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ACOFP / AOA's 122nd Annual Osteopathic Medical Conference & Exposition

# Joint Session with ACOFP, AOASM and AAO:

# Post Concussion Research and Therapy Options

P. Gunnar Brolinson, DO, FAOASM

acofp American College of Osteopathic Family Physicians

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# Post Concussion Research Update and Treatment Options

Edward Via College of Osteopathic Medicine
VIRGINIA • CAROLINAS
AUBURN

**October 7-10. 2017**
**OMED 2017**
**Philadelphia, PA**

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NCAA-DoD Care Consortium

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Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences

ICTAS

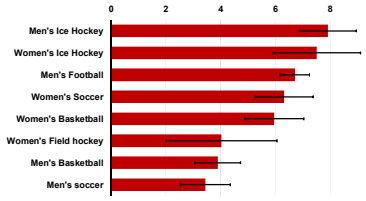
## Concussive Brain Injuries

- Nearly 90% of estimated 2.5 million TBIs in the US each year are mild
- Gross underestimates since most do not go to ED for care
- Up to 3.8 million sports-related TBIs each year
- Research suggests potential links between repetitive concussions and long-term neurodegenerative processes

www.nytimes.com

www.wired.com

## Concussive Rates by Sport




** Rates are reported per 10,000 athlete-exposures*

## Concussion Biomechanics

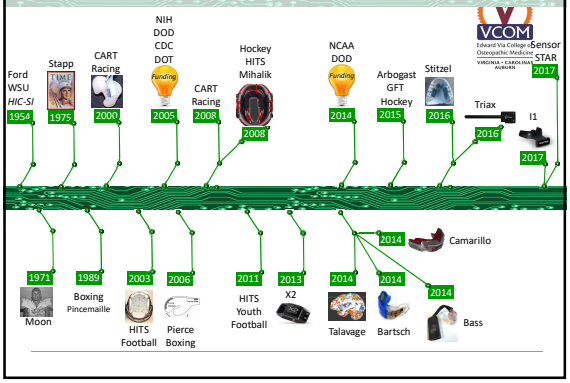
- Heading a soccer ball results in head accelerations
  - From 16 to 20g lasting 25 ms
- The average collegiate football impact
  - From 21 and 32g lasting 14-15 ms
- Impacts to the top of the head yielded the greatest linear acceleration and impact force magnitude
  - Improper tackling techniques
- Offensive and Defensive line players sustained the lowest-magnitude impacts but the highest number of impacts during games and practices

Rowson, S et al. Presented at Rocky Mountain Bioengineering Symposium & International ISA Biomedical Sciences Instrumentation Symposium 17-19 April 2009, Milwaukee, Wisconsin, www.isa.org
Halsted, M and K Walter. Pediatrics, 2010; 126 (3): 597-615
Broglio, SP, et al. Journal of Athletic Training 2009;44(4):342–349

## Sensor Systems….

- Can they be clinically useful?
- Research tool only?
- How validated?
  - Industry standards?

## Field Deployed Head Impact Sensor History




## Peak head acceleration of athletes during competition—football

MEDICINE AND SCIENCE IN SPORTS
Vol. 3, no. 1, pp. 44-50, Spring, 1971

DONALD W. MOON,* CHARLES W. BEEDLE* AND CHARLES R. KOVACIC†
*Department of Mechanical Engineering and †Department of Physical Education
University of California — Davis
Davis, California 95616

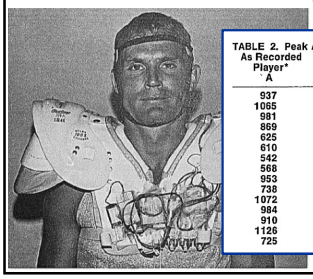
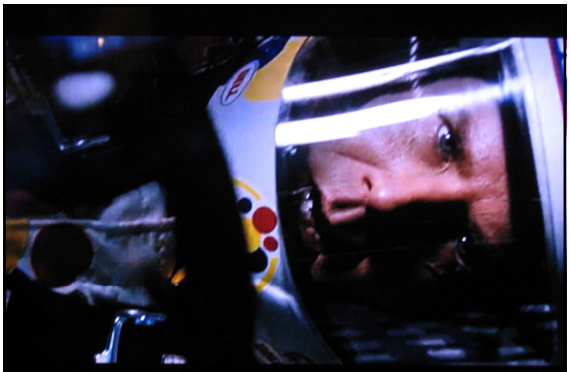


TABLE 2. Peak Acceleration data of football players' heads [G].

| As Recorded Player* | | With 750 Hz Filter Player* | |
|---|---|---|---|
| A | A | B | C |
| 937 | 867 | 108 | 1200 |
| 1065 | 960 | 108 | 985 |
| 981 | 882 | 493 | 1140 |
| 869 | 875 | 54 | 748 |
| 625 | 536 | 139 | 1053 |
| 610 | 684 | 47 | 1175 |
| 542 | 553 | 130 | 984 |
| 568 | 501 | 209 | 550 |
| 953 | 834 | 161 | 1150 |
| 738 | 643 | 350 | 1120 |
| 1072 | 1016 | 778 | 1118 |
| 984 | 997 | 596 | 1105 |
| 910 | 808 | 940 | 1135 |
| 1126 | 870 | 506 | 1130 |
| 725 | 617 | 275 | 1150 |

## 2000: CART Racing Instrumentation, Air Force Research Lab

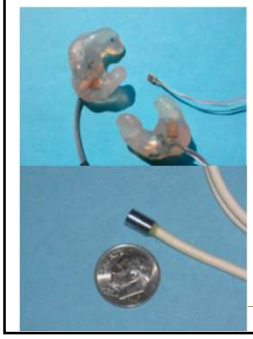
Hill, Knox, Crockett, Handman, Poff, Olvey, Cohn, Pellettiere, Bonfeld, Plaga

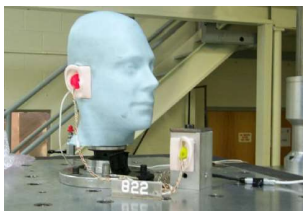


"Yep, I'm flying through the air, this is not good" Ricky Bobby

## 2008: CART Racing New Sensors

Smaller sensor located further in ear canal
Knox, Pellettiere, Panzer, Bass





## "Sensorgate"…Lights out on concussion????

## Concussion Biomechanics

- Over 225,000 head impacts recorded at Virginia Tech
  - Games (30%)
  - Practice (70%)
  - 13 years of data collection: 2003-2016
- Clinically diagnosed concussive impacts recorded for instrumented players
- Unbiased exposure data
  - Previous football work over-sampled injury data

IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, VOL. 61, NO. 11, NOVEMBER 2014 2659

### A Head Impact Detection System Using SVM Classification and Proximity Sensing in an Instrumented Mouthguard

Lyndia C. Wu, Livia Zarnescu, Vaibhav Nangia, Bruce Cam, and David B. Camarillo*, *Member, IEEE*

***Abstract*—Injury from blunt head impacts causes acute neurological deficits and may lead to chronic neurodegeneration. A head impact detection device can serve both as a research tool for studying head injury mechanisms and a clinical tool for real-time trauma screening. The simplest approach is an acceleration** pact monitoring. Previous research found statistically significant correlation between the number of head impacts and the resulting neurophysiological deficit [11]. In football players, a greater number of head impacts with high impact kinematics were more

*Stanford CAMLab MiG*

**Stanford Tab MG**
Hernandez et al., 2014

**Stanford MiG1.0**
Hernandez et al., 2014
Wu et al., 2014
Wu et al., 2015
Kuo et al., 2016

**Stanford MiG2.0**

*Cleveland Clinic – Prevent Biometrics*

*Stapp Car Crash Journal, Vol. 58 (November 2014), pp. 1-27*

2014-01

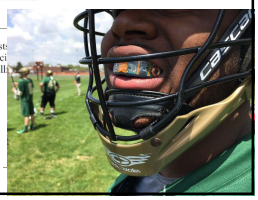
**Validation of an "Intelligent Mouthguard" Single Event Head Impact Dosimeter**

Adam Bartsch, Sergey Samorezov, Edward Benzel
Cleveland Clinic

Vincent Miele
University of Pittsburgh, Cleveland Clinic

Daniel Brett
Sportsguard Laboratories Inc.

**ABSTRACT** – Dating to Colonel John Paul Stapp MD in 1975, scientists accuracy and precision. But no instrument exists to accurately and preci develop a practical single event head impact dosimeter known as "Intell benchtop, in vitro and in vivo.



Player-specific ear molds used to create custom-fit ear piece sensors: DASHR (Duke-Bass) MVTrak

**Lacrosse Summary Data**

Linear Acceleration
18 ± 13 g

## Wake Forest Retainer System

## 20 g, 14 rad/s


**Soccer Summary Data**

Linear Acceleration
23 ± 11 g

Rotational Velocity
11 ± 5 rad/s

## Concussions in Ice Hockey

- Among the highest rates of concussion in sports
- Most result from player-player contact (45%), followed by player-boards/glass (28.8%), and player-ice contact (20%) (*Marar et al 2012*)
- Higher rates of concussion associated with body checking

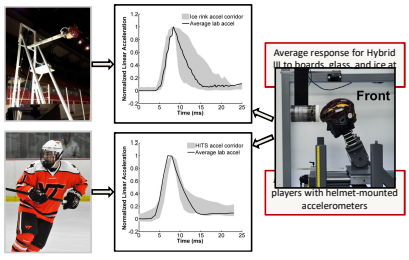
## Laboratory Testing Methods

Pendulum Impactor:

- Improved repeatability
- Variable impact energy (pendulum arm angle)
- Rigid impactor face

NOCSAE headform mounted on Hybrid III neck

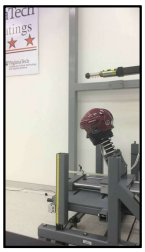
## Impact Response Corridors




Average response for Hybrid III to boards, glass, and ice at

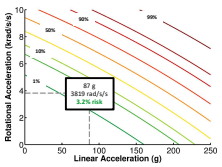
players with helmet-mounted accelerometers

## Front Impact: Medium Energy Level



Linear = 87 g Rotational = 3819 rad/s/s

$$Risk = \frac{1}{1 + e^{-(-10.2 + 0.043ra + 0.000873rx - 0.00000092\ rx)}}$$

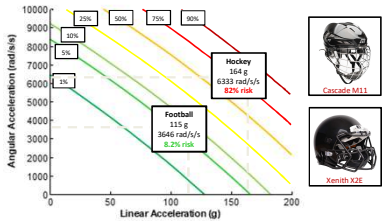



*Risk* × *Exposure* = *Incidence*

0.032 × 4.6 = 0.148

## Injury Risk Comparison

Front Impact, High Severity



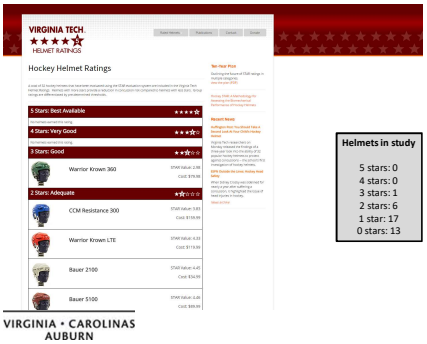



Cascade M11



Xenith X2E

## Hockey Helmet Ratings

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AUBURN

**Helmets in study**

5 stars: 0
4 stars: 0
3 stars: 1
2 stars: 6
1 star: 17
0 stars: 13

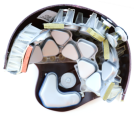
## Hockey Helmets

BAUER 5100

CCM RESISTANCE 100

## Football Helmets

RIDDELL SPEEDFLEX

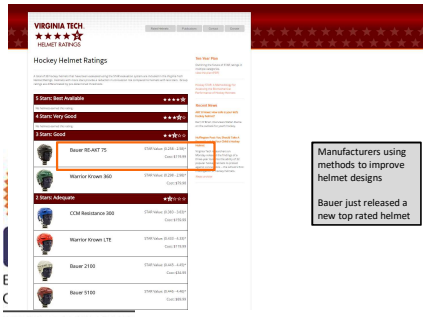


SCHUTT AIR XP PRO VTD

## Padding Thickness

(Bauer 5100 helmet and Bauer Nexus padding)

- Head: 0.7 in (18 mm)
- Shoulders: 1.0 in (25 mm)
- Elbows: 1.5 in (38 mm)
- Hands: 1.5 in (38 mm)
- Hips: 1.5 in (38 mm)
- Knees: 2.2 in (56 mm)
- Shins: 1.6 in (41 mm)




Manufacturers using methods to improve helmet designs

Bauer just released a new top rated helmet

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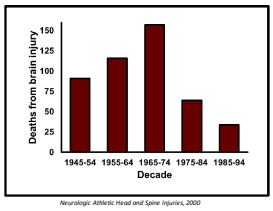
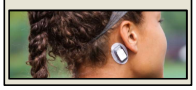
## Effects of Helmet Safety Standards



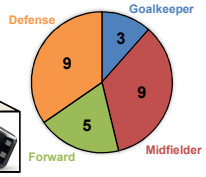

*Neurologic Athletic Head and Spine Injuries, 2000*

**Helmet standards reduced rate of fatal head injuries 74%**

## Quantifying Head Impact Exposure

| Exposure | Sensor Performance |
|---|---|
| All results from video analysis **only** | **Comparison** between video analysis and data collected by sensors |
|  |  |

## Virginia Tech Women's Soccer Team




**Concussion History**

| # Previous Concussions | 0 | ≥ 1 | ≥ 2 |
|---|---|---|---|
| # Players (26 total) | 15 | 11 | 4 |

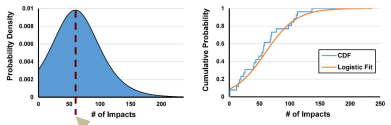
## Data Processing

- Downloaded and processed following each game and practice
- Two games excluded due to poor video quality

Video Identification → Corresponding Impact in Data → T/F Positive and Negative Classification → Impact Mechanism Identified

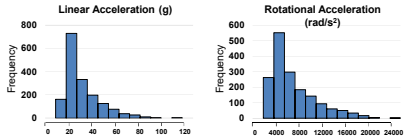
## Distribution Functions

**Head impacts per season across all players**




Median = 56.5 impacts per player

## Acceleration Distributions



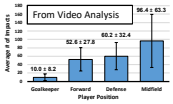

| Linear Accel. (g) | | | Rotational Accel. (rad/s²) | | |
|---|---|---|---|---|---|
| Min | Max | Avg ± SD | Min | Max | Avg ± SD |
| 6 | 113 | 25 ± 16 | 380 | 26222 | 5626 ± 4223 |

## 88g, 12,039 rad/s²

## X2 xPatch Study – Women's Soccer

- VT Women's Soccer
  - 26 players
  - 26 practices
  - 20 games
- Instrumented with xPatch
- Video footage of each practice/game used to verify every head impact events

**X2 xPatch did not accurately:**
**count head impacts**
**or**
**measure head acceleration**




## X2 xPatch Study – Women's Soccer

**Head Impact Count Comparison**
**X2 xPatch:** 8,999 events classified as head impacts
**Video:** 1,703 head impact events identified

- X2 Data
  - 1,463 True Positives
  - 7,536 False Positives
  - 8,626 True Negatives
  - 240 False Negatives
- In identifying head impacts:
  - Sensitivity: 86%
  - Specificity: 53%

**Head Acceleration Measurements**

Avg Linear Accel: 26 g
Avg Rotational Accel: 5626 rad/s²

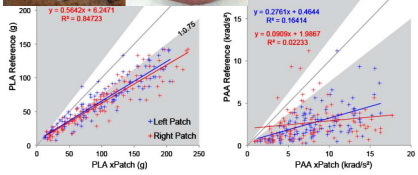
Peak linear and rotational accel. values are suspiciously high

Suspected measurement error due to motion of skin behind ear

## X2 Coupling Limitation

Over-prediction of Rotational Acceleration

Siegmund - Bass
IRCOBI 2015

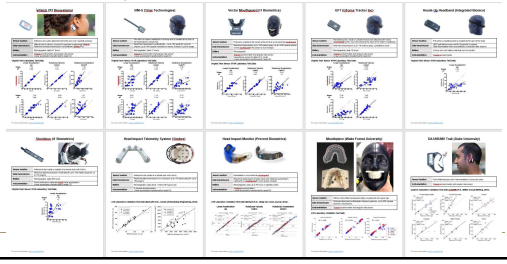



## Sensor STAR (Fall 2017)

Dummy Testing

Volunteer Testing

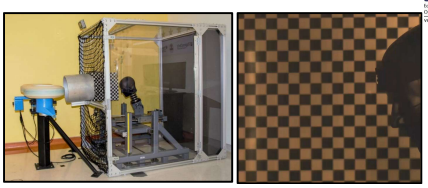
Preliminary results:



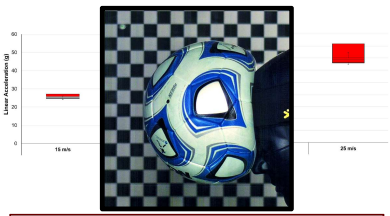
## Biomechanical Performance of Headgear Used in Soccer

| Ball-to-Head | Head-to-Head |
|---|---|
|  |  |

## Ball-to-Head Impacts

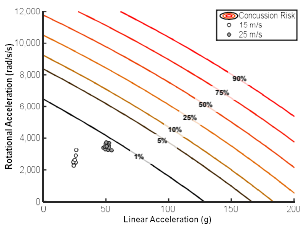



## Little Effect with Protective Headgear




**Ball modulates impact energy**

## Concussion Risk Below 1%



## Head-to-Head Impacts

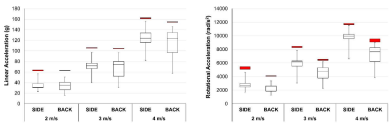
## Head-to-Head Impacts

Side Location Back Location

## Head-to-Head Impacts

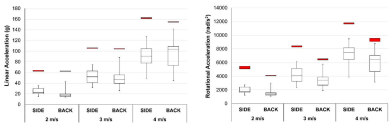
Bare Head to Bare Head Bare Head to Headgear Headgear to Headgear

## Bare Head to Headgear



**35% average reduction in linear head accelerations**

## Headgear to Headgear



**53% average reduction in linear head accelerations**

## Differences in Headgear Performance

2 m/s
3 m/s
4 m/s

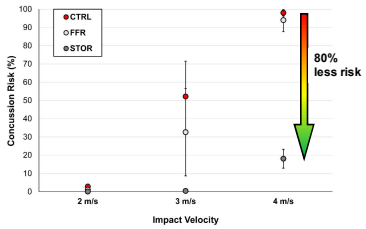


2 m/s
3 m/s
4 m/s

**1 exposure to each impact (6 total)**

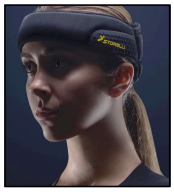
| Headgear | Overall Metric |
|---|---|
| CTRL | 3.06 |
| STOR | 0.37 |
| UN10 | 0.64 |
| UN6 | 1.12 |
| DJ | 1.63 |
| F90P | 1.81 |
| FFU | 1.92 |
| FN1 | 1.93 |
| F90S | 2.03 |
| HB | 2.29 |
| FFR | 2.55 |

## Differences in Headgear Performance




## Impact Protection Summary

- *Not effective* for ball-to-head impacts
- *Meaningful reductions* for head-to-head impacts
  - Not all headgear performed equally
- Use of protective headgear could reduce concussion incidence significantly



## The Concussion "crisis" and Chronic Traumatic Encephalopathy

- "Unlike other neurology specialties, sports concussion is driven not by science but opinion in the form of the numerous consensus conferences".
- "Accepting the assertion that football causes CTE requires the well-read and knowledgeable clinician to make a sizable leap of faith".

*JAMA Neurol*. 2014;71(5):654.
doi:10.1001/jamaneurol.2013.6408

## The Concussion "crisis" and Chronic Traumatic Encephalopathy

- In a convenience sample of 202 deceased players of American football from a brain donation program, CTE was neuropathologically diagnosed in 177 players across all levels of play (87%), including 110 of 111 former National Football League players (99%).
- In a convenience sample of deceased players of American football, a high proportion showed pathological evidence of CTE, suggesting that CTE may be related to prior participation in football.

*JAMA.* 2017;318(4):360-370.
doi:10.1001/jama.2017.8334

## The Concussion "crisis" and Chronic Traumatic Encephalopathy

- What are the potential issues with this study?
  - ascertainment bias associated with participation in this brain donation program
    - public awareness of a possible link between repetitive head trauma and CTE may have motivated players and their families with symptoms and signs of brain injury to participate in this research
  - the VA-BU-CLF brain bank is not representative of the overall population of former players of American football
  - this study lacked a comparison group that is representative of all individuals exposed to American football at the college or professional level

## Incidence of neurodegenerative disease

- 9% of Americans over 65 have dementia
  - About 5 million people
  - Expected to triple by 2050
- NFL players are 3X more likely to develop neurodegenerative disease

# HS Football and Risk of Neurodegenerative Disease

- ***To assess whether high school football played between 1946 and 1956, when headgear was less protective than today, was associated with development of neurodegenerative diseases later in life.***
- Compared 438 FB players to 140 non FB players from HS in Rochester, MN
- High school students who played American football from 1946 to 1956 did not have an increased risk of later developing dementia, PD, or ALS compared with non–football-playing high school males, despite poorer equipment and less regard for concussions compared with today and no rules prohibiting head-first tackling (spearing).
- These results should be somewhat reassuring to high school players from 50 years ago, they should give no reassurance to today's players.

High School Football and Risk of Neurodegeneration: A Community-Based Study; Savica, Parisi et al; Mayo Clin Proc. 2012;87(4):335-340

**WE HAD NO IDEA THAT THIS COULD CAUSE WHAT IT'S CAUSING. CTE? THAT'S SCARY STUFF. THAT, WE DIDN'T EVEN KNOW ABOUT UNTIL THREE YEARS AGO OR SO. ALZHEIMER'S? WE NEVER HEARD THE WORD ALZHEIMER'S IN THE '60S OR '70S.**

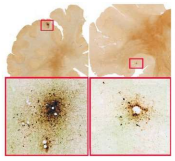
MANNY FERNANDEZ, DEFENSIVE TACKLE ON 1972 MIAMI DOLPHINS

FERNANDEZ DOESN'T REMEMBER THE END OF SUPER BOWL VII, WHICH CAPPED THE DOLPHINS' 17-0 SEASON, BECAUSE OF BLOW HE TOOK TO THE HEAD.

FERNANDEZ ESTIMATES HE SUSTAINED "DOZENS" OF CONCUSSIONS DURING HIS PLAYING CAREER. AND YET, HIS MIND IS STRONG.

# What is Chronic Traumatic Encephalopathy???

- Dementia Pugilistica…
  - "Punch Drunk Syndrome"
  - Dr. Harrison Martland 1928
  - CTE with Post Traumatic Encephalopathy
- Accumulation of Tau Protein in neurologic tissue
  - Genetically determined?
  - Head trauma triggered?
  - "Over-production" vs "Inadequate Clearance"?
  - A progressive neurodegenerative syndrome
- A composite *syndrome of mood disorders*
  - associated neuropsychiatric and cognitive impairments
- Is NOT Alzheimer's Disease
  - Not associated with cerebral atrophy
- Relationship to Lou Gehrig's Disease?
- Definitive Diagnosis by direct tissue analysis post mortum



Brain tissue from 18-year-old multi-sport athlete

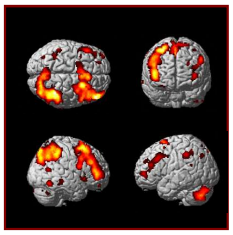
*BU Center for the Study of Traumatic Encephalopathy*

## What is Post Traumatic Encephalopathy?

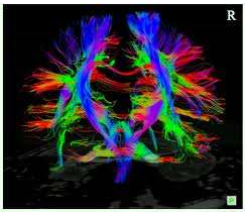
- A clinicopathologic syndrome that follows focal or diffuse brain trauma
  - Associated with gross or microspcopic destruction of brain tissue
  - Lacerations, contusions, hemorrhages, etc
- Not neurodegenerative and not progressive
- Can co-exist with CTE

## Does "Advanced Imaging" help? Maybe….

- Functional MRI
  - Measures neuronal glucose uptake while the patient performs a "task" in the magnet
  - Can see changes in brain activation patterns for "acutely injured" patients vs controls



## Does "Advanced Imaging" help? Maybe….




- Diffusion Tensor Imaging
  - can identify structural changes in the white matter of the brain that correlates to cognitive deficits even in patients with mild traumatic brain injury.
  - When white matter is damaged, other areas of the brain may appear healthy but they are actually "unplugged" and cannot function optimally.

Kraus, Little, Susmaras et al; Brain: Oct 2012

## Future Diagnostic Considerations

- Biomarkers
  - term often used to refer to a protein measured in blood whose concentration reflects the severity or presence of some disease state.
  - Troponin is a biomarker used to diagnose acute myocardial infarction (AMI) in Emergency Rooms

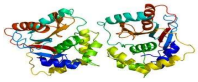
## Banyan Biomarker Panel for TBI

**GFAP**


**Glial Fibrillary Acidic Protein**

- Structural protein of the intermediate filament of Astroglia 50 kDa
- Highly enriched in the nervous system.
- 1% of total brain protein

**UCH-L1**



**Ubiquitin Carboxyl-Terminal Esterase L1**

- Small compact 24 kDa protein
- Expressed at a high level in neurons
- 5% of total brain protein

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## TBI study

**Levels of Serum GFAP Are Associated With Severity Of Injury In Patients With Mild And Moderate Traumatic Brain Injury**


**Acad Emerg Med. May 2008**

**SUMMARY:**

GFAP was systematically assessed in human serum following mild and moderate TBI.

GFAP levels were significantly elevated in this population using ELISA analysis, including those with mild TBI.

GFAP was able to discriminate TBI patients from uninjured controls and serum levels were able to distinguish orthopedic and motor vehicle controls form TBI patients

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## Mild and moderate TBI study (GFAP)

**Elevated Levels of Serum Glial Fibrillary Acidic Protein Breakdown Products in Mild and Moderate Traumatic Brain Injury Are Associated With Intracranial Lesions and Neurosurgical Intervention**


**Annals of Emergency Medicine**
**May 29, 2011**

**SUMMARY:**

GFAP-BDP is detectable in serum within an hour of injury
It is associated with measures of injury severity, including the GCS score, CT lesions, and neurosurgical intervention.
Further study is required to validate these findings before clinical application.

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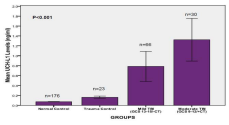
## Mild and moderate TBI Study (UCHL-1)

**Serum levels of UCHL-1 distinguishes mild and moderate traumatic brain injury from trauma controls and is associated with lesions on computed tomography.**


**Journal of Neurotrauma**
**July, 2011**

**SUMMARY:**

UCHL-1 was detected in the serum of mild and moderate TBI (MMTBI) patients within an hour of injury

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## What about repetitive "sub concussive" impacts?

- ***Millions of individuals have played contact sports for many years without obvious functionally significant adverse effects, and without developing progressive neurodegenerative disorders.***
- Nevertheless, we are concerned that repetitive head impacts may have an adverse effect on some athletes.
  - It is reasonable to speculate that individual differences such as polymorphisms in genes modulating response to neurotrauma (e.g., *APOE*, *BDNF*, *ANKK1*) or other host factors may play a role
  - it is tempting to hypothesize that risk of chronic traumatic encephalopathy or other long term effects of contact sports may represent a gene–environment interaction between repetitive mild neurotrauma and genetic vulnerability to heightened injury response or attenuated neural repair.

McAllister TW, Flashman LA, Maerlender AC, Greenwald RM, Beckwith JG, Tosteson TD, Crisco JJ, **Brolinson PG**, Duma SM, Duhaime AC, Grove MR and Turco JH. *"Cognitive Effects of One Season of Head Impacts in a Cohort of Collegiate Contact Sport".* Neuro. 2012 May 29;78(22):1777-84.

# Post Concussion Syndrome

- This Dx is a function of the length of symptom persistence
  - 3 months duration of at least 3 symptoms
- Retired NFL players who were diagnosed with post-concussion related depression
  - 87% continued to have lifelong symptoms
- Medications that address symptoms may be considered in the treatment of PCS
  - Dosing should begin low and titrated upward slowly

TABLE. Symptoms of postconcussion syndrome.

| Cognitive | Physical | Behavioral |
|---|---|---|
| Slowed response speed | Headache | Depression |
| Mental fogginess | Nausea | Anxiety |
| Poor concentration | Vision changes | Panic attacks |
| Distractibility | Light sensitivity | Irritability |
| Trouble learning | Tinnitus | Personality changes |
| Memory difficulty | Noise sensitivity | Increased emotionality |
| Disorganization | Dizziness | Clinginess |
| Problem-solving difficulty | Vertigo | Apathy |
| | Balance problems | Lowered frustration tolerance |
| | Fatigue | Increased sensitivity to alcohol |
| | Sleep disturbance | |

Jotwani, V et al. Curr. Sports Med. Rep.; 2010; 9 (1): 21-26
Halsted, M and K Walter. Pediatrics, 2010; 126 (3): 597-615

# Summary of Gunnar's clinical treatment Pearls for PCS

- Remember that dx and tx is a "team event"
  - Psychologists, neurologists, PM&R, PT's and ATC's can all be involved
- You are treating "symptoms"
- For mild insomnia with head/neck pain
  - Flexeril 10mg at hs
  - Elavil 10-25mg at hs
- For headache
  - NSAIDs
  - Topamax 25-50mg BID
  - OMT
- For depression with diffuse "body pain"
  - Effexor and Cymbalta (SNRI's)
  - Tricyclics
  - SSRI's don't seem to work well
- For "fogginess"
  - Omega 3 supplements
  - Antioxidants
    - Alpha Lipoic Acid 100mg QD
    - B Complex
    - Co Q 10 100-200mg QD
  - Amantadine
    - 100-200mg BID
- Remember to include physical therapy and neurocognitive rehab as appropriate
- In general avoid narcotics

Placebo-Controlled Trial of Amantadine for Severe Traumatic Brain Injury; Gianco et al; N Engl J Med 2012; 366:819-826March 1, 2012DOI: 10.1056/NEJMoa1102609