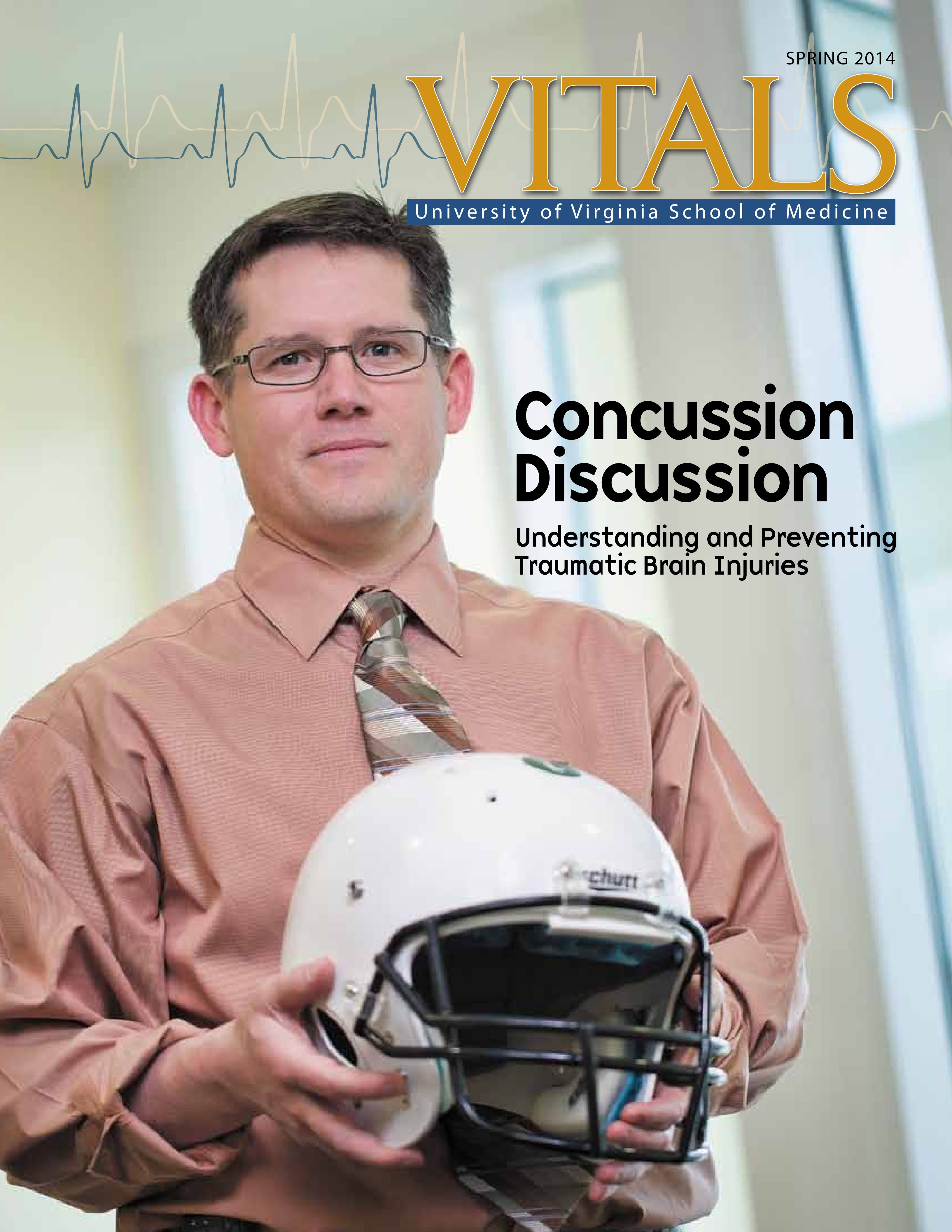
SPRING 2014

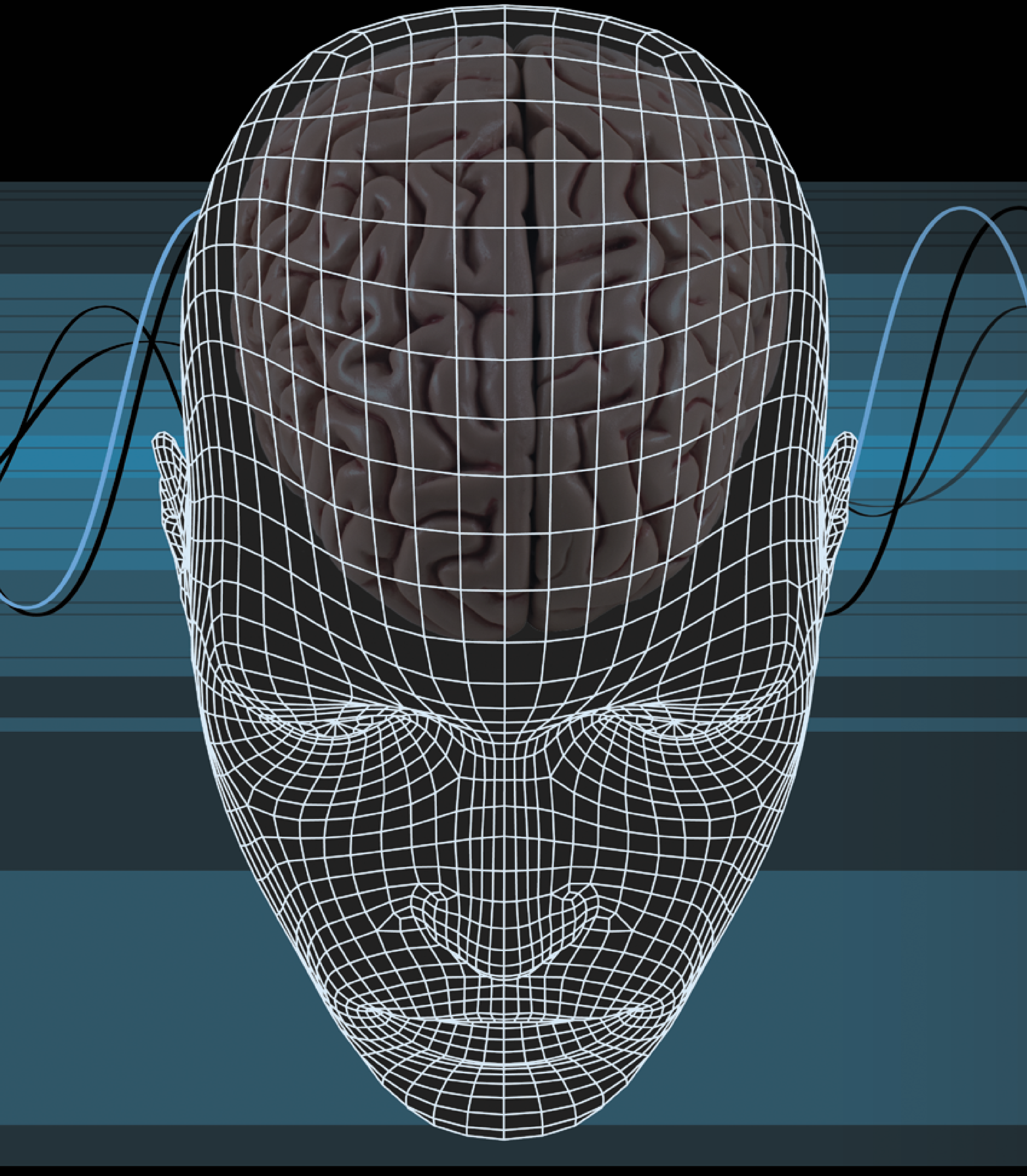
VITALS

University of Virginia School of Medicine



Concussion Discussion

Understanding and Preventing Traumatic Brain Injuries



BISC INSTITUTE CONTRIBUTES TO THE CONVERSATION

Written by Linda Kobert
Photographs by Jackson Smith

CONCUSSION DISCUSSION

Earlier this year, the National Football League reached a preliminary settlement with former players who had suffered head injuries during their careers. The amount was staggering: $765 million, and there was concern that it might not actually be enough to cover the nearly 20,000 players who would be eligible.

The settlement became part of the ongoing conversation that has taken place over the last decade or more about the risks and long-term consequences of repeated blows to the head in professional athletes, a conversation that has awakened public awareness of the topic of mild to moderate brain injury, especially sports-related injuries.

With its newly organized Brain Injury and Sports Concussion (BISC) Institute, the University of Virginia Health System is hoping to add to this dialogue, leading the way in creating new understanding about the pathophysiology, diagnosis and treatment of traumatic brain injury, understanding that will help prevent those long-term consequences.

"Analyzing these hits is complicated, but from my small sample I'm wondering if we have at least two mechanisms whereby a concussion can happen."
—Jason Druzgal, MD, PhD

Inside the Brains of Student Athletes

Among the many research initiatives within the institute is a project with student athletes led by neuroradiologist Jason Druzgal, MD, PhD. The assistant professor of radiology is trying to tease out some of the diagnostic difficulties of concussion through research that looks for correlations between physiological findings and how hard and how often an athlete sustains an impact to the head.

"We don't understand the physiology of what's happening in the brain when someone gets hit in the head, whether it's a concussion or a milder hit," says Druzgal. "So we're hoping to develop physiologic markers of what's going on in the brain of athletes while they're playing."

Druzgal leads a team of researchers funded by a clinical research grant from the UVA Medical Center and in partnership with X2 Biosystems, a medical devices company. These scientists use advanced research imaging techniques, such as functional MRI and magnetic resonance spectroscopy, to identify changes that may occur in the brains of both male and female athletes as they play football, soccer and lacrosse.

Student athletes playing for both UVA and a local high school can volunteer as re-


JAMES DAVIES/U.VA. ATHLETICS

A sensor patch is placed behind the athlete's ear to measure brain impacts.


Jason Druzgal, MD, PhD (right) with doctoral student Bryson Reynolds.

search subjects for the ongoing project. Serving as their own controls in the study, they receive scans before and after the playing season. Those who suffer a head injury during a game are scanned at that time as well. Researchers are hoping that by measuring neural activity and alterations in brain chemistry they will be able to identify changes that can be linked to the number and intensity of hits players sustain to the head.

The unique aspect of this study is that before every practice and every game during the season, student athletes apply an adhesive patch containing a computerized sensor behind their ear. This device captures and measures impacts to the head.

"It stands to reason that people who get hit harder and more often in the head will have more changes," Druzgal says. "We've implemented a way during the course of the season to measure how hard and how often they get hit."

Druzgal and his team compare preseason and postseason MRI findings with sensor data to identify any changes and how that correlates with hits to the head. They are especially interested in noting the impacts that don't result in a diagnosed concussion and whether an accumulation of subconcussive impacts produces consistent physiological changes.

While it's too early to discuss results, sensor data did provide one item of interest. "We think of concussion as this big hit phenomenon," Druzgal says. "But in the four athletes who sustained concussion during the fall season, they don't all have an identifiable big hit where we can look at the traces and say that's the hit where they got the concussion. Analyzing these hits is complicated, but from my small sample I'm wondering if we have at least two mechanisms whereby a concussion can happen."

Imaging Milder Trauma

Whatever the mechanisms by which it happens, milder trauma to the brain can be hard to identify.

"The moderate to severe brain injuries tend to manifest themselves with fairly profound symptoms, and they also have signatures that can be seen with our current clinical imaging modalities such as CT or MRI,"

Coming to Conclusions about Concussion

"Concussion occurs on a spectrum of what's called traumatic brain injury, from mild to severe," says Michael Jaffee, MD. "Mild traumatic brain injury is the technical term for concussion. It can occur from any blow or force affecting the head that results in an alteration in consciousness or awareness."

Jaffee stresses that, contrary to popular understanding, just feeling dazed or confused after receiving a blow to the head, even without loss of consciousness, is still diagnostic of concussion. In fact, according to Jaffee's own research on traumatic brain injury, approximately two-thirds of concussions occur without loss of consciousness.

"One of the important parts of concussion care is being able to recognize it," Jaffee says.

But diagnosing mild traumatic brain injury is not always easy. There are no lab tests to confirm the diagnosis, and initial indications can be vague: seeing stars, feeling dizzy, not knowing where you are for a minute, stumbling. Even those who develop symptoms later on may not connect their headache, fatigue, anxiety, forgetfulness or trouble falling asleep with the hit they sustained to the head in yesterday's game.

In trying to identify a concussion, clinicians must also rely on patients to accurately and candidly report what they're feeling, something some patients—athletes and soldiers, for example—may not be willing to do if they fear they might be taken out of the game or the field.

"There are more than 40 classification systems in the literature for diagnosing concussion," says Jason Druzgal, MD, PhD. "Most of them are based on a consensus of expert opinion, mainly because we haven't had great studies where we have a firm way to diagnose concussion. There's a lot of subjectivity to it."

Current diagnostic modalities are often not helpful in pinning down a diagnosis either. While moderate to severe brain injuries are associated with fairly profound symptoms and can be identified through CT or MRI imaging, the cellular level changes that occur with milder brain injuries cannot be detected with current clinical imaging technology.

Druzgal estimates that between 1.6 and 3.6 million concussions occur in the US each year, with the vast majority being unreported. Because mounting evidence indicates there is a dramatic and often enduring additive effect when a person sustains subsequent concussions too soon after the first, this underreporting is one of the biggest challenges in concussion care.

"The most important part of recognizing a mild traumatic head injury is to make sure individuals are not exposed to another hit until they're fully recovered from the first injury," says Jaffee. "In fact, an athlete who sustains a head injury should not go back into the same game. We don't want him or her to do anything that could result in exposure to another injury until after being evaluated and cleared."

"Our current clinical imaging paradigm allows for only the identification of macroscopic lesions. The real important advances in imaging over the next five to ten years in traumatic brain injury will be our ability to detect things that we know are occurring on the cellular and the subcellular level."

—James Stone, MD, PhD

says James Stone, MD, PhD. "The problem comes with mild to moderate brain injury."

There's a real push toward trying to develop more objective metrics for mild to moderate traumatic brain injury, so clinicians have better predictive tools to guide therapy and determine prognosis.

Stone, an assistant professor of radiology and medical imaging and a 2004 graduate of the UVA School of Medicine, leads another BISC project that probes deeper into the brain to examine the inflammation that occurs after a traumatic brain injury. His project, which uses positron emissions tomography (PET) imaging, has been characterized as a Trojan horse.

"When we talk about brain imaging, one of the major challenges is getting small molecules into the brain so they can then identify a process of interest," Stone says. "The brain is a very tightly regulated organ. So many molecular imaging approaches have failed because of the inability to get these molecules into the brain past the blood/brain and blood/CSF barriers."

Stone, however, has developed a process for tagging neutrophils with a radioactive isotope of copper. Like the Trojan horse of myth, this small white blood cell, which is mobilized as part of the body's normal response to injury, is able to carry the isotope across the barrier, enter the brain and travel to the site of injury where its activity can be detected with a PET scan.

This preclinical proof-of-concept project, funded by a sizable grant from the U.S. Army, just concluded a four-year effort looking at a variety of different markers in animal models specifically related to contusion-type brain injury. This marker of inflammation turned out to be by far the most promising of the three markers tested.

Stone and his colleagues were able to demonstrate that copper-labeled neutrophils were able to cross the blood/brain barrier and were able to identify sites of injury in the

James Stone, MD, PhD

expected acute period of 24-48 hours after injury. The results were very localizable and very predictable, proving that this concept is a potentially useful strategy that deserves further study.

"Our current clinical imaging paradigm allows for only the identification of macroscopic lesions," Stone says. "The real important advances in imaging over the next five to ten years in traumatic brain injury will be our ability to detect things that we know are occurring on the cellular and the subcellular level, to see the kinds of things that have a direct correlation with patient symptomatology and pathophysiology so we have a better sense for who will recover or who will need more intensive rehabilitation."

After the Injury

Helping patients recover is the mission of the Brain Injury and Sports Concussion Clinic. Newly organized under the direction of neurologist, psychiatrist and sleep medicine specialist Michael Jaffee, MD, this patient-focused arm of the BISC Institute brings together brain injury specialists from all over the UVA Health System in an integrated approach to patient care.

The clinic, which started seeing patients in January, allows practitioners from a number of different specialties—including adult neurology, child and adolescent neurology, physical medicine and rehabilitation, neuropsychology, occupational therapy, physical therapy, psychiatry and sleep medicine—to sit down with one another and make decisions about individual patient cases. The program also serves as a resource for the department of sports medicine, and it coordinates with a number of other departments, including trauma surgery and neurosurgery.

This is a unique model at UVA, one with a number of advantages.

"It's not just the specialty departments," says Jaffee, who also serves as an associate professor of neurology and who received his medical degree from the UVA School of Medicine in 1992. "This is a true multidisciplinary clinic where all the resources are together under one roof. This allows us to make sure we're all on the same page in developing a coordinated management plan."

Michael Jaffee, MD

The clinic covers the entire spectrum of patients, from pediatrics to geriatrics, and provides continuity of care as patients move from an inpatient situation to outpatient care. The clinic also evaluates and manages care for traumatic brain injuries from all causes and the full range of severity, not just sports injuries.

"I come from a multidisciplinary background, so I'm very comfortable with this model," says Jaffee. As a colonel in the U.S. Air Force, Jaffee served as the national director of the Defense and Veterans Brain Injury Center, a role that included oversight of brain injury programs for the US military and the Veterans Administration, the two largest health care institutions in the world.

"Virginia has a rich, long and distinguished history in dealing with concussions and traumatic brain injury," Jaffee says. "The BISC Institute is really bringing all those resources together in an integrated way. I very much appreciate the power of multidisciplinary collaboration, so I'm very excited to bring that to UVA."

TBIs by the Numbers

- Every year, at least 1.7 million traumatic brain injuries (TBIs) occur either as an isolated injury or along with other injuries.
- TBI is a contributing factor to a third (30.5%) of all injury-related deaths in the United States.
- About 75% of TBIs that occur each year are concussions or other forms of mild TBI.
- Falls are the leading cause of TBI (35.2%) in the United States. Falls cause half (50%) of the TBIs among children aged 0 to 14 years and 61%of all TBIs among adults aged 65 years and older.
- In every age group, TBI rates are higher for males than for females.
- During 2001-2009, an estimated 2,651,581 children under age 19 were treated annually for sports and recreation-related injuries. Approximately 6.5% or 173,285 of these injuries, were TBIs.
- Overall, the activities associated with the greatest estimated number of TBI-related emergency department visits were bicycling, football, playground activities, basketball, and soccer.
- TBI can cause a wide range of functional short- or long-term changes affecting thinking, sensation, language, or emotions. TBI can also cause epilepsy and increase the risk for conditions such as Alzheimer's disease, Parkinson's disease, and other brain disorders that become more prevalent with age.
- Repeated mild TBIs occurring over an extended period of time (i.e., months, years) can result in cumulative neurological and cognitive deficits. Repeated mild TBIs occurring within a short period of time (i.e., hours, days, or weeks) can be catastrophic or fatal

Source: Centers for Disease Control and Prevention