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From the 2006 NIDRR SCI Measures Meeting
Neuroimaging in Traumatic Spinal Cord Injury: An Evidence-based Review for Clinical Practice and Research

Report of the National Institute on Disability and Rehabilitation Research Spinal Cord Injury Measures Meeting

Neuroimaging Committee:

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Received January 23, 2007; accepted February 28, 2007

Abstract

Objective: To perform an evidence-based review of the literature on neuroimaging techniques utilized in spinal cord injury clinical practice and research.

Methods: A search of the medical literature for articles on specific neuroimaging techniques used in SCI resulted in 2,302 published reports. Review at the abstract and full report level yielded 99 clinical and pre-clinical articles that were evaluated in detail. Sixty nine were clinical research studies subjected to quality of evidence grading. Twenty-three articles were drawn from the pre-clinical animal model literature and used for supportive evidence. Seven review articles were included to add an element of previous syntheses of current thinking on neuroimaging topics to the committee process (the review articles were not graded for quality of evidence). A list of clinical and research questions that might be answered on a variety of neuroimaging topics was created for use in article review. Recommendations on the use of neuroimaging in spinal cord injury treatment and research were made based on the quality of evidence.

Results: Of the 69 original clinical research articles covering a range of neuroimaging questions, only one was judged to provide Class I evidence, 22 provided Class II evidence, 17 Class III evidence, and 29 Class IV evidence.

Recommendations: *MRI* should be used as the imaging modality of choice for evaluation of the spinal cord after injury. *CT* and *plain radiography* should be used to assess the bony anatomy of the spine in patients with SCI. *MRI* may be used to identify the location of spinal cord injury. *MRI* may be used to demonstrate the degree of spinal cord compression after SCI. *MRI* findings of parenchymal hemorrhage/contusion, edema, and spinal cord disruption in acute and subacute SCI may contribute to the understanding of severity of injury and prognosis for neurological improvement. *MRI-Diffusion Weighted Imaging* may be useful in quantifying the extent of axonal loss after spinal cord injury. *Functional MRI* may be useful in measuring the anatomic functional/metabolic correlates of sensory-motor activities in persons with SCI. *MR Spectroscopy* may be used to measure the biochemical characteristics of the brain and spinal cord following SCI. *Intraoperative Spinal Sonography* may be used to identify spinal and spinal cord anatomy and gross pathology during surgical procedures. Further research in these areas is warranted to improve the strength of evidence supporting the use of neuroimaging modalities. *Positron Emission Tomography* may be used to assess metabolic activity of CNS tissue (brain and spinal cord) in patients with SCI.

J Spinal Cord Med. 2007;30:205–214

Key Words: Spinal cord injuries; Evidence-based medicine; Neuroimaging; spinal sonography; Magnetic resonance imaging; MRI-diffusion weighted imaging; Functional MRI; Positron emission tomography; Computerized tomography; National Institute on Disability and Rehabilitation Research

INTRODUCTION

With the field of SCI research now in the era of clinical trials of interventions targeting improved neurological outcome, the need for precise and clinically meaningful measurement of spinal cord pathophysiology is evident. While neuroimaging modalities have commonly been used in SCI clinical practice and research, an evidence-based review of the existing literature has not been conducted. The following review is intended to provide guidance for clinicians and researchers in the use of selected neuroimaging modalities in the assessment of spinal cord injury. The clinical questions posed by the

National Institute on Disability and Rehabilitation Research (NIDRR) SCI Measures Meeting Neuroimaging Committee included:

- What is the role of MRI in the assessment of spinal cord injury?
- What is the role of MRI-Diffusion Weighted Imaging in SCI assessment?
- What is the role of functional MRI (fMRI) in SCI assessment?
- What is the role of MR Spectroscopy in SCI assessment?
- What is the role of Intraoperative Spinal Sonography (IOSS) in SCI assessment?
- What is the role of Positron Emission Tomography (PET) in SCI assessment?

Description of the Analytical Process

The Committee: The committee was formed in late 2005. The committee chair invited participation from recognized experts in the fields of SCI Medicine, Neuroradiology, and Neurosurgery. The committee has conducted its work by email periodically since December 2005.

The Task: The committee's task was to develop preliminary evidence-based guidelines for a defined set of neuroimaging modalities used in spinal cord injury clinical practice and research. As a volunteer effort with limited methodological and technical support, the committee's scope of work was by necessity, a preliminary review of a circumscribed list of neuroimaging techniques. The committee sees this project as the first step in the development of comprehensive evidence-based neuroimaging guidelines in SCI clinical care and research.

Literature Search: A literature search for relevant published articles in the medical literature was performed utilizing three electronic databases: PubMed, OVID, and Google Scholar. Database search terms of spinal cord injury, MRI, functional MRI, MRI-Diffusion-Weighted Imaging, Intraoperative Spinal Sonography, ultrasonography, PET, and MR spectroscopy were used. The reference lists of SCI neuroimaging literature were also reviewed for relevant studies. In addition, nominations for published articles were forwarded by committee members. This search process yielded 2,302 abstracts published between 1984 and 2006 for review, the majority of which were from electronic database queries.

Preliminary Review: The 2,302 abstracts were reviewed for relevance, specifically the likelihood that the published article would contain scientific evidence on a neuroimaging topic in SCI that could be used in the development of a guideline. The primary criterion for more detailed review was that a published article described SCI research that included neuroimaging as an important element of outcome measurement. While the primary focus of the guideline development process was on human research, the committee also considered preclinical (animal model) research findings since they may lay the groundwork for validation of specific modalities. After review of the abstracts, 119 articles were selected for more detailed assessment and distributed to the committee.

Literature Review and Evidence Grading: The 123 full-text articles were distributed to the committee for review. After review of these articles, 24 were judged to be inappropriate for inclusion in the in-depth analysis because they did not provide sufficient evidence on the use of imaging modalities in traumatic spinal cord injury. Of the 99 remaining articles, 92 were original research publications and 7 were review articles. The review articles were included to add an element of previous syntheses of current thinking on neuroimaging topics to the committee process (the review articles were not graded for quality of evidence). A list of questions were posed in broad topic areas (eg, What is the role of MRI in the assessment of spinal cord injury?) and more narrowly focused topics (eg, Do MRI findings in acute/subacute SCI predict neurological outcome?) that might be addressed in a neuroimaging guideline. The questions were intended to guide the committee in its review of the literature. An evidence table was created, grading each original research article for quality of evidence utilizing the American Academy of Neurology (AAN) criteria for evaluating literature on diagnostic and prognostic accuracy questions (1). Since preclinical animal model research reports often do not comment on blinding procedures, which are critical for evaluation by AAN criteria, it was difficult to apply evidence criteria to the 23 preclinical research articles, leaving 69 clinical research articles for grading. The AAN criteria were developed as a method of estimating the risk of bias in published medical research using a 4-tiered classification scheme. The AAN criteria are as follows:

Class I (Low risk of bias): Evidence is provided by a prospective study of a broad spectrum of persons who

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The views expressed in this article are the result of independent research and do not necessarily represent the views of the US Department of Education or the United States.

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may be at risk for developing the outcome. The study measures the predictive ability using an independent gold standard for case definition. The predictor is measured in an evaluation that is masked to clinical presentation and the outcome is measured in an evaluation that is masked to the presence of the predictor. All patients have the predictor and outcome variables measured.

Class II (Moderate risk of bias): Evidence is provided by a prospective study of a narrow spectrum of patients at risk for having the condition or outcome, or by a retrospective study of a broad spectrum of persons with the condition compared to a broad spectrum of controls. The study measures the prognostic accuracy of the risk factor/predictor using an acceptable gold standard for case definition, measured in an evaluation that is masked to the clinical presentation.

Class III (Moderate to High risk of bias): Evidence is provided by a retrospective study in which either the persons with the condition/outcome or the controls are of a narrow spectrum. The study measures the predictive ability using an acceptable independent gold standard for case definition. The outcome, if not *objective*, is determined by someone other than the person who measured the predictor.

Class IV (Very High risk of bias): Any design where the predictor is not applied in an independent evaluation *or* evidence is provided by expert opinion *or* case series without controls.

In applying this classification scheme, it was assumed all studies were retrospective that did not explicitly state the use of a prospective protocol-defined application of neuroimaging technique. As an example, a "look back" at those patients enrolled in a prospective database for that subset of them that had clinical neuroimaging is assumed to be a retrospective study.

In answering the specific questions posed by the committee, a modified version of the AAN Guidelines for rating the strength of conclusion was utilized. The committee elected to add consideration of pre-clinical animal model research results in recognition of the contribution of that branch of SCI inquiry to the validation of neuroimaging techniques. Understanding that some neuroimaging modalities used for SCI have been adapted from use in other related CNS disorders (eg, traumatic brain injury, cerebrovascular disease—beyond the scope of this review) or have been widely adopted as accepted practice, the Committee also added a category of Expert Consensus to enable recommendations in areas where strict evidence support in SCI is lacking. The Level of Recommendation criteria used by the Committee were as follows:

Level A (Established as effective): Requires at least two consistent Class I studies.

Level B (Probably effective): Requires at least one Class I study or two consistent Class II studies or one Class II study with at least two controlled preclinical animal studies that provide indirect support.

Level C (Possibly effective): Requires at least one Class II study or two consistent Class III studies or one Class III study with at least two controlled preclinical animal studies that provide indirect support.

Level EC (Expert Consensus): When published literature was not available to establish an evidence basis for specific recommendations on SCI neuroimaging modalities that are in common clinical usage; where there is an accepted usage among experts in the field. Specific validation in spinal cord injury is lacking. This rating was also used for recommendations beyond the scope of the SCI neuroimaging literature review that were discussed and approved at the measures meeting (eg, the recommendation on the use of CT and plain radiography).

Level U (Data inadequate or conflicting): Studies not meeting criteria for Class I-III.

Neuroimaging Session at the SCI Measures Meeting: Presentations of the committee's recommendations on specific neuroimaging modalities were made at the SCI Measures Meeting sponsored by the National Institute on Disability and Rehabilitation Research (NIDRR) on June 24, 2006 in Boston, Massachusetts. The SCI Measures Meeting session on Neuroimaging in SCI was attended by 40 international SCI clinician scientists. An interactive attendee participation format was used to determine the consensus status of the specific recommendations. All of the recommendations presented in this report achieved consensus approval of the SCI clinician scientist participants at the meeting.

Analysis of Evidence

Magnetic Resonance Imaging: The topic of magnetic resonance imaging (MRI) of the spinal cord was subdivided into "standard" clinical MRI used for imaging the injured spinal cord, magnetic resonance imaging-diffusion weighted imaging (MRI-DWI)—an evolving technique targeted at quantifying preservation or loss of specific axon tracts in the spinal cord, functional MRI (fMRI)—the use of special imaging techniques to assess functional activity of the CNS during sensory stimulation or motor activity, and MR spectroscopy.

- **MRI:** Forty clinical and 12 preclinical studies utilizing standard MRI as an assessment tool were reviewed. Evidence rating of the 40 clinical studies produced one Class I article, 7 Class II articles, 17 Class III articles, and 15 Class IV articles. The studies fell into several broad categories:
  1. Correlation of MRI imaging findings with clinical status:
     - Pathology: MRI is an imaging technique that can assess abnormality of soft tissues such as the spinal cord. Since the "gold standard" for assessment of tissue changes after injury is pathological examination, correlation of MRI signal abnormalities with the gross and histopathology of spinal cord would

validate the use of MRI to diagnose such pathological correlates as contusive hemorrhage, hematomyelia, edema, cord compression, cord laceration/transection, etc. While there were only 4 Class IV studies (1–4) that examined the correlation between MRI findings and pathology of the spinal cord on post-mortem examination, there were 6 controlled pre-clinical studies that demonstrated the ability of MRI to detect a variety of pathological findings including edema, hemorrhage, cystic cavitation, and length of lesion (5–10). The use of Computed Tomography (CT) was compared to MRI for assessment of acute spinal trauma in a single Class III study (11) which showed that MRI was superior to CT for measuring cord compression. The ability of MRI to measure cord atrophy in chronic SCI patients was reported in one Class II study (12).

- Impairment: Correlation of acute MRI findings with SCI impairment was demonstrated by two Class II (13,14), 9 Class III (15–23), and one Class IV (24) studies as well as 3 pre-clinical investigations (7,8,10). Patients with no or minimal MRI signal change showed the least amount of motor-sensory impairment (19,22,24). Patients with parenchymal hemorrhage (14–16,18–24). and transection (19,22) had the most severe functional deficits. There was a correlation with length of signal abnormality and degree of impairment (15,16,20). A single Class I study showed evidence of increased MRI signal abnormality in the grey matter immediately rostral to the spinal cord lesion of chronically injured patients with central pain compared to those who were pain-free (25).

2. Use of MRI findings for prognostic purposes: As an extension of the investigation of MRI and severity of injury correlates, 6 Class II studies (14,15,26–29), 13 Class III studies (16,17,19,21–24,30–35), 6 Class IV studies (5,25,36–39), one Class III clinical animal study (40), and 4 preclinical studies (7,8,10,11) have shown a relationship between acute SCI MRI signal abnormality and neurological outcome over time—the use of early MRI findings as a prognostic indicator for recovery of function. Parenchymal hemorrhage (7,9,11,14,16,17,19–25,27,28,30,31,33,34,36,40), transection (19,22), and longer lesion length (8,16,20,25,28,30,41) were correlated with less favorable neurological outcome. Lack of MRI signal abnormality (19,21,22,24,32,33,36,39) was associated with greater recovery. Several studies which examined the relative prognostic value of initial neurological examination and MRI concluded that the initial physical examination findings were the best single predictor of outcome (17,25).
3. Use of MRI findings as a secondary outcome measure: MRI has been utilized in one Class II (41) and 4 Class IV (42–45) interventional studies as a secondary outcome measure of response to treatment. A study of omentum transposition surgery for improvement in neurological function used MRI to track the secondary outcomes of spinal cord size, omentum pedicle graft contact with the spinal cord, omental enhancement, degree and anatomical extent of signal change in the graft and spinal cord, and spinal cord cyst size following the surgical intervention (42). A study of surgical treatment to arrest neurological deterioration of progressive post-traumatic cystic and non-cystic myelopathy with tethered cord used MRI as a secondary outcome measure of signal abnormality and cyst size response to intervention (44). Two studies of embryonic spinal cord tissue implant therapies for arresting neurological loss in persons with progressive post-traumatic cystic myelopathy have used MRI to track cyst cavity response to the implant intervention (43,46). They both showed persistent cyst cavity obliteration in the region of tissue implantation which was interpreted as evidence suggestive (but not conclusive) of graft survival. One of the studies also noted that there was no evidence of tissue overgrowth at the site of the implant, but concluded that MRI was not able to delineate the boundary between host and graft tissue and that "conventional MRI may not be sufficient to unequivocally determine graft survival or failure" (46). This same research group had previously conducted a pre-clinical animal study of implanted fetal tissue into two distinct injury models (hemisection and compression), using MRI to track the fate of the implants (46). MRI of the grafted animals in that study showed homogeneous, slightly hyperintense signal at the graft site relative to the neighboring host tissue which was felt to be indicative of graft survival in most of the animals. Hypointense transplant site signal changes in the remainder of the transplanted animals was interpreted as an indication of failure of transplant survival and was similar to the signal abnormality seen in the lesion-only control animals. These findings led the authors to conclude that MRI could be used to detect the presence of transplanted neural tissue in living animals after experimental spinal cord injury. The search for a more reliable means to track the anatomical location of cellular implants has led to the study of MRI assessment of labeled cells (47). A number of preclinical animal studies have documented the ability of MRI to localize superparamagnetic iron oxide (SPIO)-labeled cells (autologous inflammatory cells and homologous implants) delivered to lesion sites in the central nervous system in a variety of experimental models (48,49). The utility and safety of SPIO or other labeling techniques in human SCI cellular therapies has not been studied.

- **MRI-DWI:** Magnetic Resonance Imaging-Diffusion Weighted Imaging is an MRI-based imaging modality that measures the free diffusion (Brownian motion) of water molecules, enabling the detection of imaging information beyond the resolution of conventional MRI techniques (50,51). MRI-DWI data derive from the differential directional diffusivity of water molecules and are analyzed and commonly reported as one or more distinct parameters: Apparent Diffusion Coefficients (ADC) measured, for example, longitudinally and transversely to the axis of the spinal cord, tensors derived from diffusion tensor imaging (DTI), and measures of anisotropy. Specifically, it has been proposed as a technique for detecting axon integrity, myelin disruption, and axon swelling. For these reasons, it has been studied as a neuroimaging measure of spinal cord injury, specifically the integrity of white matter. While it has come into common clinical usage in brain imaging, the technical challenges of this modality related to its susceptibility to motion artifact (arising from cardiorespiratory activity and CSF pulsations) as well as the small size of the spinal cord have significantly limited its clinical application in SCI and other spinal cord disorders to date. Only one Class IV report (single case report) of the use of MRI-DWI in traumatic SCI was found (52). This report compared MRI-DWI within 2 hours of injury to standard clinical MRI with T2-weighted images in a patient with acute upper cervical SCI. The investigators found that DWI was more sensitive than T2-weighted MRI for the detection of spinal cord injury in their patient examined in the first several hours post injury. A class II study on the use of MRI-DWI in patients with symptomatic cervical spondylotic myelopathy showed that DWI improved the sensitivity for detection of spinal cord imaging abnormality compared to standard MRI (53). Another Class IV study of the use of MRI-DWI in the assessment of a variety of spinal cord intramedullary lesions reported the ability to detect different patterns of DWI signal abnormalities in the various disorders, prompting the investigators to suggest that the imaging technique had diagnostic promise (54). The application of MRI-DWI in the assessment of spinal cord injury has been much more extensively studied in pre-clinical animal model investigations where the technical difficulties of this technique can be more easily overcome with experimental examination paradigms which might include controlled ventilation or ex-vivo imaging. Nine controlled preclinical animal studies were reviewed, four of which described DWI assessments of experimental SCI of rats using various injury models (55–58), while two described DWI techniques using non-injured rat spinal cord (59,60), and thee utilized MRI-DWI to investigate response to cellular interventions after SCI (61–63). These studies show that MRI-DWI values correlate with axon counts and thus are an indicator of white matter integrity (57,59), that ex-vivo DWI of the spinal cord is influenced by fixative technique (60), and that DWI may be more sensitive in detection of early pathological change after excitotoxic and contusive injury than conventional MRI (56,58,59). The three studies that utilized MRI-DWI to measure response to various cellular therapy interventions after experimental SCI demonstrated that this technique could be used as an outcome measure of tissue destruction and subsequent repair beyond the capabilities of standard MRI, and that correlated to behavioral outcomes (61–63).
- **Functional MRI (fMRI):** Fifteen clinical studies were reviewed that used fMRI to assess CNS activation with motor or sensory activation paradigms, including 11 Class II articles (64–73) and 4 Class IV articles (74–77). Three Class II studies examined the fMRI activation of the spinal cord either in response to a motor task (66) or thermal stimulation of the skin (70,73). These studies showed that fMRI can reliably detect motor and sensory activation of the spinal cord. In the study of motor activation, the Blood Oxygen Level Dependent (BOLD) fMRI signal changes indicating functional activity of the spinal cord were examined in uninjured subjects and found to be anatomically localized to the appropriate myotome and proportional to the level of activity (66). The studies of sensory (thermal) activation of the spinal cord were conducted in persons with complete and incomplete SCI compared to uninjured controls, utilizing thermal (10°C) (70,73) or 2°C (70) stimulation of the L4 dermatome at the calf with fMRI signal analysis of the lumbar spinal cord. In these studies of sensory activation of the spinal cord, fMRI image quality and signal changes were enhanced by use of an imaging protocol that utilizes detection of tissue water content changes termed Signal Enhancement by Extravascular water Protons (SEEP). In the uninjured control subjects, there was a pattern of spinal cord activation detected by fMRI that was consistent with animal-derived physiological data. In the subjects with SCI, the thermally stimulated activation of the spinal cord was altered with an absence or diminished activation of ipsilateral dorsal grey matter, but increased activation of contralateral ventral spinal cord. Twelve studies examined fMRI to detect brain responses to motor (65,67–69,71,72,74,75,78) or sensory (68, 75–77) activation paradigms in persons with SCI. The 8 Class II and two Class IV studies that examined fMRI response to motor tasks showed variable degrees of reorganization of motor activation in the subjects with SCI, not only in areas associated with motor impairment, but also in cortical regions representing motor function unaffected by SCI. Evidence of motor reorganization observed in these studies included shifts of somatotopic representation, changes in pattern of activation, volume of activation, and modulation of activation. The single Class II and three Class IV studies

that investigated brain fMRI response to sensory stimulation also showed evidence of reorganization of sensory processing. One of these sensory investigations studied SCI patients with phantom pain (76), while another studies a variety of patients with allodynia, 3 of whom had a spinal cord locus of pathology (77). A single Class IV study of 4 SCI subjects participating in a body weight-supported treadmill training program (BWSTT) utilized fMRI as an interventional outcome measure (78). The investigators reported greater activation of cortical sensorimotor regions and the cerebellum following BWSTT and noted that only the subjects with increased cerebellar activation achieved independent over-ground ambulation.

- **MR Spectroscopy:** Only two Class II studies on the use of MR Spectroscopy in patients with SCI were reviewed (78,79). MR Spectroscopy is a technique that allows the non-invasive measurement of various biochemical metabolites by in vivo analysis of the magnetic resonance spectrum of a specified volume of tissue. MR Spectroscopy has been used to analyze a variety of metabolites including compounds containing choline, creatine, phosphocreatine, N-acetyl aspartate, glutamate and glutamine. A controlled study of brain MR Spectroscopy of the thalamus in patients with paraplegia with and without neuropathic pain compared to uninjured control subjects showed that the concentration of N-acetyl (NA) was negatively correlated with pain intensity (80). The authors concluded that the presence of neuropathic pain after SCI is associated with biochemical changes in the thalamus. The other MR Spectroscopy study was an investigation of biochemical changes in N-acetyl aspartate (NAA) and creatine in the motor cortex and ipsilateral occipital cortex in patients with motor-functional (ASIA D) incomplete SCI (81). Compared to uninjured control subjects, the patients with functionally incomplete SCI showed an increased NAA/creatine ratio in the motor cortex which was interpreted as an increase in NAA due to adaptive dendritic sprouting accompanying recovery after injury.

Intraoperative Spinal Sonography (IOSS): One Class II (81) and 4 Class IV (82–85) articles on Intraoperative Spinal Sonography were reviewed. IOSS is the measurement of spinal cord and spinal canal abnormalities utilizing real time ultrasound technology in the operating room. The technique is widely used in the clinical practice of spinal surgery to assess bony anatomy of the spinal canal as well as anatomy and pathology of the spinal cord and meninges. The Class II study correlated the ultrasound, MRI findings, and motor impairment in patients with cervical spine lesions and neurological deficits who underwent spinal surgery. IOSS abnormality was assigned a grade determined by the fraction of spinal cord diameter exhibiting increased echogenicity. IOSS grade was correlated with the initial and follow-up motor scores but did not add to the prognostic information gained from initial neurological examination. IOSS was able to confirm spinal cord lesions seen on MRI and showed some abnormalities which were missed on suboptimal preoperative MRI examinations. The Class IV studies described the variety of intraoperative spine and spinal cord abnormalities that can be detected and measured with IOSS: bone fragments, spinal malalignment, spinal cord and thecal sac compression, disk material, foreign bodies, spinal cord motion, syrinx cavities, and myelomalacia. These studies also suggest that IOSS can be used to document initial intraoperative response to intervention such as decompression, untethering, and cyst shunting.

Positron Emission Tomography (PET): Five Class IV articles on PET imaging in patients with SCI were reviewed. A single Class IV PET imaging article was found that assessed PET of the *spinal cord* in the assessment of patients with compressive myelopathy (86). This study utilized high resolution fluorodeoxyglucose-positron emission tomography (FDG-PET) to evaluate the metabolic characteristics of the spinal cord in myelopathy patients and concluded that the standardized uptake values for FDG-PET in the cervical spinal cord correlated better than MRI with pre- and postoperative neurological scores in these nontraumatic subjects. Four Class IV articles were found describing PET assessment of the *brain* in persons with SCI (87–90). One of the articles utilized PET scanning to assess brain metabolism after sensory stimulation of the vagina and foot to elucidate the sensory pathways which convey genital stimulation to the brain in women with SCI (87). Two articles studied regional brain response to unilateral hand movement in persons with SCI determined by PET, showing changes in activation patterns compared to uninjured control subjects (88,89). One additional article assessing resting brain metabolism showed alterations in the distribution of PET glucose utilization in persons with SCI compared to uninjured control subjects (90). These studies suggest that PET may be used to assess the metabolism of spinal cord and brain in patients with SCI.

Other imaging modalities:

- **Computerized Tomography (CT):** CT imaging of the spinal column was not specifically covered in this review of spinal cord neuroimaging because it does not adequately image the spinal cord. Current clinical convention holds that CT is the superior modality for measuring bony canal dimension and MRI is the superior modality for assessing spinal cord compression and pathology of spinal cord parenchyma (80). Two Class III studies and one Class IV study of neuroimaging in SCI considered in the above MRI evidence review also included CT imaging data, supporting the conclusion that MRI is the superior modality for assessment of spinal cord injury and contribution to clinical prognostication (12,22,38).

Specific SCI Neuroimaging Recommendations

Based on the evidence of the medical literature that was reviewed by the committee and the discussion held at the SCI Measures Meeting Neuroimaging Session, the Neuroimaging Committee makes the following recommendations:

MRI:

1. MRI should be used as the imaging modality of choice for evaluation of the spinal cord injury. Level of Recommendation: B
2. MRI may be used to identify the location of spinal cord injury. Level of Recommendation: B
3. MRI may be used to demonstrate the degree of spinal cord compression after SCI. Level of Recommendation: B
4. MRI findings of parenchymal hemorrhage/contusion, edema, and spinal cord disruption in acute and subacute SCI may contribute to the understanding of severity of injury and prognosis for neurological improvement. Level of Recommendation: B
5. MRI-DWI may be useful in quantifying the extent of axonal loss after spinal cord injury. Level of Recommendation: B
6. Functional MRI may be useful in measuring the anatomic functional/metabolic correlates of sensory-motor activities in persons with SCI. Level of Recommendation: B
7. MR Spectroscopy may be used to measure the biochemical characteristics of the brain and spinal cord following SCI. Level of Recommendation: C
8. MRI assessment of patients with suspected injury of the spinal cord should include the following views and pulse sequences:
   a. Sagittal Views: T1, T2 Fast Spin Echo, T2 Gradient Echo
   b. Axial Views: T2 Fast Spin Echo, T2 Gradient Echo

   Level of Recommendation: EC

CT and Plain Radiography:

1. CT and plain radiography should be used to assess the bony anatomy of the spine in patients with SCI. Level of Recommendation: EC (Note: while the literature review did not specifically target CT and Plain Radiography, the attendees at the Neuroimaging Session of the SCI Measures Meeting agreed that this recommendation was an appropriate expert consensus addition to the list of neuroimaging recommendations.)

Intraoperative Spinal Sonography:

1. Intraoperative Spinal Sonography may be used to identify spinal and spinal cord anatomy and gross pathology during surgical procedures. Level of Recommendation: C

Positron Emission Tomography:

1. Positron Emission Tomography may be used to measure metabolic characteristics of the brain and spinal cord following SCI. Level of Recommendation: C

Future Research Recommendations: In its review of the current evidence basis for neuroimaging in SCI, the committee identified a number of areas for future research.

1. All neuroimaging modalities:
   a. The use of neuroimaging measurement in SCI research should include the blinding/masking of key clinical correlates from interpreters of neuroimaging information. Research reports should include documentation of blinding/masking protocols. The quality of evidence rating assigned to a number of reports was downgraded because of failure to document the investigator's efforts to eliminate bias by masking the evaluators from the treatment status of the subjects.
   b. Research involving the use of neuroimaging measurement should include reliability/reproducibility testing (inter-rater reliability). Investigators are encouraged to document efforts to promote the reliability and reproducibility of key outcome measures. This can include specification of key neuroimaging assessment criteria as well as the training and assessment of evaluators on the consistent application of such criteria.
   c. Future research on imaging modalities should include larger sample sizes and multiple levels and severities of injury.
2. MRI
   a. Research on the correlation of MRI findings with clinical outcome should investigate specific lesion size (contusion and edema) measurement. With the development of imaging software that allows specific measurement of dimension, correlational studies can be further refined.
   b. The committee anticipates that further research on the clinical and prognostic capability of MRI will be appropriate with improvements in field strength and software.
   c. As the field of SCI interventional research enters the era of cellular therapies, the study of clinical safety and effectiveness of cellular tracers to enable tracking of cellular implant migration and fate will be important.
3. MRI-DWI
   a. Specific "lesion size" measurement correlations with clinical status should be undertaken.
   b. Refinement of clinical and prognostic capability should be anticipated with improvements in field strength and software.
4. fMRI
   a. The standardization of activation paradigms utilized for SCI would allow comparison of fMRI outcomes across studies.
   b. Refinements in hardware and software should improve the feasibility of fMRI assessment of the spinal cord in patients with SCI.
5. MR Spectroscopy

a. Refinements of hardware and software should improve the feasibility of MR Spectroscopy to assess the biochemistry of the spinal cord after SCI.

6. IOSS
   a. With refinements in the resolution of ultrasound imaging, specific lesion size correlation with MRI and other clinical/pathological indicators should be undertaken (eg, can IOSS identify contusion boundary?).
7. PET
   a. The standardization of activation paradigms utilized for SCI would allow comparison of PET outcomes across studies.
   b. Refinements in hardware and software should improve the feasibility of PET assessment of the spinal cord in patients with SCI.

SUPPORT

The SCI Measures Meeting was supported by grant funds from the National Institute on Disability and Rehabilitation Research, Office of Special Education and Rehabilitation Services in the US Department of Education.

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