRI: neutral sitting position (n = 50) uMRI: flexion sitting position (n = 50) uMRI: extension (standing) position (n = 49) rMRI: supine position (n = 32) **Assessed:** Rate, location, and size of juxtafacet cysts, vertebral slips, lordosis angle, angular movement in the affected segment	Rate, location, and size of juxtafacet cysts: based on signal intensity **Vertebral slips:** The distance between 2 measured lines: a line on a midline sagittal image between the bony structures connecting the upper and lower dorsal edge of the cranial	2 patients could not complete extension (standing) MRI because of pain and resulting movement artifacts

Author (Year)	LoE	Study design	Demographics	Patients	uMRI	rMRI	Protocol	Diagnostic criteria	Methods concerns
							Interpretation: All images visualized by a board-certified senior neuroradiologist and a board-certified senior neurosurgeon specialized in spinal neurosurgery; measurements were performed conjointly and in agreement between the two physicians **Blinding:** NR	vertebra; a second, parallel line drawn by the viewing software after pointing to the upper dorsal edge of the caudal vertebra **Lordosis angle:** angle between the upper margin of L1 and the upper margin of S1 **Overall movement rate:** the difference in the lordosis angle between flexion (sitting) and extension (standing) position	

Abbreviations: A-P: anterior-posterior; DCSA: dural sac cross-sectional area; LoE: level of evidence; rMRI: standard, recumbent magnetic resonance imaging; Specs: specifications; ST: slice thickness; uMRI: upright magnetic resonance imaging

Appendix D. Summary table of results of included articles in updated literature search

Table 4. Mean values of the 4 positions (H0- horizontal with no applied axial load; H40- Horizontal with 40% load; H50- horizontal with 50% load; V- vertical) in 16 patients with lumbar spinal stenosis. Results: Madsen 2008.

Variable	H0 Mean (95% CI)	H40 Mean (95% CI)	H50 Mean (95% CI)	V Mean (95% CI)	*P*†
Cumulative disc height (mm)*	174.7 (166.7; 182.7)	174.0 (165.5; 182.5)	175.6 (166.1; 185.1)	172.2 (162.9; 181.5)	NS
Lordosis (˚)*	49.9 (45.6; 54.2)	49.5 (45.5; 53.5)	49.6 (44.1; 55.1)	43.9 (38.4; 49.4)	0.04
DCSA (mm^2)*					
L1-L2	175 (147; 202)	178 (153; 203)	195 (167; 224)	194 (161; 227)	NS
L2-L3	146 (118; 173)	136 (106; 166)	150 (125; 174)	150 (112; 187)	NS
L3-L4	128 (94; 162)	115 (84; 147)	146 (112; 180)	117 (84; 150)	NS
L4-L5	123 (91; 155)	121 (82; 160)	138 (101; 175)	136 (101; 171)	NS
L5-S1	126 (87; 164)	129 (85; 172)	132 (88; 176)	146 (115; 176)	NS

*Two patients did not complete the last scan, H50, because of discomfort. Seven image-files with axial T1-weighted sequences were excluded because the contours of the dural sac were not satisfyingly defined.

†Evaluating differences between V and H0, H40, H50 combined by two-way ANOVA. NS = not statistically significant, $P > 0.05$.

Table 5. Mean juxtafacet cyst (JFC) size, detection rate, lordosis angle and amount of vertebral slip in 50 patients with a total of 67 JFCs acquired in three positions: supine, sitting, and standing (extension). Results: Niggemann 2012.

	Supine	Sitting	Standing (extension)	Significance
Size of JFC (mm)*	5.5 ± 2.9	4.6 ± 3.0	6.7 ± 2.3	all $p < .05$
Detection rate	89% (32/36)	78% (52/67)	97% (65/67)†	
Lordosis angle (˚)	53.4 ± 11.4	Flexion: 9.7 ± 13.1 Neutral: 23.2 ± 14	50.1 ± 13	
Vertebral Slip	Less pronounced	Most pronounced		

*34 segments in which axial images were acquired in all three positions: supine, sitting, and standing

† In two patients the standing examination could not be completed because of pain and resulting movement artifacts, therefore the detection rate was 100% for completed examinations and 97% for all examinations.