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Executive Summary

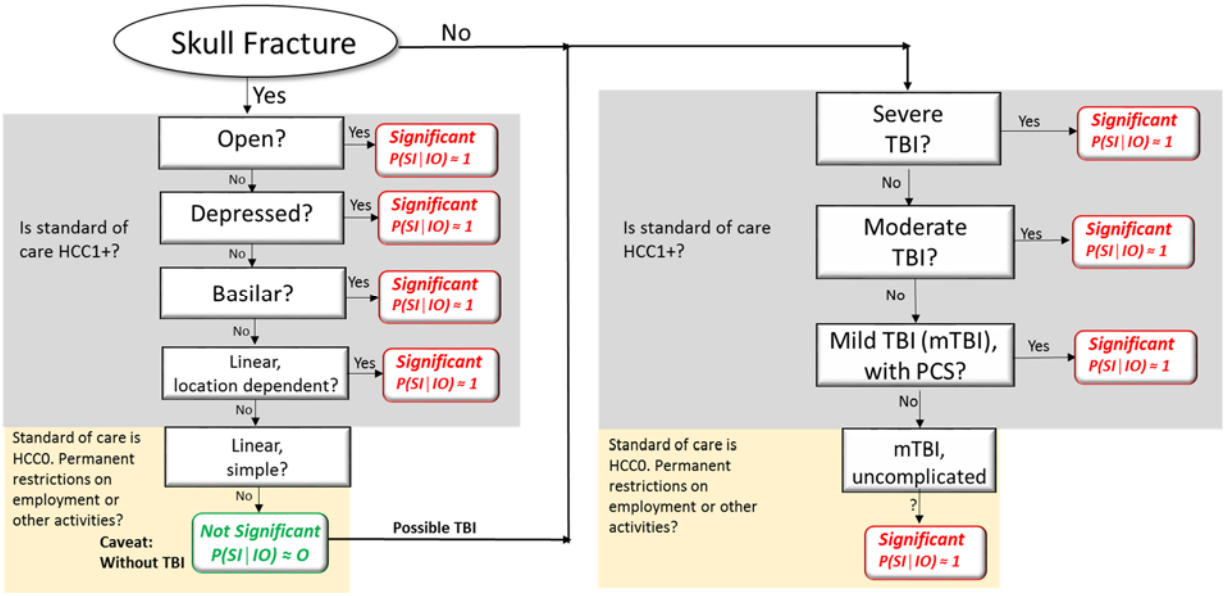
Department of Defense Directive 3000.3E defines non-lethal weapons (NLWs) as

> weapons, devices, and munitions that are explicitly designed and primarily employed to incapacitate targeted personnel or material immediately, while minimizing fatalities, permanent injuries to personnel, and undesired damage to property in the target area or environment … NLWs are intended to have reversible effects on personnel and material. (DoD 2013, 12)

This document considers effects from non-lethal blunt-impact munitions, such as rubber bullets and beanbags. Often employed in crowd control, these munitions act as a deterrent by inducing pain or muscle spasm at the site of impact of the targeted individual. These weapons may induce head injuries, including skull fractures and traumatic brain injury (TBI).

During the Department of Defense (DoD) technology-development and acquisition process, developers compare the capabilities of novel NLW systems to requirements, including the key performance parameters (KPPs) and key system attributes (KSAs) addressed in capability documents (DoD 2015, B-24). Counter-personnel NLW requirements often include a KPP or KSA pertaining to risk of significant injury (RSI). The RSI metric estimates the reversibility of a system's effect on targeted personnel (DoD 2012, 14). During the development acquisition process, developers must quantify the NLW's total RSI (DoD 2012), demonstrating an RSI less than or equal to a numerical threshold value. DoD Instruction (DoDI) 3200.19 defines a significant injury as death, permanent injury, or injury that requires medical treatment with a Health Care Capability (HCC) index of 1 (HCC1) or higher (HCC1+) (DoD 2012, 14). An HCC index of 0 (HCC0) medical treatment requires "limited first-responder capability including self-aid, buddy-aid, and combat lifesaver skills" (DoD 2012, 13).

This objective of this study was to examine the relevant academic and medical literature to identify attributes of skull fractures and TBI that can quantitatively, accurately, and precisely approximate the significance of the skull fracture type or TBI type according to the definitions established in DoDI 3200.19 (DoD 2012) and consider how these predictive attributes can be estimated during the development acquisition phase for a novel, blunt-impact NLW. The results of our analysis are shown in the figure below.



Decision Flow Diagram: Classifying Head Injuries (skull fractures and TBI) as Significant Based on Skull Fracture Type or TBI Type

Findings

- Available blunt-impact head trauma data is from motor vehicle accidents, falls, sports injuries, bicycle accidents, pedestrian accidents and assaults (Stiell et al. 2001), which have different injury mechanisms than blunt-impact NLWs. Our analysis utilizes all data regardless of injury mechanism.
- The medical literature does not study skull fracture in isolation, and the majority of skull fracture data are from traumatic brain injury studies.
- Linear fractures are the most prevalent skull fracture, occurring in 70%–80% of all reported cases (Oehmichen, Auer, and Konig 2006, 475). Of those linear fractures, we can determine types that are significant, but the incidence of these types is unclear.
- Currently, no objective metrics exist to gauge and compare recovery from TBI.
- Treatments and outcomes of mild TBI (mTBI) are heterogeneous among patients, because it is generally unknown how the applied forces to the head cause specific brain injuries and how individual patient factors contribute to recovery.
- The Glasgow Coma Scale, the Glasgow Outcome Scale, and the Glasgow Outcome Scale-Extended are flawed subjective metrics currently used to assess mTBI injury and predict outcome in the civilian world.
- The flawed nature of these tests makes the return-to-duty and duty-readiness decision after mTBI still a major concern for DoD (Radomski et al. 2018).

- Mild TBI damage to the brain is now thought to be on the cellular and molecular level and cannot be detected using current imaging diagnostics (Huang, Risling, and Baker 2016).
- Fluid-based biomarkers are now starting to be validated in the clinic for their diagnostic value for mTBI. Several candidate biomarkers have gone through some clinical assessment and been shown to have diagnostic value. Although this development is encouraging, there is a need to develop larger panels of biomarkers that are capable of both diagnosing and stratifying mTBI.
- Since mTBI is so heterogeneous and ill-defined clinically, IDA cannot define attributes to distinguish between a not significant, uncomplicated mTBI and a significant mTBI with long-term cognitive impairment or post-concussive symptoms.
- The Advanced Total Body Model (ATBM) includes a finite-element model (FEM) of a head and an injury model for skull fracture, including location of fracture and distinction between linear and depressed skull fracture. Error on the predictions has not yet been adequately quantified, but relative results can be used in design stages of weapons.
- While the ATBM includes several brain injury models, we conclude that at this time, the ATBM cannot be used to predict brain injuries.

Recommendations

Based on our findings, we make the following recommendations for NLW developers:

- Classify the following skull fracture and TBI types as significant because the medical treatment for the injuries or the complications have HCC1+ standards of care:
  - Skull fracture types:
    - Open skull fracture
    - Depressed skull fracture
    - Basilar skull fracture
    - Linear, location dependent (includes linear fractures at or near meningeal groove or major venous sinuses)
  - TBI types:
    - Severe TBI
    - Moderate TBI

    - Mild TBI (mTBI) with post-concussion syndrome (PCS)

- Classify the following skull fracture type as not significant because the literature suggests HCC0 standard of care, with low likelihood of permanent disability:
  - Linear, simple skull fracture with no TBI.
- Classify the following TBI type as significant because, although the medical treatment is an HCC0 standard of care, the permanent disability cannot be adequately assessed at this time.
  - mTBI, uncomplicated
- Until biomarker research reaches a maturity where mTBI attributes are sufficiently validated and mTBI can be diagnosed, stratified, and outcomes predicted, all mTBI should be classified as significant.
- With the exception of linear, simple skull fractures with no TBI, the current approach of treating blunt force head trauma as significant should continue.
- Future study of permanent injury from mTBI should closely follow state-of-the art fluid biomarker research as a metric to diagnose, guide treatment for, and predict mTBI outcomes. A large panel of biomarkers will be needed to capture the subtle differences between individual mTBI cases and be able to predict their outcome.
- For skull injury, continue investment in validation and uncertainty quantification of the ATBM head FEM and skull fracture injury models.
- For brain injury, update of the ATBM injury model for brain injuries is necessary, but may require additional fidelity in the FEM. We recommend waiting for further developments in medical research before investing in an update. Extrapolation of TBI mechanisms and thresholds from medical research to NLW regimes must be done with care.

Contents

1. Introduction

A. Non-lethal Weapons

Department of Defense Directive 3000.3E defines non-lethal weapons (NLWs) as "weapons, devices, and munitions that are explicitly designed and primarily employed to incapacitate targeted personnel or material immediately, while minimizing fatalities, permanent injuries to personnel, and undesired damage to property in the target area or environment" (DoD 2013, 12). Furthermore, "NLWs are intended to have reversible effects on personnel and material" (DoD 2013, 12).

This document considers effects from non-lethal blunt-impact munitions, such as rubber bullets and bean bags. Often employed in crowd control, these munitions function as a deterrent by causing pain or muscle spasm at the site of impact of the targeted individual. These weapons may also cause head injuries such as skull fractures and traumatic brain injury (TBI)—the focus of this document.

B. Why Assess Head Injury Significance?

This document informs the Joint Non-Lethal Weapons Directorate (JNLWD) of the risk of significant injury (RSI) from blunt-impact NLWs by categorizing the potential injuries caused by these weapons as either significant or not significant. While blunt impact NLWs are not intended to be aimed at the head, field data show that impacts to the head have occurred in routine police use in the United States and that potentially significant injuries have occurred. Currently, JNLWD assesses all head injuries as significant. Our goal is to more accurate and precise RSI estimates.

C. Risk of Significant Injury (RSI)

Part of the DoD NLW technology-development acquisition process is for developers to compare novel NLW systems' capabilities to requirements, including the key performance parameters (KPPs) and key system attributes (KSAs) considered in capability documents (DoD 2015, B-24). Counter-personnel NLW requirements often include a KPP or KSA relating to RSI. The RSI metric approximates the reversibility of a system's effect on targeted personnel (DoD 2012, 14). During the development acquisition process,

developers must quantify the NLW's total RSI (DoD 2012), showing a RSI less than or equal to a numerical threshold value.[1]

To approximate the RSI metric for an injury (e.g., skull fracture), one must first examine the term "significant." DoD Instruction (DoDI) 3200.19 defines[2] a significant injury as death, permanent injury, or injury that requires medical treatment with an Health Care Capability (HCC) index of 1 (HCC1) or higher (HCC1+) (DoD 2012, 14) as follows:

- Permanent injury is "physical damage to a person that permanently impairs physiological function and restricts the employment or other activities of that person for the rest of his or her life" (DoD 2012, 14).
- Medical treatment with an HCC index of 1 (HCC1) is defined as "first responder capability including resuscitation, stabilization, and emergency care" (DoD 2012, 13). Medical treatment with an HCC index of 2 (HCC2) is defined as "forward resuscitative and theater hospitalization capabilities including advanced emergency, surgical, and ancillary services" (DoD 2012, 13).
- In contrast, medical treatment with an HCC index of 0 (HCC0), that is, below the threshold for significance, is defined as "limited first-responder capability including self-aid (Samuels and Ellyson 2006), buddy-aid, and combat lifesaver skills" (DoD 2012, 13).

To summarize, DoD categorizes an injury as significant if the injury requires HCC1+ medical treatment or leads to permanent injury.[3]

We use a multistep estimation process to determine RSI (Burgei et al. 2014). The first step estimates $P(\textit{injury occurs})$, the probability that a particular injury (e.g., skull fracture) occurs when the NLW system is used as intended. This metric can be estimated via modeling and simulation and animal or human cadaver experimentation. The second step estimates $P(\textit{injury is significant} \mid \textit{injury occurred})$, the probability that the injury (e.g., skull fracture) is significant, given that it has occurred. The third step estimates RSI for the injury as the product of these two quantities:

$$RSI = P(\textit{injury occurs}) \times P(\textit{injury is significant} \mid \textit{injury occurred}),$$

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1 See Cazares et al. (2017) and Burgei et al. (2104) for a detailed explanation of total RSI for a NLW system.

2 DoDI 3200.19 specifically defines "risk of significant injury" rather than "significant injury." For this reason, the "significant injury" definition given here is our derivation from DoDI 3200.19's definition of "risk of significant injury" (see DoD 2012, 14).

3 In this document, we consider "death" to be a subset of "permanent injury."

where the *injury* can be any particular injury under investigation (e.g., skull fracture, TBI, rib fracture, tympanic membrane rupture, photothermal retinal lesion, etc.).

This document focuses on the second RSI quantity, *P*(*injury is significant* | *injury occurred*). The estimation of the first quantity, *P*(*injury occurs*), is beyond the scope of this project.[4] Previous projects for JNLWD have estimated the second RSI quantity through an extensive search of academic and medical literature to determine the physical attributes of an injury that can determine the injury's significance (Hirsch et al. 2015; King and Cazares 2015; Cazares, Hirsch, and King 2015; Cazares et al. 2016; Cazares et al. 2017).

D. Objective

This study examined the relevant academic and medical literature to:

- Identify physical attributes of head injuries (skull fractures and TBI) that allow us to consistently bin any occurrence of a head injury into a set of mutually exclusive and collectively exhaustive types, such that we can quantitatively, accurately, and precisely approximate each head injury type as either nonsignificant or significant according to definitions established in DoDI 3200.19 (DoD 2012).
- Evaluate how these attributes can be estimated during the development acquisition phase for a novel blunt-impact NLW.

E. Overview

In this document, we summarize the field-use data and the types of skull fracture and TBI expected with blunt-impact NLWs. We review the anatomy of the skull and brain and blunt-impact injuries, including skull fractures, TBI, and other potential injuries and complications. We discuss standards for, and research toward, rating long-term disability due to head injuries. We report our findings from the academic and medical literature for data on head injuries and propose recommendations for evaluating a head injury as significant or not significant, based on the definitions established in DoDI 3200.19. (DoD 2012). Finally, we review relevant modeling capabilities and conclude with our recommendations for how NLW developers might further develop computational modeling to estimate the likelihood of head injury for blunt-impact NLWs.

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[4] Refer to Cazares et al. (2017) for a more detailed discussion of how our approximation of *P*(*injury is significant* | *injury occurred*) can assist the NLW developer's approximation of *P*(*injury occurs*), allowing for a more straightforward approximation of the NLW system's RSI for the specific injury in question.

2. Injuries and Complications of Blunt-Impact NLWs

In this chapter, we provide definitions for the terms "injury" and "complication" used throughout this document. We then summarize injury data on blunt-impact NLW injuries that guide our selection of head injuries as the primary focus of our significance analysis.

A. Defining Injuries and Complications

The head (skull and brain) conditions described in this chapter fall into two categories: injuries and complications. An injury is "damage, harm, or loss to a person, particularly as a result of external force" (Stedman 2012, 868). A complication is a "morbid process or event occurring during a disease [or injury] that is not an essential part of the disease [or injury], although it may result from it or from independent causes" (Stedman 2012, 375). We consider skull fracture and TBI primary injuries, and complications that may result from these injuries as secondary (causal). Because skull fracture can occur in absence of TBI, and vice versa, these injuries can both be classified as primary injuries. In Chapter 4, the distinction between head (skull and brain) injuries and complications (those likely caused by either the skull fracture or brain injury) becomes important and will be discussed.

B. Blunt-Impact NLW Injuries: Review of Field-Use Data

Kramer, Macheret, and Teichman (2016) report that non-lethal blunt-impact weapons are currently used against U.S. citizens by law enforcement and corrections personnel, and many attempts to identify and characterize the likely injuries resulting from field use have been made. Field-use data, which are necessarily limited to the observations available to the officers at the time of reporting, may not include conditions such as TBI that may take time to develop and may require clinical expertise beyond first-responder care to diagnose. We therefore supplement the field-use data with medical case studies to gain insight into the more serious injuries.

Reported blunt-impact injuries include abrasions, lacerations, rib fractures, skull fractures, and heart and pulmonary contusions (Kobayashi and Mellen 2009; Pavier et al. 2015). Each part of the body will respond differently to blunt impact, which requires studying the specific region of interest (Pavier et al. 2015).

Two sources documenting the injuries from field use of blunt-impact NLWs, previously summarized in 2017 Cazares et al., informed this report:

- A 2013 study (Kenny and Bovbjerg) conducted by Penn State University and funded by the Joint Non-Lethal Weapons Program (JNLWP) focused on use-of-force records detailing 1,398 non-lethal blunt-impact weapon uses between 1995 and 2010, as maintained by the Los Angeles Sheriff's Department (LASD). Weapons reported were Stinger (37 mm round containing .32 cal rubber balls), flash-bang, Sting-ball grenade, and 12-gauge beanbag.
- A 2004 study (Hubbs and Klinger) conducted by the National Institutes of Justice (NIJ) analyzed case studies from 106 agencies nationwide after a targeted data call, resulting in 373 separate case reports during which 979 blunt-impact weapon munitions were fired. Weapons reported in these case reports were 337 mm plastic batons, 12-gauge bean-bag, 12-gauge "super-sock," and 40 mm "eXact iMpact™" rounds. (Cazares et al. 2017).

While blunt impact NLWs are not intended to be aimed at the head, field data show that impacts to the head have occurred in routine police use in the United States and that potentially significant injuries have occurred. The 2013 Penn State/JNLWP (Kenny and Bovbjerg 2013) study estimates that face and head injuries account for 115 out of 638 total reported injuries (18%) induced by blunt- impact NLWs over the period of data collection. These data also indicate the type of injury that occurred but are not mapped to body part. Nine fractures (anywhere on the body) were reported. We can therefore state that there were nine or fewer skull fractures reported (7.8% of head injuries; 1.4 % of all injuries). In addition, one concussion (i.e., mTBI) was reported (0.9% of head injuries, 0.2% of all injuries). Unfortunately, these data do not report impacts where no injuries occurred, so it is impossible to report the probability of injury given a hit to the head.

The 2004 study by the National Institute of Justice (Hubbs and Klinger 2004) finds a much lower likelihood of head injury at 2.8%, or 19 out of 691 reported injuries. This study also reports the types of injuries that were sustained to the head. Five reported injuries were fractures (26% of head injuries; 0.7% of all injuries), two were penetrating, and the remainder were bruises, abrasions and lacerations (Hubbs and Klinger 2004).

We chose to focus this document on head injuries such as skull fractures and TBI and identify the physical attributes of such injuries that can be used to determine the significance based on skull fracture and TBI types. Before we evaluate head injury significance, the following sections provide an overview of skull and brain anatomy and details of blunt-impact head injuries, their complications, and their HCC level of care as documented in the medical literature. This background information will be helpful for

evaluating the significance of head injuries. For reasons of scoping, analysis of penetrating injuries,[5] facial fractures, and injuries to the eyes will not be considered here.

[5] Penetrating injuries, including lacerations and incised wounds, are IDA's next RSI area of investigation for JNLWD.

3. Anatomy of the Skull and Brain

A. Bones of the Skull

The human head contains the concentration of sensory organs in the body, which includes the eyes, ears, tongue, and olfactory system (Hansen 2014). A collection of 22 bones called the skull constitutes the skeletal support for the head. Table 3-1 and Figure 3-1 describe the function and indicate the position of the bones of the skull. The brain and its associated meninges (tissues between brain and skull) are protected within a subset of skull bones that form the cranium; the remaining bones of the skull form the face (also known as the viscerocranium). The bones of the skull are united through joints made of a thick fibrous material known as *sutures* (Stedman 2012); see Figure 3-1. The skull also contains *foramina,* openings that allow nerves and blood vessels to pass (Figure 3-2). For example, the foramen magnum in the base of t he skull allows the spinal cord to exit from the skull. The *frontal, parietal, and occipital bones* form the top surface of the cranium as well as the base (Figure 3-2). The *temporal bone* is located on the sides of the skull and also forms part of the base of the skull. The *ethmoid and sphenoid bones* are complex bones that contribute to both the nasal cavity and the eye orbits.

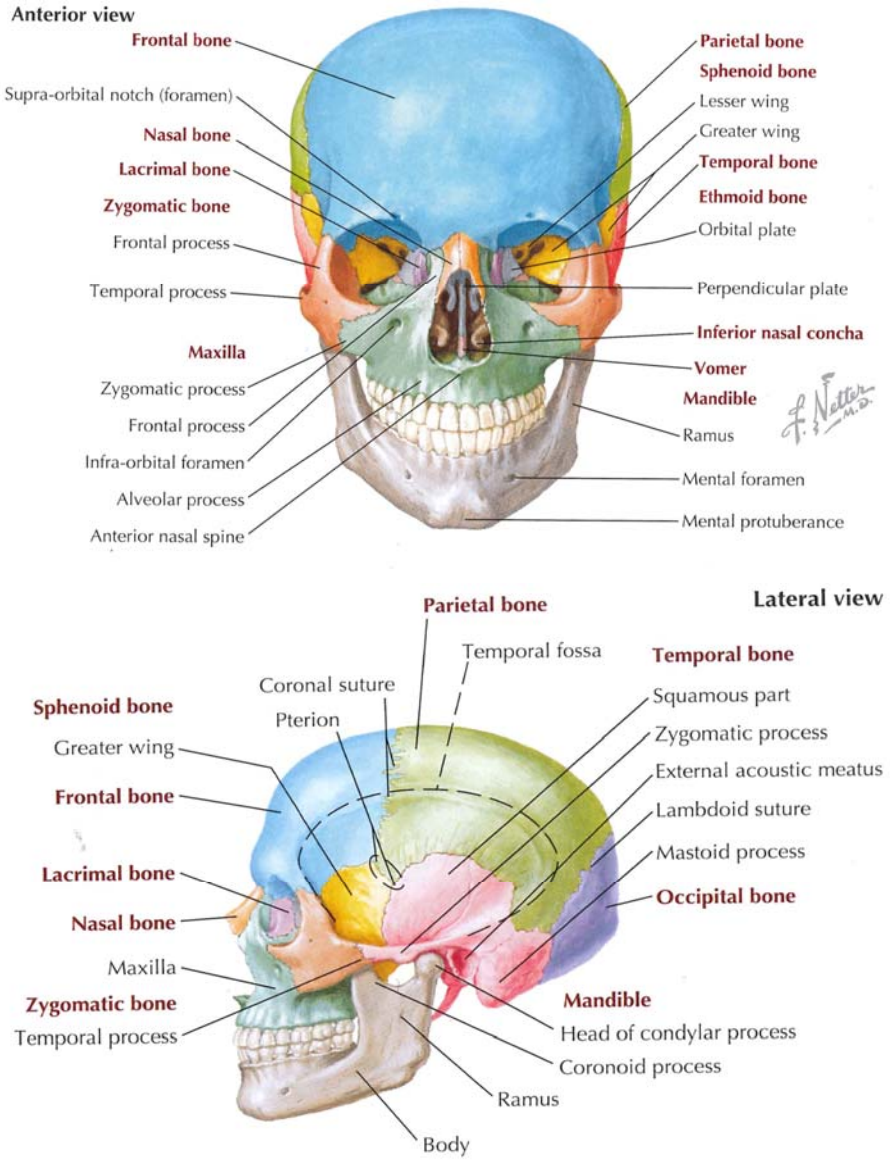
Certain skull bones provide support for the muscles of the face and neck and also can be located near vital blood vessel and nerves. For example, the temporal and sphenoid bones are located close to cranial nerves that control human senses; damage to these bones can affect those senses. In the case of the sphenoid bone, many nerves and blood vessels pass through the foramina in the bone, including the optic nerve (Ghobrial, Amstutz, and Mathog 1986). The sphenoid bone is also an attachment for muscles of the face. As will be seen in Chapter 4, the location of a blunt-impact skull fracture will have bearing on the severity, significance, and complications due to the initial fracture.

Table 3-1. Bones of the Skull

Cranium (neurocranium)		Face (viscerocranium)	
Bone	**Description**	**Bone**	**Description**
Frontal	Forms the forehead	Nasal (2)	Forms root of nose
Parietal (2)	Forms the superolateral portion of the neurocranium	Inferior concha (2)	Forms lateral nasal wall
Temporal (2)	Forms the lower portion of the neurocranium	Vomer	Forms lower nasal septum
Sphenoid	Forms parts of both orbits and sides of skull	Palatine (2)	Contributed to nasal wall and hard palate

Cranium (neurocranium)		Face (viscerocranium)	
Occipital	Forms the inferoposterior portion of the neurocranium	Lacrimal (2)	Forms part of orbit and contains lachrymal sac
Ethmoid	Contributes to nasal cavity	Zygomatic (2)	Cheekbones
		Maxilla (2)	Forms part of orbit and contains maxillary teeth
		Mandible	Lower jawbone that contains mandibular teeth

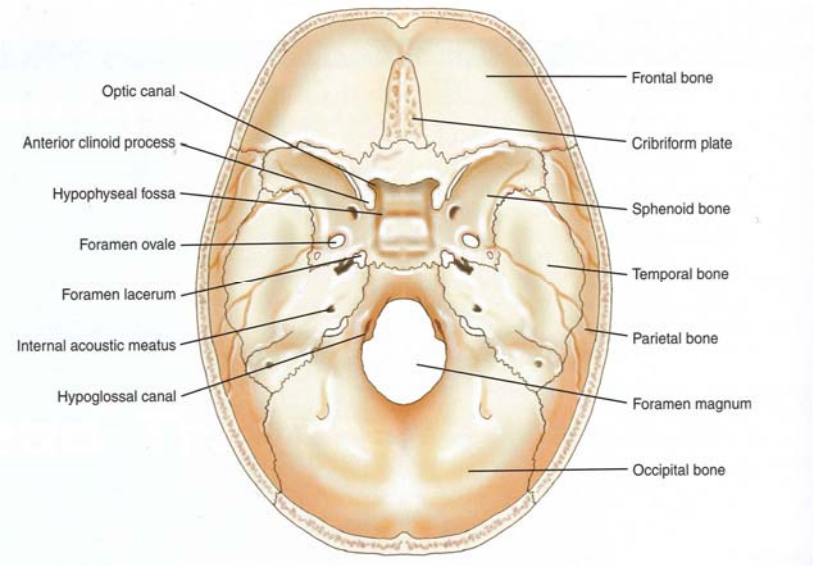
Source: (Hansen 2014, 412–14).



Source: Hansen (2014, 413–14).

Top: Forward view of the skull. The bones are labeled and colored to give definition. Bottom: The left side of the skull.

Figure 3-1. The Skull



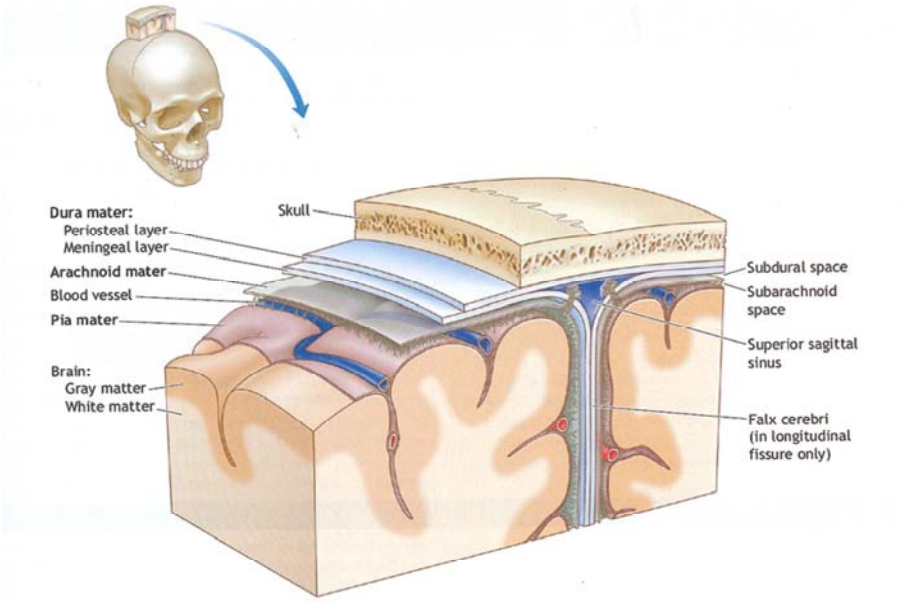
Source: NAMET (2016, 260).

Figure 3-2. Base of the Skull

B. The Brain and Meninges

The brain is located within the neurocranium and has three meningeal tissue layers that separate it from the inner surface of the skull (Figure 3-3). The meninges, which are composed of fibrous tissue, help cushion and protect the brain. The outermost layer, which is attached to the inside of the cranium, is called the *dura mater*. Beneath the dura is the *arachnoid mater;* the layer that closely surrounds the brain is called the *pia mater*. Between the arachnoid and pia mater is the *subarachnoid space*, which contains the *cerebrospinal fluid* (CSF). The CSF surrounds organs of the central nervous system, such as the spine and brain, and it cushions and protects these organs from trauma.

The brain has a number of blood vessels to supply it with oxygen and nutrients (Felton, O'Banion, and Maida 2016, 93–124). Blunt-impacts to the head have the potential to generate force that can tear blood vessels, leading to bleeding into the skull cavity (Young et al. 2015). Of particular importance to this study is the *middle meningeal artery* (MMA) that runs along a groove called the middle meningeal groove in the base of the skull (Yu et al. 2016). Damage to the MMA is can result in very severe bleeding in the cranial cavity and potentially fatal epidural hematoma (EDH) (Pascual and Prieto 2012).



Source: NAMET (2016, 261).

Figure 3-3. The Meningeal Layers between the Skull and Brain

The gross anatomy of the brain divides it into two hemispheres. A slice between the two hemispheres reveals several structures in the brain, among them the cerebellum, the thalamus, the corpus callosum, the pons, and the medulla oblongata (Hansen 2014). Each of these structures has been shown to serve a different brain function. The higher cognitive functions of the human brain occur in the cerebral cortex, which is the outer gray matter of the brain (Kandel and Hudspeth 2013). The cerebral cortex is divided into four lobes (frontal, parietal, occipital, and temporal) and designated by the skull bones that overlie that particular area of the brain. The four lobes have subsequently been shown to carry out defined cognitive functions, including processing motor, visual, auditory, or sensory input. TBIs to these lobes can result in cognitive deficits.

In the next section, we examine potential blunt-impact head injuries and complications to assess the HCC level of care.

4. Blunt-Impact Head Injuries and Their HCC Level of Care

Blunt impact to the head can result in a number of different types of injuries depending upon conditions of the initial insult (Kerr 2013). Blunt-impact head trauma data are from motor vehicle accidents, falls, sports injuries, bicycle accidents, pedestrian accidents, and assaults (Stiell 2001), all of which have different injury mechanisms than blunt-impact NLWs. Our analysis utilizes all data regardless of injury mechanism.

A spectrum of injuries from simple scrapes, bruises, and abrasions to severe TBI can occur with potential outcomes of complete reversibility to mortality. This study concerns itself with head injuries including skull (neurocranium) fractures and brain injuries, such as TBI and associated hematomas. Other head injuries, including facial fractures, and injuries to the eyes will not be considered here.

1. Skin Bruises and Abrasions

A bruise (also known as a contusion) is a common skin injury that results from damage to blood cells beneath the skin. Bruising is extremely common with blunt-impact NLWs, and the treatment protocol is known as the RICE method (rest, ice, compression, elevation) (Mayo Clinic 2017). More severe impacts can cause a scalp hematoma (a lump produced by the pooled blood outside of the skull), which also usually resolves on its own. Infrequently, a scalp hematoma must be surgically drained. We therefore conclude that bruises require only HCC0 care. Hematomas, however, may require surgical treatment (HCC1 or greater). In young children (<24 months), scalp hematoma could indicate more serious head trauma, including intracranial injury (Burns et al. 2016, 576), but is generally not significant in adults and typically heals on its own (Wedro 2017). Further analysis is required to establish the attributes that will enable determining a given hematoma's needed level of care.

Abrasions are wounds caused by superficial damage to the skin, specifically no deeper than the epidermis. Abrasions can be defined as level 1 (epidermal only) or level 2 (also involving the dermis). Head abrasions must be cleaned, and topical antibiotics can be used to prevent infection and promote healing (Kerr 2013). The level of care required for abrasions is HCC0.

Lacerations occur when there is a tear of skin tissue. Lacerations that occur over areas of the skull that do not have high skin tension can be closed with a simple dermal adhesive. These types of lacerations require HCC0 level of care. Lacerations over areas of dynamic

muscle contraction, such as the forehead, or lacerations greater than 4 cm in length, or those that involve separation of deep tissue, require suturing (Kerr 2013). We consider suturing HCC1 level of care. Open head wounds require surgical intervention, and we consider these injuries to require HCC1+ level of care.

2. Skull Fractures

Skull fractures generally refer to fractures of the neurocranium (see Table 3-1) and can be classified by several criteria (Hansen 2014; Valadka 2017). First, the wound can be open (compound) or closed. Skull fractures can present as a *linear fracture* where there is no displacement of the bone or as *depressed fractures* where the bone fragments are offset from each other. Linear fractures are the most prevalent skull fracture, occurring in 70%–80% of all reported cases (Oehmichen 2006, 475). They can occur along a suture line that joins to skull bones (diastatic), involve the base of the skull (basilar), or involve the cranial vault (hairline). The majority of linear fractures will not harm other structures if the fractured piece stays in place (Black, Gargallo, and Lipson 2009). Depressed fractures can present as one fragmented piece or multiple fragments (comminuted). Each of these criteria, as well as fractures to a particular bone, can affect the standard of treatment and potential outcome (Valadka 2017; Saraiya and Aygun 2009).

a. Open (Compound) Skull Fracture

An open (compound) skull fracture is a fracture where there is an open wound and the cranial cavity is exposed (*Segen's Medical Dictionary* 2018) and there is shattering of the bone (MedLine Plus 2018). Open skull fractures often require surgical intervention to remove pieces of bone (debridement); they require prescription antibiotics for infection prevention and control. Both surgical intervention and antibiotics are HCC1+ levels of medical treatment.

b. Depressed Skull Fracture

Depressed skull fractures that include a depression of more than 8–10 mm or a depression that is greater than the thickness of the surrounding skull bone require surgical intervention (Valadka 2017; Neville et al. 2014) to remove pieces of bone (debridement) and elevate the depressed skull bones to their original position (Masters 1980, 329). Any depressed skull fracture that includes a complication of damage to the underlying dura mater (the outermost layer of the meninges) requires surgical intervention to repair the dura and reduce the risk of meningitis.[6] CSF leakage can be a sign of damage to the meninges

[6] Meningitis is "[i]nflammation of the membranes of the brain or spinal cord" (Stedman 2012, 1044).

and indicates that surgical intervention may be required (Schmidt 2009). Depressed skull fractures require surgical interventions, which require HCC1+ levels of medical treatment.

c. Basilar Skull Fracture

Basilar fractures are linear fractures of the base of the skull (see Figure 3-2). They do not require surgical treatment the vast majority of time, but potential complications warrant hospitalization for observation (Simon and Newton 2017; Heegaard, Moreira, and Grayzel 2011. Basilar fractures can have a CSF leak as a complication (Baugnon and Hudgins 2014). In this case, surgical repair is necessary (McCutcheon et al. 2013). Other complications include "meningitis, pneumocephalus,[7] cavernous sinus thrombosis,[8] Carotid dissection,[9] pseudoaneurysm,[10] or thrombosis,[11] carotid-cavernous fistula,[12] [and] injury to cranial nerves…" (Simon 2017). Basilar fractures can also be associated with complications including nerve damage since nerves enter and exit the skull at the foramen (Figure 3-2). The surgical interventions for basilar skull fracture complications are HCC1+ medical treatments.

Treatment protocols in the past included the use of prophylactic antibiotics to mitigate the risk of meningitis (Masters 1980, 335), an HCC1+ medical treatment. This standard of care remains controversial, however, and the utility of such treatment has not been clearly established (Ratilal 2015).

d. Linear Skull Fracture: Location Dependent

1) Linear Skull Fracture at or near the Middle Meningeal Artery or at or near Major Venous Sinuses

Linear skull fractures close to vascular structures (i.e., at or near the middle meningeal artery or at or near major venous sinuses) have potential complications. Fractures that occur at or near the middle meningeal artery can cause either EDH or arteriovenous fistula (AVF), an irregular connection between an artery and a vein caused by trauma and resulting in an aneurysm (Yu 2016, 792; Stedman 2012). Fractures that occur at the major venous sinuses can cause potentially fatal hemorrhaging (Bond, Vierra, and Yates 1999, 3).

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7 "Presence of air or gas within the cranial cavity" (Stedman 2012).

8 Blood clot behind the eye socket.

9 Separation of the carotid artery.

10 A pseudoaneurysm is a result of an injured blood vessel wall and blood enters the adjacent tissues (Mankad 2015).

11 Blood clot within a blood vessel.

12 An abnormal connection between and artery and a vein within the cavernous sinus (i.e., a venous cavity located next to the temporal bone and the sphenoid bone) (Scott 2017).

Temporal and temporo-parietal skull fractures run the risk of intracranial bleeding including EDH because of their proximity to the middle meningeal artery (Kerr 2013, 280; Bond, Vierra, and Yates 1999, 3). Complications from these types of linear skull fractures require significant clinical intervention; therefore, we consider these types of skull fractures to require HCC1+ level of medical treatment.

2) Linear Skull Fracture at or near Suture

Linear fractures that occur at or near a suture can cause suture diastasis, a separation of the skull sutures. Suture diastasis is more prevalent in children than adults, but when it occurs in adults, the lamboid suture is the one most affected (see Figure 3-1) (Grossart and Samuel 1961, 167). It is commonly accepted in the medical community that suture diastasis is a significant injury generally indicative of additional trauma in both children and adults, but we cannot find any protocols in the literature regarding medical treatment.

3) Temporal Bone Fractures

The temporal bone is very resistant to damage; therefore, with fractures of this type there is usually damage to underlying structures, including vascular structures (Saraiya and Aygun 2009; White and Folkens 2005), cranial nerves (Dubal et al. 2015), and internal structures of the ear (Saraiya and Ayugun 2009). As discussed previously, temporal linear fractures that intersect the middle meningeal artery can result in intracranial bleeding and EDH, both of which require HCC1+ medical treatment (Kerr 2013, 280; Zuckerman and Conway 1997, 624). Patients with nerve injury require surgical intervention, which is HCC1+ medical treatment (Patel and Groppo 2010, 111).

The most prevalent complication associated with temporal fractures is conductive, sensorineural, and/or mixed hearing loss (24%–81%) (Saraiya and Augun 2009, 257). Patients with temporal fractures and conductive hearing loss (caused by tympanic membrane rupture) as the only complication can be treated conservatively because most TMRs heal spontaneously and sensorineural hearing loss has poor outcomes despite level of medical treatment (Patel 2010, 105; Qureshi and Harsh 2017).[13]

4) Sphenoid Bone Fractures

Fractures to the sphenoid bone can cause several significant injuries such as hematoma, loss of vision, and muscular dysfunction. As with most head bone fractures, "expectant waiting" with prophylactic antibiotics is an appropriate treatment in cases that are not severe without neurologic or bleeding complications. The severity of injury is generally dependent on the location of the fracture on the sphenoid bone. Fractures of the

[13] Refer to Cazares, Hirsch, and King (2015) and King and Cazares (2015) for detailed analysis of hearing loss significance (sensorineural and conductive).

greater wing of the sphenoid are generally not associated with other cranial injuries. Other portions of the sphenoid are in contact with vital nerves, blood vessels, and muscles and fractures in those areas result in more severe injuries such as neurologic, hematomas, or vision loss that require advanced HCC1+ level of clinical care (Ghobrial et al. 1986).

e. Linear Skull Fracture: Simple

In general, closed linear skull fractures are considered non-operative lesions and do not require any surgical intervention (Valadka 2017; Neville et al. 2014). Treatment of linear skull fractures in the absence of any co-injuries or complications is therefore considered HCC0.

3. Intracranial Injuries

a. Traumatic Brain Injury

In addition to potentially causing a skull fracture, blunt-impact also has the potential to cause intracranial co-injuries and complications (Young et al. 2015). Damage can occur to the meninges and the brain itself, which can result in neurological and cognitive deficits (Valadka 2013). Bleeding or leakage of CSF can cause fluid buildup inside the skull, resulting in the increase in intracranial pressure (ICP). Physical damage to neural cells and brain structures can also occur due to external forces. These injuries are collected under the term "traumatic brain injury."

Clinically, TBI is very difficult to diagnose and manage, and it is difficult to predict outcomes accurately (Sandsmark 2016). Many types of injuries are collected under the TBI moniker, and the trajectory of each of these injuries are not completely understood. TBI is also a dynamic injury that can evolve over time differently, depending upon the conditions of the injury and patient (Valadka 2013). All these factors contribute to the subjective metrics for TBI treatment as well as the diagnosis of a specific TBI. TBI is classified as a *functional* injury where the course of injury and recovery are measured by somewhat subjective measures of cognitive function, such as the Glasgow Coma Scale (GCS; Teasdale and Jennett 1974). Objective clinical metrics that can drive reliable treatment options or accurately predict outcome of a TBI are also lacking in the clinical literature (Levin and Diaz-Arrastia 2015). All these factors contribute to the difficulty of ascribing specific attributes of a TBI from an NLW blunt impact.

In the following sections we describe attributes of head injuries that contribute to TBI and their medical treatment in the current medical literature. Basic research continues to evolve the clinical thinking surrounding these injuries, and these attributes will continue to change in the future. Appendix A describes research to develop more objective biomarkers or attributes of TBI.

b. Definition of TBI

Until recently, a consistent definition for TBI was lacking in the clinical literature (Menon et al. 2010). An interagency group of clinicians has developed a working definition of TBI in which "TBI is defined as an alteration in brain function, or other evidence of brain pathology, caused by an external force" (Menon et al. 2010).

An alteration of brain function can mean a period of loss or decreased consciousness, or a loss of memory before or after the injury, or a neurological deficit (weakness, loss of balance, change in vision, paralysis, etc.), or a change in mental state (such as confusion, slowed thinking or disorientation.). Evidence of brain pathologies in TBI will be discussed in later sections. External forces that can cause TBI include the following:

- The head being struck by an object.
- The head striking an object.
- Acceleration of the brain without trauma to the head.
- Foreign body penetration.
- Blast forces.

c. Classification of TBI

The clinical literature indicates that the heterogeneity of injuries and the dynamic nature of TBI is the greatest impediment to the development of effective therapies (Pasqual and Prieto 2012). These same qualities also prevent a rigorous clinical classification and stratification of TBI to allow an effective prediction of clinical outcome. To understand the injury mechanism, develop effective therapies, and be able to reliably predict clinical outcomes, attempts have been made to classify TBI according to five qualities:

- *Injury Severity*—Classification based on cognitive impairment.
- *Pathoanatomic Findings*—Classification by location and type of injury.
- *Biomechanical Mechanism*—Blunt-impact or inertial loading.
- *Pathophysiology*—Metabolic processes set in motion by the TBI.
- *Prognostic Modeling*—Classification based upon predicted clinical outcome of TBI.

1) Injury Severity Classification

An ideal classification system should take into account all five of these qualities in order to fully understand the injury. However, in practice usually one quality is used depending upon the goals of clinical treatment or research. Injury severity is generally the most quoted quality, and for civilian trauma triage, GCS, along with other tests such as

structural imaging of the head, are used to stratify TBI during the acute phase for initial treatment (Swanson et al. 2017). The GCS has limited prognostic capability, and other criterion are used to assess outcome.

The GCS is intended to assess the level of consciousness of a patient. The clinician rates the responses of an injured person along three components:

1. Motor response.
2. Verbal response.
3. Eye-opening response.

Table 4-1. The Glasgow Coma Scale Components and Ratings

Score	Best Motor Response	Best Verbal Response	Best Eye-Opening Response
6	Obeys commands	N/A	N/A
5	Localizes movements toward painful stimuli	Oriented	N/A
4	Withdraws from pain	Confused fluent speech	Spontaneously
3	Flexor response by pain	Inappropriate words	To speech
2	Extensor response by pain	Incomprehensible	To pain
1	None	None	None

Table 4-1 shows the criteria for the assessment. The ratings for the three components are totaled for a final GCS score. The severity of TBI is then classified according to GCS total score (Schmidt 2009):

- **Severe TBI**: GCS < 8–9
- **Moderate TBI**: GCS = 9–12
- **Mild TBI**: GCS = 13–15

Despite its almost universal adoption in the civilian clinical assessment of TBI, the GCS has been criticized as being too subjective or not necessarily a mathematically rigorous assessment of conscious state (Levin and Diaz-Arrastia 2015, Reith et al., 2017). A Department of Veteran's Affairs and DoD working group on the management of mild TBI (mTBI) states that the departments do not use the GCS as criteria to define and stratify TBI (DoD 2015; VA and DoD 2016). However, other publications by VA and DoD physicians and researchers indicate that the GCS is used for diagnosis (Swanson 2017). It may be that GCS can be used in the DoD to assess cognitive function, but it is not part of

the formal definition of TBI. The DoD definition and criteria for stratifying TBI is given in Table 4-2.

Table 4-2. DoD Definition and Stratification of TBI

Criteria	Mild	Moderate	Severe
Structural imaging	Not indicated/Normal	Normal or Abnormal	Normal or Abnormal
Loss of Consciousness (LOC)	0–30 min	>30 min and <24 hrs.	>24 hrs.
Alteration of Consciousness (AOC)	Up to 24 hrs.	>24 hrs. Severity based on other criteria	
Post-traumatic Amnesia (PTA)	0–1 day	>1 and <7 days	>7 days
GCS Score	13–15	9–12	3–8

2) Pathoanatomic Findings Classification

Structural imaging of the brain has also been incorporated into classification of the severity of TBI. Identifying structural injuries to the brain such as hematomas, hemorrhages, and diffuse axonal injuries (DAIs) has been used successfully to classify some TBIs, and that information has been to treat the injury and predict the outcome of treatment. Computed tomography (CT) findings have been used in Marshall's CT classification (Pasqual and Prieto 2012) to develop six classes of TBI injury. Marshall's classification scheme has been identified as the most successful in classifying severity and outcome of TBI (Pasqual and Prieto 2012, 1516).

3) Biomechanical Mechanism Classification

Numerous studies have been performed to understand the physical mechanism of TBI. For example, it is known that blunt impact can cause the brain to impact the side of the skull, causing contusions of the brain (Young et al. 2015). Even less forceful impacts can cause increases of intracranial pressure (ICP) on the side of brain impact and decreasing ICP on the lagging side of the brain. The pressure gradients can cause diffuse (i.e., widespread) injury throughout the brain such as diffuse axonal injury. Rotational motions are also deleterious since the brain is held fairly rigidly in place by the brain stem. Rotations can then cause gradients of shear stress, although the exact mechanisms are not well understood (Young et al. 2015) Progress has been made to understand the mechanisms of TBI injury, but a clearer understanding is needed to reliably predict the effect of physical force on the brain and resulting injuries (Bandak et al. 2015).

4) Pathophysiology Classification

Metabolic processes that respond to a TBI can have an effect on the trajectory of the injury. Molecular, cellular, and immunological factors respond to TBI. It is becoming increasingly clear that these factors contribute to the heterogeneity and dynamic nature of TBI (Pasquale and Prieto 2012). Our lack of complete understanding of these factors also clouds prognostic capabilities.

5) Prognostic Modeling Classification

As stated previously, the complexity, heterogeneity, and dynamic nature of TBI makes outcome prognostication difficult; developing the attributes of TBI that can predict recovery is still nascent. Despite this, there are attempts to develop prognostic models of TBI (Sandsmark 2016). These models use the standard of clinical assessment of outcome of TBI called the Glasgow Outcome Scale (GOS; Jennett et al. 1976). Similar to the GCS, the GOS is a simple scoring scale from 1 to 5 to assess the functional capability of a patient. A score of 5 means that the patient can resume a normal life; a score of 1 is death. The simplicity of the GOS contributes to the lack of effectiveness of prognostic tools to understand outcomes of TBI.

d. Management and Treatment of TBI

Injuries to the brain resulting from blunt impact can classified as either focal (located in a clearly defined area) or diffuse in nature. The majority of focal injuries of TBI are the result of bleeding or fluid buildup in the brain, which causes an increase in ICP. TBI definition associates these focal injuries mainly with severe or moderate TBI. Mild TBI does not necessarily require a focal lesion for its diagnosis. Therefore, we will consider focal intracranial injuries as severe or moderate TBI injuries.

Management of focal injuries involves monitoring and managing ICP by stopping bleeding or fluid drain within the cranium (Pascual and Prieto 2012). Normal ICP for adults is 10–15 mm Hg; ICP that exceeds 20–25 mm Hg is considered the threshold for clinical intervention (Valadka 2017). Surgical intervention is usually warranted (Schmidt 2009), and the majority of the focal injuries described below are therefore significant. However, there are no accepted rigorous (clinical trial based) attributes that can be used to define a management approach. It is usually left to the clinician's judgement. All attributes below reflect clinical uncertainty and are used as guides only (Pascual and Prieto 2012). A brief description of focal TBI injuries follows (since the majority of these injuries are considered significant, we will not concentrate this analysis on those injuries).

Diffuse injuries, such as mTBI or diffuse axonal injury, occur in the vast majority (70%–90%) of TBI cases in civilian and military populations (Levin and Diaz-Arrastia 2015). Diffuse injuries usually require a "watchful waiting" management approach. Some cases of these diffuse injuries can be considered not significant because full recovery can

be spontaneous in "a few days" (Levin and Diaz-Arrastia 2015). The U.S. Army's Borden Institute has published an extensive textbook on the management of mTBI (Weightman et al. 2015).

e. Focal Injuries

1) Intracerebral Hemorrhages and Contusions

Contusions of the brain parenchyma often leads to massive edema, and despite clinical intervention, intracerebral hemorrhage (ICH) is often fatal (Pascual and Prieto 2012). Surgical intervention for intracerebral hemorrhage and contusions is recommended for patients who present with a GCS score of 6–8 (Severe TBI) and where the volume of fluid buildup volume exceeds 50 cm^3. Non-surgical management is recommended only if the patient is fully conscious and if lesion does not expand or shift structure of the brain (midline shift). We consider all ICH and contusions to require HCC1+ level of care.

2) Epidural Hematoma

On a CT scan, an EDH appears as a convex mass. It is caused by an accumulation of fluid between the dura mater (the outermost layer of the meninges) and the skull (Valadka 2017). EDHs must be monitored and managed expediently. Surgical intervention is needed when the volume of the EDH exceeds 30 cm^3 (Pascual and Prieto 2012). Craniotomy, surgical opening of the skull, is the suggested treatment for removal of the hematoma. (Bullock et al. 2006). Non-surgical management can be used when the volume is less and the patient has a GCS score greater than 8. Note, however, that the patient must be monitored in a neurosurgical center for potential delayed or expanding EDH. Outcome is related to level of consciousness of the patient. Of patients who are conscious at the time of surgery, nearly all survive (Maugeri et al. 2015), but mortality rates can climb to 50% for patients who never regain consciousness following EDH. Since EDH always requires surgery or condition monitoring in an ICU if non-surgical management is provided, we treat all EDH as requiring HCC1+ level of care.

3) Subdural Hematoma

A subdural hematoma (SDH) occurs when blood accumulates between the dura and arachnoid layers of the meninges (Valadka 2017). An SDH with a thickness of 1 cm is surgically drained regardless of GCS score. Surgery is also recommended when there is a GCS of less than 9, a midline shift of the brain past 5 mm, and an SDH thickness of less than 1 cm. Otherwise, non-surgical monitoring similar to EDH can be performed (Pascual and Prieto 2012). For similar reasons as with EDHs, all SDHs require HCC1+ level of medical care.

4) Subarachnoid Hemorrhage

Subarachnoid hemorrhage (SAH) is the pooling of blood between the pial and arachnoid layers of the meninges (Valadka 2017). There are no specific guidelines for the treatment of SAH since associated injuries usually take precedence. ICP monitoring and relief of pressure may be needed, so ICU monitoring is essential. We therefore consider all SAH as requiring HCC1+.

f. Diffuse Injuries

1) Mild Traumatic Brain Injury

mTBI or concussion is estimated to encompass the majority (70%–90%) of TBI diagnoses in military and civilian populations (Levin and Diaz-Arrastia 2015). The criteria for such a diagnosis is subjective, however. Since there is no indication of physical injury using current clinical imaging techniques for mTBI, a diagnosis is mainly based on cognitive function and the GCS (Table 4-1; Kay et al. 1993; Renjilian and Grady 2017). Currently accepted clinical practice for the treatment of mTBI is for physical and cognitive rest for the patient (Stillman et al. 2017; Renjilian and Grady 2017; VA and DoD 2016; Levin and Diaz-Arrastia 2015), and mTBI symptoms typically resolve within 7–10 days. We consider this form of uncomplicated mTBI as self-resolving and therefore classified as HCC0 level of medical care. However, an estimated 10%–30% of mTBI cases do not self-resolve and require further clinical intervention (VA and DoD, 2016). These complicated mTBI cases are considered an HCC1+ level of care.

Note that recent research is starting to cast doubt on the current accepted ideas about mTBI. Research is indicating that despite the lack of injury apparent on CT scans and other imaging techniques, damage does occur in the nervous system on the cellular level (Levin and Diaz-Arrastia 2015). Cellular stretching and twisting and molecular damage repair mechanisms disrupt the energy balance within the brain (Renjilian and Grady 2017). Synaptic reorganization and immune mechanisms can also affect cognitive function (Algattas and Huang 2014). Molecular and cellular damage is not detectable using typical imaging methodologies in the clinic. In response, the DoD is advocating the development of more objective metrics for the diagnosis of mTBI and deemphasizing the GCS (VA and DoD, 2016; DoD 2015b). Current research is concentrating on developing objective biomarkers of these cellular and molecular damage mechanisms (see Appendix A). However, DoD currently *does not* recommend using biomarkers for the diagnosis, treatment, and prognosis of mTBI due to their technological immaturity (VA and DoD 2016). From this assessment of the literature, IDA concludes that there are no reliable physical attributes that can distinguish an uncomplicated and self-resolving mTBI from an mTBI with persistent symptoms. With the development of biomarker panels of mTBI, specific attributes for mTBI may be possible in the future based on this research.

2) Post-Concussive Syndrome

A subset of complicated mTBI symptoms known as post-concussion syndrome (PCS) have been known to occur in some mTBI patients. These symptoms are loosely defined cognitive deficiencies such as “trouble thinking,” “trouble concentrating,” or “memory problems,” as well as emotional problems such as anxiety, depression, or irritability (Dischinger et al. 2009). Like mTBI, PCS symptoms are not rigorously defined, and the mechanistic cause of these cognitive difficulties is not understood (Bigler 2008; Levin and Diaz-Arrastia 2015). There is debate about whether PCS is even associated with mTBI (Mears et al. 2011) because base rates for PCS symptoms among those who have never suffered an mTBI are similar to those who have (Chan 2001; Asken et al. 2017).

If PCS symptoms do not resolve within 3 months, patients are referred to a TBI clinical specialist for further treatment (VA and DoD 2016). We consider PCS symptoms that do not resolve within 3 months as requiring an HCC1+ standard of care.

3) Diffuse Axonal Injury

Diffuse (or traumatic) axonal injury (DAI) involves mechanical stress forces upon parts of the neuron called axons. Axons are long, thin projections from the cell body of neurons; axons contain long and thin protein structures called microtubules. Motor proteins transport material along these microtubules; the damage of DAI is thought to disrupt this process (Hill, Coleman, and Menon 2016). DAI damage occurs mainly in the brainstem and corpus callosum, and severe DAI can lead to significant morbidity and mortality (Vieria et al. 2016). A grading system of three tiers for the severity of DAI has been developed based upon length of coma and imaging findings (Adams et al. 1989). The least severe, grade 1, can be difficult to diagnose due to the absence of lesions in imaging diagnosis. A clear diagnosis cannot be made in many cases until a post-mortem autopsy (Valadka 2017; Smith 2013). All grades of DAI involve some length of coma in patients (Vieria et al. 2016) and ICU monitoring (Hamdeh et al. 2017). There is no current specific therapeutic intervention for DAI other than clinical support functions and monitoring for cognitive improvement (Smith, Hicks, and Povlishock 2013). However, improvements in the understanding of the pathology of DAI could lead to the development of biomarkers and therapeutic interventions in the future (Hill, Coleman, and Menon 2016). Because all grades of DAI require ICU stay in the majority of cases, and because of the lack of specific therapeutics for improvement, we consider DAI to require a HCC1+ standard of medical care.

5. Head Injury Disability

In this chapter, we discuss the limited standards for and research toward rating long-term disability due to head injury. We first provide an overview of U.S. military medical standards and Veteran Affairs Schedule for Rating Disabilities (VASRD), which could be useful in evaluating permanent head injury disability.

A. U.S. Military

DoDI 6130.03 (DoD 2010) establishes medical standards for new recruits in the military Services. This instruction provides information on a range of head injuries from headaches to the loss of the skull bone. We will focus our efforts on the injuries where HCC0 is the standard of care because these are the types of injuries that we evaluate for permanent disability. These include "moderate" and "mild" head injuries.

"Moderate head injury" is:

a) Unconsciousness of more than 30 minutes but less than 24 hours, or

b) Amnesia, or disorientation of person, place, or time, alone or in combination, more than 24 hours but less than 7 days duration post-injury, or

c) Linear skull fracture.

Moderate head injury prevents military enlistment in the military for the first 12 months following the injury. Candidates can later qualify if a "neurological examination shows no residual dysfunction or complications" (DoD 2010, 44–45).

"Mild head injury" is:

a) Unconsciousness of less than 30 minutes post-injury.

b) Amnesia or disorientation of person, place, or time, alone or in combination, of less than 24 hours post-injury. (DoD 2010, 45)

Mild head injury precludes enlistment in the military for the first month post-injury, but candidates may qualify after 1 month if a "neurological examination shows no residual dysfunction or complications" (DoD 2010, 45).

B. U.S. Department of Veterans Affairs

The VASRD details requirements for assigning a rating between 0% and 100% to a veteran's conditions (DVA 1992). This assignment of a rating is done to reflect the extent to which a condition impairs a veteran's ability to work (CBO 2014).

1. Skull

Ratings are given for the skull if part of the skull is missing with or without brain protruding from the skull (DVA 2015). If a portion of the skull is missing, but there is no brain displacement, the disability rating reflects the size of the missing skull bone (from 10% to 50%). If the brain protrudes from the skull, the rating is 80% irrespective of missing skull bone size (DVA 2015 code 5296). We consider missing pieces of a skull a significant injury since this requires surgical intervention, an HCC1+ level of care. Brain injuries are rated separately from skull injuries (DVA 2015).

2. Traumatic Brain Injury

The VA rates disability due to TBI differently than a clinical diagnosis. Whereas a physician will classify the severity of TBI based on the GCS and other clinical criteria (see Section 4.3.c), as well as indicate any PCS in the case of mTBI, these terms do not necessarily factor into disability ratings. The VASRD rates disability due to TBI according to the *symptoms and conditions* that it causes rather than the severity of the clinical TBI, which can be a very complex process. Disability ratings for TBI can be thought of as divided into two stages. First, disability is rated due to initial clinical diagnosis of conditions and symptoms:

- *Diagnosed conditions* caused by the TBI: stroke, infection, dementia, seizure, etc.
- *Symptoms:* memory loss, dizziness, headaches, decreased vision, etc.

For example, if a patient is diagnosed with stroke and memory loss due to a TBI, the VASRD will rate disability according to the stroke (diagnosed condition) and memory loss (symptom) conditions regardless of the severity of the TBI.

Second, to take into account residual injury from the TBI that might develop after initial clinical treatment, the VASRD rates TBI disability for residual *undiagnosed* symptoms and conditions under a TBI residuals code. Thus, a TBI disability is rated with two distinct ratings, one for diagnosed conditions and symptoms and one for undiagnosed residual symptoms and conditions. Undiagnosed residual conditions or symptoms are given in the VASRD TBI Residuals Table (Table 5-1):

Table 5-1. VASRD TBI Residuals Table

TBI Residuals Table	
Executive Functions	Neurobehavioral Effects
Judgement	Communication
Social Interaction	Consciousness
Orientation	Subjective Symptoms
Motor Activity	

Both diagnosed and undiagnosed residual symptoms and conditions are then given impairment ratings according to Table 5-2, and the highest rated impairment due to a symptom or condition is then taken as the overall disability rating for the TBI.

Table 5-2. VASRD Level of Impairment Equivalent Ratings

Level of Impairment Equivalent Ratings	
0 – normal	0%
1 – mild	10%
2 – moderate	40%
3 – moderately-severe	70%
Total	100%

6. Assessing Head Injury Significance

In this chapter, we categorize head injuries (i.e., skull fracture and TBI) as different types and then approximate whether $P(\textit{head injury}_{\textit{type}}\ \textit{is significant} \mid \textit{head injury}_{\textit{type}}\ \textit{occurred})$, the probability that a head injury type is significant, given that it has occurred.

A. Overview: HCC Standard of Care to Treat Head Injuries

The following probability expressions are a review of information presented in Cazares et al. (2017). The expression for the probability that a head injury type is significant, given that the injury type occurred, is as follows:

$$P(\textit{head injury}_{\textit{type}}\ \textit{is significant} \mid \textit{head injury}_{\textit{type}}\ \textit{occurred}).$$

We assign the probability that the injury is not significant to 0 if our analysis finds that the medical literature indicates that the standard of care for this injury type is HCC0 *and* this injury type does not result in permanent injury that limits employment or other activities for the rest of an individual's life. That is,

$$P(\textit{head injury}_{\textit{type}}\ \textit{is significant} \mid \textit{head injury}_{\textit{type}}\ \textit{occurred}) = 0.$$

We assign the probability that the injury is significant to 1 when the medical literature suggests that the standard of care for this type of head injury is HCC1+ *or* this injury type results in permanent injury. That is,

$$P(\textit{head injury}_{\textit{type}}\ \textit{is significant} \mid \textit{head injury}_{\textit{type}}\ \textit{occurred}) = 1.$$

In addition, $P(\textit{head injury}_{\textit{type}}\ \textit{is significant} \mid \textit{head injury}_{\textit{type}}\ \textit{occurred})$ for a head $\text{injury}_{\text{type}}$ that includes any causal complication(s) is the product of two expressions that should be evaluated for significance independently:

$$\begin{aligned} &P(\textit{head injury}_{\textit{type}}\ \textit{is significant} \mid \textit{head injury}_{\textit{type}}\ \textit{occurred}) \\ &= P(\textit{complication is significant} \mid \textit{complication occurred}) \\ &\times P(\textit{complication occurs} \mid \textit{head injury}_{\textit{type}}\ \textit{occurred}). \end{aligned}$$

We methodically evaluate head injury type (i.e., skull fracture type then TBI type) significance using HCC standards of care and illustrate this process in a decision flow diagram. Each rectangular box in the decision flow diagram is a head injury type (where "head injury" is either skull fracture or TBI), each of which is discussed in the context of

this framework. The decision flow diagram is broken down into sequential steps, and each new step also includes all preceding steps to logically guide the reader through this framework. We begin our analysis by assessing the significance of "open skull fracture".

B. HCC Standard of Care to Treat Skull Fracture

1. An Open Skull Fracture Is a Significant Injury

An open skull fracture, also referred to as a compound fracture, is a fracture where there is an open wound with the cranial cavity exposed (*Segen's Medical Dictionary* 2018) and a shattering of the bone (MedlinePlus 2018). Open skull fractures often require surgical intervention to remove pieces of bone (debridement) and infection prevention and control with a prescription antibiotic (Valadka 2017, 385). We propose that an open skull fracture is a significant injury. We stop the analysis at this step because debridement and infection prevention and control with a prescription antibiotic are both HCC1+ treatments, regardless of any complications (see Figure 6-1).

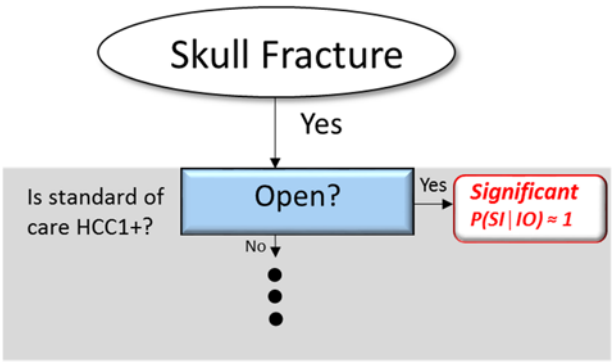


Figure 6-1. Decision Flow Diagram: An Open Skull Fracture Is a Significant Injury

In the first rectangular box (shaded blue) of the decision flow diagram, we consider the HCC standard of care to treat an open skull fracture.

We can now write the following equation:

$$P(\textit{skull fracture}_{\textit{open}}\ \textit{is significant} \mid \textit{skull fracture}_{\textit{open}}\ \textit{occurred}) \approx 1$$

That is, we bin open skull fracture as a significant injury. At this point in the decision flow diagram, open skull fracture is a significant injury, and we are left to evaluate the significance of closed skull fractures.

2. A Depressed Skull Fracture Is a Significant Injury

Depressed skull fractures have bone fragments that are offset from each other and can present as one fragmented piece or multiple fragments (comminuted). We propose that a

depressed skull fracture is a significant injury because, like open skull fracture, it often requires surgical intervention to remove pieces of bone (debridement).[14] A depression of more than 8–10 mm or a depression that is greater than the thickness of the surrounding skull bone will also require surgical intervention (Valadka 2017; Neville 2014), including elevation of the depressed skull to its original position (Masters 1980, 329). Both of these surgical interventions are HCC1+ standards of care (Figure 6-2).

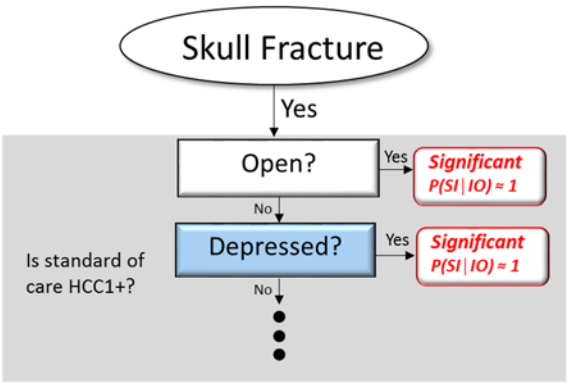


Figure 6-2. Decision Flow Diagram: Depressed Skull Fracture Is a Significant Injury

In the second rectangular box (shaded blue) in the decision flow diagram, we consider the HCC standard of care to treat depressed skull fracture. Debridement and surgical elevation are both HCC1+ standards of care, and we can stop the analysis at this step, regardless of the surgical interventions needed to treat the complications.

$$P(skull\ fracture_{depressed}\ is\ significant \mid skull\ fracture_{depressed}\ occurred) \approx 1$$

At this point in the decision flow diagram, open skull fracture is a significant injury, and depressed skull fracture is also a significant injury. We are left to evaluate the significance of "closed skull fracture, with no displacement of the bone." We next consider a basilar skull fracture.

3. A Basilar Skull Fracture Is a Significant Injury

Basilar fractures are linear fractures in any one of the five bones at the base of the skull (see Figure 3-2). They do not require surgical treatment the vast majority of time, but the seriousness of potential complications necessitates hospitalization for observation (Simon and Newton 2107; Heegaard 2011). The Canadian CT head rule sets to establish CT screening guidelines for patients with minor head injuries. It considers any indication

[14] Note that a skull fracture can present as both open and depressed and, in the literature, skull fractures are sometimes described as "open, depressed" skull fractures. For purposes of our study, we are classifying them as different types of skull fracture because each can be assessed for significance independently.

of a suspected basal skull fracture a "high" risk factor for CT screening, because these patients are "at substantial risk for requiring neurosurgical intervention and we believe that CT is mandatory in these cases" (Stiell 2001, 1394).

We propose that basilar skull fracture is a significant injury due to the need for hospital observation, which we consider an HCC1+ medical treatment, regardless of any complications (see Figure 6-3).

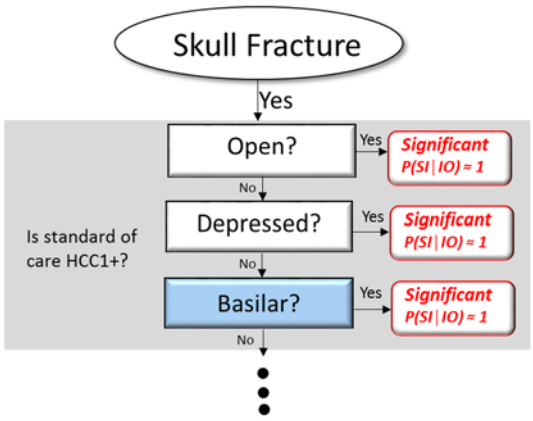


Figure 6-3. Decision Flow Diagram: A Basilar Skull Fracture Is a Significant Injury

In the third rectangular box, shaded blue in the decision flow diagram, we consider the HCC standard of care to treat basilar skull fracture. We can now write the following equation:

$$P(skull\ fracture_{basilar}\ is\ significant \mid skull\ fracture_{basilar}\ occurred) \approx 1$$

That is, we bin basilar skull fracture as a significant injury.

At this point in the decision flow diagram, open skull fracture is a significant injury (see Figure 6-1), depressed skull fracture is a significant injury (see Figure 6-2), and basilar skull fracture is a significant injury (see Figure 6-3). We are left to evaluate the significance of "closed skull fracture, with no displacement of the bone." We next consider linear, location dependent skull fractures.

4. Linear, Location Dependent Skull Fracture Is a Significant Injury

A linear skull fracture is a fracture where there is no bone displacement or "splintering" (Medline Plus 2018). Most linear fractures are not considered significant injuries with the exception of those close to vascular structures (i.e., at or near the meningeal groove or major venous sinuses) (Walls, Hockberger and Gausche-Hill 2018, 361) in the temporal, tempoparietal, and sphenoid regions. We propose that linear, location-dependent (including linear fractures at or near meningeal groove or major venous

sinuses) skull fracture is a significant injury because of increased risk of potentially life-threatening causal complications that have an HCC1+ standard of care. See Figure 6-4.

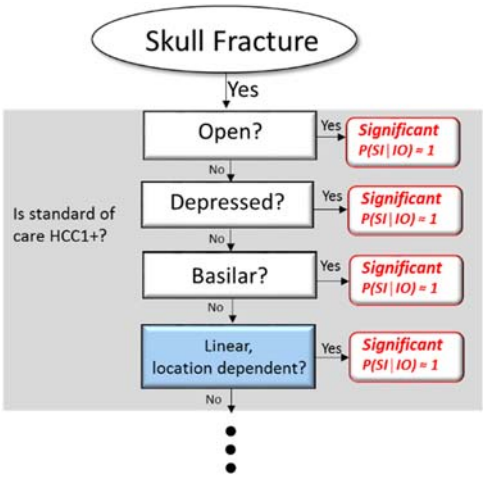


Figure 6-4. Decision Flow Diagram: Linear, Location Dependent Skull Fracture Is a Significant Injury

Linear fractures that occur at or near the middle meningeal artery (temporal or tempoparietal region) can cause either EDH (Kerr 2013, 280; Bond, Viera, and Yates 1999, 3) or traumatic AVF, an irregular connection between an artery and a vein caused by trauma and resulting in an aneurysm (Yu et al. 2016, 792; Stedman 2012). Skull fractures that intersect the meningeal groove in the temporal region are the most fatal as they manifest quickly (Pascual and Prieto 2012,1513).

Fractures that occur at the major venous sinuses can cause potentially fatal hemorrhaging (Bond, Viera, and Yates 1999, 3). Complications from these types of linear skull fractures require significant clinical intervention; therefore, we consider these types of skull fractures to require HCC1+ level of medical treatment.

In the fourth rectangular box (shaded blue) in the decision flow diagram (see Figure 6-4), we consider the HCC standard of care to treat linear, location-dependent skull fracture. We can now write the following equation:

$$P(\textit{skull fracture}_{\textit{linear, location}}\ \textit{is significant} \mid \textit{skull fracture}_{\textit{linear, location}}\ \textit{occurred})$$

$$= P(\textit{complication is significant} \mid \textit{complication occurred})$$

$$\times P(\textit{complication occurs} \mid \textit{skull fracture}_{\textit{linear, location}}\ \textit{occurred})$$

where “complication” can be EDH, AVF, or hemorrhage.

For the first term in the preceding equation, we know that the probability that the complication is significant, given that the complication occurred, is 1 because HCC1+ is the standard of care for each potential complication. Therefore,

$P(\textit{complication is significant} \mid \textit{complication occurred}) = 1.$

For the second term in the equation, we do not know the probability that a complication occurs, given that a linear, location-dependent skull fracture occurred. The literature does not provide enough detail to independently quantify the conditional likelihood of these complications. Therefore, we err on the side of caution and approximate this term as 1:

$P(\textit{complication occurs} \mid \textit{skull fracture}_{\textit{linear, location}}\ \textit{occurred}) \approx 1.$

Multiplying these terms together, we find that we can approximate the probability that linear, location-dependent fracture is significant, given that the linear, location-dependent fracture occurred, as follows:

$P(\textit{skull fracture}_{\textit{linear, location}}\ \textit{is significant} \mid \textit{skull fracture}_{\textit{linear, location}}\ \textit{occurred}) = 1 \times (\approx 1) = \approx 1.$

That is, we bin linear, location-dependent skull fracture as a significant injury.

At this point in the decision flow diagram, open skull fracture is a significant injury (Figure 6-1), depressed skull fracture is a significant injury (Figure 6-2), basilar skull fracture is a significant injury (Figure 6-3), and linear, location-dependent skull fracture is a significant injury (Figure 6-4). This concludes our analysis of the types of skull fractures that have HCC1+ standards of care.

5. Linear Simple Skull Fractures without TBI Are Treated with HCC0

The types of skull fractures not yet considered include skull fractures that are not open, not depressed, not basilar, and not linear, location dependent. The only type of skull fracture that fits these criteria is a simple linear fracture. We define a simple linear fracture as one that is not location dependent.

In general, closed linear skull fractures do not require surgical intervention (Valadka 2017; Neville et al. 2014; Pascual and Prieto 2012). The general consensus among clinicians is the majority of linear fractures are "clinically insignificant" (Smits et al. 2008, 506) unless there is indication of "concussive symptoms or other evidence of mild traumatic brain injury" (Heegaard 2011).

6. Restrictions to Life Caused by Linear Skull Fracture, Simple

In the previous section, we evaluated skull fracture types that are significant injuries because they have an HCC1+ standard of care. For skull fracture types that have an HCC0 standard of care, DoDI 3200.19 specifies a second way in which an injury can be considered significant: the injury results in death or "physical damage … that … restricts the employment or other activities of the person for the rest of his or her life" (DoD 2012, 14).

Linear, simple skull fractures without TBI have an HCC0 standard of medical care. DoDI 6130.03 (DoD 2010) establishes medical standards for new recruits in the military Services. For this project, we approximate that failure to meet pre-enlistment standards in the U.S. military is an adequate surrogate for "restrictions on employment." Per DoDI 6130.03, linear skull fracture prevents military enlistment for the first 12 months following the injury. However, candidates can later qualify if a "neurological examination shows no residual dysfunction or complications" (DoD 2010, 45). The VASRD does not rate linear skull fracture as a disability, but brain injuries receive a separate disability rating.

For our analysis, we consider a "non-rating" from the VASRD as a proxy for "restrictions on employment," per DoDI 3200.19 language (DoD 2012). Therefore, linear, simple skull fracture in the absence of other complications (including TBI) should *not* be considered significant:

$$P(\textit{skull fracture}_{\textit{liner, simple}}\ \textit{is not significant} \mid \textit{skull fracture}_{\textit{linear, simple}}\ \textit{occurred}) = 0$$

Figure 6-5 shows the final step in the skull fracture branch of the decision flow diagram for linear, simple skull fractures without TBI. We are left to consider (1) linear, simple skull fractures with possible TBI and (2) TBI injuries independent of skull fracture.

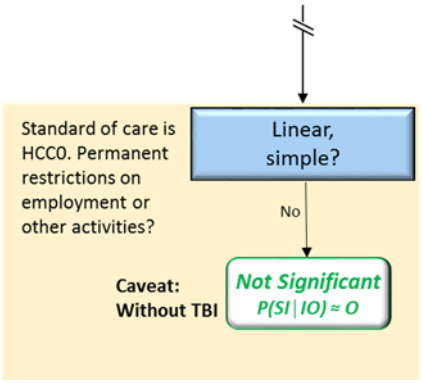


Figure 6-5. Decision Flow Diagram: Linear, Simple Skull Fracture Is Not a Significant Injury

C. HCC Standard of Care to Treat Traumatic Brain Injury

1. Severe TBI Is a Significant Injury

We propose that severe TBI is a significant injury due to increased mortality and increased risk of causal complications, generally focal injuries that have an HCC1+ standard of care (see Figure 6-6).

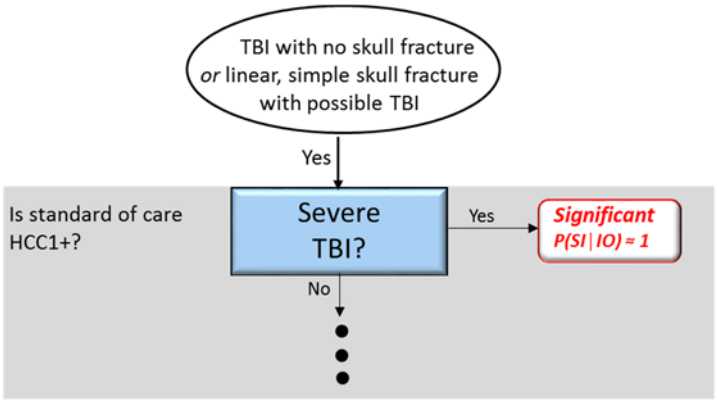


Figure 6-6. Decision Flow Diagram: Severe TBI Is a Significant Injury

In the first rectangular box (shaded blue) of the TBI branch of the decision flow diagram, we consider the HCC standard of care to treat severe TBI. Patients with severe TBI require hospitalization with acute trauma care to stabilize blood pressure, oxygen levels, and respiration (Carney et al. 2017; NAMET 2016, 284).

Increased mortality can be linked to hypotension (low blood pressure, <90 mm Hg) in patients with severe TBI caused by resuscitation efforts. In a retrospective study of 717 patients with severe TBI, hypotension occurred in 34.6% of these patients, which correlates with a 150% increase in mortality (Chesnut et al. 1993, 216). Management of potential focal injuries includes monitoring and managing ICP by stopping bleeding or fluid drain within the cranium (Pascual and Prieto 2012). Of these same 717 patients, 72% had a craniotomy to alleviate ICP and reduce the risk of causal complications (Bell et al. 2008, 2). Patients with severe TBI have a greater risk of other complications, including but not limited to, intracerebral hemorrhage and contusion, epidural hematoma, SDH, SAH (Pascual and Prieto 2012 1514), and dementia (Elder 2015).

We can now write the following equation:

$$P(TBI_{severe}\ is\ significant \mid TBI_{severe}\ occurred)$$

$$= P(complication\ is\ significant \mid complication\ occurred)$$

$$\times P(complication\ occurs \mid TBI_{severe}\ occurred)$$

where "complication" can be intracerebral hemorrhage and contusion, epidural hematoma, SDH, and SAH.

For the first term in the equation above, we know the probability that the complication is significant, given that it has occurred, is 1 because the standard of care for the above complications is HCC1+ (see Section 4.3). Therefore,

$$P(complication\ is\ significant \mid complication\ occurred) = 1.$$

For the second term in the equation, we do not know the probability that a complication occurs, given that severe TBI occurred. The literature does not give enough detail to independently quantify the conditional likelihood of these complications. Therefore, we err on the side of caution and approximate this term as 1:

$$P(\textit{complication occurs} \mid \textit{TBI}_{\textit{severe}}\ \textit{occurred}) \approx 1.$$

Multiplying these terms together, we find that we can approximate the probability that severe TBI is significant, given that that severe TBI occurred, as follows:

$$P(\textit{TBI}_{\textit{severe}}\ \textit{is significant} \mid \textit{TBI}_{\textit{severe}}\ \textit{occurred}) = 1 \times (\approx 1) = \approx 1$$

2. Moderate TBI Is a Significant Injury

Like severe TBI, moderate TBI clinical treatment is based upon managing symptoms of cerebral, blood flow, ICP, and any seizures that develop (Swanson et al. 2017; NAMET 2016, 284). We propose that moderate TBI is a significant injury due to increased risk of causal complications, generally focal injuries that have an HCC1+ standard of care (see Figure 6-7).

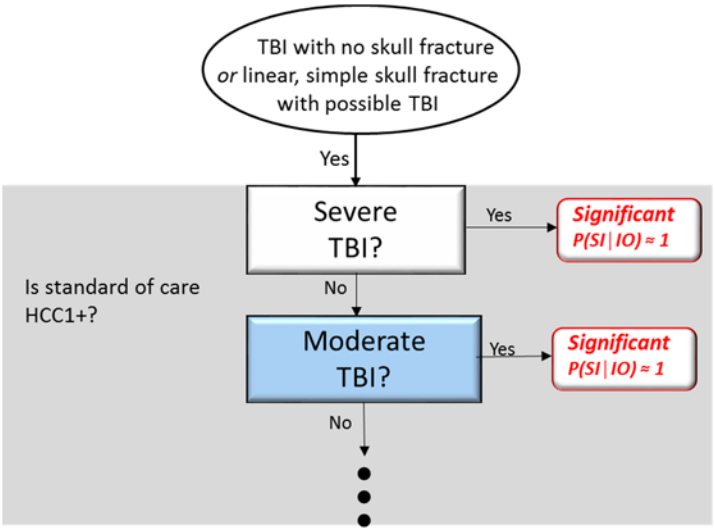


Figure 6-7. Decision Flow Diagram: Moderate TBI Is a Significant Injury

In the second rectangular box (shaded blue) of the TBI branch of the decision flow diagram, we consider the HCC standard of care to treat moderate TBI. Similar to patients with severe TBI, patients with moderate TBI have a greater risk of causal complications, including but not limited to intracerebral hemorrhage and contusion, epidural hematoma, SDH, and subarachnoid hemorrhage. Therefore,

$$P(\textit{TBI}_{\textit{moderate}}\ \textit{is significant} \mid \textit{TBI}_{\textit{moderate}}\ \textit{occurred})$$

$$= P(\textit{complication is significant} \mid \textit{complication occurred})$$

$\times P(complication\ occurs \mid TBI_{moderate}\ occurred)$

where "complication" can be focal injuries, including intracerebral hemorrhage and contusion, epidural hematoma, SDH, and subarachnoid hemorrhage.

For the first term in the equation above, we know the probability that the complication is significant, given that it has occurred, is 1 because the standard of care for the focal injuries listed above is HCC1+ (see Section 4.3). Therefore,

$P(complication\ is\ significant \mid complication\ occurred) = 1.$

For the second term in the equation, we do not know the probability that a complication occurs, given that moderate TBI occurred. The literature does not give enough detail to independently quantify the conditional likelihood of these complications. Therefore, we err on the side of caution and approximate this term as 1:

$P(complication\ occurs \mid TBI_{moderate}\ occurred) \approx 1.$

Multiplying these terms together, we find that we can approximate the probability that severe TBI is significant, given that that severe TBI occurred, as follows:

$P(TBI_{moderate}\ is\ significant \mid TBI_{moderate}\ occurred) = 1 \times (\approx 1) = \approx 1$

3. mTBI with PCS Is a Significant Injury

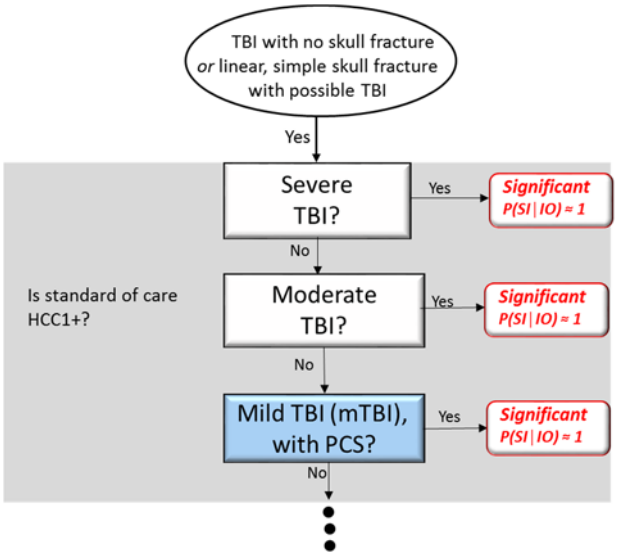


Figure 6-8. Decision Flow Diagram: mTBI with PCS Is a Significant Injury

In the third rectangular box (shaded blue) of the TBI branch of the decision flow diagram (see Figure 6-8), we consider the HCC standard of care to treat mTBI with PCS. Patients with mTBI with PCS have persistent cognitive symptoms that can last beyond to the typical 7–10 day period of uncomplicated mTBI recovery. PCS is ill-defined clinically,

heterogeneous, and unable to be predicted *a priori*. As stated in Chapter 3, PCS symptoms include, but not limited to, dizziness, blurred vision, difficulty concentrating, emotional problems, and memory problems. PCS symptoms can last for variable periods of time after the initial mTBI up to several months McCrea et al. 2013; Eisenberg, Meehan, and Mannix 2014). If PCS symptoms do not resolve within three months, patients are referred to an mTBI clinical specialist for further treatment (VA and DoD 2016). We propose that mTBI with PCS is a significant injury due to the necessity of specialized clinical care to treat PCS symptoms and we consider such care to have an HCC1+ standard.

We can now write the following equation:

$$P(TBI_{mild\ with\ PCS}\ is\ significant \mid TBI_{mild\ with\ PCS}\ occurred)$$

$$= P(complication\ is\ significant \mid complication\ occurred)$$

$$\times P(complication\ occurs \mid TBI_{mild\ with\ PCS}\ occurred)$$

Where "complication" is PCS.

4. mTBI, Uncomplicated Is a Significant Injury

In the previous section, we evaluated TBI types that are significant injuries because they have an HCC1+ standard of care. For TBI types that have an HCC0 standard of care, we assess significance by evaluating if the injury results in death or "physical damage … that … restricts the employment or other activities of the person for the rest of his or her life" (DoD 2012, 14). Mild TBI, uncomplicated, that is, an mTBI without any PCS, is the only TBI type that fits this criterion.

DoDI 6130.03 (DoD 2010) establishes medical standards for new recruits in the military Services. For this project, we approximate that failure to meet pre-enlistment standards in the U.S. military is an adequate surrogate for "restrictions on employment." Per DoDI 6130.03, "mild head injury," which we equate with mTBI, prevents military enlistment for the first month following the injury. However, candidates may later qualify if a "neurological examination shows no residual dysfunction or complications" (DoD 2010, 45).

The established clinical practice for treating mTBI, uncomplicated, involves physical and cognitive rest (Stillman et al. 2017; Renjilian and Grady 2017; VA and DoD 2016; Levin and Diaz-Arrastia 2015), an HCC0 standard of care, and mTBI symptoms typically resolve within 7–10 days. Despite this clinical standard in the literature, recovery from uncomplicated mTBI can be very variable (Levin and Diaz-Arrastia 2015), with some patients requiring weeks for symptoms to resolve. It is therefore difficult to diagnose and prognosticate in the acute phase of mTBI whether an mTBI will resolve in 7–10 days or persist. Also, metrics for a clearly defined decision for "recovery" from mTBI are sorely lacking (see Appendix A), and the military is still looking for validated and trusted metrics

to clarify the return-to-duty decision (Radomski et al. 2018). Mild TBI has a substantial effect on the quality of life of patients within the first year after injury (Chiang et al. 2016), including an effect on employment, and research is ongoing to try to understand factors of mTBI that can affect quality of life. Finally, new mTBI research is discovering that in cases of uncomplicated mTBI, there is significant damage to the brain at the cellular and molecular level (see Appendix A). All these factors above combine to cast doubt on clinician's current clinical ability to adequately diagnose, predict the outcome of, and understand if a patient has sufficiently recovered from an uncomplicated mTBI. With this in mind, IDA has chosen to be conservative and treat uncomplicated mTBI as a significant injury. Therefore, uncomplicated mTBI with or without simple linear skull fracture should be considered significant. Therefore,

$$P(TBI_{mild,\ uncomplicated}\ is\ significant \mid TBI_{mild,\ uncomplicated}\ occurred) = 1$$

Figure 6-9 shows the final step in the TBI branch of the decision flow diagram for mTBI, uncomplicated. Therefore, *all* TBIs are significant injuries.

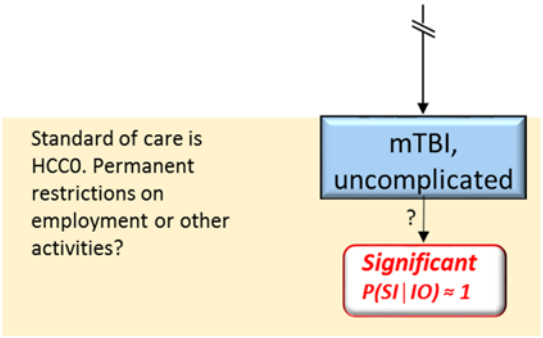


Figure 6-9. Decision Flow Diagram: mTBI, Uncomplicated Is a Significant Injury

7. Computational Modeling of Head Injuries Caused by NLWs

A. Evidence of NLW-Induced Injuries to the Head

Given the LASD and NIJ blunt-impact field use data described in Section 2.B, we find there is a need to model impacts to the head. We have also concluded that skull fractures can be distinguished into significant and nonsignificant depending on where they occur on the skull and if they are open or depressed fractures. We have found that mTBI cannot at this time be parsed into significant and nonsignificant based on physical features, and we consider all mTBI to be significant. Below, we discuss the capability of existing models to meet these needs and challenges associated with modeling the necessary attributes of head injuries.

B. Advanced Total Body Model

The Advanced Total Body Model (ATBM) is a collection of finite-element models (FEMs) used to predict the likelihood of blunt-impact NLW injuries. The ATBM was funded by JNLWD and developed by L3. ATBM includes a finite-element model (FEM) of the head, as well as injury models (risk) curves for both skull fracture and concussion. In addition, the ATBM contains injury models for head contusion, SDH, and SAH (Shen et al. 2012). The ATBM FEM is used to predict internal metrics such as stresses, strains, and displacements of organs during an impact. Experimental data, for which injury outcomes are known, are simulated, to identify risk curves associated with those metrics. The threshold for injury occurrence is set to 50% on the risk curve. New rounds and conditions are then simulated, and calculated metrics are compared to the threshold. One of the major limitations of such models is the availability of relevant, detailed injury data with which to identify these thresholds.

1. Skull Fracture

In the case of skull fracture, sufficient data exist in the literature to allow development of a reasonably accurate threshold of stress associated with fracture. IDA's analysis concludes that stress is an appropriate predictor for bone fracture (skull and otherwise), following many literature results and comprehensive analysis of existing data by L3 (Shen et al. 2012; Wood 1971). Wide error bars are associated with the prediction, however, and it has not been validated against an independent data set. But we believe that the foundation of the model is sound, and with further calibration and validation of the model, such

predictions can be used with confidence. Error bars associated with the risk curve include error associated with the prediction of stress values, inherent variability in the subjects, and statistical uncertainty based on small sample sizes. The 50% threshold effective stress in the cranial bone that is associated with skull is currently estimated to be 93.4 MPa, with a 95% confidence band between 85.4 and 104.1 MPa.

A separate model has been demonstrated within ATBM that can be used to qualitatively distinguish between linear and comminuted (depressed) skull fractures (a valuable distinction based on the results of the current analysis). This implementation replaces the elastic model describing the skull tables and diploe (the spongy cancellous bone separating the inner and outer layers of the cortical bone of the skull) with an elastic failure model. When the effective plastic strain exceeds a certain threshold, the material is modeled as a fluid.

As shown in Figure 7-1 and Figure 7-2, different patterns of crack growth can be modeled. The simulation conditions were chosen to match experiments impacts on the skull, using a projectile known as the waterball to compare model and experimental results. The crack associated with Figure 7-1 was described by the original experimenter (Mickiewicz, Lewis, and Clare 1975) as a "hairline fracture 5.0 cm long through right parietal bone" and that associated with Figure 7-2 as a "massive comminuted, depressed fracture of left side of skull. Cracks extend through left orbit and nasal bones and across the occipital bone." Final images from the original source are available, but the quality is not sufficient to visually compare the experiment and simulation.

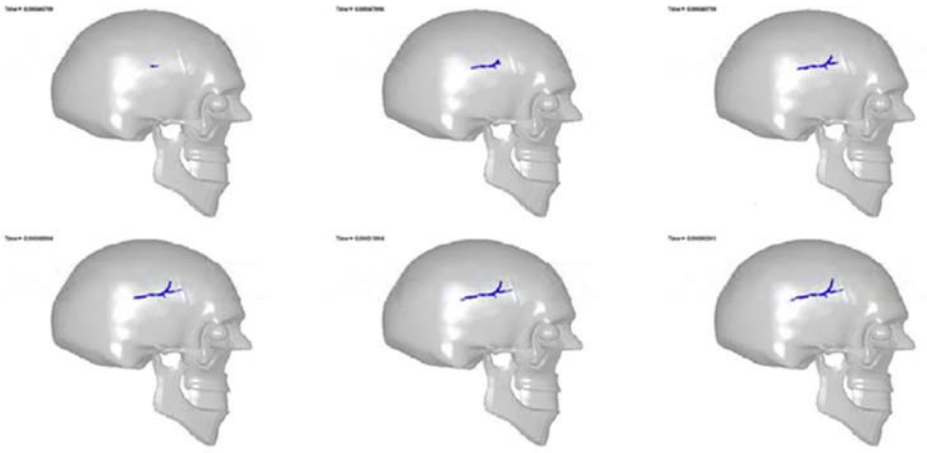


Figure 7-1. Crack Propagation of Right Parietal Bone under the Impact of a Waterball at *v* = 45 m/s as Modeled by L3/ATBM (Shen et al. 2012). Crack initiated at time 0.46 ms (displayed time step is 0.02 ms). This pattern of propagation qualitatively compared favorably to the reported experimental crack.

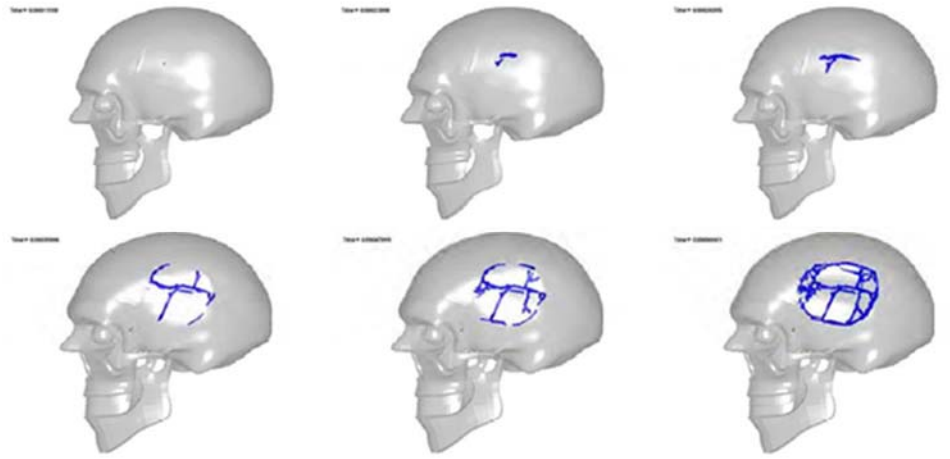


Figure 7-2 Left Parietal Bone Crack Propagation under the Impact of a Water Ball at Velocity 61.4 m/s at 0.11, 0.24, 0.26, 0.40, 0.48, and 0.8 ms

A single experiment producing a penetrating skull (Shen et al. 2012 using data from Hodgson and Thomas 1972) was also modeled and demonstrated qualitative agreement. This feature of the model shows promise but has not been validated at all. (Some aspects of the model response validation of the original head model may be relevant, but that requires a separate analysis). The three simulations described in Shen et al. (2012) are the extent of effort in this area.

2. Brain Injuries

ATBM includes risk curves for four brain injuries: concussion (a.k.a. mTBI), head contusion, SDH, and SAH. Besides the single reported concussion (Hubbs and Klinger 2004), there is no evidence one way or the other that blunt-impact NLWs cause these injuries, nor is there evidence one way or the other that other brain injuries described in previous sections are not caused by NLWs. These four injuries were included based on non-human primate testing reported in Vorst et al. (2007) and performed by the Japanese Automobile Research Institute (JARI). Test subjects were struck by a padded impactor with varied duration and intensities and from the front, back and side. Data include acceleration waveforms, peak linear and angular acceleration of the head, and injury outcomes. Vorst et al. (2007) conclude that peak angular acceleration of the head combined with the cumulative number of impacts is the best predictor for these four injuries. ATBM uses the developed thresholds, scaled to human, with number of impacts set to one (Shen et al. 2012).

A FEM is not needed to predict global quantities such as acceleration; if such quantities are actually the best predictors, then the already-developed ATBM head model is not necessary for this application. Brain injury is an active area of research, however, and there have been many advancements made since 2007. It is almost certainly the case

that tissue-level stresses or strains in the brain are related to brain injury. But without experimental data to support development of a risk curve, the detailed resolution provided by a FEM cannot be used. Here, we briefly explore the data set underlying ATBM's current risk curves and some of the new data, as well as their relevance to NLW impacts. Finally, we assess modeling needs in light of what is currently known about brain injuries.

In the 1950's researchers at Wayne State (Williams and Lissner 1992) inducing traumatic brain injury in rats identified the relationship between acceleration and duration of insult in what is known as the Wayne State Tolerance Curve (see Figure 7-3).

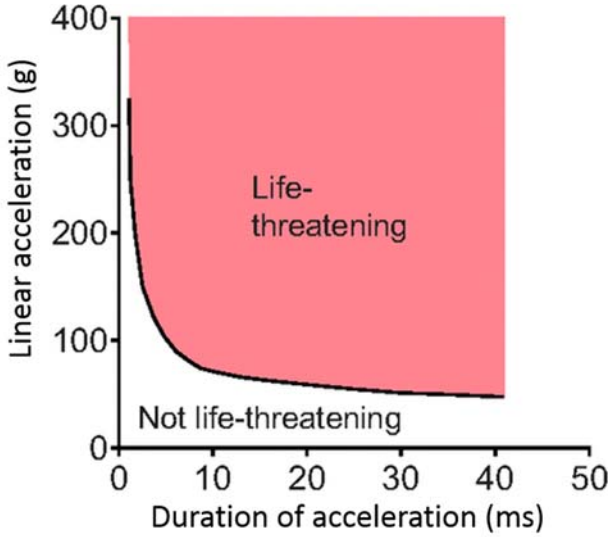


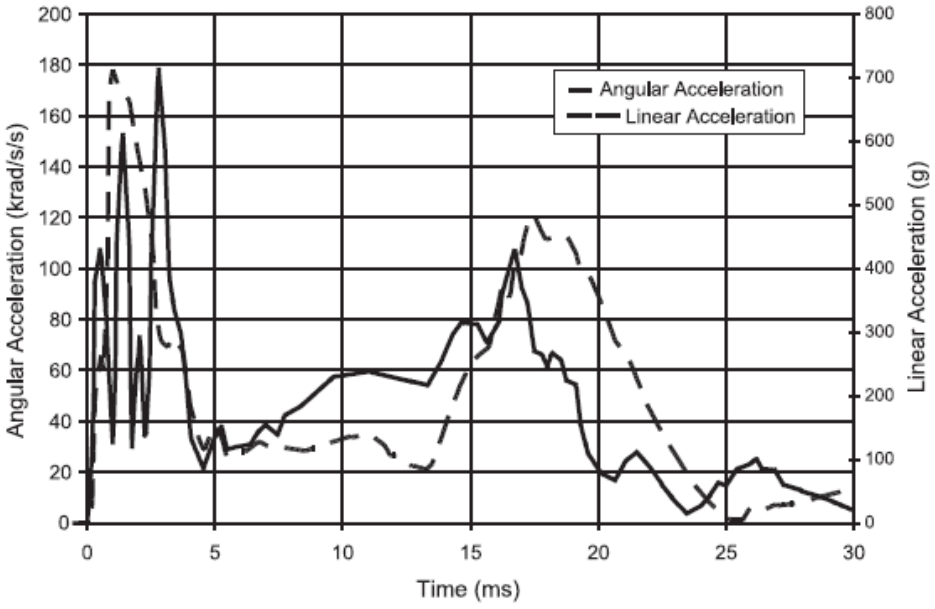
Figure 7-3. Wayne State Tolerance Curve

Since then, many researchers have developed more nuanced relationships between predictor variables and specific TBIs. Much effort has gone into understanding the mechanism of mTBI. The STC is included here because the relationship between amplitude and duration of the insult is fundamental to understanding brain injury. When studying a certain type of impact with a consistent relationship between amplitude and duration (e.g., automotive conditions), amplitude of the acceleration (linear or rotational) alone may be sufficient to distinguish injurious from non-injurious conditions. When using that threshold with another waveform (e.g., blunt-impact NLW conditions), one must remember to consider the effects of duration as well.

a. Mild Traumatic Brain Injury

IDA does not have access to the JARI database of non-human primate impacts used by Vorst et al. (2007). A sample acceleration curve from that source is displayed in Figure 7-4. Subsequent analyses of the database report that peak values of translation acceleration

were between 185 and 1282 g, and angular acceleration peak values were from 5762 to 51253 $\mathrm{rad/s^2}$, over a duration of 2.4 to 11.7 ms (Antona-Makoshi 2013).



Source: Vorst et al. (2007).

Note: The acceleration waveforms exhibit two peaks. A short-duration peak was caused by the initial impact, followed by a longer duration lower intensity second peak.

Figure 7-4. Sample Angular and Linear Acceleration Waveforms

Table 7-1 shows the conclusions drawn from Vorst et al.'s (2007) analysis. The authors note that they find a higher threshold than a similar analysis of non-human primates from Pellman et al. (2003): 10% risk at 9 and 13 krad/s^2 for concussion and SDH, respectively, compared with a reconstruction of head impacts in football by 5 krad/s^2 for concussion. These are likely the thresholds used in ATBM, but the reported regressions do not relate directly to these results and have not been explained by L3.

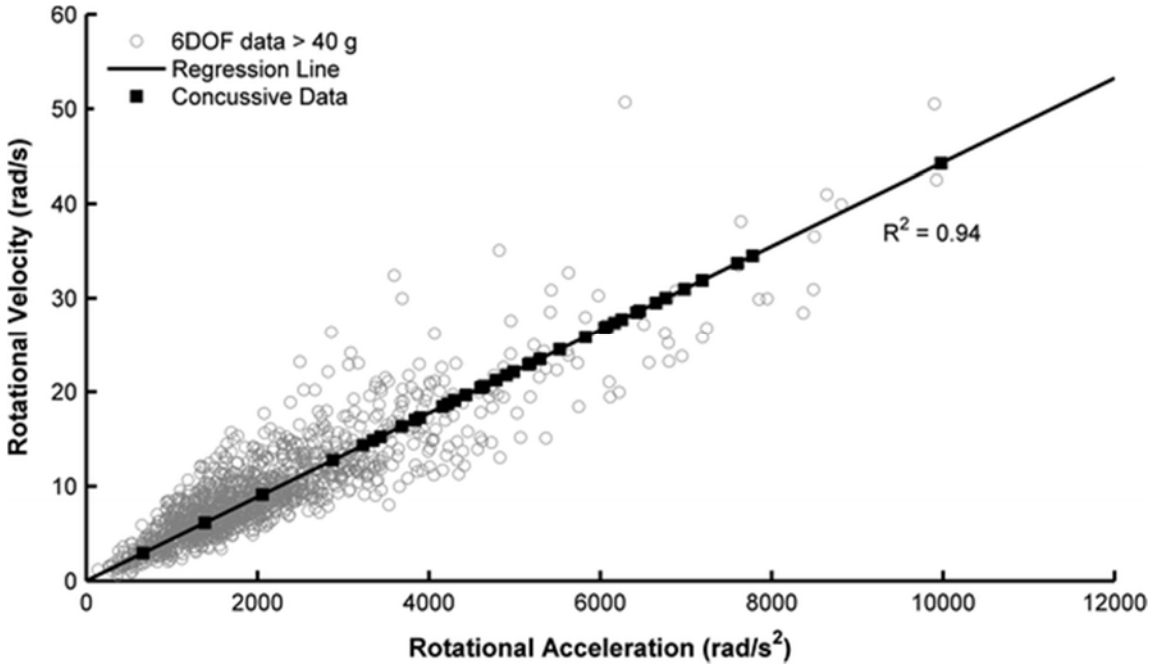
Table 7-1. TBI Prevention Criteria Based on Mean Condition at 10% Probability of Injury to Japanese Monkey and Scaled to Man

Injury	Correlate	Japanese Monkey	Man
Concussion	$\Omega_{max}\ N_f^{0.84}$	<69 krad/s/s	<13 krad/s/s
SAH	$\Omega_{max}\ N_f^{0.70}$	<160 krad/s/s	<30 krad/s/s
Contusion	$\Omega_{max}\ N_f^{0.35}$	<160 krad/s/s	<30 krad/s/s
SDH	$\Omega_{max}\ N_f^{0.60}$	<280 krad/s/s	<53 krad/s/s

Source: Vorst et al. (2007).

b. Football

More recent analyses such as Rowson et al. (2012) using data from instrumented football helmets establish the 10% risk of concussion at 5.26 krad/s^2 and also display the relationship between peak angular acceleration and peak angular velocity of the head (i.e., taking into account the duration of impact). The football impacts all lie on a line, with a slope of approximately 4.4 ms (the approximate duration of impact from beginning to peak). On average, we can assume that all the instrumented data from football impacts have a similar waveform, with an average duration close to the slope. Because the impacts are all so similar, it may be possible to develop a threshold based on only one dimension (angular acceleration).

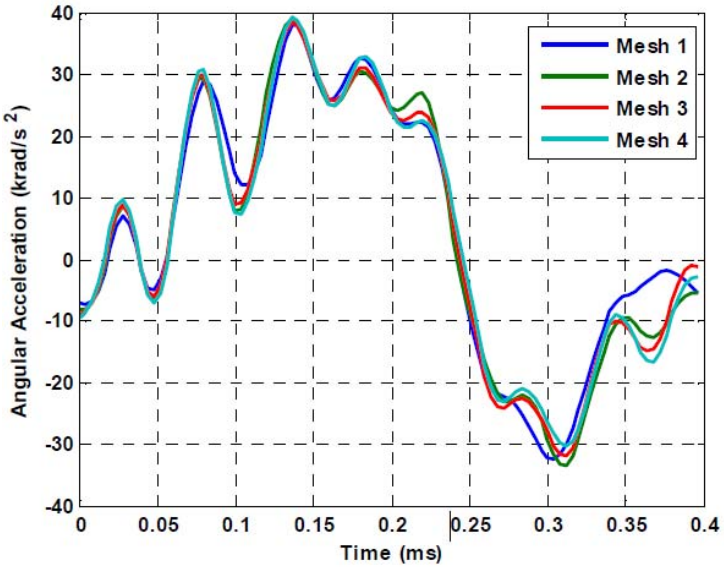


Source: Rowson et al. (2012).

Figure 7-5. Linear Regression Relating Peak Rotational Acceleration to Peak Rotational Velocity for 1285 Impacts Recorded Using the 6DOF Measurement Device That Had Peak Linear Accelerations Greater Than 40 g. Using this model, rotational velocities were estimated for concussive impacts recorded using the HIT System.

c. Relevance of Existing Data to NLW Impacts

Can thresholds developed from either of these types of data sets be used to predict the likelihood of brain injury from NLW-like impacts? At this time, IDA only has access to a single trace of a simulated impact that is depicted in Figure 7-6 (Shen et al. 2012). This trace, which was used for mesh verification testing of ATBM, represents a 20.5 g M1052 impacting the forehead at 80 m/s. The peak angular acceleration seen is ~40 krad/s^2, which is greatly in excess of most of the concussion (or other head injury) thresholds established in the literature.



Source: Shen et al. (2012).

Note: The modeled round was a 20.5 g M1052 impacting the forehead at 80 m/s. The peak angular acceleration seen is ~40 krad/s^2 in excess of most of the concussion (or other head injury) thresholds established in the literature, but the duration is ~5% of that in either the JARI database, or recorded by the HITS system.

Figure 7-6. Reported Time History for Angular Acceleration Performed for ATBM Mesh Verification Testing

Recall, however, that the upper bound of the rate of concussions is estimated by field data to be less than 1% *given* a hit to the head. We do not know how representative of a real hit this particular shot is. But there is substantial evidence regarding the effect of duration on brain injury, and the paradox between a predicted angular acceleration that far exceeds the nominal threshold and the observed rate in the field calls into question the validity of using the JARI data set for an NLW application The duration of the NLW hit is ~5% of that in either the JARI database or recorded by the HITS system. We conclude that a threshold that combines angular acceleration with duration is needed or an angular acceleration threshold must be set using NLW-like experimental conditions; we believe that such a threshold would be significantly higher than that found in any of the sources discussed in this chapter. At this time, we conclude that the ATBM cannot be used to predict brain injuries.

8. Findings and Recommendations

Figure 8-1 shows the results of our analysis, which are summarized in the findings and recommendations that follow.

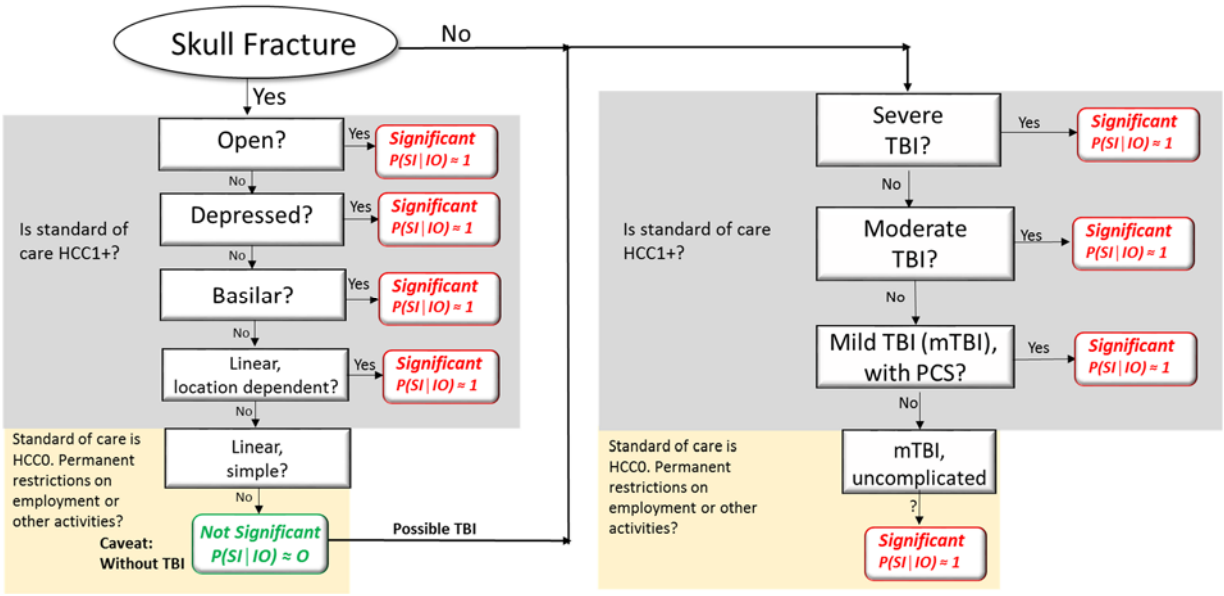


Figure 8-1. Classifying Head Injuries (skull fractures and TBI) as Significant Based on Skull Fracture Type or TBI Type

A. Findings

- Available blunt-impact head trauma data are from motor vehicle accidents, falls, sports injuries, bicycle accidents, pedestrian accidents, and assaults (Stiell 2001), all of which have different injury mechanisms than blunt-impact NLWs. Our analysis utilizes all data regardless of injury mechanism.
- The medical literature does not study skull fracture in isolation, and the majority of skull fracture data are from traumatic brain injury studies.
- Linear fractures are the most prevalent skull fracture, occurring in 70%–80% of all reported cases (Oehmichen 2006). Of those linear fractures, we can determine types that are significant, but the incidence of these types is unclear.
- Currently, no objective metrics exist to gauge and compare recovery from TBI.

- Treatments and outcomes of mTBI are heterogeneous among patients, which is because it is generally unknown how the applied forces to the head cause specific brain injuries and how individual patient factors contribute to recovery.
- The Glasgow Coma Scale, the Glasgow Outcome Scale, and the Glasgow Outcome Scale-Extended are flawed, subjective metrics currently used to assess mTBI injury and predict outcome in the civilian world.
- The flawed nature of these tests makes the return-to-duty and duty-readiness decision after mTBI still a major concern for DoD (Radomski et al. 2018).
- Mild TBI damage to the brain is now thought to be on the cellular and molecular level and cannot be detected using current imaging diagnostics (Huang, Risling, and Baker 2016).
- Fluid-based biomarkers are now starting to be validated in the clinic for their diagnostic value for mTBI. Several candidate biomarkers have gone through some clinical assessment and have been shown to have diagnostic value. While this development is encouraging, there is a need to develop larger panels of biomarkers that are capable of both diagnosing and stratifying mTBI.
- Since mTBI is so heterogeneous and ill-defined clinically, IDA cannot define attributes to predict a nonsignificant, uncomplicated mTBI from a significant mTBI with long-term cognitive impairment or post-concussive symptoms.
- The ATBM includes a FEM of a head and an injury model for skull fracture, including location of fracture and distinction between linear and depressed skull fractures. Error on the predictions has not yet been adequately quantified, but relative results can be used in design stages of weapons.
- While the ATBM includes several brain injury models, we conclude that at this time, the ATBM cannot be used to predict brain injuries.

B. Recommendations

Based on our findings, we make the following recommendations for NLW developers:

- Classify the following skull fracture and TBI types as significant because the medical treatment for the injuries or the complications have HCC1+ standards of care:
  - Skull fracture types:
    - Open skull fracture
    - Depressed skull fracture

    - Basilar skull fracture
    - Linear, location dependent (including linear fractures at or near meningeal groove or major venous sinuses)
  - TBI types:
    - Severe TBI
    - Moderate TBI
    - mTBI with PCS
- Classify the following skull fracture type as not significant because the literature suggests HCC0 standard of care, with low likelihood of permanent disability:
  - Linear, simple skull fracture with no TBI.
- Classify the following TBI type as significant because, although the medical treatment is an HCC0 standard of care, the permanent disability cannot be adequately assessed at this time.
  - mTBI, uncomplicated
- Until biomarker research reaches a maturity where mTBI attributes are sufficiently validated and mTBI can be diagnosed, stratified, and outcomes predicted, all mTBI should be classified as significant.
- With the exception of linear, simple skull fractures with no TBI, the current approach of treating blunt force head trauma as significant should continue.
- Future study of permanent injury from mTBI should closely follow state-of-the art fluid biomarker research as a metric to diagnose, guide treatment for, and predict outcomes of mTBI. A large panel of biomarkers will be needed to capture the subtle differences between individual mTBI cases and predict their outcome.
- For skull injury, continue investment in validation and uncertainty quantification of the ATBM head FEM and skull fracture injury models.
- For brain injury, an update of the ATBM injury model for brain injuries is necessary, but may require additional fidelity in the FEM. We recommend waiting for further developments in medical research before investing in an update. Extrapolation of TBI mechanisms and thresholds from medical research to NLW regimes must be done with care.

Appendix A.
Biomarkers as Attributes of mTBI

This appendix serves as a primer for state-of-the-art research in using fluid biomarkers to diagnose, guide treatment for, and predict outcome of mTBI. We also assess how likely these research efforts will be successful in developing biomarkers for mTBI or post-concussive symptoms in the near term and far term.

Fluid Biomarkers as Attributes of mTBI

No Attributes to Accurately Predict HCC Level of Care, Outcome, or Impact to Quality of Life

As discussed in Section 4.3, the treatments and outcomes of mTBI are heterogeneous among patients because it is generally unknown how the applied forces to the head cause specific brain injuries and how individual patient factors contribute to recovery. Specifically, there are no objective metrics that can be used to gauge and compare recovery from TBI (Sandsmark 2016; Meehan and Mannix 2018). To develop objective attributes of mTBI, it will be necessary to develop fluid molecular or imaging biomarkers to diagnose and predict outcomes for mTBI.

Definition of Fluid Biomarker and Desired Characteristics of mTBI Biomarkers

A fluid biomarker is a molecule (e.g., a protein, DNA, RNA, or metabolite) that is measured in a sample of biological fluid whose measure relates to a physiological or pathological process. Current validated medical biomarkers include cholesterol level in blood for risk of arteriosclerosis and blood sugar level for risk of diabetes. A desired fluid biomarker for would have the following characteristics:

- Its measure relates to the physiological or pathological process of mTBI.
- It must be sampled at the appropriate time after initial mTBI injury.
- It must be able to be sample reliably and easily from a biological fluid of a patient.
- A candidate mTBI should be stable over time, reproducible, and thoroughly validated.

For mTBI, the physiological or pathological processes are complex (see Chapter 3). mTBI from blunt-impact to the head is believed to proceed through three stages—early,

intermediate, and late. These stages are characterized by cell damage due to ischemia, neuroinflammation due to disruption of the blood-brain barrier, and neuronal rewiring, respectively (Algattas and Huang 2014). Current research seeks to develop candidate biomarkers for all three of these stages of mTBI damage (Zetterberg and Blennow 2016). An ideal mTBI biomarker or set of biomarkers should be able to correlate with these phases of damage to become an attribute that can predict severity and outcome.

Due to the hierarchy and temporal nature of the damage in mTBI pathophysiology, timing of sampling for biomarkers is crucial. Appropriate sampling of the desired biomarker at a known time post-injury must be performed to capture that marker during the appropriate time in the damage process (Zetterberg and Blennow 2016).

The potential biomarker must be sampled from an appropriate fluid. Since the cerebrospinal fluid (CSF) is known to be in contact with the brain and exchanges metabolites and other molecules with the brain (Zetterberg and Blennow 2016), some researchers have proposed that the CSF will be the best source of mTBI biomarkers. Other biofluids like blood or saliva reside outside the blood-brain barrier and are less likely to be in contact with the brain. But because blood has the advantage of being easily sampled, much ongoing research searching for blood-based biomarkers of mTBI (Mondello, Maas, and Buki 2017).

TBI Fluid Biomarkers in Clinical Practice

TBI Diagnosis

Several proteins have been identified in clinical research to be signs of neural cell damage associated with TBI or mTBI. Most of these markers have been identified as diagnostic markers that are beginning to be used in civilian clinical settings to diagnose and distinguish mTBI from cases of mTBI with intracranial injury visible on imaging methods (subdural or epidural hematoma, subarachnoid hemorrhage, or edema). Table A-1 summarizes these candidate biomarkers and their appropriateness for clinical application.

Table A-1. Summary of Candidate Biomarkers

Biomarker	Location	Function/pathogenic process	Clinical Application		Comment
			Diagnosis	Prognosis	
UCH-L1	Neuronal cell body	Indicator of neuronal damage or death	Yes	Yes, for severe TBI	FDA-approved diagnostic
NSE	Neuronal cytoplasm	Released from damaged axons.	Not clear	Not clear for severe TBI No for mTBI	
pNF-H	Axon	Component of axonal cytoskeleton.	Not clear	Not clear	
Tau	Axon	Indicator of axonal injury	No	Not clear for severe TBI or mTBI	
S100B	Astroglial cells		Yes	Yes for severe TBI No for mTBI	In clinical trials
GFAP	Glial filaments and Astrocytes	Cytoskeleton support	Yes	Yes for both severe TBI and mTBI	FDA-approved diagnostic

S100B, GFAP, and UCH-L1 are the most studied and most promising biomarkers in diagnosing injury due to mTBI. Even though it has not been approved by FDA for this purpose, S100B has been introduced into some clinical guidelines in mTBI diagnosis (Jagoda et al. 2008; Unden, Ingebrigtsen, and Rommer 2013). These recommendations are based on limited clinical study and on clinical judgement of panels such as the American College of Emergency Physicians. Note, however, S100B has been shown in several studies to predict visible intracranial damage with sensitivities in the range of 75% to 100%. Similarly, GFAP levels in serum have also shown to be able to distinguish TBI patients with and without intracranial lesions on CT scans with high sensitivities (Papa et al. 2014). UCH-LI is a neuronal cell protein that has also shown utility in diagnosing and stratifying mTBI (Papa et al. 2012). All three of these promising biomarkers are the subject of a recent clinical trial, and each one has shown utility as a classifier for mTBI versus no mTBI (Lewis et al. 2017). Recently, Banyan Biomarkers has won approval for its brain trauma indicator that measures blood levels of GFAP and UCH-L1 to help detect the presence of intracranial brain lesions within 12 hours of head injury (FDA 2018).

TBI Prognosis

Several research studies have shown that high serum concentrations of S100B, GFAP, or UCH-L1 can be used to predict mortality outcomes in TBI patients, but these same biomarkers, except for GFAP, are poor at predicting the outcome of mTBI (Mondello, Maas, and Buki 2017). There is no evidence that fluid biomarkers can currently be used for prognosis in mTBI. Further, as stated in Chapter 3, a subset of mTBI patients have extended symptoms and have post-concussion syndrome. IDA was unable to find attributes in the literature that could define an uncomplicated mTBI that self-resolves from an mTBI with PCS that persists. There have been some studies in the literature to find fluid biomarkers that describe PCS with conflicting results. There are no biomarkers that can currently predict the severity and outcome from PCS (Mondello, Maas, and Buki et al. 2017; Zetterberg and Blennow 2016).

Discovery Research Studies for mTBI Biomarkers

Because of the complexity and heterogeneity of the pathophysiology of mTBI, researchers generally believe that a single biomarker will not be able to describe all the damage processes of head trauma to the brain (Sharma et al. 2017). Researchers are targeting multiple panels of biomarkers to improve statistical rigor of diagnosing, stratifying, and predicting outcomes of mTBI. Researchers are casting a wide net to discover potentially powerful biomarkers for mTBI (Zetterberg and Blennow 2016) through a two-pronged approach:

1. Targeting multiple modalities of biomarker discovery (Wright et al. 2016) including:
    a. Imaging biomarkers
    b. Proteins
    c. Metabolites
    d. Nucleic acids
2. Trying to understand these biomarker modalities in the context of the current thought of damage mechanisms and pathophysiology of mTBI (Carpenter et al. 2015). These mechanisms include
    a. Neural cell death
    b. Axon stretching
    c. Changes in energy utilization or metabolism by the brain
    d. Neuroinflammation
    e. Damage to the blood-brain barrier

Imaging Biomarkers for mTBI

Current imaging techniques for the diagnosis of TBI, which include computed tomography (CT) and magnetic resonance imaging (MRI), are ideal for detecting macrostructure changes such as bleeding from torn capillaries (Shenton et al. 2012). Bleeding is indicative of more severe forms of TBI, and many times this damage is not present in mTBI. Damage mechanisms that are indicative of mTBI on the cellular and molecular level are not detectable by these methods (Huang, Risling, and Baker 2016). New imaging methods that detect changes on the microstructure level, such as cell or axonal damage, are needed for diagnosing and describing attributes for mTBI. Therefore, new biomarkers need to be developed to detect brain damage due to mTBI.

MRI uses measurements of the local magnetic environment surrounding protons[15] to develop images of the brain. Despite success in detecting gross pathologies of the brain, the resolution of this imaging technique is insufficient to detect damage to the brain in cases of mTBI. Imaging techniques that measure the diffusion of water in a sample, such as diffusion weighted imaging (DWI) or diffusion tensor imaging (DTI), have been recently applied to studies of mTBI due to their success in detecting other brain injuries from stoke or Alzheimer's disease (Shenton et al. 2012). DWI has had limited success in detecting mTBI changes in the brain, but DTI has been more promising. Evidence indicates that DTI is sensitive to axonal injury, as well as blood-brain barrier disruption and edema (Wright et al. 2016). Despite this promise, however, the studies that support this idea are heterogeneous in their methodologies, study population, and goals, so no definitive conclusion can be drawn regarding the utility of DTI to detect imaging biomarkers of mTBI (Shenton et al. 2012).

Magnetoencephalography (MEG) is another imaging technique that has recently been applied to detecting mTBI damage. MEG uses SQUID magnetometers to detect changes in magnetic fields in the brain due to neural activity. MEG can detect changes with spatial resolution to the various oscillating waves generated by the brain, which can then be interpreted into functional or pathophysiological changes. Several studies have detected changes in delta- or theta-band frequencies associated with mTBI (Huang, Risling, and Baker 2016).

Proteins

Many of the protein biomarkers described above that are now entering clinical practice were derived from a hypothesis-driven approach where the proteins were suspected to be reasonable biomarkers by their natural biological functions in the nervous system. There may be additional undiscovered proteins or panels of proteins that could be

[15] It is possible that other nuclei have the proper magnetic moment; however, protons are useful for human imaging due to the pervasiveness of water in the body.

useful biomarkers as well. Discovery of these potential markers generally occurs through high-throughput methods such as proteomics. Proteomics is an unbiased methodology for the discovery of proteins that may be biomarkers of mTBI. A sample of a biofluid, tissue, or cell is subjected to a proteomics technique such as mass spectrometry or electrophoresis to assess its protein complement in both healthy and mTBI patients. Different levels of a protein between the two sets can indicate a potential marker of mTBI damage. These biomarker candidates need to be then validated for their use as a biomarker for mTBI. Early studies have investigated such candidate protein markers for mTBI (Kulbe and Geddes 2016). Further validation studies for these candidates are needed to determine the usefulness of these candidate biomarkers.

Metabolites

Metabolites of biochemical activity of the brain can also be used to identify mTBI damage-induced chemical or energy utilization changes of the brain. Similarly to proteomics, high throughput methods for scanning metabolites as potential mTBI biomarkers can be used (metabolomics). High-throughput analytical chemistry methods such as mass spectrometry or NMR are used to compare healthy and mTBI patient sample to look for changes in various metabolites (Wolahan et al. 2016). Although marker studies for mTBI are not as well developed, recent studies have shown that some fatty acids and sugar moieties have the potential to be markers for severe TBI (Oresic et al. 2016). Metabolomics for the study of mTBI is an emerging endeavor, but there may be potential to develop clinically relevant TBI metabolic fingerprints (Posti et al., 2017)

Nucleic Acids

Small ribonucleic acids (22 nucleotides long) called microRNAs are currently being studies as potential diagnostic (Kulbe and Geddes 2016) and outcome (DiPietro et al. 2017) biomarkers for TBI. These studies have found candidate microRNAs that can be diagnostic for severe TBI and mTBI, as well as for short-term outcome for mTBI.

Microvesicles/Exosomes

Microvesicles and exosomes are very small lipomembrane-bound structures that naturally bud off from cells. Their exact function is unknown, but they are believed to be involved in cell-cell communication by transferring protein and nucleic acids between cells. Recent studies have shown that exosomes from neural cells can contain protein or nucleic acid biomarkers of TBI (Goetzl et al. 2017; Manek et al. 2017). These exosome “cargoes” are being studied for changes after mTBI for diagnostic or outcome predictability for mTBI.

Conclusions

Fluid-based biomarkers are now starting to be validated in the clinic for their diagnostic value for mTBI. Several candidate biomarkers have gone through some clinical assessment and been shown to have diagnostic value. While this is encouraging, larger panels of biomarkers that are capable of both diagnosing and *stratifying* mTBI need to be developed. Since mTBI is heterogeneous in its characteristics and outcomes for different patients, researchers think that a large panel of biomarkers will be needed to capture the subtle differences between individual mTBI cases and to predict their outcome. Since mTBI is so heterogeneous and ill-defined clinically, IDA was unable to define specific attributes that could delineate an uncomplicated and not significant mTBI from a complicated and significant mTBI.

In addition, the damage mechanisms on cellular and molecular levels for mTBI need to be clarified, and appropriate biomarkers and metrics to describe attributes need to be found. Based on our assessment of the literature, both these research thrusts are still firmly in the beginning phase of development. It may take several years until these damage and outcome attributes are validated for IDA to have confidence that attributes exist that define an uncomplicated mTBI that is not significant. On the other hand, it appears that with additional cellular and molecular studies of mTBI that evidence is increasingly pointing to the fact that all mTBI may be significant. Until this discovery research reaches a maturity where mTBI attributes are sufficiently validated and mTBI can be diagnosed, stratified, and outcomes predicted, IDA will continue to be cautious and classify all mTBI as a significant injury.

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Abbreviations

ATBM	Advanced Total Body Model
AVF	arteriovenous fistula
cal	caliber
CT	computed tomography
DAI	Diffuse Axonal Injury
DoD	Department of Defense
DoDI	Department of Defense Instruction
EDH	Epidural Hematoma
FEM	finite element model
GCS	Glasgow Coma Scale
GOS	Glasgow Outcome Scale
HCC	Health Care Capability
HCC0	HCC index of 0
HCC1	HCC index of 1
HCC2	HCC index of 2
ICH	Intracerebral Hemorrhage
ICP	intracranial pressure
IDA	Institute for Defense Analyses
J	joule
JNLWD	Joint Non-Lethal Weapons Directorate
JNLWP	Joint Non-Lethal Weapons Program
kPA	kilopascal
KPP	key performance parameter
KSA	key system attribute
LASD	Los Angeles Sheriff's Department
ml/kg	milliliters per kilogram
m/s	meters per second
mm	millimeter
mmHg	millimeter of mercury
MPa	megapascal
ms	millisecond
mTBI	mild traumatic brain injury
NAMET	National Association of Emergency Medical Technicians
NDIA	National Defense Industrial Association
NIJ	National Institutes of Justice
NLW	non-lethal weapon
PCS	post-concussive syndrome
RICE	rest, ice, compression, elevation
RSI	Risk of Significant Injury

SAH	subarachnoid hemorrhage
SDH	subdural hematoma
TBI	traumatic brain injury
USD(AT&L)	Under Secretary of Defense for Acquisition, Technology, and Logistics
VASRD	Veteran Affairs Schedule for Rating Disabilities

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14. ABSTRACT

Non-lethal weapons (NLWs) are systems designed to immediately and reversibly incapacitate targeted personnel or materiel, while minimizing fatalities, permanent injuries to personnel, and undesired damage to property. Often employed in crowd dispersal, NLWs serve as a deterrent by inducing pain or muscle spasm at the site of impact of the affected individual, but they may also induce skull fractures and traumatic brain injury, which are the focus of this document. As part of the DoD acquisition process, combat developers must compare the capabilities of NLW systems to requirements to assess technical maturity. One important requirement stipulates the acceptable likelihood of injury, often quantified as the risk of significant injury (RSI). A NLW's RSI is a compound metric that estimates the likelihood that the NLW will cause an injury and the significance of that injury. Computational models could potentially estimate the first part of RSI, the likelihood that the blunt impact produced by a NLW will cause skull fracture or TBI. This report focuses on the second part of RSI, the significance of these injuries, which could guide future Joint Non-Lethal Weapons Directorate modeling efforts.

15. SUBJECT TERMS

blunt-impact NLW; mild TBI; mTBI; NLW; non-lethal weapon; Risk of Significant Injury; RSI; skull; skull fracture; TBI; traumatic brain injury

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