Return to Play Following Concussion: Role for Imaging?

Drew Sanclemente[1] Jeffrey A. Belair, MD[2] Kiran S. Talekar, MD[3] Johannes B. Roedl, MD[2]
Stephen Stache, MD[4,5]

[1] Medical Student, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania
[2] Department of Radiology, Thomas Jefferson University, Philadelphia, Pennsylvania
[3] Department of Radiology, Brain Mapping (fMRI and DTI) in Neuroradiology, Thomas Jefferson University, Philadelphia, Pennsylvania
[4] Division of Non-Operative Sports Medicine, Department of Orthopaedics and Family and Community Medicine, Rothman Orthopaedic Institute, Thomas Jefferson University, Sidney Kimmel Medical College, Philadelphia, Pennsylvania
[5] Department of Orthopaedics and Pediatrics, University Athletics, Drexel University and Drexel College of Medicine, Philadelphia, Pennsylvania

Address for correspondence Stephen A. Stache, MD, Rothman Orthopaedic Institute, 925 Chestnut Street, 5th Floor, Philadelphia, PA 19107 (e-mail: stephen.stache@rothmanortho.com).

Semin Musculoskelet Radiol 2024;28:193–202.

Abstract

This review surveys concussion management, focusing on the use of neuroimaging techniques in return to play (RTP) decisions. Clinical assessments traditionally were the foundation of concussion diagnoses. However, their subjective nature prompted an exploration of neuroimaging modalities to enhance diagnosis and management. Magnetic resonance spectroscopy provides information about metabolic changes and alterations in the absence of structural abnormalities. Diffusion tensor imaging uncovers microstructural changes in white matter. Functional magnetic resonance imaging assesses neuronal activity to reveal changes in cognitive and sensorimotor functions. Positron emission tomography can assess metabolic disturbances using radiotracers, offering insight into the long-term effects of concussions. Vestibulo-ocular dysfunction screening and eye tracking assess vestibular and oculomotor function. Although these neuroimaging techniques demonstrate promise, continued research and standardization are needed before they can be integrated into the clinical setting. This review emphasizes the potential for neuroimaging in enhancing the accuracy of concussion diagnosis and guiding RTP decisions.

Keywords
- magnetic resonance spectroscopy
- diffusion tensor imaging
- functional magnetic resonance imaging
- positron emission tomography
- amyloid imaging

In recent years, particularly in sports, the issue of concussions has garnered significant public attention and concern. The media has extensively covered the experiences of high-profile athletes and aspiring young individuals engaged in a wide range of sports, from American football to rugby, soccer, ice hockey, skiing/snowboarding, and others. This growing spotlight has prompted national and international organizations to dedicate substantial efforts to disseminating comprehensive reviews, guidelines, position statements, and recommendations regarding sports-related concussions.

The primary focus in sports-related concussion management focused traditionally on preventing a premature return to contact activities and thus avoiding the risk of concussion-related complications, such as dangerous subsequent blows

Issue Theme Return to Play in Sport: The Role of the Radiologist; Guest Editors, Jeffrey A. Belair, MD and Vishal Desai, MD

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0043-1778031.
ISSN 1089-7860.

to the head and persistent postconcussion symptoms.[1–13] However, an emerging concern now centers on the potential for cumulative long-term impairments resulting from recurrent concussions and sub-concussive hits sustained throughout an athlete's career.[2–14] The multifaceted medical considerations surrounding sports concussions emphasize the need for a multidisciplinary approach to assess and manage these injuries comprehensively.

Concussions, as a form of mild traumatic brain injury (mTBI), have become a significant public health concern, with an annual influx of ~ 200,000 individuals into emergency departments, as estimated by the Centers for Disease Control and Prevention (CDC).[1,14–16] Diagnosing and managing concussions present complex challenges, primarily relying on clinical symptoms, physical examinations, behavioral assessments, and cognitive deficits. Precise determination of the juncture at which an athlete can safely return to competitive activities remains a formidable clinical quandary.[1,14,17]

Traditional neuroimaging, in the form of computed tomography (CT) or magnetic resonance imaging (MRI), often fails to reveal structural brain injury because concussive events rarely result in macroscopic anatomical abnormalities.[18–22] As a result, the contemporary management of concussions relies on other objective and subjective indicators, such as symptomatic checklists, physical examinations, comparisons with baseline testing, balance assessments, and computerized neuropsychological testing.[15,17–19,23–26] Furthermore, the quantification of concussion severity is inundated with challenges, requiring an exploration of advanced diagnostic modalities and methodologies capable of providing more precise and objective measures to aid in diagnosis and in turn inform return to play (RTP) decisions.[4,5,15,27]

Given the global participation of > 200 million individuals in organized physical activities, the development of objective diagnostic and management strategies for concussions is of paramount importance.[28] Although tools like the Sport Concussion Assessment Tool have gained wide validation and adoption in sporting institutions, the limitations of conventional neuroimaging techniques highlight the need for more advanced diagnostic paradigms.[29–33]

This article explores the role of imaging modalities in the context of concussion management and their potential impact on RTP decisions. It delves into the intricacies of concussion diagnosis, the constraints of existing assessment tools, and the emerging necessity to develop advanced neuroimaging methodologies capable of providing deeper insights into the pathophysiology and severity of concussive injuries. Ultimately, we hope to contribute to the ongoing discourse aimed at refining the diagnostic and management landscape of sports concussions, with the ultimate goal of safeguarding the welfare of athletes at all levels of competitive play.

Defining Concussion

A sports-related concussion (SRC) is a form of TBI that occurs due to a direct blow to the head, neck, or body during a sports or exercise activity.[1,7,29,34–37] This blow generates an impulse force transmitted to the brain and initiates a complex physiologic process.[12,15,26,38] The pathophysiologic basis of concussion involves underlying changes in the brain due to the microtrauma of neuronal cell membranes.[1,15,39–41] This microtrauma triggers a cascade of ionic and metabolic events: changes in intracellular ion concentrations, release of neurotransmitters, mitochondrial dysfunction leading to reactive oxygen species production, increased glucose utilization, and decreased blood flow.[42–45] The cascade involves three phases: an initial period characterized by hyperglycolysis, followed by metabolic depression, culminating in a recovery phase.[42,43]

Deciphering the precise point at which cerebral restitution permits the athlete's safe return to competitive activity presents a formidable clinical dilemma. Concussion symptoms can manifest instantly or gradually over minutes to hours following the traumatic event.[2,23,26,30] Symptoms typically resolve within a few days, but in some cases, they can persist for weeks.[11,13,14,23,26,39] It is also important to ensure that symptoms are not attributable to other external factors, such as alcohol, drugs, medications, or additional unrelated injuries.[15]

Nonimaging Diagnosis of Concussion

The American Medical Society for Sports Medicine's "Position Statement on Concussions in Sports" underscores the challenges in diagnosing concussions due to the absence of validated tests and a reliance on self-reported symptoms that can be nonspecific.[1,14,29] These symptoms may include headaches, fogginess, dizziness, visual changes, fatigue, neck pain, sleep changes, and more.[1,6,30–32,46–49]

Because of the nuances in presentation, thorough preseason physical evaluations and consideration of factors such as a history of prior concussions or TBIs, preexisting conditions, learning disorders, attention-deficit hyperactivity disorder, motion sickness, mood disorders, migraines, and current medications are crucial.[33,50] Some organizations recommend baseline evaluations using tools like SCAT6, Computerized CogSport, ANAM, CNSVS, and Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT).[1,7,29–33,47,51]

Best practices endorsed by the National Collegiate Athletics Association include baseline assessments of symptom checklists, cognitive function, and balance.[52] On the sidelines, athletes should be removed from the game if they exhibit signs such as loss of consciousness, tonic posturing, gross motor instability, confusion, amnesia, seizures, a vacant look, or balance and coordination issues.[1,6,30–32,46–49] If a concussion is suspected, clinicians should conduct a brief history, assess orientation, memory, concentration, balance, and speech patterns, and perform cervical spine evaluation with palpation and range of motion checks during the evaluation process.[1,6,9,10,14,29,35,53–55]

Current Protocol for Return to Play

The current RTP guidelines for SRCs have evolved significantly based on the latest research and a heightened awareness of SRC. These guidelines emphasize the importance of medical oversight and the careful management of athletes to ensure adequate time for recovery before resuming competitive play.[8,29,56]

The CDC and the National Federation of State High School Associations Sports Medicine Advisory Committee recommend a Six-Step Return to Play Progression structured to ensure athlete health and safety.[53,56] Only after being symptom free and cleared by a health care professional can athletes progress through the steps.[8,29,53,56] The stepwise approach includes increasing physical activity levels, from light aerobic exercise to full competition, carefully monitoring symptoms and cognitive function at each stage.[8,29,53,56] The process considers individual variability, with athletes moving between stages at their own pace, and it emphasizes the importance of medical oversight and communication among all involved parties.[8,29,53,56] Each step of the process takes a minimum of 24 hours for a gradual progression.[29,56]

Unlike past practices that advocated for strict physical and cognitive rest, the current approach emphasized in the most recent "Consensus Statement on Concussion in Sport" encourages athletes to engage in daily activities including walking immediately after the injury.[1,6–8,14,29,34,53,56] Light physical activity and prescribed aerobic exercise within specified thresholds are introduced early in the treatment plan.[29,56] Athlete symptoms, cognitive function, clinical findings, and the judgment of a health care provider guide progression through these steps.[29,56] Although unrestricted RTP typically occurs within 1 month of injury, individual characteristics may extend this time frame.[8,29,53,56] Overall, the current RTP guidelines emphasize a personalized, multidisciplinary approach to concussion management that considers both preexisting and postinjury factors that can impact an athlete's recovery trajectory.[8,29,53,56]

Imaging Modalities in Management

The following discussion provides a thorough understanding of the diverse and complex neuroimaging methods and approaches of neuroimaging techniques for managing and diagnosing concussions, delving into each imaging modality and discussing its potential contribution to the intricate decision-making processes associated with the return to sport in athletes. A detailed evaluation of various neuroimaging modalities has revealed their promise in augmenting the understanding of the pathophysiologic underpinnings and severity assessment of concussions, especially in cases where conventional imaging methods fall short.

The discussion synthesizes the findings and explores the clinical implications of these modalities, considering their respective strengths, limitations, and evolving roles in concussion management. But it important to note that many, if not all, of the imaging modalities discussed here are not currently ready for real-time use in clinical management. A considerable amount of additional research is necessary to refine, simplify, and validate these novel techniques.

Magnetic Resonance Imaging

As previously mentioned, routine clinical MRI sequences obtained in patients with SRC often fail to reveal structural brain injury because concussive events rarely result in macroscopic structural changes.[18–22] In some cases, mTBI may result in cerebral microhemorrhage that can be detected on certain MRI sequences due to the paramagnetic properties of blood degradation compounds, specifically deoxyhemoglobin, ferritin, and hemosiderin.[57] Susceptibility weighted imaging (SWI) has been found to be more sensitive for detecting microbleeds compared with T2*-weighted gradient-echo (GRE) imaging. Some evidence indicated that traumatic microbleeds predict cognitive outcome and persistent posttraumatic complaints in patients with mTBI.[58] Therefore, when performing routine noncontrast brain MRI in the work-up of patients, substituting the more commonly performed T2*-weighted GRE sequence with SWI is highly recommended (►Fig. 1).

Magnetic Resonance Spectroscopy

Proton magnetic resonance spectroscopy (MRS), a noninvasive technique, has displayed substantial promise by shedding light on neurochemical changes that might remain hidden when relying solely on conventional MRI for structural assessments. Specifically, MRS has uncovered crucial alterations in critical metabolites such as N-acetyl aspartate (NAA), choline (Cho), and creatine-phosphocreatine (Cr) ratios, even when no discernible structural injury is apparent

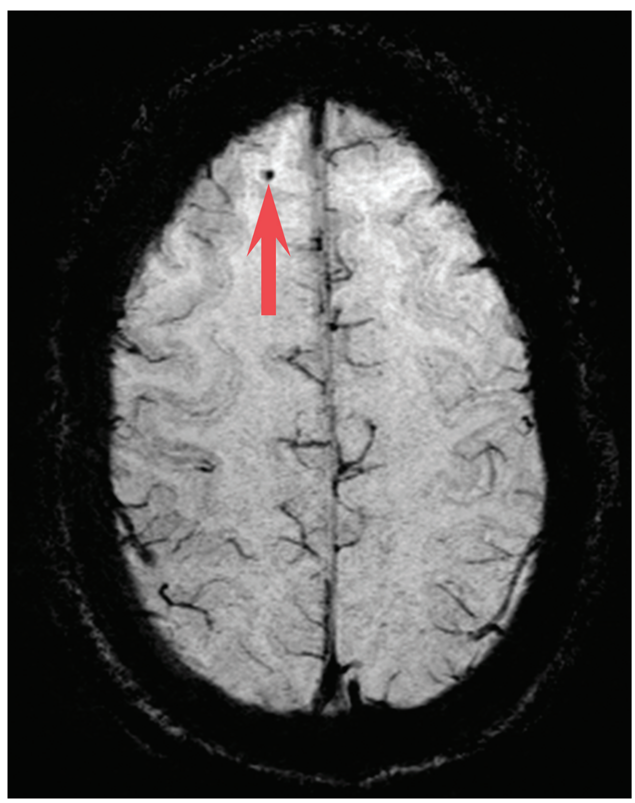

Fig. 1 A 45-year-old former football player with a history of multiple prior concussions. Axial susceptibility weighted imaging minimum intensity projection image reveals a small focus of susceptibility artifact in the anterior right frontal lobe (arrow), consistent with prior microhemorrhage. Other routinely obtained magnetic resonance imaging sequences in this patient revealed no other structural or anatomical abnormality.

on standard MRI.[59] Studies focusing on SRCs have demonstrated the diminished NAA-to-Cr ratio during the acute phase of injury that signifies metabolic disturbances.[60,61]

Importantly, these ratios have shown signs of recovery within 30 days postinjury, underlining the potential of MRS to monitor metabolic changes longitudinally and thus potential application to RTP decision making. NAA relates to neuronal and axonal integrity. Altered NAA levels provide insights into neuronal loss, metabolic disruptions, or myelin repair processes.[62,63] Cho levels, in contrast, tend to increase after head trauma, pointing to dynamic cell membrane turnover. At the same time, the Cr peak emerges as a reliable indicator of baseline cellular energy metabolism and serves as a reference peak for calculations of the NAA-to-Cr ratio and Cho-to-Cr ratios.[64]

Despite the wealth of information MRS provides, there is a notable gap in research on mTBIs both in SRC and non–sports-related forms. Existing studies have predominantly focused on moderate to severe TBI. Although common trends in MRS studies of mTBI, both in SRC and non–sports-related incidents, often involve reduced NAA and increased Cho levels, with Cr levels presumed to be stable, emerging research suggests that this presumed stability may not hold true.[20,64] In conclusion, using MRS in the context of concussion management and RTP decision making offers a valuable window into the dynamic metabolic changes occurring in the brain after injury. Understanding the subtle abnormalities inherent in concussive injuries is important and emphasizes the need for further research in this area.

Diffusion Tensor Imaging

Diffusion tensor imaging (DTI), an advanced MRI technique that harnesses the directional analysis of water diffusion within white matter (►**Fig. 2**), offers a unique window into the brain's microstructural changes following concussions.[20–22,65–67] Studies using DTI have mainly centered on nonathletes, providing valuable insights into the alterations occurring in white matter regions.[21,22] DTI has shown a remarkable ability to detect white matter injuries even when conventional MRI sequences appear normal, making it a valuable tool for concussion assessment.[20–22,65] More recently, quantitative DTI, and one key metric in particular, fractional anisotropy (FA), showed potential for assessing the severity of concussions.[22,65,66,68] Reduced FA is correlated with more severe symptoms, even in subjects with structurally normal imaging.[69] Abnormal findings on quantitative DTI correlate with impaired reaction time, emphasizing its practical relevance in concussion management.[66]

Despite the potential of DTI, its utility is influenced by various factors, including the timing of imaging postinjury.[22,65] Studies indicate that the results of DTI can vary as time elapses from the initial insult.[22,65] Understanding the complex and dynamic nature of brain injuries, particularly SRC, is vital when interpreting DTI findings. The heterogeneity of results observed in different studies underscores the importance of considering the time elapsed since the injury, the age of the patient, and the presence of previous concussions when analyzing DTI data.

As DTI continues to gain prominence in concussion research, it is essential to address the need for data collection and analysis standardization. Uniformity in DTI protocols and data interpretation across different platforms remain critical challenges. The emergence of other advanced diffusion imaging techniques, such as diffusion spectrum imaging, hybrid diffusion imaging (HYDI), q-ball imaging, and high angular resolution diffusion imaging (HARDI), presents new avenues for improving our understanding of concussions.[70,71] DTI has already made significant contributions to

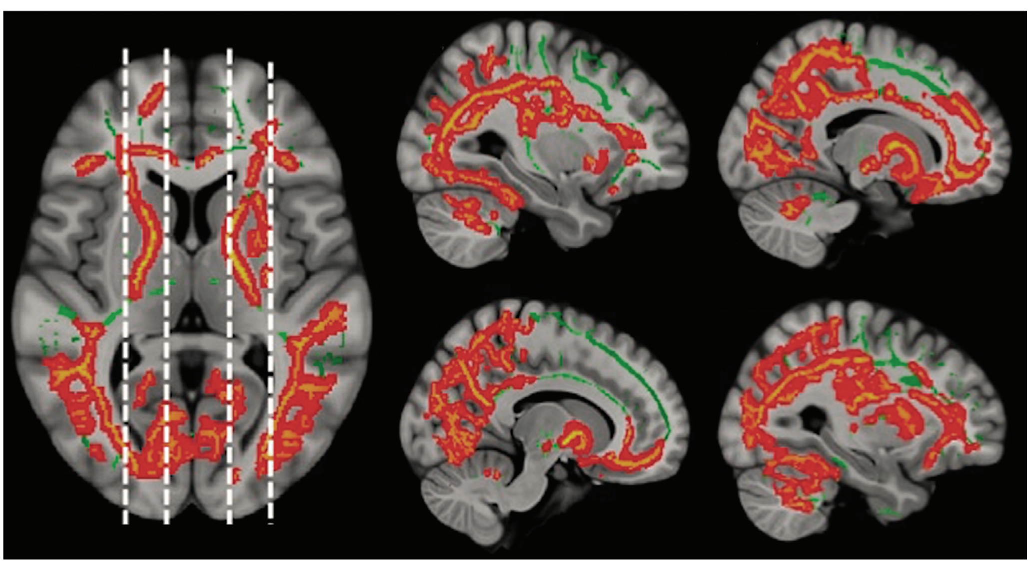

Fig. 2 Usage of hybrid diffusion imaging (HYDI) to detect white matter microstructure alterations in patients with chronic traumatic brain injury (TBI). Tract-based spatial statistics (TBSS) maps of significant differences of intra-cellular volume fraction (V_{ic}) between TBI patients and healthy controls. Red-orange voxels indicate regions with significantly lower V_{ic} values in TBI versus controls, whereas green voxels indicate no significant differences. Abnormal fiber tract diffusion metrics are useful for detecting long-term alterations of declining neurite density. Specifically, decreased V_{ic} within the posterior periventricular regions may be disruptive to the overall integrative of the whole-brain white matter network, which can help explain long-term cognitive and behavioral symptoms after TBI. Image courtesy of Dr. Andrew B. Newberg.

the field, but ongoing research and advancements in neuroimaging will likely further enhance our ability to assess and manage concussions effectively.

Functional Magnetic Resonance Imaging

Functional magnetic resonance imaging (fMRI) uses the blood oxygen level-dependent (BOLD) contrast to provide insights into neuronal activity within the brain (►**Fig. 3**).[18,72] The BOLD signal in fMRI is sensitive to blood-based properties, particularly the magnetic susceptibility produced by deoxyhemoglobin.[17,18,20,63] The fundamental principle underlying fMRI is that increased neuronal activity in a specific brain region leads to an elevation in local blood flow, resulting in reduced deoxyhemoglobin concentrations in nearby vessels.[17,18,20,63] The heightened presence of oxyhemoglobin, corresponding to neuronal activity, results in higher signal intensities, allowing for the indirect assessment of neuronal responses to cognitive and sensorimotor tasks.[17,18,20,63]

Despite its proven efficacy in probing brain function, discussions continue regarding the clinical utility of fMRI in concussion assessment, especially in the context of SRC. Studies using fMRI in individuals with mTBI have shown alterations in the BOLD signal during various cognitive tasks, including working memory, attention, and sensorimotor functions.[17,18,20,63] Task-related fMRI may be a sensitive tool for evaluating residual motor and cognitive deficits in the subacute phase of mTBI.[27,63,72]

The prefrontal cortex, particularly the dorsolateral prefrontal cortex (DLPFC), consistently exhibits increased neural activity in response to cognitive tasks in patients with postconcussive symptoms.[27,63] This phenomenon, often termed "neural inefficiency," may be linked to diminished cognitive performance in SRC patients.[27,63,73] Recent research delving into spatial memory navigation tasks using fMRI in athletes with SRC demonstrated distinctive brain activation patterns.[18,20,27,63,73–75] Although no significant differences in task performance were observed between concussed individuals and neurologically normal controls, fMRI revealed more extensive cortical networks with additional activation outside the study's regions of interest.[27,63,76] The enhanced activation was evident in the parietal cortex, right DLPFC, and right hippocampus.[17,27,63]

The bilateral recruitment of the DLPFC in concussed subjects further emphasized the complexity of neural responses following SRC.[27,51,63] The increased neural recruitment observed in studies of working memory dysfunction in SRC can be attributed to three possible explanations: "brain reorganization," "neural compensation," and the "latent support hypothesis."[20,27,77,78] These explanations

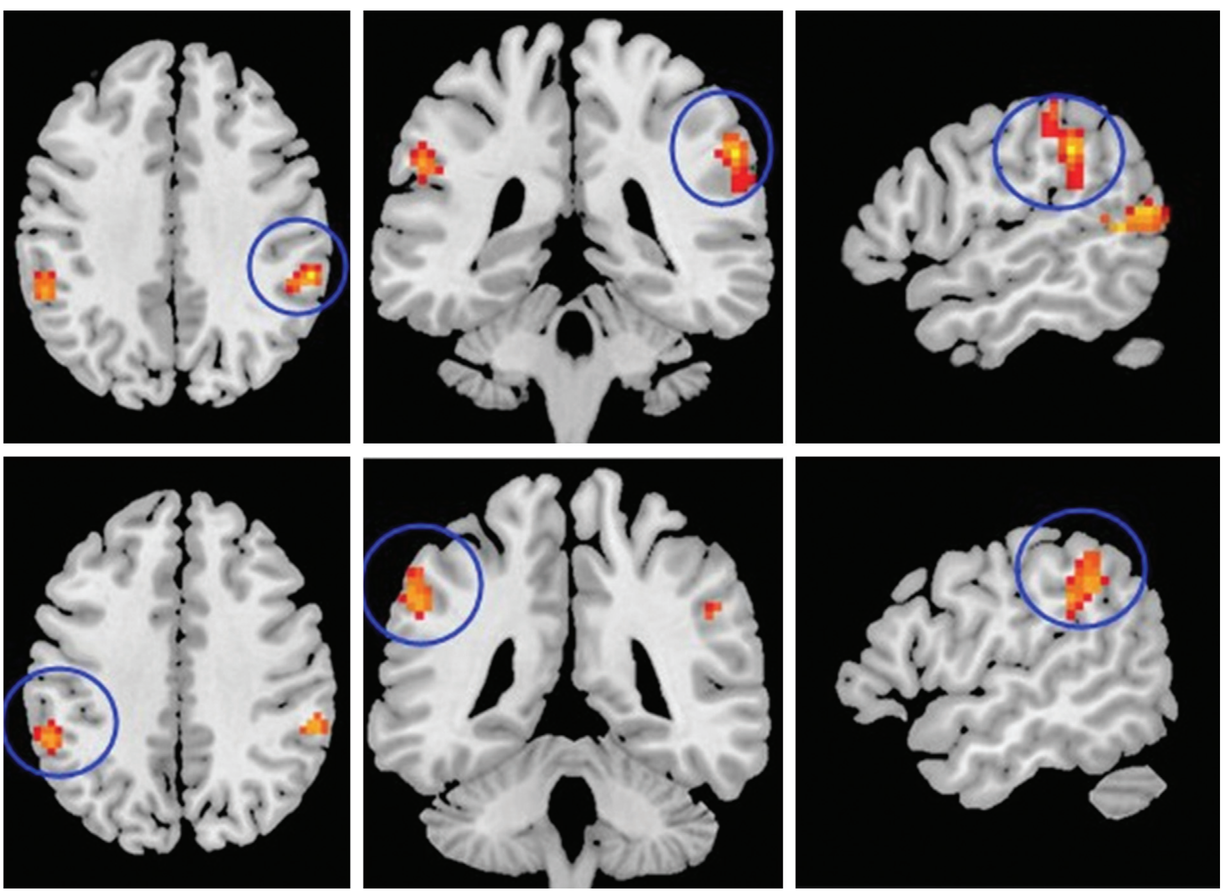

Fig. 3 Increased fractional amplitude of low-frequency fluctuations (fALFF) on blood-oxygen-level-dependent (BOLD) imaging in mild traumatic brain injury (mTBI) patients compared with healthy controls. Hot colors denote areas of increased fALFF in the mTBI group, including the circled regions in the right supramarginal gyrus (top row) and the left inferior parietal region (bottom row). Areas of significantly different resting functional connectivity reflect increased spontaneous brain activity at rest. Image courtesy of Dr. Andrew B. Newberg.

differ in their interpretations of the permanence and purpose of additional neural recruitment in response to cognitive challenges. Research findings in this area have been somewhat controversial, with some studies suggesting hypoactivation in specific brain regions, particularly the mid-DLPFC, and variations in activation patterns based on the presence of depression in concussed athletes.[27,63,73,75]

Positron Emission Tomography

Positron emission tomography (PET) imaging, with its capability to measure brain metabolism, has emerged as a powerful neuroimaging technique for assessing metabolic disturbances.[18,24,74,79–83] This technology offers a unique window into the functional alterations in the brain and holds particular promise for SRCs. Conventional imaging modalities such as MRI or CT lack the ability to capture the nuanced metabolic changes seen in SRC.[18–22] PET provides a more thorough understanding of the metabolic activity of brain regions and their correlation with the associated neurovascular changes linked to symptomatology through the use of radionucleotide tracer fludeoxyglucose F18 (abbreviated as 18F-FDG) that measures local glucose metabolism in various brain regions.[74,84,85] PET imaging can be combined with CT or MRI for anatomical localization (►**Fig. 4** and ►**Fig. 5**).

A recent study compared patients with a single blunt mTBI from a vehicle accident with age-matched controls. The study revealed a complex pattern of hypermetabolism in some brain regions (parahippocampal gyrus, middle temporal gyrus, cingulate, precuneus, and brainstem) and concurrent hypometabolism in others (angular gyrus, calcarine cortex, and middle/superior frontal brain regions).[84] This novel approach highlighted the association between hypometabolism in frontal brain regions and decreased cognitive scores. These results provided clear evidence for the sensitivity of 18F-FDG PET in linking changes in glucose metabolism with cognitive function.[84] The lack of specificity of 18F-FDG PET, combined with the complexity of understanding changes in glucose metabolism, raises questions about its utility as a diagnostic biomarker for SRC.[24,84]

Tau PET imaging has emerged as a promising avenue of research in this field, especially for assessing tau pathology in patients with TBI.[76,79,80,83,84] Following a single TBI, of any type, including sports-related concussion, pathologic findings suggest that a third of subjects exhibit neurofibrillary tangles at autopsy years after injury.[86] Currently, research indicates that axonal injury leads to tau hyperphosphorylation and aggregation.[79,83] However, the precise mechanisms remain unclear. Recent advancements in tau-selective radiotracers have provided opportunities to visualize tau pathology in patients with TBI. The most widely used tau PET tracer, 18F-AV-1451 (18F-flortaucipir), was evaluated in patients with a single moderate to severe TBI history.[84] The findings revealed significant differences in the spatial extent of 18F-flortaucipir signals in gray and white matter regions compared with age-matched controls, suggesting distinctive tau deposition patterns in TBI patients.[84]

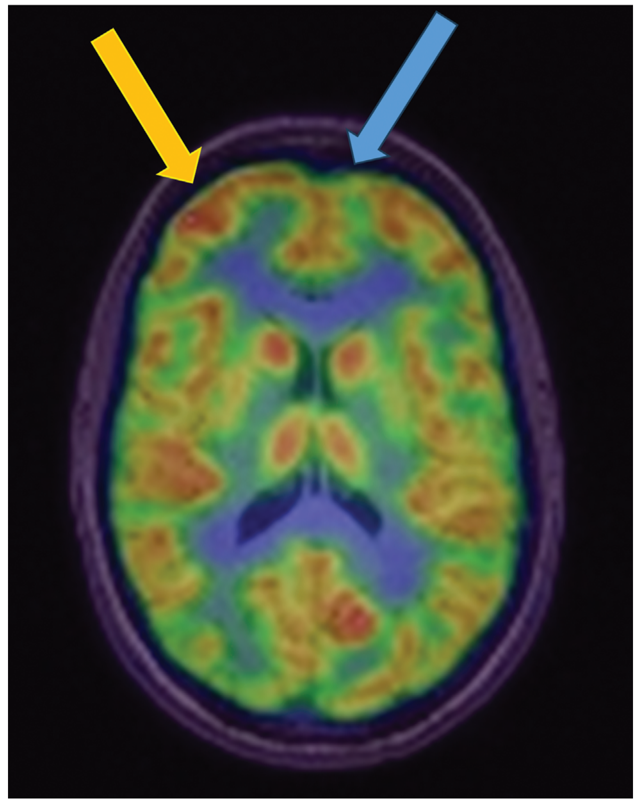

Fig. 4 Axial attenuation corrected fused FDG PET-MR images of the brain in a 35-year-old female with history of prior concussions particularly to the front of the head, obtained for research purposes. In this case, there was decreased metabolism in the left superior frontal region (blue arrow) along with increased metabolism in the right frontal region. A common finding in patients with post-concussion syndrome is a mix of areas of increased and decreased metabolism. These findings correlate with symptoms such as poor concentration when frontal lobe metabolism is abnormal. Image courtesy of Dr. Andrew B. Newberg.

Various radiotracers have provided insights into the dynamics of β-amyloid deposition within the brain.[87–89] Recent case reports using 18F-florbetapir have demonstrated intriguing patterns of β-amyloid deposition in the aftermath of TBI.[84] Although there is an initial increase, this deposition appears to clear over time in specific brain regions.[87,88] These findings highlight the complexity of β-amyloid accumulation dynamics following TBI and emphasize the need for comprehensive investigation.[87,88] If researchers can quantify β-amyloid deposition models, it would be possible to develop the ability to monitor SRC in cases of subclinical symptomatology. Factors beyond the occurrence of TBI, such as age, genetic risk, or vascular factors, may influence β-amyloid deposition and need to be controlled for in future studies and could hinder potential future applications.[84,87,88]

In the context of SRC, PET has the potential to provide invaluable insights into the metabolic and functional alterations in the brain. The challenges of interpreting these findings within the broader clinical context further emphasize the multifaceted nature of RTS decision making. As research in this field continues to evolve, PET remains a promising tool with the potential to enhance our understanding.

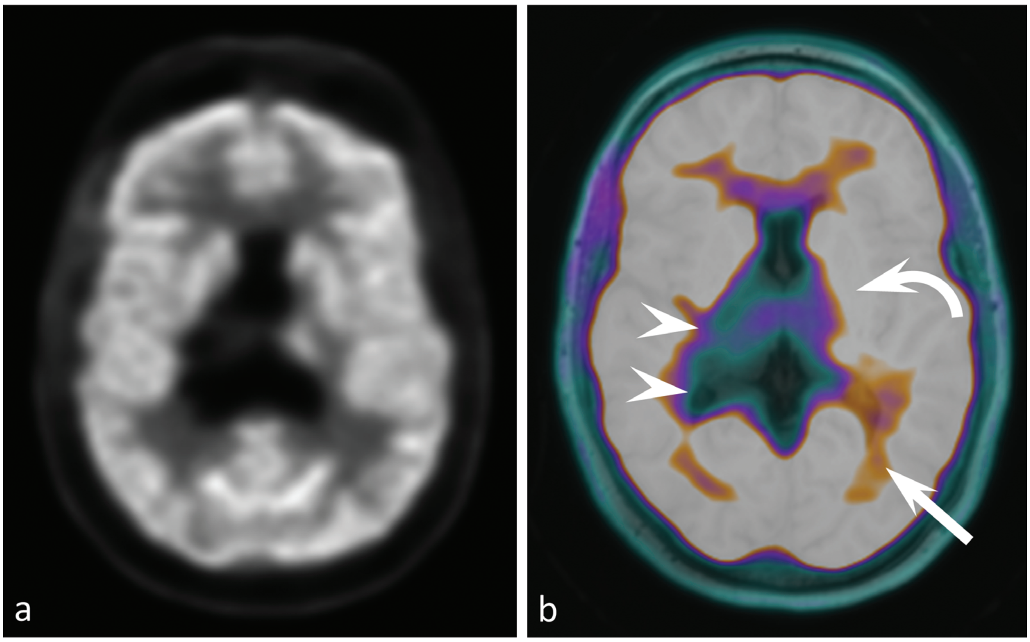

Fig. 5 Axial PET attenuation corrected (a) and axial fused PET-MR (b) images of the brain in a 52-year-old female with history of multiple prior concussions, obtained for research purposes. In this case, there was mildly decreased metabolism in the left inferior occipital region (arrow) and right fusiform gyrus and superior temporal region (arrowheads). There was mildly increased metabolism in the left insula (curved arrow), as well as the hypothalamus, midbrain, left orbital gyrus, right thalamus, and right nucleus accumbens (not shown). Decreased metabolism in the occipital lobe along with increased metabolism in the thalamus and temporal regions can be associated with visual processing problems, including hypersensitivity to light. Abnormal function in the superior temporal region can also be associated with verbal processing problems. Increased metabolism in the hypothalamus, nucleus accumbens, insula, and midbrain can be associated with emotional dysregulation as well as general problems with cognitive processing speed. Increased metabolism in the orbital regions can be associated with impaired concentration and cognition. In general, areas of increased metabolic activity are typically associated with inflammation or a persistent neuroexcitatory state associated with a history of head injury, and areas of decreased metabolic activity are associated with reduced neuronal function, most likely from injury.

Vestibulo-Ocular Dysfunction and Eye Tracking

The prevalence of vestibulo-ocular dysfunction in concussions is evident, with vestibular and oculomotor symptoms frequently reported.[6,15,29,30,47,90–93] Screening using tools like vestibular/ocular motor screening (VOMS) has shown promise in detecting changes in symptom provocation and components of vestibular function.[29,91,93] Eye tracking, although challenging to implement on the sidelines, can detect abnormal ocular motility patterns associated with concussions, necessitating establishing appropriate error thresholds and optimizing sensitivity and specificity.[30,47,91–93] Emerging technology that attempts to track eye movements digitally and produce imaging reports shows significant promise and will allow further objective assessment of eye movements that can be combined with reported symptom provocation related to eye-tracking testing.[93]

Chronic Traumatic Encephalopathy

Chronic traumatic encephalopathy (CTE) is a neurodegenerative disease linked to repetitive head impacts.[74,76,79,80,86–88,94] CTE, which occurs predominantly in contact sports and military service, presents a significant challenge because a diagnosis can only be made postmortem at this time. This limitation prevents intervention and comprehensive patient care.

The emerging role of neuroimaging techniques in the in vivo diagnosis of CTE is a promising development.[74,76,79,94] MRI has revealed significant alterations in brain structure and function among individuals with CTE including changes in brain volume, ventricular enlargement, cerebral atrophy, white matter organization, cortical thinning, and functional connectivity.[74,80,94] These findings are indicative of the neuropathologic changes associated with CTE and provide a potential tool for early diagnosis and intervention.

MRS has proven to be sensitive in detecting neuroinflammation, neuronal loss, and axonal injury, all of which are characteristics observed in CTE.[70,72,75,] Studies indicate that MRS can correlate neurochemical changes associated with neuroinflammation with mood symptoms and behavioral changes in former NFL players.[95] Advancements in two-dimensional MRS allow more precise measurements of metabolites and neurotransmitters.[59,64] A further subtype of MRS, localized correlated spectroscopy, allows detection of different brain metabolites in various brain regions.[96]

PET and radionucleotides are promising future methods of diagnosing CTE by detecting tau aggregates.[79,83] Radionuclide 18F-FDDNP has shown potential in distinguishing CTE from other conditions.[74] The limitation of these methods includes financial coverage, nonspecific binding, and safety concerns.[74] In Shin's 2023 review in the *National High School Journal of Science,* there is a discussion about the need for personalized models of tau-induced atrophy in CTE, allowing clinicians to understand the trajectory of individual disease processes and intervene accordingly.[94] Diagnosing CTE in living patients remains a significant challenge, but neuroimaging will likely emerge as the center point of in vivo diagnosis.

Conclusion

The management and RTP decision making in SRCs have evolved significantly over recent years, driven by increasing public awareness and the multidisciplinary approach adopted by medical professionals, researchers, and sports organizations. This article illuminated the multifaceted nature of concussions, emphasizing the significance of various imaging modalities in enhancing our understanding of these injuries.

The discussion surrounding imaging modalities, including MRS, quantitative DTI, fMRI, PET, and VOMS, highlighted their potential to offer valuable insights into the pathophysiologic processes and severity assessment of concussions. These technologies offer a dynamic and comprehensive perspective on brain function and structure, with each modality contributing to a more complete understanding of the intricacies of concussions.

Despite the progress made in the field of concussion-related neuroimaging, significant challenges and gaps in research remain. The need for standardization in data collection and analysis within the development of advanced imaging techniques, such as tau PET imaging, are ongoing areas of exploration. Additionally, integrating imaging data with clinical assessments and neuropsychological tests is crucial for making informed RTP decisions and monitoring recovery. Thus all of the imaging modalities described here remain outside the scope of standard practice and are primarily limited to research applications.

This literature review underscored the evolving landscape of concussion management, guided by the promise of advanced imaging modalities in elucidating the complex nature of concussions. As research continues to advance, these tools hold the potential to improve the accuracy of diagnosis, inform treatment strategies, and ultimately enhance the welfare of athletes who sustain head trauma. Integrating these imaging techniques into the broader context of clinical care and RTP decision making would represent a significant step forward in mitigating the short- and long-term consequences of SRCs.

Conflict of Interest
None declared.

References

1 Harmon KG, Drezner JA, Gammons M, et al. American Medical Society for Sports Medicine position statement: concussion in sport. Br J Sports Med 2013;47(01):15–26
2 Harmon KG. Assessment and management of concussion in sports. Am Fam Physician 1999;60(03):887–892, 894
3 McCrea HJ, Perrine K, Niogi S, Härtl R. Concussion in sports. Sports Health 2013;5(02):160–164
4 Slobounov SM, Sebastianelli WJ. Foundations of Sport-Related Brain Injuries. New York, NY: Springer Science & Business Media; 2006
5 Difiori JP, Giza CC. New techniques in concussion imaging. Curr Sports Med Rep 2010;9(01):35–39
6 Putukian M. Clinical evaluation of the concussed athlete: a view from the sideline. J Athl Train 2017;52(03):236–244
7 McCrea M, Guskiewicz K. Evidence-based management of sport-related concussion. Prog Neurol Surg 2014;28:112–127
8 Teare-Ketter A, Ebert J, Todd H. The implementation of a return-to-play protocol with standardized physical therapy referrals in a collegiate football program: PT's role in return-to-play, a clinical commentary. Int J Sports Phys Ther 2023;18(02):513–525
9 Fick DS. Management of concussion in collision sports. Guidelines for the sidelines. Postgrad Med 1995;97(02):53–56, 59–60
10 McCrea M, Kelly JP, Kluge J, Ackley B, Randolph C. Standardized assessment of concussion in football players. Neurology 1997;48 (03):586–588
11 Mayers L. Return-to-play criteria after athletic concussion: a need for revision. Arch Neurol 2008;65(09):1158–1161
12 Neumann KD, Broshek DK, Newman BT, Druzgal TJ, Kundu BK, Resch JE. Concussion: beyond the cascade. Cells 2023;12(17): 2128
13 Bytomski J. Sports medicine: concussion. FP Essent 2022; 518:11–17
14 Harmon KG, Clugston JR, Dec K, et al. American Medical Society for Sports Medicine position statement on concussion in sport. Br J Sports Med 2019;53(04):213–225
15 Bolouri H, Zetterberg H. Animal models for concussion: molecular and cognitive assessments—relevance to sport and military concussions. In: Kobeissy FH, ed. Brain Neurotrauma: Molecular, Neuropsychological, and Rehabilitation Aspects. Boca Raton, FL: CRC Press/Taylor & Francis; 2015:Chapter 46
16 Traumatic brain injury data. Available at: https://www.cdc.gov/traumaticbraininjury/data/index.html. Accessed October 30, 2023
17 Saluja RS. The Use of Functional Magnetic Resonance Imaging in the Assessment of Pediatric Patients Post Concussion. Montreal, QC, Canada: McGill University Libraries; 2017
18 Riascos R, Bonfante-Mejia EE. Imaging of Brain Concussion, an Issue of Neuroimaging Clinics of North America. Philadelphia, PA: Elsevier Health Sciences; 2017
19 Yuh EL, Hawryluk GWJ, Manley GT. Imaging concussion: a review. Neurosurgery 2014;75(Suppl 4):S50–S63
20 Slobounov S, Gay M, Johnson B, Zhang K. Concussion in athletics: ongoing clinical and brain imaging research controversies. Brain Imaging Behav 2012;6(02):224–243
21 Schrader H, Mickeviciene D, Gleizniene R, et al. Magnetic resonance imaging after most common form of concussion. BMC Med Imaging 2009;9:11
22 Wilde EA, McCauley SR, Hunter JV, et al. Diffusion tensor imaging of acute mild traumatic brain injury in adolescents. Neurology 2008;70(12):948–955
23 Gay M, Slobounov S. Concussion: a window into brain–movement relations in motor control. Kinesiol Rev (Champaign) 2018;7(01): 51–57
24 Chen SHA, Kareken DA, Fastenau PS, Trexler LE, Hutchins GD. A study of persistent post-concussion symptoms in mild head trauma using positron emission tomography. J Neurol Neurosurg Psychiatry 2003;74(03):326–332
25 Abraham L, Bell KR. The use of neuroimaging by community physicians in children with mild traumatic brain injuries. Presented at: 13th World Congress on Brain Injury, March 13–16, 2019; Toronto, ON, Canada
26 Hainline B, Gurin LJ, Torres DM. Concussion. New York, NY: Oxford University Press; 2020
27 Dettwiler A, Murugavel M, Putukian M, Cubon V, Furtado J, Osherson D. Persistent differences in patterns of brain activation after sports-related concussion: a longitudinal functional magnetic resonance imaging study. J Neurotrauma 2014;31(02): 180–188
28 Data finder: Health, United States. Available at: https://www.cdc.gov/nchs/hus/data-finder.htm?&subject=Physical%20activity. Accessed October 30, 2023
29 Patricios JS, Schneider KJ, Dvorak J, et al. Consensus statement on concussion in sport: the 6th International Conference on

Concussion in Sport-Amsterdam, October 2022. Br J Sports Med 2023;57(11):695–711
30 Yue JK, Phelps RRL, Chandra A, Winkler EA, Manley GT, Berger MS. Sideline concussion assessment: the current state of the art. Neurosurgery 2020;87(03):466–475
31 Podell K, Presley C, Derman H. Sideline sports concussion assessment. Neurol Clin 2017;35(03):435–450
32 Yengo-Kahn AM, Hale AT, Zalneraitis BH, Zuckerman SL, Sills AK, Solomon GS. The Sport Concussion Assessment Tool: a systematic review. Neurosurg Focus 2016;40(04):E6
33 Katz BP, Kudela M, Harezlak J, McCrea M, McAllister T, Broglio SPCARE Consortium Investigators. Baseline performance of NCAA athletes on a Concussion Assessment Battery: a report from the CARE Consortium. Sports Med 2018;48(08):1971–1985
34 Herring S, Kibler WB, Putukian M, et al. Selected issues in sport-related concussion (SRC|mild traumatic brain injury) for the team physician: a consensus statement. Curr Sports Med Rep 2021;20(08):420–431
35 Gregory A, Poddar S. Diagnosis and sideline management of sport-related concussion. Clin Sports Med 2021;40(01):53–63
36 Okonkwo DO, Tempel ZJ, Maroon J. Sideline assessment tools for the evaluation of concussion in athletes: a review. Neurosurgery 2014;75(Suppl 4):S82–S95
37 Hyden J, Petty B. Sideline management of concussion. Phys Med Rehabil Clin N Am 2016;27(02):395–409
38 Sussman ES, Ho AL, Pendharkar AV, Ghajar J. Clinical evaluation of concussion: the evolving role of oculomotor assessments. Neurosurg Focus 2016;40(04):E7
39 Giza CC, Kutcher JS. An introduction to sports concussions. Continuum (Minneap Minn) 2014;20(6 Sports Neurology):1545–1551
40 Makdissi M, Cantu RC, Johnston KM, McCrory P, Meeuwisse WH The difficult concussion patient: what is the best approach to investigation and management of persistent (> 10 days) post-concussive symptoms? Available at: https://bjsm.bmj.com/content/47/5/308.short. Accessed October 30, 2023
41 Toledo E, Lebel A, Becerra L, et al. The young brain and concussion: imaging as a biomarker for diagnosis and prognosis. Neurosci Biobehav Rev 2012;36(06):1510–1531
42 Giza CC, Hovda DA. The new neurometabolic cascade of concussion. Neurosurgery 2014;75(0 4, Suppl 4):S24–S33
43 MacFarlane MP, Glenn TC. Neurochemical cascade of concussion. Brain Inj 2015;29(02):139–153
44 Hovda DA. The neurophysiology of concussion. Prog Neurol Surg 2014;28:28–37
45 Giza CC, Hovda DA. The neurometabolic cascade of concussion. J Athl Train 2001;36(03):228–235
46 Davis G, Makdissi M. Use of video to facilitate sideline concussion diagnosis and management decision-making. J Sci Med Sport 2016;19(11):898–902
47 Ventura RE, Jancuska JM, Balcer LJ, Galetta SL. Diagnostic tests for concussion: is vision part of the puzzle? J Neuroophthalmol 2015;35(01):73–81
48 Echemendia RJ, Broglio SP, Davis GA, et al. What test and measures should be added to the SCAT3 and related tests to improve their reliability, sensitivity and/or specificity in sideline concussion diagnosis? A systematic review [abstract]. Available at: https://bjsm.bmj.com/content/51/11/895 Accessed October 30, 2023
49 Patricios J, Fuller GW, Ellenbogen R, et al. What are the critical elements of sideline screening that can be used to establish the diagnosis of concussion? A systematic review. Br J Sports Med 2017;51(11):888–894
50 McCrea M. Standardized mental status testing on the sideline after sport-related concussion. J Athl Train 2001;36(03):274–279
51 Wang Y, Nelson LD, LaRoche AA, et al. Cerebral blood flow alterations in acute sport-related concussion. J Neurotrauma 2016;33(13):1227–1236
52 National Collegiate Athletics Association. Concussion safety protocol management. Available at: https://www.ncaa.org/sports/2016/7/20/concussion-safety-protocol-management.aspx. Accessed October 30, 2023
53 National Federation of State High School Associations (NFHS). NFHS sports medicine position statements and guidelines. Available at: https://www.nfhs.org/sports-resource-content/nfhs-sports-medicine-position-statements-and-guidelines/. Accessed October 30, 2023
54 ImPACT Applications. Concussion protocol 101: For team physicians, athletic trainers, healthcare providers, and rehab professionals. Available at: https://impacttest.com/wp-content/uploads/Concussion-Protocol-101-Guide.pdf Accessed October 30, 2023
55 Gianotti S, Hume PA. Concussion sideline management intervention for rugby union leads to reduced concussion claims. NeuroRehabilitation 2007;22(03):181–189
56 Centers for Disease Control and Prevention. Managing return to activities. Available at: https://www.cdc.gov/headsup/providers/return_to_activities.html Accessed October 30, 2023
57 Schweser F, Deistung A, Lehr BW, Reichenbach JR. Differentiation between diamagnetic and paramagnetic cerebral lesions based on magnetic susceptibility mapping. Med Phys 2010;37(10):5165–5178
58 Hageman G, Hof J, Nihom J. Susceptibility-weighted MRI and microbleeds in mild traumatic brain injury: prediction of post-traumatic complaints? Eur Neurol 2022;85(03):177–185
59 Gujar SK, Maheshwari S, Björkman-Burtscher I, Sundgren PC. Magnetic resonance spectroscopy. J Neuroophthalmol 2005;25(03):217–226
60 Ellemberg D, Henry LC, Macciocchi SN, Guskiewicz KM, Broglio SP. Advances in sport concussion assessment: from behavioral to brain imaging measures. J Neurotrauma 2009;26(12):2365–2382
61 Viano DC, Hamberger A, Bolouri H, Säljö A Concussion in professional football: animal model of brain injury—part 15. Neurosurgery 2009;64(06):1162–1173; discussion 1173
62 Weinberg BD, Kuruva M, Shim H, Mullins ME. Clinical applications of magnetic resonance spectroscopy in brain tumors: from diagnosis to treatment. Radiol Clin North Am 2021;59(03):349–362
63 Dean PJ, Sato JR, Vieira G, McNamara A, Sterr A. Multimodal imaging of mild traumatic brain injury and persistent postconcussion syndrome. Brain Behav 2015;5(01):45–61
64 Holshouser B, Pivonka-Jones J, Nichols JG, et al. Longitudinal metabolite changes after traumatic brain injury: a prospective pediatric magnetic resonance spectroscopic imaging study. J Neurotrauma 2019;36(08):1352–1360
65 Lees B, Earls NE, Meares S, et al. Diffusion tensor imaging in sport-related concussion: a systematic review using an a priori quality rating system. J Neurotrauma 2021;38(22):3032–3046
66 Gonzalez AC, Kim M, Keser Z, et al. Diffusion tensor imaging correlates of concussion related cognitive impairment. Front Neurol 2021;12:639179
67 Muller J, Middleton D, Alizadeh M, et al. Hybrid diffusion imaging reveals altered white matter tract integrity and associations with symptoms and cognitive dysfunction in chronic traumatic brain injury. Neuroimage Clin 2021;30:102681
68 Virji-Babul N, Borich MR, Makan N, et al. Diffusion tensor imaging of sports-related concussion in adolescents. Pediatr Neurol 2013;48(01):24–29
69 Wada T, Asano Y, Shinoda J. Decreased fractional anisotropy evaluated using tract-based spatial statistics and correlated with cognitive dysfunction in patients with mild traumatic brain injury in the chronic stage. AJNR Am J Neuroradiol 2012;33(11):2117–2122
70 Alexander AL, Wu YC, Venkat PC. Hybrid diffusion imaging (HYDI). Conf Proc IEEE Eng Med Biol Soc 2006;2006:2245–2248
71 Wu YC, Mustafi SM, Harezlak J, Kodiweera C, Flashman LA, McAllister TW. Hybrid diffusion imaging in mild traumatic brain injury. J Neurotrauma 2018;35(20):2377–2390
72 Vedaei F, Newberg AB, Alizadeh M, et al. Resting-state functional MRI metrics in patients with chronic mild traumatic brain injury and their association with clinical cognitive performance. Front Hum Neurosci 2021;15:768485

73 Dunst B, Benedek M, Jauk E, et al. Neural efficiency as a function of task demands. Intelligence 2014;42(100):22–30
74 Dallmeier JD, Meysami S, Merrill DA, Raji CA. Emerging advances of in vivo detection of chronic traumatic encephalopathy and traumatic brain injury. Br J Radiol 2019;92(1101):20180925
75 Lovell MR, Pardini JE, Welling J, et al. Functional brain abnormalities are related to clinical recovery and time to return-to-play in athletes. Neurosurgery 2007;61(02):352–359; discussion 359–360
76 Barrio JR, Small GW, Wong KP, et al. In vivo characterization of chronic traumatic encephalopathy using [F-18]FDDNP PET brain imaging. Proc Natl Acad Sci U S A 2015;112(16):E2039–E2047
77 Levin HS. Neuroplasticity following non-penetrating traumatic brain injury. Brain Inj 2003;17(08):665–674
78 Hillary FG, Genova HM, Medaglia JD, et al. The nature of processing speed deficits in traumatic brain injury: is less brain more? Brain Imaging Behav 2010;4(02):141–154
79 Filippi L, Schillaci O, Palumbo B. Neuroimaging with PET/CT in chronic traumatic encephalopathy: what nuclear medicine can do to move the field forward. Expert Rev Mol Diagn 2022;22(02):149–156
80 Sparks P, Lawrence T, Hinze S. Neuroimaging in the diagnosis of chronic traumatic encephalopathy: a systematic review. Clin J Sport Med 2020;30(Suppl 1):S1–S10
81 Glaudemans A, Dierckx R, Gielen J, Zwerver J. Nuclear Medicine and Radiologic Imaging in Sports Injuries. New York, NY: Springer; 2015
82 Raji CA, Henderson TA. PET and single-photon emission computed tomography in brain concussion. Neuroimaging Clin N Am 2018;28(01):67–82
83 Marklund N, Vedung F, Lubberink M, et al. Tau aggregation and increased neuroinflammation in athletes after sports-related concussions and in traumatic brain injury patients—a PET/MR study. Neuroimage Clin 2021;30:102665
84 Bischof GN, Cross DJ. Brain trauma imaging. J Nucl Med 2023;64(01):20–29
85 Byrnes KR, Wilson CM, Brabazon F, et al. FDG-PET imaging in mild traumatic brain injury: a critical review. Front Neuroenergetics 2014;5:13
86 Shively S, Scher AI, Perl DP, Diaz-Arrastia R. Dementia resulting from traumatic brain injury: what is the pathology? Arch Neurol 2012;69(10):1245–1251
87 Stein TD, Alvarez VE, McKee AC. Concussion in chronic traumatic encephalopathy. Curr Pain Headache Rep 2015;19(10):47
88 Nicks R, Clement NF, Alvarez VE, et al. Repetitive head impacts and chronic traumatic encephalopathy are associated with TDP-43 inclusions and hippocampal sclerosis. Acta Neuropathol 2023;145(04):395–408
89 Hong YT, Veenith T, Dewar D, et al. Amyloid imaging with carbon 11-labeled Pittsburgh compound B for traumatic brain injury. JAMA Neurol 2014;71(01):23–31
90 Ellis MJ, Cordingley D, Vis S, Reimer K, Leiter J, Russell K. Vestibulo-ocular dysfunction in pediatric sports-related concussion. J Neurosurg Pediatr 2015;16(03):248–255
91 Kontos AP, Deitrick JM, Collins MW, Mucha A. Review of vestibular and oculomotor screening and concussion rehabilitation. J Athl Train 2017;52(03):256–261
92 Murray NG, Ambati VNP, Contreras MM, Salvatore AP, Reed-Jones RJ. Assessment of oculomotor control and balance post-concussion: a preliminary study for a novel approach to concussion management. Brain Inj 2014;28(04):496–503
93 Wolf A, Tripanpitak K, Umeda S, Otake-Matsuura M. Eye-tracking paradigms for the assessment of mild cognitive impairment: a systematic review. Front Psychol 2023;14:1197567
94 Shin J. The role of medical imaging in the diagnosis of chronic traumatic encephalopathy in vivo. Available at: https://nhsjs.com/2023/the-role-of-medical-imaging-in-the-diagnosis-of-chronic-traumatic-encephalopathy-in-vivo/. Accessed October 30, 2023
95 Peters ME, Rahman S, Coughlin JM, Pomper MG, Sair HI. Characterizing the link between glial activation and changed functional connectivity in National Football League players using multimodal neuroimaging. J Neuropsychiatry Clin Neurosci 2020;32(02):191–195
96 Kirov II, Whitlow CT, Zamora C. Susceptibility-weighted imaging and magnetic resonance spectroscopy in concussion. Neuroimaging Clin N Am 2018;28(01):91–105

