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Mild traumatic brain injury: Is DTI ready for the courtroom?

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ABSTRACT

Important advances in neuroscience and neuroimaging have revolutionized our understanding of the human brain. Many of these advances provide new evidence regarding compensable injuries that have been used to support changes in legal policy. For example, we now know that regions of the brain involved in decision making continue to develop into the mid-20s, and this information weighs heavily in determining that execution or automatic sentence of life without the possibility of parole for someone younger than 18 years old, at the time of the crime, violates the 8th Amendment prohibition against "cruel and unusual punishment." The probative value of other testimony regarding neuroimaging, however, is less clear, particularly for mild traumatic brain injury (mTBI), also known as concussion. There is nonetheless some evidence that new imaging technologies, most notably diffusion tensor imaging (DTI), may be useful in detecting mTBI. More specifically, DTI is sensitive to detecting diffuse axonal brain injuries in white matter, the most common brain injury in mTBI. DTI is, in fact, the most promising technique available today for such injuries and it is beginning to be used clinically, although it remains largely within the purview of research. Its probative value is also not clear as it may be both prejudicial and misleading given that standardization is not yet established for use in either the clinic or the courtroom, and thus it may be premature for use in either. There are also concerns with the methods and analyses that have been used to provide quantitative evidence in legal cases.

It is within this context that we provide a commentary on the use of neuroimaging in the courtroom, most particularly DTI, and the admissibility of evidence, as well as the definition and role of expert testimony. While there is a great deal of evidence demonstrating cognitive impairments in attention, processing speed, memory, and concentration from neuropsychological testing following mTBI, we focus here on the more recent introduction of DTI imaging in the courtroom. We also review definitions of mTBI followed by admissibility standards for scientific evidence in the courtroom, including Daubert criteria and two subsequent cases that comprise the so-called Daubert trilogy rulings on the admissibility of expert testimony. This is followed by a brief review of neuroimaging techniques available today, the latter with an emphasis on DTI and its application to mTBI. We then review some of the court rulings on the use of DTI. We end by highlighting the importance of neuroimaging in providing a new window on the brain, while cautioning against the premature use of new advances in imaging in the courtroom before standards are established in the clinical arena, which are informed by research. We also discuss further what is needed to reach a tipping point where such advances will provide important and meaningful data with respect to their probative value.

1. Introduction

1.1. Advances in neuroimaging

In the past 40 years, beginning with the introduction of computed axial tomography (CT) in the mid-1970s, there have been important advances in medical imaging technology that have truly revolutionized nearly every area of medicine, including our ability to investigate the brain, perhaps one of the most exciting and far-reaching areas of medical imaging technology. With these new advances, our ability to go

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beyond what is gleaned from post-mortem studies has elevated neuroimaging to a central role in neuroscience research and in clinical practice, where researchers are beginning to understand associations between brain and behavior in both healthy and impaired brains, and where clinicians routinely use such tools to assist in the diagnosis, staging, and follow up of neurological disorders – all in a manner that was heretofore not possible. Indeed, we need look only in a small number of areas to see the impact of these advances, as for example, pre-surgical planning for neurosurgery, where often several imaging modalities are used simultaneously to localize and to characterize brain tumors in order to best excise them while avoiding eloquent cortex. Advances in imaging technology in psychiatry have also led to the confirmation of the long-held speculation that schizophrenia is a disorder of the brain. We now know that there are subtle brain abnormalities in schizophrenia that would not have been appreciated without the advent of novel imaging techniques. Where this knowledge will lead, however, is still an open question (see review in Shenton, Dickey, Frumin, & McCarley, 2001).

These remarkable advances in imaging were propelled by dramatic improvements in image resolution and in the development of novel imaging techniques, including CT, positron emission tomography (PET), single photon emission tomography (SPECT), magnetic resonance imaging (MRI), functional MRI (fMRI), diffusion weighted imaging (DWI)/ diffusion tensor imaging (DTI), magnetic resonance spectroscopy (MRS), susceptibility weighted imaging (SWI), and magnetoencephalography (MEG) – all of which provide an unprecedented view of anatomical structures and/or functions in the *living* human body (see below, under IV. Neuroimaging Techniques Available Today and Their Application to Mild Traumatic Brain Injury, for a description of the different imaging modalities).

The brain and our ability to view its inner workings have thus become an important new area of scientific inquiry, and have captured the imagination of the popular press as well as been integral to the development of several new fields of academic inquiry, including behavioral economics (Laibson & List, 2015) and neurolaw (Shen, 2010). These advances have also captured the attention of politicians, with President George H. W. Bush proclaiming the 1990s as “the Decade of the Brain,” and President Barack Obama announcing the White House initiative to support the National Institute of Health's Brain Research through Advancing Innovative Neurotechnologies (BRAIN Initiative; https://www.braininitiative.nih.gov/). The latter initiative is aimed at revolutionizing our understanding of the human brain.

Recent attention in the media about the effects of repetitive head trauma in professional athletes has also raised public awareness of mild traumatic brain injury (mTBI), also known as concussion, to the point where it has been referred to as a “concussion epidemic” (Grey & Marchant, 2015). Moreover, with this newfound public awareness, the number of lawsuits alleging brain injuries has increased three-fold in the last 20 years (Woodard, Kendall, & Spartaro, 2016). This becomes particularly challenging in cases of mTBI where there is often no radiological evidence of brain injury and where self-reported symptoms are the mainstay of diagnosis following a head trauma (see review in Shenton et al., 2012; see also discussion below under Impact on the Legal System and Probative Value of Neuroimaging Techniques in the Courtroom; see also II. Definitions of Mild Traumatic Brain Injury).

1.2. Impact on the legal system

Some progress in neuroscience has had an immediate impact on the legal system as it has provided heretofore missing evidence regarding the existence of compensable injuries and biological evidence that support changes in legal policy. For example, with respect to legal policy, neuroimaging has led to a more comprehensive understanding of the developing brain, which in turn has catalyzed a dramatic shift in how we understand adolescent behavior. More specifically, in a trilogy of cases between 2005 and 2012, the Supreme Court relied in part upon neuroscience research findings which suggest that the frontal lobes of the brain do not reach full maturity until the age of the mid-20s, or even older. The legal implications of these findings were instrumental in determining that execution or an automatic sentence of life without the possibility of parole for someone younger than 18 years old, at the time of the crime, violates the 8th Amendment prohibition against “cruel and unusual punishment” (see Roper v. Simmons, 2005; Graham v. Florida, 2011; Miller v. Alabama, 2012).

1.3. Probative value of neuroimaging techniques in the courtroom

With more and more advances in brain imaging the legal system will face greater pressure to determine which imaging techniques have probative value in a given case and which may be prejudicial or even misleading (see also 2014 articles included in the Hastings Center Report: Farah, 2014; Mayberg, 2014; Parens & Johnston, 2014; Wasserman & Johnston, 2014; as well as Morse, 2006; Patel, Meltzer, Mayberg, & Levine, 2007; Granacher, 2008; Moriarty, 2008; Johnson, Blum, & Giedd, 2009; Roskies, Schweitzer, & Saks, 2013; Meltzer et al., 2014). There are also significant concerns about what can be inferred from brain images, and this area warrants further investigation to elucidate the role of neuroimaging in the courtroom (Appelbaum, 2009). Moreover, it is important to note that the inordinate power of medical imaging is not new but is more than a century old. For example, even in the early part of the 1900s, courts admitted X-ray evidence through expert testimony to prove the presence of bone fractures including fractures of the skull [see Moriarty, 2008, see also United Laundries Co. v. Bradford (1918), as noted in Glasser (1931)].

Nonetheless, the rapid advances in brain imaging become more challenging to the legal system, where judges are asked to determine the admissibility of expert neuroimaging testimony in the courtroom. It is thus not surprising that the limits of scientific inference and expert opinion have been the subject of attempts at common law and statutory codifications of appropriate guidelines (Grudzinskas & Appelbaum, 1998). The state and federal standards for the admissibility of this evidence will be reviewed below in the context of understanding what we know and don't know about the implications of introducing neuroimaging expertise into both civil and criminal litigation. While an extensive review of neuroimaging evidence in the criminal context is beyond the scope of this review, it is important to note that the same imaging modality may receive differing levels of evidentiary scrutiny in civil versus criminal contexts. This difference results from many factors, including different levels of Constitutional protection, procedural differences between these contexts, and legal policy considerations which inform these proceedings (Denno, 2016; Denno, 2015).

Rapid advances in neuroimaging technologies have also raised valid concerns that many of the methods developed may be adopted too quickly, and perhaps even prematurely, without the kind of standardization that is needed for aiding in the diagnosis of brain pathology, or for determining associations between brain and behavior. One such debate surrounds diffusion imaging, an imaging technique that characterizes microstructural changes and white matter connectivity patterns in the brain. For example, as recently as 2013, the Institute of Medicine sponsored a meeting to review the use of diffusion imaging to detect diffuse axonal injuries in mTBI and to diagnose stroke. The main objective of this meeting was to develop standards in diffusion imaging for use in clinical settings for diagnosing mTBI, as there are currently no clear standards for diagnosing mTBI using diffusion imaging (see report by the Institute of Medicine's Forum on Neuroscience and Nervous System Disorders, Health Arm of the Institute of Medicine and the National Academy of Science, Meeting held in August 2013; see also review in Shenton et al., 2012).

The use of diffusion tensor imaging (DTI) in the courtroom will be reviewed in detail below, because more and more legal cases involve mTBI, where there are as yet no standards that support the probative value of DTI in the courtroom. This is despite the fact that such testimony has been allowed (see below in V. Magnetic Resonance Diffusion Imaging, mTBI, and Admissibility Standards of Evidence in the Courtroom).

Conventional MRI and CT, for example, often do not show the kind of subtle brain injuries that characterize mTBI, which can be appreciated using diffusion imaging techniques (see reviews in Niogi & Mukherjee 2010; and Shenton et al. 2012; see also Wortzel et al., 2011 for implications of diffusion imaging in mTBI brain injury litigation). The standardization of these techniques, however, lags behind their measure of sensitivity to white matter microstructure (see previously cited report by the Institute of Medicine's Forum on Neuroscience and Nervous System Disorders, Health Arm of the Institute of Medicine and the National Academy of Science, Meeting held in August, 2013).

The precipitous adoption of DTI is nonetheless not surprising, as new technologies appear to be imported more quickly into the courtroom when they purportedly offer the fact finder objective proof of significant injury. This is particularly true for claims that rely upon the articulation of subjective symptoms for the establishment of compensable damages, such as damages for Post Traumatic Stress Disorder or chronic pain syndromes (Edersheim & Wei, 2018; Pustilnik, 2015). Granacher (2008) has suggested that in legal cases involving mTBI, which rely heavily upon an event (head impact) and self-reported symptoms for diagnosis, "mTBI is easy to obfuscate and difficult to detect" (p. 324), thereby being *reminiscent of legal cases involving back pain, whiplash, or headaches*. This is captured even more clearly in a 2014 Hastings Center Report where Aguirre (2014) dubbed this phenomenon "imaging colonization" to describe what happens when an established method in one area moves too quickly to a new area, such as the law, where attorneys are using neuroimaging findings as scientific evidence in both criminal and civil cases. As Aguirre notes, this "imaging colonization" may be without "hard won cautionary experience" (p. 8), and thus may be lacking in "the methodological rigor" used in the application of neuroimaging techniques in scientific discovery.

Meltzer et al. (2014), in an attempt to deal with these growing concerns, summarized guidelines for the ethical use of neuroimaging in medical testimony, reported in a conference in 2012 at Emory University entitled the "Use and Abuse of Neuroimaging in the Courtroom." Among the important questions posited at this conference were: 1) what are the standards or guidelines to be used for testimony involving inferences about abnormal brain and behavior associations? 2) What testimony should be considered outside the expert's purview? 3) How does one diminish bias in medical testimony when using neuroimaging evidence?

These questions, and the timing and topic of the conference, are important, particularly in light of the increasingly robust and advanced neuroimaging techniques that can presumably be used in the courtroom to prove brain damage and disease. But, as the first part of the title of an article by Baskin, Edersheim, & Price (2007) cautions, "Is a Picture Worth a Thousand Words?" The answer to this question is, "not always," particularly when the jury believes that the colored areas on the brain that depict injury are actually the injury itself rather than statistical maps generated from post-processing of images of the plaintiff's brain, compared to an ill-defined control group. Moreover the colored areas on the brain may vary depending upon the quality of the images, the similarity of the imaging sequences, and the comparability of the control group (i.e., if plaintiff is left handed and male, controls should be left handed and male and of roughly the same age and education) – all factors that can influence possible findings of brain injury in a plaintiff compared to an ill-defined control group (see, for example, Craffey v. Embree Constr. 2017, where a left-handed plaintiff was compared with controls who were not well matched on age, gender, or handedness). It is thus important to know whether or not appropriate methods are used for comparison and whether or not sensitivity and specificity measures are used to characterize the findings.

The main point here is that there are many important advances in neuroimaging, and there are many ways in which such knowledge can assist in legal determinations. Unfortunately, there are also many advances in neuroimaging that are not ready to be adopted outside the fields in which the methods have been developed and applied. Some importation of neuroimaging into the courtroom is so clearly premature that its adoption is baffling and concerning to the scientific community. There has been, for example, extensive criticism of the courtroom use of an EEG based lie detection method developed by Farwell and Smith (2001) termed "Brain Fingerprinting" (Nature Neuroscience Editorial, 2008; Meijer et al., 2013). However, in many instances, the suitability of a particular neuroimaging modality for the courtroom is less clear and requires more nuanced judgments. An imaging technique may be inappropriate for use in the courtroom for many reasons, for example, because there are no agreed upon standards or because the methods are used inappropriately, or because the answers provided by the methods are more ambiguous than enlightening in the legal system, where truth is thought, ideally, to evolve from the adversarial system where clear, unambiguous evidence is presented on each side, and a binary decision is made based on the weight of the evidence.

1.4. Summary of what follows

Below we review definitions of mTBI, followed by a review of the history of the admissibility of evidence from scientific and medical experts, and how the rules of evidence have evolved. This is followed by a brief review of neuroimaging techniques that are in use today, some of which have a place in the new "Neurolaw" (see Jones et al., 2014) and some of which are likely premature with respect to their use in the courtroom. We note, however, that we do not intend this to be an exhaustive review of neuroimaging. We intend instead for this information to provide a perspective, or commentary, on the challenges that these new tools bring to the courtroom, particularly with respect to mTBI.

This is followed by a discussion of how we should scrutinize neuroimaging in the courtroom and admissibility standards of evidence in a new light, given the growth in neuroimaging technology. Here we attempt to elucidate what we know and do not know from this brave new world, and how these new technologies impact the legal system. We focus specifically on mTBI, as this is an area where, unlike an X-ray that shows whether or not a bone is broken, there are difficulties in interpreting findings. Problems with interpreting findings are due in part to the fact that much of what is used currently for the diagnosis of mTBI is the brain trauma event itself, and a cluster of symptoms that are nonspecific, as they overlap with other disorders such as post-traumatic stress disorder and depression, including dizziness, headache, nausea, problems with attention, memory problems, impulsivity, and poor judgment, to name just a few (e.g., Bigler, 2008).

The most promising radiological evidence of mTBI, however, is DTI, which is the most sensitive neuroimaging tool available today to detect microstructural integrity and diffuse axonal injury, the most common injury observed in mTBI, an injury which, as noted previously, is not easily detected using conventional MRI and CT. Additionally, we note that the good news is that for most of those who suffer from symptoms following concussion, these symptoms generally resolve over days or weeks, although for some, the symptoms continue and can lead to disability (see review in Shenton et al., 2012).

Finally, we summarize the role of DTI in the courtroom for determining the presence or absence of mTBI, and how this area is particularly murky since secondary gain in terms of monetary compensation, subjective symptoms, and the use of only conventional CT or MRI, which can miss subtle diffuse axonal injuries, make this area similar to the lack of clarity which has long been extant in legal cases involving back pain, headache, and whiplash. We end with a cautionary note about the premature use of new advances in imaging, before standards are established in the clinical arena, which are informed by research. However, we note that some of these tools can be used now if they are used appropriately in conjunction with other information and with all the caveats as reviewed in this commentary.

2. Definitions of mild traumatic brain injury

Brain trauma affects 1.7 million individuals each year with 85–90% of these cases classified as mTBI, also known as concussion (CDC 2010; Faul et al., 2010). This number, however, does not include those seen in private clinics or by primary care physicians, nor does it include those seen for medical treatment outside an emergency room (Langlois et al., 2006). Thus 1.7 million is likely an underestimate of the number affected by TBI each year, with an estimated 14% of mTBI patients seen in private clinics or by their own physicians, and another 25% not receiving medical attention (Sosin et al., 1996). This large unknown number of mTBI cases has been referred to by Goldstein (1990) as a "silent epidemic."

It is also not unexpected that mTBI is a controversial diagnosis. First, it is not clear how many people are actually affected, and second, as described above, the brain often appears quite normal on conventional computed CT and MRI (e.g., Bazarian et al., 2007; Inglese et al., 2005; see also review in Shenton et al., 2012). This is because, as described above, conventional CT and MRI do not accurately depict brain injury in mTBI since these techniques are not sensitive to detecting diffuse axonal injuries, the most common brain injuries in mTBI.

Such injuries are caused by physical forces that result in rotational and/or acceleration/deceleration forces that may occur from a blunt force to the head, a fall, a bicycle or motor vehicle accident, or from blasts from an explosive device. These forces to the head result in the brain moving within the skull, where shearing and stretching of the axons (white matter) may occur throughout the brain, which, in turn, results in what is known as diffuse axonal injury (e.g., Young et al., 2015).

Thus when there is, more often than not, no conventional radiological evidence to diagnose mTBI, the diagnosis is made based on the event itself (head trauma) and upon clinical and cognitive symptoms, which are generally self-reported, and, as noted previously, tend to be non-specific, and overlap with other disorders such as depression and PTSD (e.g., Hoge et al., 2008). This has led Hoge et al. (2008) to conclude that mTBI does not exist when both depression and PTSD are taken into account. While this is an extreme point of view, it highlights the critical challenge faced in documenting clearly what mTBI is and is not.

It is also noteworthy that TBI and PTSD are sometimes presented as co-morbid in the same person. This is common in the military but is also observed in civilian cases. See for example Nelson v. BNSF Railway Company Case No.27-CV-12-9171 (2013) where the plaintiff claimed to have both TBI and PTSD. The claim was also made that moderate to severe TBI was present, as evident from DTI. The arguments for TBI were from scientific testimony that went well beyond what was credible in terms of moderate to severe TBI (i.e., the Glasgow Coma Scale indicated mTBI – see below for details), and the methods and approach used to quantify DTI were not appropriate. The finding in the case was for PTSD but not for TBI.

Table 1 describes the major classifications of TBI based on the Glasgow Coma Scale (Teasdale and Jennett, 1974; Teasdale et al., 2014) and the Committee on Mild Traumatic Brain Injury, the American Congress of Rehabilitation Medicine (Table 2; 1993). The Glasgow Coma Scale is commonly used by emergency medical technicians at the scene of a head trauma, where it is used to assess 3 behaviors, and the scale is often repeated in the emergency room. The 3 behaviors assessed include eyes opening, verbal response, and motor response (see Table 2). The totals under each of these areas are then added together to define the severity of the head injury where mTBI is scored between 13 and 15, moderate TBI between 9 and 12, and severe between 3 and 8. Additional measures such as alteration in consciousness, loss of consciousness, and post-traumatic amnesia (PTA) are also used to define mTBI, moderate TBI, and severe TBI (see Table 1). In reviewing Table 1, it is clear that mTBI may be present in the absence of loss of consciousness.

Table 1
Glasgow coma scale.

Behavior	Response	Score
Eye opening response	Spontaneously	4
	To Speech	3
	To Pain	2
	No Response	1
Best verbal response	Oriented to time, place, and person	5
	Confused	4
	Inappropriate words	3
	Incomprehensible words	2
	No Response	1
Best motor response	Obeys commands	6
	Moves to localized pain	5
	Flexion withdrawal from pain	4
	Abnormal flexion (decorticate)	3
	Abnormal extension (decerebrate)	2
	No response	1
Total score	Best response possible [mild injury]	15
	Moderate injury	9 to 12
	Comatose client [severe injury]	8 or less
	Totally unresponsive [most severe]	3

Adapted from Teasdale and Jennett (1974).

Table 2
Severity rating criteria.

Severity of trauma	Glasgow coma scale	Alteration in consciousness	Loss of consciousness	Post-traumatic amnesia
Mild TBI	13–15	≤24 h	0 to 30 min	≤24 h
Moderate TBI	9–12	> 24 h	> 30 min, < 24 h	> 24 h, < 7 days
Severe TBI	3–8	> 24 h	≥24 h	≥7 days

Parenthetically, we note that neurocognitive impairments, assessed using neuropsychological measures, are also evident in mTBI, including cognitive impairments in attention, processing speed, memory, and concentration following mTBI. Fortunately, these impairments typically improve over days to weeks post-injury. However, in some cases, they may persist for months or years, and legal action may be pursued. Such legal cases are the most frequent type encountered by neuropsychologists conducting forensic work in personal injury litigation. These issues have been covered well in other reviews (e.g., see for example reviews in Larrabee and Rohling, 2013, and Williams, Potter, and Ryland, 2010) and will not be covered here. Instead, our focus is on the recent introduction of DTI in cases of mTBI in the courtroom.

A further diagnostic conundrum is "complicated" mTBI. This classification is based on a head injury meeting the criteria for mTBI, as listed in Tables 1 and 2, but in addition, the person has a "positive" finding on CT or MRI such as a hematoma (generally a subdural hematoma, which is a collection of blood outside the brain but within the cavity itself) or a contusion (a bruise to the brain that may include multiple micro-hemorrhages). The difficulty here is in discerning whether or not complicated mTBI is more similar to moderate TBI or to mTBI. While there is considerable debate on this topic, recent research suggests that while there are some differences observed in DTI between those with complicated versus uncomplicated mTBI at the time of injury such that those with complicated mTBI return to work later than those with uncomplicated mTBI, at 8 to 10 weeks post-injury, there are no differences between these two groups on DTI measures (Panenka et al., 2015). This thus places the classification of complicated mTBI closer to mTBI than to moderate TBI.

A further challenge both in the clinic and in the courtroom is that approximately 15 to 30% of those diagnosed with mTBI continue to experience symptoms 3 months post-injury (Alexander 1995; Bazarian et al., 1999; Bigler 2008; Rimel et al., 1981; Vanderploeg et al., 2007). Symptoms that continue 3 months post-injury are referred to as "persistent post-concussive symptoms." This minority has been referred to as the "miserable minority" (Ruff et al., 1996) because while these individuals report continued symptoms, there is often no radiological evidence observed that is consistent with the presence of such symptoms. This has led some to purport a psychogenic origin to the persistence of such symptoms (see review in Shenton et al., 2012). These attributions are understandable and easy to make, but the question becomes one of whether or not persistent post-concussive symptoms that go beyond the expected time of recovery are: (1) self-reported symptoms related to a psychiatric illness such as PTSD, depression, or a somatization disorder that preceded the head trauma; (2) related to individuals seeking secondary gain such as monetary compensation in a legal case (a neuropsychologist can help here with such tests at the TOMM – Test of Memory Malingering, 2018, or the Green Nonverbal Medical Symptom Validity Test, Green, 2004, and other such validity/malingering measures); or (3) self-reported symptoms related to the brain trauma but where the imaging techniques used, such as conventional CT or MRI, are insensitive to the kind of diffuse axonal injury that may be present but is not appreciated using these more conventional imaging techniques.

The answer to these questions is quite challenging and it is primarily *individuals with a single mTBI and persistent post-concussive symptoms who are also challenging to the legal system*. We are only just beginning to address some of the questions raised in the research arena, where neuroimaging tools such as DTI may make it possible to better characterize the extent of brain injuries in mTBI. Such advances in DTI may also lead to the development of markers of injury and to the staging of reorganization in the brain, and even to quantifiable reversal of brain injury following trauma. These advances, however, are more futuristic, albeit promising. And, as described below (see IV. Neuroimaging Techniques Available Today and Their Application to mTBI), there are concerns regarding their probative value in the courtroom.

3. Admissability standards for scientific evidence in the courtroom

3.1. Scientific and medical experts

In order to understand the role of the expert in the courtroom, it is important to know something about the basic requirements for courtroom testimony. Witnesses, both fact and expert, are part of the adversarial legal system. A fact witness is someone who has some knowledge of the facts of a specific case either because this person has direct involvement or because this person has observed an event or a series of events. Expert witnesses, on the other hand, are the exception to these restrictions, as they are, by definition, brought into the courtroom because they have specialized knowledge relevant to the outcome that the judge or jury cannot glean by listening to fact witnesses and by using their own experience. Expert witnesses may also offer opinions, based on their expertise, in order to assist the jury or the judge in understanding the facts at issue. Thus expert witnesses are given far more leeway than fact witnesses in the information they provide as part of the legal process. Expert witnesses include, although are not limited to, physicians who provide expert testimony on standards of medical care, engineers who provide expert testimony on specialized knowledge, as well as scientists who provide expert testimony on scientific evidence in cases.

3.2. Scientific evidence

With respect to scientific evidence, it is important to recognize that law and science are quite different in their approaches. Science is based on the quest for knowledge, and the tools used to get to this end point are broad, although the goal is to discover new truths. Here, knowledge changes over time, and is an iterative process where provisional knowledge changes as new discoveries lead to still newer truths. The legal system, in contrast, seeks an immediate and final resolution of a dispute, based on an adversarial system where each side presents facts that support their position and the judge or jury is given the role of finder of facts, or truth. Decisions in law are thus more binary and are not in flux, as is the case in science. Moreover, these facts are deliberated upon by the jury or judge and a verdict is rendered (Haack, 2014; Kaye, 1992).

Because of the law's inherent suspicion of expert testimony and preference for fact testimony, and the vast differences in these truth-seeking approaches, the legal system has tried to grapple with expert testimony from scientists by developing standards of evidence regarding what should be admissible. Some considerations here, which will be discussed in more detail below, include how relevant or helpful the information may be in a given case, what standards of scientific validity should be proxies for reliability in the courtroom, and whether or not even reliable opinions should be excluded because they unfairly bias or prejudice the outcome of the case.

3.3. Evolution of the standards for admissibility of scientific evidence. Frye rule

One of the earliest American attempts to grapple with standards for the admissibility of scientific evidence was the Frye standard or general acceptance test, articulated by the District of Columbia Circuit Court in 1923 (*Frye v. United States*, 1923; see also Table 3). The *Frye* court held that using systolic blood pressure as scientific evidence of lying (i.e., a polygraph precursor) did not reach the threshold of acceptance standards of science from the larger scientific community, and was therefore not admissible. Importantly, for the Frye standard, the issue was not one of reliability or reproducibility, which are among the standards used in science, but whether or not the method or scientific principle at issue was "sufficiently established to have gained general acceptance in the particular field in which it belongs."

In the ensuing nine decades, the courts have attempted to unpack the meaning of the notion of "general acceptance" while retaining a flexible approach to scientific testimony. One of the persistent difficulties with the Frye test has been identifying the tipping point where something novel or new in the scientific arena becomes sufficiently standardized and accepted as to be applicable and admissible in legal proceedings (see also Bertin & Henifin, 1994; Moriarty, 2008; O. D. Jones, Buckholtz, Schall, & Marois, 2009; Meltzer et al., 2014).

Farah (2014), in the Hastings Center Report, observed that the issue of a tipping point tends particularly to afflict young fields of science such as cognitive neuroscience and advanced neuroimaging techniques, where some things are known, but much is still not known. More specifically, in her discussion of functional magnetic resonance imaging (fMRI) she notes that while there are gaps between neural events in the brain, and images of the brain that are purported to represent such events, she cautions that we not throw out the baby with the bathwater, in that we need "to distinguish between specific criticisms of particular applications"… and "wholesale criticisms of the entire enterprise of functional neuroimaging" (p. S28). These arguments hold up equally well for scientific findings in general, although here we will focus primarily on neuroimaging and advances in neuroimaging, which highlight the new challenges that must be met in determining what does and does not (or should not) meet evidentiary standards for admissibility.

While the *Frye* standard governed the admissibility of expert scientific testimony for so many decades, its use was superseded completely in the federal courts and only eight states still use the Frye standard for state court admissibility (CA, IL, MD, MN, NY, NJ, PA, WA).

3.4. Daubert trilogy

The Frye standard was, in many jurisdictions (see above), superseded by a new standard articulated by the U.S Supreme Court in the landmark case of *Daubert v. Merrell Dow* (1993; see also Table 1).

Table 3
Evidence criteria for expert/technical knowledge.

Case	Year	Issue	Effect on standards	Reference
Frye v. United States	1923	Can a primitive form of polygraph lie detection be admitted as evidence?	Frye Standard – The court must determine whether or not the method by which scientific evidence is obtained is generally accepted by experts in the larger scientific community.	Frye v. United States, 293 F. 1013 (D.C. Cir. 1923).
Daubert v. Merrell Dow Pharmaceuticals	1993	Can the anti-nausea drug Bendectin cause birth defects?	Daubert Criteria – A judge must evaluate scientific evidence based on the following: 1. Whether or not the theory can be or has been tested. 2. Whether or not the theory has been subjected to peer review and is published. 3. The known or potential error rate. 4. Whether or not standards and controls exist and are maintained. 5. Whether or not the theory has been accepted in the larger scientific community and to what degree.	Daubert v. Merrell Dow Pharmaceuticals Inc., 509 US 579, 589 (1993). Daubert v. Merrell Dow Pharmaceuticals Inc., 727 F Supp 570 (SD Cal 1989. Daubert v. Merrell Dow Pharmaceuticals Inc., 951 F2d 1128 (9th Cir 1991).
General Electric Co. v. Joiner	1997	Can exposure to toxic PCBs in the workplace promote the later development of lung cancer?	A judge can exclude an expert testimony when there are gaps between the data used as evidence and the conclusions drawn.	General Electric Co. v. Joiner, 522 U.S. 136 (1997).
Kumho Tire Co. v. Carmichael	1999	Is a technician's testimony that only a manufacturing defect could have caused a tire to blow out admissible as evidence?	The Daubert Criteria apply not only to scientific knowledge, but also to technical or other specialized knowledge that a juror would be unlikely to have.	Kumho Tire Co, Ltd. v. Carmichael, 526 US 137 (1999).

Daubert, and two subsequent cases elaborating on the Daubert standard - *General Electric Company v. Joiner* (1997), and *Kumho Tire Company, Ltd. v. Carmichael* (1999; see also Table 3) – form the so-called Daubert trilogy, which articulated a new Federal framework for the admissibility of expert scientific testimony based upon an updated interpretation of the Federal Rules of Evidence.

The Daubert case was a toxic tort case involving Bendectin (doxylamine), a once widely prescribed medication for morning sickness during pregnancy that was developed and marketed by Merrell Dow Pharmaceutical, Inc. The plaintiffs in the case were two sets of parents, each with a child born with limb deformities. These plaintiffs claimed that the drug Bendectin had caused birth defects in their children as a result of the mothers being prescribed Bendectin during pregnancy. The plaintiffs offered testimony from eight scientific experts who provided evidence that indicated that the drug caused birth defects. This evidence came from animal studies, from the chemical structure of the drug and its analysis, as well as from a new method of combining epidemiological data across several published studies to reanalyze it and interpret it, whereupon the reanalysis provided evidence that the drug did, indeed, cause birth defects. On the defendant side, expert opinion was that Bendectin did not cause birth defects, as there were no established correlations in the published literature between the use of this drug and birth defects. The judge in the case ruled that the evidence from the plaintiffs was inadmissible because it did not meet the general acceptance standards (Frye standards).

A federal appeals court upheld the trial court ruling (*Daubert v. Merrell Dow Pharmaceuticals*, 1989) but the Supreme Court (*Daubert v. Merrell Dow Pharmaceuticals*, 1991) decided otherwise. The opinion of the court, written by Justice Blackmun, determined that trial court judges should be the "gatekeepers" of the admissibility of scientific evidence in expert testimony and that the standards should be based on reliability and relevance, where reliability would be determined by error rates, peer reviewed articles, accepted methodology, etc. (see Table 3), and where relevance would be determined by whether or not it was relevant to the specific case and would be useful (see *Daubert Criteria* - Table 3 and Federal Rule of Evidence 402 - Table 4). The court also ruled that Federal Rule of Evidence 702 did not incorporate the *Frye* general acceptance test but, instead, principles of sound scientific inquiry, including, whether or not the expert has scientific, technical, or other specialized knowledge that will be helpful to the jury, whether or not the testimony is rooted in facts or data, whether or not the principles and methods used to produce the testimony are reliable, and whether or not the principles and methods have been reliably applied to the facts of the case (see Table 4). This landmark decision put judges in the role of gatekeeper for all scientific evidence and its admissibility in the courtroom. In addition, Federal Rule of Evidence 702 provides guidance to judges on how to evaluate the scientific method, as well as guidelines to consider with respect to relevance on a case-by-case basis (see also Gold, Zaremski, Lev, & Shefrin, 1993; Bertin & Henifin, 1994; Cecil, 2005; Grivas & Komar, 2008).

The second case in this lineage was *General Electric Company v. Joiner* (1997), which involved toxic exposure to polychlorinated biphenyls (PCBs) in the workplace and their causal link to the development of lung cancer. The outcome in this case was that the judge, as gatekeeper, could exclude expert testimony where there were gaps between the data used as evidence by the expert testimony and the conclusions drawn (see Table 3). An expert's opinion now also needed justification, *as "nothing in either Daubert or the Federal Rules of Evidence requires a district court to admit opinion evidence which is connected to existing data only by the ipse dixit of the expert"* (*General Electric Co. v. Joiner*, 1997). However, whether the judge, as gatekeeper, could apply the Daubert standard to non-scientific expert witness testimony was not addressed until the *Kumho Tire Company Ltd. v. Carmichael* case, which reached the Supreme Court in 1998, with a ruling in 1999 (*Kumho Tire Co. v. Carmichael*, 1999).

The Kumho Tire case involved whether or not a technician's expert testimony that only a manufacturing defect could have caused a tire to blow out was admissible evidence. The decision rendered was that the Daubert criteria apply not only to scientific knowledge, but also to technical or other specialized knowledge that a juror would be unlikely to possess. The gatekeeper role also was interpreted as one of following flexible guidelines as opposed to following strict rules, where judges were given the latitude to apply some, or none of the Daubert criteria, depending upon the testimony (Berger, 2000; Sanders, 2001; Federal Rule of Evidence 702 – See Table 4; Grivas & Komar, 2008). Nonetheless, if a judge does not use Daubert criteria, or only some criteria, the judge must justify the decision (Sanders, 2001).

This final case of the Daubert trilogy expands the role of judges and is quite important because it is difficult to differentiate between scientific and technical expert opinions, and judges are now allowed to

Table 4
Synopsis of federal rules of evidence.

104(a)	The trial judge must decide the admissibility of an expert testimony before the jury hears it.
401	The *relevancy* of evidence depends on if (a) it could make a fact more or less probable than it would be otherwise and (b) that fact will affect the outcome of the case.
402	Evidence that is not relevant is not admissible.
403	The trial judge can exclude evidence if it has a danger of causing unfair prejudice, confusing the issues, misleading the jury, or wasting time.
702	An expert witness may testify if: (a) The expert has scientific, technical or other specialized knowledge that will help the jury to determine a fact or understand evidence. (b) The testimony is rooted in facts or data. (c) The principles and methods used to produce the testimony are reliable. (d) These principles and methods have been reliably applied to the facts of the case.
703	An expert witness can use facts of the same sort that are normally used by experts in his or her field in forming an opinion, even if those facts are not admissible evidence. However, if inadmissible facts are used, they may only be disclosed to the jury for the purpose of evaluating the expert's opinion.
704	Generally, an expert can give an opinion on "ultimate issues," which are those determining the outcome of the case. However, in a criminal case, an expert may not state an opinion on whether the mental state or condition of the defendant affected an element of the crime or defense.
705	An expert may state an opinion to the jury without first stating all the facts underlying it, however, the trial judge may require the facts to be disclosed upon cross-examination.
706	The court may appoint its own expert witnesses in order to help elucidate discrepancies in the conclusions drawn by the expert witnesses of each party.
1101(d) (1)	The rules of evidence – except for those relating to privilege – do not apply to a trial judge's determination of admissibility under rule 104(b).

evaluate all forms of expert testimony to determine relevance and reliability, thereby extending the gatekeeper role of admissibility of evidence to <u>all</u> expert testimony. This expansion of the gatekeeper role has led to debates about how this role may be in conflict with the adversarial legal system (see Boxler, 2011; Pikus, 2014; Vidmar, 2005), although in many respects this expansion ensures that some of the same rigor in evaluating expert testimony is applied not just to expert testimony by scientists, but to all expert testimony. In 2011, Federal Rule 702 was formally amended to incorporate all of the evidentiary principles articulated in the Daubert Trilogy (see Table 4).

The Daubert trilogy and the Federal Rules of Evidence, while imperfect, reflect the legal system's attempt to understand that scientific inquiry is substantially broader than a specific technical expertise, and that applying one set of standards, or applying very rigid criteria, may not be appropriate. Making broad and explicitly flexible guidelines, however, is also challenging, as judges are not trained as scientists (Slovenko, 2003; Stern, 2000). In fact one study showed that only 5% of judges understood what falsifiability meant and only 4% understood the meaning of error rate, both part of Daubert's criteria for making determinations of admissibility of evidence (Gatowski et al., 2001). While somewhat disappointing, this finding does highlight the need for educating both judges and lawyers in how to evaluate what constitutes appropriate expert testimony in terms of meeting admissibility standards of evidence.

Further difficulties arise when judges attempt to determine admissibility standards of evidence for advanced neuroimaging techniques, particularly as they pertain to mTBI, where there is less standardization in the clinical and scientific arenas, and where there is an increasing need to make legal decisions in cases involving mTBI. Parenthetically, as noted previously, the number of mTBI cases brought to litigation has increased three-fold over the last 20 years (Woodard, Kendall, & Spartaro, 2016). And, also, as alluded to previously, this is likely in part due to public awareness based on news reports of sports injuries leading to long-term effects of repetitive trauma to the brain in professional football players, as well as to news reports of more than 1.64 million soldiers deployed to Iraq or Afghanistan with 320,000 of those returning estimated to have head injuries from improvised explosive devices (Tanielian, Jaycox, & Rand Corporation, 2008; Weinberger, 2011).

Below we review some of the advanced neuroimaging techniques in use today, some of which are used clinically but most of which are not applicable to mTBI, and some, as described in a recent White Paper by the American College of Radiology (Wintermark et al., 2015) are simply not ready to be used for the clinical evaluation of <u>*individual*</u> patients as they are still being developed and refined in the research arena.

4. Neuroimaging techniques available today and their application to mTBI

4.1. Introduction

Table 5 provides information regarding some of the imaging techniques that are available today, not all of which are suitable for detecting brain injury in mTBI. We review a number of imaging modalities so as to provide a context for DTI, which has the most promise of any neuroimaging tool for detecting diffuse axonal injuries in the brain, the most common mTBI injury.

4.2. Imaging modalities reviewed

Table 5 is divided into structural, functional, and metabolic imaging modalities. With respect to structural measures, X-ray is the earliest technique for imaging the body and it is based on differences in the absorption rate of different tissues. It is particularly good for imaging bone. A fractured skull, for example, would be visible on an X-ray of the skull. Such imaging has been accepted in the courtroom since the Hayes murder trial (see Table 6). This is less useful for evaluating mTBI as mTBI does not generally involve a fractured skull and if there is evidence showing either a positive X-ray or CT finding (blood or skull fracture or any positive finding), and the criteria listed in Table 5 are still met for mTBI, then this is referred to as complicated mTBI. Complicated mTBI has been debated with respect to whether it truly impacts outcome and, if not, then the issue becomes one of whether it should be categorized separately from mTBI. The previously cited Panenka et al. (2015) study suggests that outcome for complicated versus uncomplicated mTBI is the same after 8 to 10 weeks following injury, suggested that complicated mTBI does not impact outcome.

CT combines X-ray images from many different angles to create a three-dimensional image. It is commonly used to detect gross abnormalities or injuries to the brain and skull including skull fracture and subdural hematoma (blood just under the skull) and it is used when there is a question of a need for surgical intervention. For the most part it is <u>not</u> used routinely for mTBI as generally CT and MRI scans show no radiological evidence of mTBI (e.g., Bazarian et al., 2007; Inglese et al., 2005; Hughes et al., 2004; Iverson, Lovell, Smith, & Franzen, 2000; Miller, 1996; Mittl et al., 1994; Povlishock, 1989; Scheid et al., 2003). This lack of radiological evidence has, as noted previously, led clinicians typically to diagnose mTBI on the basis of clinical and cognitive symptoms, which, also as noted previously, are generally based on self-report, and are non-specific as they overlap with other diagnoses (e.g., Hoge et al., 2008; Stein & McAllister, 2009). CT is, nonetheless inexpensive, although among its drawbacks are that CT does not provide

Table 5
Summary of imaging modalities.

	Image modality	Mechanism	Applications/Advantages
Structural			
	X-Ray	Based on the differing x-ray absorption rate of different tissues such as bone, fat and air.	Primarily used for detecting fractures.
	Computed Tomography (CT)	Combines X-ray images of an object taken from many angles into a 3D image.	Detects gross abnormalities or injuries to brain and skull such as bone fracture and subdural hematoma, used when immediate surgical intervention is needed, can have medical equipment in area.
	Magnetic Resonance Imaging (MRI)	Uses radiofrequency pulses to measure the spin signal of hydrogen atoms placed in a magnetic field.	High resolution, can provide gross delineation between gray and white matter structures.
	Diffusion Tensor Imaging (DTI)	A type of MRI that characterizes microstructural changes by measuring signal attenuation due to water diffusion.	Best available technique for detecting white matter integrity, able to detect microscopic damage to neural tracts.
	Susceptibility Weighted Imaging (SWI)	A type of MRI that uses the different magnetic susceptibility of different tissues to produce high contrast images.	Detection of tiny bleeds (micro-hemorrhages) in TBI not detectable on standard MRI.
Functional			
	Functional Magnetic Resonance Imaging (fMRI)	A type of MRI that measures changes in activity level in the brain by detecting associated changes in blood flow.	Can assess the effect of injury or disease on brain functions such as language, movement, sensation and thinking.
	Single Photon Emission tomography (SPECT)	Uses radiotracers labeled with different isotopes that emit signals indicating where blood is flowing in the brain.	Can detect brain injury based on reduction of blood flow to injury sites.
	Magnetoencephalography (MEG)	Detects very small magnetic fields that occur due to the electrical currents that underlie neural activity.	Non-invasive and has very high temporal and spatial resolution compared to other techniques.
	Electroencephalography (EEG)	Detects electrical activity in the brain using electrodes placed on the scalp.	Non-invasive but has low spatial resolution.
	Positron Emission Tomography (PET)	Uses radiotracers labeled with different isotopes that emit signals indicating areas of uptake or binding in the brain.	Provides information on the concentration of a chemical or protein in the brain.
Metabolic			
	Magnetic Resonance Spectroscopy (MRS)	Measures brain chemistry by producing a spectrum where individual chemicals, or metabolites can be identified and concentrations can be measured.	Provides neurophysiological data that are related to structural damage/changes, neuronal health, neurotransmission, hypoxia, and other brain functions.

clear differentiation between gray and white matter, and it uses radiation.

In contrast to CT, MRI uses radiofrequency pulses to measure the spin of hydrogen atoms that are placed in a magnetic field. The resolution of brain tissue is much higher than in CT and gray matter and white matter are clearly delineated. Neither CT nor MRI, however, is particularly useful for detecting diffuse axonal injuries in mTBI. That these injuries exist has been demonstrated at post-mortem where CT and MRI did not detect these injuries prior to death (Bigler, 2004).

DTI is an MR sequence that characterizes microstructural changes by measuring water diffusion in the brain. Different tissues restrict the flow of water in different ways. More specifically, while water in an unrestricted medium such as cerebrospinal fluid flows equally in all directions (i.e., isotropic, spherical shape), water in brain's white matter cannot cross axonal membranes, myelin, or other barriers, and is therefore restricted to flow that is primarily parallel to the direction of the axons (i.e., anisotropic, elliptical shape). The shape of the diffusion can be quantified using the measure of fractional anisotropy (FA), which ranges from 0 (representing perfectly spherical diffusion) to 1 (representing perfectly linear diffusion). This characteristic of water diffusion in brain tissue is used to detect white matter pathology in multiple sclerosis and it may also show what is known as “shearing” of axons in mTBI.

DTI is the most promising technique available today as it is able to detect microscopic damage to neural tracts. Standards for the use of DTI, however, are still being developed. Accordingly, findings using methods such as voxel-based morphometry (VBM), which were developed for evaluating gray matter, do not work well with white matter measured with DTI. The problem here is that DTI images are inherently low resolution. Essentially, what one is trying to do is to align fuzzy images from a number of subjects in order to create a control group where a group of individuals is combined. An analogy would be to think of trying to line up five fingers of a hand across many images of the hand of one person, and then combining these images with many images of a hand with the fingers of a hand from many other people. If the alignment is not good, then not all of the fingers will be aligned properly, i.e., they will be misregistered to each other. This is a well-known problem with using voxel-based analyses with DTI images. Moreover both this approach and a method of post-processing of images known as tract-based spatial statistics (TBSS; Smith et al., 2006; Smith et al., 2007) were designed for group comparisons and not for comparing an individual to a group, where such comparisons can lead to possible erroneous findings (see the American Society of Functional Neuroradiology – ASFNR – 2012: http://www.asfnr.org/wp-content/uploads/ASFNR-Guidelines-for-DTI.pdf; see also Smith et al., 2006; Smith et al., 2007; and “do's and don'ts” of using diffusion imaging in Jones, Knösche, & Turner, 2013). Using either voxel based or TBSS approaches are therefore not appropriate for comparing an individual mTBI subject with a group of controls for use in the clinic or in the courtroom.

Inappropriate consideration given to magnet strength and image acquisition protocols may also confound interpretations and meaning of information from DTI. For example, DTI can be acquired on a 1.5 Tesla magnet or on a 3 Tesla magnet. Tesla (T) is a unit of measure of the strength of the magnetic field. The larger the Tesla, the stronger is the magnetic field. An analogy would be to look at the moon with a low powered telescope versus a high powered one that provides more detailed information. Thus combining control subjects from, for example,

Table 6
Relevant exemplars of the use of imaging in the courtroom.

Year	Case	Modality	Purpose	Outcome
1897	Haynes Murder Trial	X-Ray	Examination of bullet wounds (Halperin, 1988).	Admitted as evidence of bullet fragments rather than multiple bullets.
1982	Hinckley v. United States	CT	Evidence of brain shrinkage as support for insanity defense of John Hinckley, who had attempted to assassinate president Ronald Reagan.	Admitted as evidence, jury found Hinckley not guilty by reason of insanity.
1992	People v. Weinstein	PET	PET is admitted as evidence of reduced brain function in defendant due to an arachnoid cyst in frontal lobe.	Admitted as evidence, case is settled by plea bargain.
1996	Hose v. Chicago Northwestern Transportation Company	PET	Used as evidence of manganese induced encephalopathy.	Admitted as reliable and relevant evidence for diagnosing cause of the defendant's condition.
1997	Penney and Penney v. Praxair, Inc.	PET	Used as evidence of TBI following a car collision.	Evidence is rejected because comparison of patient's scan with control group is not deemed reliable.
1998	Rhilinger v. Jancsics et al	SPECT	Used as evidence of toxic solvent induced encephalopathy.	Massachusetts court rejects Daubert challenge to use of SPECT images, stating that SPECT is an undisputed method for showing abnormalities in brain function.
2000	Jackson v. Calderon	PET	Used as evidence of chronic abuse of the drug PCP.	Evidence is rejected as PET is not a widely accepted method of diagnosing PCP abuse
2000	Van Middlesworth v. Century Bank & Trust Co.	MRI	Used as evidence of dementia and mental incompetency in a case regarding whether a sales contract was voidable.	Evidence was admitted and contract was found voidable.
2005	Entertainment Software Ass'n v. Blagojevich	fMRI	Evidence of brain changes due to violent video games in support of new video game laws.	Evidence is admitted but fails to convince jury that new laws are necessary.
2009	Brian Dugan Murder Trial	fMRI	Evidence of brain activity levels characteristic of psychopathy in murderer Brian Dugan (Hughes, 2010).	Judge does not allow scans to be seen by the jury but does allow them to be described using graphs.
2010	U.S. v. Semrau	fMRI	Used to prove that testimony is truthful in a case involving intention to commit billing fraud.	Federal court rules that fMRI based lie detection fails to meet Daubert standards.
2010	Wilson v. Corestaff Services, L.P.	fMRI	Used to prove that testimony is truthful in a case involving alleged retaliation against sexual harassment claims.	New York Trial Court concludes that fMRI based lie detection does not pass Frye test.
2011	Byers v. Sec'y of HHS	DWI	Used to prove that a child's status epilepticus followed a hemiplegic stroke and neurological damage from Measles-Mumps-Rubella vaccine.	Federal court rules that DWI can be used to show status epilepticus following hemiplegic stroke from Measles-Mumps-Rubella vaccine.
2011	Ruppel v. Kukanin	DTI	Used to prove diffuse axonal injury after motor vehicle accident.	DTI admitted as evidence of mTBI.
2012	Brown v. Sec'y of HHS	DWI	Used to prove acute Ischemic injury in a case claiming vaccine injury.	Federal court rules that DWI can be used to show acute ischemic brain injury after vaccine administration.
2013	Nelson v. BNSF Railway Company	DTI	Used to prove brain injury after train derailment.	DTI admitted as evidence of mTBI.
2014	Andrew v. Patterson Motor Freight	DTI	Used to prove frontal lobe injuries sustained in motor vehicle accident.	DTI admitted as evidence of frontal lobe injuries.
2016	White v. Deere & Co.	DTI	Used to prove mTBI after plaintiff hit by bale of hay.	DTI admitted as evidence of mTBI.
2017	Siracusa v. City Ice Pavillion	DTI	Used to prove mTBI and exacerbation of previous damage after ice bucket challenge injury.	DTI admitted and defense request for underlying individual and control group data denied.

Abbreviations; CT = Computed Tomography; DWI = Diffusion Weighted Imaging; fMRI = Functional Magnetic Resonance Imaging; MRI = Magnetic Resonance Imaging; PET = Positron Emission Tomography; SPECT = Single Photon Emission Computed Tomography.

a 3 T magnet with subjects from a 1.5 T magnet is not appropriate as the information from each is quite different, making any findings uninterpretable. Unfortunately such combining of 3 T and 1.5 T data is frequently performed, and is not interpretable (see also the description of the use of DTI and some of the inappropriate analyses used in the courtroom, below, under V. Magnetic Resonance Diffusion Imaging, mTBI, and Admissibility of Evidence in the Courtroom).

Susceptibility Weighted Imaging (SWI) is a type of MRI that uses the different magnetic susceptibility of different tissues to produce high contrast images that are useful for visualizing venous blood, hemorrhage, and iron storage in the brain (e.g., Haacke, Xu, Cheng, & Reichenbach, 2004). In mTBI it may be useful to determine whether or not there are any small micro-hemorrhages present in the brain, although, as noted below, the *American College of Radiology* (ACR) does not list SWI in its list of appropriateness criteria for imaging techniques for the diagnosis of closed head injury that is minor (see; https://acsearch.acr.org/docs/69481/Narrative/).

In reviewing functional measures of the brain listed in Table 5, functional MRI (fMRI) is a type of MRI that measures changes in activity level in the brain by detecting associated changes in blood flow. It can assess the effect of injury or disease on brain function but it is more in the purview of research and it is not listed as a modality to be used for diagnosing head trauma (see below). Single Photon Emission Tomography (SPECT) uses radiotracers labeled with different isotopes that emit signals indicating where blood is flowing in the brain. It can detect brain injury based on reduced blood flow to the injury sites and it is useful in cases where the injury is moderate or severe rather than mild. Positron Emission Tomography (PET) also uses radiotracers that emit signals indicating areas of uptake or binding in the brain. It provides information relevant to the concentration of a chemical or protein in the brain. Its use in mTBI is not established. Additionally, EEG detects electrical activity in the brain from electrodes placed on the scalp. It is non-invasive but has low spatial resolution and it has limited utility for diagnosing mTBI. Finally, magnetic resonance spectroscopy (MRS) measures brain chemistry where metabolites can be identified and concentrations measured. This information provides data related to structural damage, neuronal health, and other brain functions. While MRS has been investigated in mTBI, it is primarily a research tool that is not as yet a useful clinical tool for diagnosing mTBI.

4.3. Appropriateness of imaging modalities for use in the diagnosis of mTBI

The *American College of Radiology* (ACR) lists the appropriateness of different imaging modalities for diagnostic purposes. For minor or mild acute closed head injuries (no opening in the skull from the injury; https://acsearch.acr.org/docs/69481/Narrative/), imaging is not generally recommended. The ACR uses a point system where 1, 2, or 3 is defined as "usually not appropriate," 4, 5, or 6 as "maybe appropriate," and 7, 8, or 9 as "usually appropriate." Of the structural imaging modalities listed in Table 5, a 1 is listed for MRI, and CT with contrast agent, although a 2 is listed for CT with no contrast agent. Similarly, PET and SPECT, under functional imaging modalities, are listed as 1 on the appropriateness rating. Finally, susceptibility weighted imaging is not listed by the ACR for use in diagnosing mTBI nor are fMRI, DTI, MEG, EEG, or MRS.

Thus for mTBI, the use of DTI for diagnosing individuals suffering from mTBI is problematic in both the clinical and the legal system as there are as yet no standards developed for diagnosis, and the gold standard for interpreting these images on an individual basis remains the clinical interpretation by a radiologist, most particularly a neuroradiologist. And, while DTI is used in mTBI litigation (see below; V. Magnetic Resonance Diffusion Imaging, mTBI, and Admissibility of Evidence in the Courtroom), its trajectory through the legal system, and the challenges to its application to legal questions, illustrate both the evidentiary and ethical dilemmas highlighted above. Below we detail the use of DTI as evidence for mTBI in the courtroom.

5. Magnetic resonance diffusion imaging, mTBI, and admissibility of evidence in the courtroom

5.1. Using DTI as evidence for mTBI in the courtroom

It is clear that DTI studies have identified clinical biomarkers that may have a prognostic role in patients with moderate to severe traumatic brain injury (Tollard et al., 2009). Such studies have also been used to track neural recovery in severe TBI (Sidaros et al., 2008). In studies of mTBI, DTI is promising in that it is superior to other imaging modalities for identifying subtle injuries observed in white matter that otherwise would not be seen using conventional CT or MRI (see review in Shenton et al., 2012). Nonetheless, it is important to note that such studies only began in 2001, they are based on comparisons between groups (i.e., controls and mTBI patients), and, as previously noted, while they have potential, they are not as yet standardized for use in individual patients, in either the clinic or the courtroom.

5.2. Evolution of the use of DTI in the courtroom

Over the past 15 years, the courts' initially cautious approach to the use of DTI in personal injury litigation has given way to more liberal patterns of admission. This has occurred despite continuing lack of standardization with respect to the methods for acquiring and analyzing DTI data, and its uncertainty as a clinical metric in cases of mTBI. This has also occurred despite sound neurologic and medicolegal critiques that legal inferences from group DTI data to individual diagnosis and prognosis would rarely withstand a Daubert analysis (Wortzel et al., 2011). Further, an analysis of the small number of published traumatic brain injury litigations involving the use of DTI indicates that the courts have thus far failed to understand the distinction between the use of DTI in more well-established diagnostic domains (i.e., moderate to severe TBI) and less established domains (i.e., mTBI; see Table 6 for example cases). The courts have, as noted previously, also struggled to understand the importance of control group data for the interpretation of individual scans, and are also unclear regarding which experts are technically qualified to interpret the data derived from these scans. With respect to the latter, post-processing analyses of the scan data can be applied inappropriately, leading to erroneous findings and interpretations. It is thus crucial for the courts to be able to discriminate what information is helpful versus what is prejudicial or even misleading or erroneous.

5.3. Admissibility: Frye, Daubert, and general acceptance

In the early cases that examined the use of DTI in head injury litigation, the courts expressed wariness about the new technology and its general acceptance within the relevant scientific community. For example in *LaMasa v. Bachman* (2005) the plaintiff LaMasa was the driver of the front vehicle that was rear-ended by Bachman. At the trial, the judge allowed a neuroradiologist to present DTI evidence alongside other expert testimony offered to support the existence of a brain injury. The plaintiff was awarded medical damages, and the defendant filed post-verdict motions, including that the court was erroneous in allowing the plaintiff's expert to testify about an "innovative MRI modality utilizing Diffusion Tensor Imaging (DTI) as this modality is not generally accepted in the field of radiology or neuroradiology to diagnose TBI or diffuse axonal injury." (p. 2.) Despite repeating this criticism, the court declined to overturn the original admissibility decision since the defendant was given sufficient time to produce his own rebuttal expert witnesses. Similarly in 2009, the court in *Bowles v. Pennington* (2009) refused to admit DTI into evidence to show mTBI because the party moving to admit the evidence did not include any articles illustrating that DTI could be used for that purpose.

More recent case law regarding general scientific acceptance and admissibility indicates that the courts are taking a more liberal approach to admitting DTI in cases of traumatic brain injury in both *Frye* and *Daubert* jurisdictions. More specifically, in *Hammar v. Sentinel Insurance Co.* (2010) a Florida court rebuffed a challenge to the admissibility of DTI evidence in a civil brain injury litigation, using *Frye* standards for the admissibility of expert scientific evidence. The *Hammar* court used language indicating a general endorsement for DTI in mTBI: "DTI is FDA approved, peer reviewed and approved, and a commercially marketed modality which has been in clinical use for the evaluation of suspected head traumas including mild traumatic brain injury" (*Hammar v. Sentinel Insurance Co. Ltd.,* 2010, p. 2). Similarly in *Whilden v. Cline* (2010), the plaintiff claimed to have suffered a mTBI in a motor vehicle accident. The court ruled that the DTI evidence was "sufficiently reliable and scientifically accepted so as to be of benefit to the jury," but qualified this holding with the caveat that it would have "serious concerns" about the appropriateness of diagnosing mild traumatic brain injury as the cause of abnormality solely from the presence of the abnormalities revealed by the technology." The court elaborated that "the technology has not yet been proven to be of sufficient value as to reasonably exclude other reasonably possible causes" (*Whilden v. Cline,* 2010, p.3), noting that the abnormalities shown could result from different causes ranging from multiple sclerosis to dementia.

Several cases using *Daubert* standards for expert testimony gatekeeping have also made blanket declarations that the use of DTI is reliable, subject to peer review, and has low error rates, making no distinction between its use in mTBI or more serious head injuries. For example, in *Ruppel v. Kucanin* (2011), defendant Dragan Kucanin, a driver for defendant FedEx Ground Package System, Inc., drove his semi-tractor trailer rig into a semi-tractor trailer rig driven by plaintiff Dale Ruppel when the latter was stopped in a construction zone. Ruppel sued FedEx and Kucanin for damages that he allegedly sustained as a result of the accident. Defendants moved to exclude Ruppel's evidence related to an alleged diffuse axonal brain injury under Federal Rule of Evidence 702 and *Daubert.* Defendants asserted that the methods of DTI and fractional anisotropy quantification used to show diffuse axonal injury were controversial and should be excluded. The court found that DTI could be used to demonstrate mTBI because it is a method that, despite being a relatively new technology, is "gaining general acceptance as a method for detecting TBI" and has FDA approval. The court cited "numerous validation studies, published in peer reviewed journals, on the use of DTI to detect diffuse axonal injuries" and opined that DTI is "regularly used as a diagnostic tool … [at] locations throughout the country" (*Ruppel v. Kucanin,* 2011, p. 20–21).

A trial court in Louisiana reached a similar result in *Andrew v. Patterson Motor Freight* (2014). This was a case in which the plaintiff was struck by a tractor-trailer and alleged frontal lobe injuries. The defense moved to exclude the evidence of DTI, citing one research article questioning its validity for that purpose. However, the court stated, "In sum, the evidence shows that DTI has been tested and has a low error rate; DTI has been subject to peer review and publication and DTI is a generally accepted method for detecting TBI" (*Andrew v. Patterson Motor Freight,* 2014, p. 9).

In another federal court case, *White v. Deere and Company* (2016), the plaintiff sued a manufacturer after she was hit by a bale of hay while operating her tractor and suffered a head injury. The defendants sought to exclude the plaintiff's DTI evidence under *Daubert* standards. However the court determined that defendants failed to establish that "DTI is an unreliable technology to detect mild TBI-associated changes in the brain."

5.4. Individual to group comparisons, standardization, and the relevancy of control groups

As reviewed extensively above, there are significant methodological hurdles facing the use of DTI in mTBI, including the standardization of measurement techniques, the acquisition protocol for images, the magnet strength, the composition of the control group and its relevance to the individual scanned, as well as the misuse of voxel based morphometry and Tract Based Spatial Statistics (TBSS; Smith et al., 2006, 2007) for the post-processing of DTI images.

With respect to controls, a careful selection of appropriate controls is critical to findings because if the control group is not carefully selected than differences reported between controls and mTBI subjects may be due to confounding factors rather than to differences between controls and mTBI groups which are relevant to brain injury. It is thus important that the control group not vary in age, gender, or handedness from the plaintiff. Otherwise the data are not interpretable and, if interpreted, are likely erroneous. Further, it is not clear that comparing an individual case to a control group makes sense using the methods frequently used for DTI, which were intended to be used for group comparisons and not to compare an individual to a group (i.e., voxel based morphometry and TBSS; Smith et al., 2006, 2007). Moreover, a change in the size of the control group is important to take note of in legal cases. For example, in one case [(*Craffey v. Embree Contr. Grp Inc.*, 16-P-791 (Mass.App.Ct. March 29, 2017)] the scientific expert for the plaintiff presented a control group composed of 62 control subjects that were used for comparison to DTI data from the plaintiff, and yet the actual comparisons completed were with 37 control subjects and another comparison with 25 control subjects. It was not evident why the control groups differed, although it was clear that the controls were not well matched on such factors as age, handedness, or gender to the plaintiff. More specifically, the plaintiff in this case was left-handed, whereas the control sample included right-handed individuals of varying age and gender. The expert for the plaintiff stated that he controlled for age, which is very difficult given that different white matter tracts develop over different ages (e.g., Lebel et al., 2012), there are also known differences in the brains of left versus right-handers which were not taken into account in this case (e.g., Geschwind and Levitsky, 1968; Toga and Thompson, 2003), and there was also no consideration given to gender differences in the brain which are also well known (e.g., Goldstein et al., 2001; Simmonds et al., 2014).

A further review of the few reported court decisions indicates that the gatekeepers have not completely understood the nature of these challenges, and have categorized them instead as issues that go to the weight of the evidence at trial, rather than as reliability and validity thresholds, which might require pre-trial exclusion.

More specifically, in *Siracusa v. City Ice Pavillion* (2017), the plaintiff participated in an ALS Ice Bucket Challenge at a Hockey Rink owned by the defendant and alleged that she sustained a traumatic brain injury and exacerbation of prior brain injuries. Her expert conducted a DTI examination and concluded that she had "abnormally low FA levels, which is consistent with traumatic axonal injury although also consistent with other non-traumatic causes" (*Siracusa v. City Ice Pavillion,* 2017, p. 268.). The defendant then served a demand upon the plaintiff for the complete data set pertaining to the DTI examination, asserting that "The individual FA levels of each member of the control group, the data as to the ages and other demographics all affect the final opinions/conclusions about what the MRI-DTI examination allegedly establishes" (*Siracusa v. City Ice Pavillion,* 2017, p. 269). The plaintiff asserted that she did not have control over the data underlying the DTI analysis, that the data set belonged to the expert and the hospital not the plaintiff, and that disclosure of the underlying statistical data was not required. The court, in denying the request for control group and other underlying statistical information, relied on its concurrent decision in *Sylvestre Jean-Francois v. The Port Authority of New York and New Jersey* (2014), involving the same expert neuroradiologist and medical center. The *Siracusa* Court concluded that the information which the neuroradiologist was ordered to produce was not under his control, the hospital should not be ordered to produce data when it is not a party to the action, and the information is "tangentially relevant at best, on issues of the general acceptance of the underlying scanning technology, which have already been determined and need not be revisited in this litigation." The court also raised a privacy and confidentiality concern regarding the possible unauthorized release of identifying information regarding the control population. Finally, the *Siracusa* court termed the defense request for disclosure "detailed" and "overly broad" pointing to requests for hardware specifications and coil design (*Siracusa v. City Ice Pavillion*, 2017, p. 271).

Other courts have similarly opined that once DTI has been deemed a reliable and peer-reviewed technique, both generally and when specifically applied in the individual case, subsequent disagreements among experts should be decided according to the weight of the evidence at trial rather than by pre-trial exclusion (*Booth v. Kit, Inc*, 2009, as cited in Kerkmans & Gaudet, 2016).

5.5. Diffusion tensor imaging and expert qualifications

The courts have also been faced with challenges regarding the admissibility of DTI expert testimony based upon whether the proffered expert is qualified to administer the scan or interpret the data derived therefrom. For example, in *Andrew v. Patterson Motor Freight* (2014), a case discussed above regarding *Daubert* criteria, the court grappled with whether the expert, a self-described "medical doctor specializing in neuroradiology" had sufficient specialized knowledge to assist the trier of fact. The expert in question was noted to have "prior certifications in neurosurgery and radiology from Argentina" but was only licensed to practice radiology in the relevant jurisdiction. After a thorough review of the expert's academic and clinical qualifications, the court denied the defense motion to prohibit his testimony but suggested that the subject of his qualifications was open to cross examination at trial (*Andrew v. Patterson Motor Freight*, 2014, p. 5).

Overall, the plaintiffs appear most frequently to offer experts who specialize in neuroradiology to administer and interpret DTI in the context of alleged traumatic brain injury (see *Ahsan v. Staples, Inc*., 2017). However, some courts have excluded the testimony of neuroradiologists regarding fiber tract abnormalities on DTI suggestive of TBI if the expert has not established himself/herself in the field of post-processing of DTI scans for quantitative analyses (*Wagoner v. Schlumberger Tech Corp*, 2008).

The cases summarized above reveal a concerning pattern. The courts appear to be making blanket endorsements of the use of DTI in mTBI by analogizing from the use of this modality in the diagnosis of moderate and severe brain injury. This facile analogy overlooks the challenges of using DTI to diagnose individual cases of mTBI, and the pitfalls of failing to examine the appropriateness of the underlying imaging data and control groups, as well as the appropriateness of the methods of analysis, and the variability in post processing and interpretation of the data.

6. Summary

DTI, with its great promise as a tool to detect objective signs of neuronal injury, is an attractive modality for the legal arena. It promises to solve many of the pitfalls surrounding mTBI litigation, including an over-reliance on subjective symptom reporting, in the context of secondary monetary gain. Conventional brain imaging modalities such as CT and MRI also often miss subtle diffuse axonal injuries, raising the specter of false negative findings. It is, consequently, highly tempting to bring a novel technology such as DTI into the courtroom, even in its infancy. In fact, as noted previously, there are many fast paced important advances in the field of neuroscience and neuroimaging that have revolutionized what we know about the human brain. The probative value of testimony regarding DTI by experts in the area of mTBI is, however, most problematic and is perhaps best described, as noted previously, by Granacher (2008) who observed that mTBI is "easy to obfuscate" but "difficult to detect."

We thus caution against the premature use of new advances in imaging such as DTI, before standards are established in the clinical arena, which are well informed and validated in the research arena. Judges, who are now gatekeepers with respect to evaluating the admissibility of evidence, need also to be informed with respect to the sensitivity and specificity of scientific measures, to issues of standardization, to appropriate methods of analyses, etc. in the use of DTI as evidence of mTBI in the courtroom.

Further, while DTI is the most promising technique available today for detecting diffuse axonal injury, and is beginning to be used clinically, it remains largely within the purview of research. Its probative value is also not clear as it may be both prejudicial and misleading given that standardization is not yet established in either the clinic or in the courtroom, and thus it may be premature for use in either. There are also concerns, as noted previously, regarding the methods and analyses that have been used to provide quantitative evidence in legal cases.

Finally, we also caution against the use of neuroimaging techniques such as DTI in the courtroom as we are not yet at the tipping point where these advances provide important and meaningful data with respect to their probative value. There is much to be learned and much to support evidence of subtle brain injury that will move from the purview of research in the near future. Additionally, we note that while it may be premature now to bring new imaging tools into the courtroom, we should remain hopeful that such tools will be ready in the very near future. At this time, however, the gold standard remains the clinical interpretation by the neuroradiologist. In the not too distant future, when standardization of some of these new technologies such as DTI are in place, we will move beyond the "new whiplash" and have hard-won evidence based on factual information that is both standardized and validated for use in the clinic and the courtroom. In the interim we do not want to "throw the baby out with the bathwater," as Professor Farah (2014), since what is premature today for use in the courtroom will not be premature tomorrow.

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