NEUROIMAGING IN TRAUMATIC BRAIN INJURY
OBJECTIVES

- Discuss standard accepted imaging tools in the context of the existing SABS definition
- Understand uses and limitations of standard imaging tests
- Understand basic physics of these tests
- Review the strength of evidence in the medical literature
Current SABS definition

(1)4. If the insured person was 18 years of age or older at the time of the accident, a traumatic brain injury that meets the following criteria:

i. The injury shows positive findings on a computerized axial tomography scan, a Magnetic resonance imaging or any other medically recognized brain diagnostic

Technology indicating intracranial pathology that is a result of the accident, including, but not limited to, intracranial contusions or haemorrhages, diffuse axonal injury, cerebral edema, midline shift or pneumocephaly
Intracranial Pathology

- Definition
- Not specifically addressed in the guidelines
- Standard medical definition
  - “within the skull or cranium”.
Basic technologies used

- **CT Scan**
  - Utilizes ionized radiation to produce an image
  - Works on the differential attenuation of specific body tissues to X-ray
  - Tissues absorb X-rays at different degrees and this slight difference can be exploited to produce an image
  - Metal, bone, soft tissue, fat, air
Technology has evolved dramatically in the past few years
It is now a “volumetric scan” which means a specific volume of tissue can be scanned at a time
Result. Extremely rapid scan times (seconds)
Results in “isotropic” voxels. Means the axial images obtained in the scan can be reconstructed in multiple planes with essentially no loss of resolution
The “postprocessing” of the data can be manipulated

Specific Kernels used by vendors to accentuate specific elements
  - Bone windows, lung windows

By manually “windowing” the data
  - Can bring out certain elements and show pathology better

Uses a contrast agent which is Iodine based
Mri Imaging

- Does not utilize radiation
- Works by exciting hydrogen molecules in specific ways and measuring their effects and return to resting state
- Requires use of multiple “sequences” to produce different images
- Each sequence can be used to answer specific questions
  - T1,T2, FLAIR, diffusion, gradient echo, etc
- Results in long scan times 20 minutes to 1 hour
- Can be difficult in the acute setting or with agitated or claustrophobic patients
- Contrast agent is Gadolinium based.
Specific Pathology

- Cranium or skull vault
- Guidelines mention Pneumocephaly
- Can only happen when skull vault is breached in some way
- Suggest presence of skull fracture
- This is best detected by CT scan
- Plain x-rays likely of historical significance only
Skull Fractures

- Many different classifications
- Commonly accepted
  - Linear
  - Depressed
  - Diastatic fracture
  - Basal skull fracture
  - Compound fracture
- Focus on those fractures that are challenging to identify
Skull fractures can be challenging to identify because of how the skull forms and grows.

It is different from the long bones of the body.

Terms are “intramembranous” vs “endochondral” ossification respectively.
In the skull this means that the separate bones are defined by sutures. They may or may not fully fuse with age. Multiple variations exist. Can be hard to separate a fracture from a persistent or anomalous suture.
Linear fractures

- Simply a faint line in the skull
- No displacement
- Can involve only one of the 2 sides of the skull bone wall
- Can be very faint and difficult to resolve
Diastatic fractures

- The fractures are partly or completely within the underlying suture plane
- They can be very challenging to assess
Skull Fracture: Diastatic

- Fracture along suture lines “traumatic sutural separation”
- Usually affected newborns and infants (unfused sutures)
- Commonly unilateral
- Most common location = lambdoid and sagittal sutures
- >2 mm separation that is asymmetric

Nazeer et al 2017
These fractures involve separation or diastasis of a suture.
Can be very challenging when multiple sutures are present and nonfused.
Basilar Skull fractures

- They are fractures that occur at the base of the skull
- Issues
  - Can affect a sinus
  - Can affect other neurologic structures
    - Cranial nerve V11, fascial palsy
    - Cranial nerve V111, hearing loss
    - Disruption of ossicular chain, hearing loss
    - Arterial structures, stroke
Intracranial Hemorrhage

- Bleeding in the brain
- Need to know some neuroanatomy
- Intracranial structures are highly compartmentalized
The Dura Mater

- Skin of scalp
- Periosteum
- Bone of skull
- Periosteal
- Meningeal
- Arachnoid mater
- Pia mater
- Arachnoid villus
- Blood vessel
- Falx cerebri

Superior sagittal Sinus
Subdural space
Subarachnoid space
The Three Layers of Meninges

- Dura mater
- Arachnoid
- Pia mater

Parasagittal Region

Subarachnoid Space

Tentorium

Posterior Fossa

Cerebello-Pontine Angle

Spinal Cord
Hemorrhage will behave differently depending on its cause and location.

Imaging tools will depict them differently.
CT Scan

- Is an excellent test for acute bleeding (macro bleeding)
- Doesn’t do well with tiny micro bleeding
- Acute blood has a high specific radiation attenuation
  - Shows up as bright white on CT
  - As it ages, it begins a healing process and will lessen in density
    - Highly dependent on cause and location of bleed
MRI Scan

- We can exploit the broader range of functionality of MRI.
- Can utilize specific sequences to augment the visualization of blood to a much better degree.
- Type of bleeding and location will determine which sequence is best.
Visualization of Blood on MRI

- The perception of blood on MRI is highly dependent and varies over time.
- Depends on location:
  - Intraparenchymal:
    - intra or extra cellular
  - In a specific space:
    - Subdural, subarachnoid
- Depends on time
- Blood degrades over time
  - Results in change in paramagnetic properties
    - Affect imaging and best sequences
Oxyhemoglobin (O₂)

Deoxyhemoglobin (empty)

Methemoglobin (H₂O or OH⁻)

Hemichromes (E7 His residue)

HEMOSIDERIN
Transition from Intracellular to Extracellular Met-Hb:
Lysis of RBC Destroys T2/T2* Susceptibility Effect

**Intracellular** Met-hemoglobin concentrates/distorts magnetic field
T2 is short (dark)

**Extracellular** Met-hemoglobin in solution produces NO local susceptibility effects
T2 is long (bright)
- General rule
- Early on when blood is in oxy HBG to met HBG state
  - Standard images useful
    - T1, T2, Flair, etc
As hgb degrades to hemosiderin

Standard images become much less useful

Especially with very small microbleeds

Need to utilize specific paramagnetic properties to bring out the artifact caused by hemosiderin

blooming effect
Hemosiderin helpful sequences

- Diffusion sequences
  - Can be helpful but limited
- Gradient echo
  - First sequence to capitalize on this artifact from hemosiderin
  - Limited sensitivity
  - Not volumetric, slice by slice, some areas not covered
- Susceptibility Weighted Imaging. SWI
- Much more sensitive for the presence of hemosiderin
- Can see much smaller amounts and more of them
- Can be volumetric
  - Whole brain covered
  - Faster
- Highly susceptible to artifacts
Epidural hemorrhage

- Bleeding between skull and dura
- Classic scenario
- Trauma to skull
  - Often to squamous temporal region
  - Fracture of bone injures vessel that runs in the bone covered by dura
  - Middle Meningeal Artery. Tear
  - Bleeding is arterial. Under pressure
Over time hematoma expands and strips dural away from bone

Results in a lentiform mass
  - Compresses adjacent brain
  - Causes midline shift
  - Hydrocephalus
  - Can injure vessels by compression against dura
 Patients have a characteristic “lucid interval”

 Initially well. Often completely normal GCS

 Over next few hours deteriorate

 Life threatening

 Immediate decompression
Because of the acuity and seriousness of the situation

Rarely need MRI to diagnose
Subdural Hematoma

- Bleeding between the dura and subarachnoid membrane
- Usually considered venous in origin, but not always
- This is a potential space with few cross limiting connections
  - Can extend large distances in the skull
- Appearance on CT will be dependent on age
  - Acute. Very bright
  - Chronic. Much lower density
  - Acute on chronic. Combination of the 2
On MRI

Subdurals will vary with age and sequences used

Due to multiplanar potential

Usually better seen
Other areas of Subdurals

- Classically along surface of brain adjacent to skull
- But can occur along essentially any dural reflection
  - Flax
  - Tentorium
Subarachnoid Blood

- Bleeding between the arachnoid membrane and pial membrane
- This is where the major arteries and veins supplying the brain substance reside
- Most nontraumatic causes of Subarachnoid bleeding (SAH) are arterial from a ruptures aneurysm
In Post Traumatic situations

Bleeding can be from
- Combination of venous and arterial blood in that space
- Extension from other compartments such as parenchymal contusion

Tends to be more diffuse

Localizes often to areas of potential impact and shearing effects

It is a measure of force transmission

Tends to have a worse prognosis
- The blood in this space ultimately resolves
- Is the finding in a positive CSF lumbar tap
- This bleeding can predispose to
  - Delayed strokes from vasospasm
  - Hydrocephalus
  - Hearing loss
  - Visual issues
  - Hemosiderin deposition over surface of brain
Ct Scan

- Very nicely depicts acute SAH
- Is the modality of choice in the acute phase
- Will often see other injuries on CT
The Subarachnoid space

- Fluid filled. CSF fluid
- Highly oxygen rich

Significantly affects blood breakdown and therefore imaging
Parenchymal Contusions

- Trauma results in brain injury with concomitant rupture and bleeding
- Can be from direct impact
  - Skull vault
  - Tentorial edges
- Shear effects
  - usually at interfaces of adjacent structures
  - Superficial
    - Cortical/subcortical interface
  - Deeper
    - Junction of deep nuclei/white matter
The bleeding damages underlying neurologic structures

Creates a cascade of pathologic processes

- Inflammatory cascade
- Increased local/global Intracranial Pressure
- Release of toxic neuromodulators
- Direct toxic effect of released heme products

Combine to produce ongoing expansion of damage
Mri imaging

- In the acute phase will show the lesion based on its state of hemoglobin degradation
- Can be highly variable
With chronicity

Looking for hemosiderin residuum

Best seen with sequences that will accentuate these artifact
  • Blooming

Diffusion

Gradient echo

Susceptibility SWI imaging
Both modalities are helpful in identifying the long term sequelae of the injury
- Volume reduction
- Encephalomalacia
- Wallerian degeneration
Diffuse Axonal Injury

- Rotational injury disrupts axons in white matter tracts
- Traditionally visualization has been challenging
- Relying on seeing any focal hemorrhage that has occurred rather than the axonal damage itself
- Don’t need to have bleeding to have axonal disruption
Grey matter vs. White matter
Direct Imaging of Tract Pathology

- Diffusion Tensor Imaging (DTI)
- It is an extension of standard diffusion imaging which was initially utilized for stroke imaging
- Based on the concept of free water motion
  - Brownian motion
- Restricted motion
  - Along a fiber tract
- It utilizes advanced mathematical processing to identify a specific trajectory of fibers
  - Eigenvector
- Utilized to look for specific tracts
- Disruption or distortion
- Depends on many factors
- Dependent on signal strength
- Artifact susceptibility
- Crossing and abutting fiber tracts are difficult to resolve
Newer more robust post processing mechanisms and field strength issues hold great promise

- Kurtosis imaging
- Constrained spherical convolution
Vascular Imaging

- Will divide this into the acute and chronic setting
- Acute setting
- Indications
  - Look for ischemic stroke
  - Global / local perfusion
Ct Angiography

- Intravenous contrast is injected
- Scan is timed to assess the Arterial System usually from Aortic arch to Vertex
- Very rapid
- Highly reproducible
In the acute setting
  - Dissection
  - Vessel occlusion
Mri Imaging

- Can achieve very similar results
- Patient has to be well enough to tolerate long scan times
  - Ct angiography very rapid. Seconds
- Can be done without or with gadolinium
Perfusion Imaging

- In MRI and Ct imaging
- Allows a very robust data set
- Involves injecting a contrast agent and watching how the brain is perfused over time
- Great deal of basic science behind this
- Creates specific maps
- Commonly used maps
  - CVF, CBV, MTT, TTP
Neuronal activation is a highly energy dependent process

- Heavily ATP driven
  - Requires constant oxygen supply
- With neuronal activation
  - ATP requirement increases
  - Metabolic products accumulate
- Arteriolar dilatation
  - Increased O2 delivery/extraction
  - Occurs in 1-2 sec
- Functional MRI can measure this increase and map it to a specific area of the brain
- Great deal of basic and clinical science
Studies in TBI

Executive/frontal lobe function
Episodic memory function
mTBI in military population
  mTBI vs PTSD
Functional connectivity abnormalities
  assess resting state default mode connectivity
Intervention after mTBI
  cognitive rehab and pharmacologic treatment
Spect nuclear medicine imaging

- Involves injection of a technetium based agent
- Crosses blood brain barrier
- Incorporated into cells
- Undergoes metabolic change
  - Remains within the cell
- Emits gamma radiation
- Detected by external camera
2 basic radionucleotides used
Tc99m hexamethylpropylene-amine oxime
  Tc HMPAO
Tc99methyl cysteinate dimer
  Tc ECD
Main differences are in intracellular metabolism of agent
The injection, crossing BBB, cell uptake
Is considered a measure of cerebral perfusion
Indirectly metabolism and neuronal activity
Patient injected
  Wait usually 30 minutes
  Scanned.
    20-30 minutes
There are 2 very basic methods of processing

Conventional

- Entire data set is utilized and processed in conventional tomographic images
- Multiplanar
- Interpretation is reader dependent
- Data set can be manipulated by "windowing"
3D Threshold SPECT

- Same raw data set obtained
- A threshold value is predetermined
- All data below this value are rejected
- Remaining data combined into a 3D surface rendered model
Co-Registered SPECT

- Combining SPECT data with MRI images
- Considered to give improved accuracy
The SPECT literature is extensive

- Mostly observational trials
- Few if any proper RCT
- Relative paucity of basic science regarding the mechanisms of how brain spect works
What is the Summary of Evidence In Advanced Neuroimaging

- Looking for seminal usually society based papers
- Have done an extensive review of literature
- Rate literature on strength of utility
- Meta analysis reviews
- Reviews based on Oxford center for evidence based medicine
  Levels of Evidence
Metaanalysis reviews

- Standard epidemiologic technique to assess broad ranges in literature
- This is done to look at only those articles that properly fulfil evidence based proper criteria and exclude the rest
- Selected articles are then individually reviewed and given a strength based on guidelines
- Allows an overall strength of the existing evidence
# Oxford Levels of Evidence

## Table 1: Levels of evidence for studies of the accuracy of diagnostic tests

<table>
<thead>
<tr>
<th>Levels of Evidence</th>
<th>Type of Evidence</th>
</tr>
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<tbody>
<tr>
<td>Ia</td>
<td>Systematic review (with homogeneity)(^b) of level-1 studies(^c)</td>
</tr>
<tr>
<td>Ib</td>
<td>Level-1 studies(^c)</td>
</tr>
<tr>
<td>II</td>
<td>Level-2 studies(^d)</td>
</tr>
<tr>
<td></td>
<td>Systematic reviews of level-2 studies</td>
</tr>
<tr>
<td>III</td>
<td>Level-3 studies(^e)</td>
</tr>
<tr>
<td></td>
<td>Systematic reviews of level-3 studies</td>
</tr>
<tr>
<td>IV</td>
<td>Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research, or “first principles”</td>
</tr>
<tr>
<td>Class</td>
<td>Description</td>
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<td>----------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Class I</td>
<td>Conditions for which there is evidence for and/or general agreement that a procedure or treatment is beneficial, useful, and effective</td>
</tr>
<tr>
<td>Class II</td>
<td>Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment</td>
</tr>
<tr>
<td>Class IIa</td>
<td>Weight of evidence/opinion is in favor of usefulness/efficacy</td>
</tr>
<tr>
<td>Class IIb</td>
<td>Usefulness/efficacy is less well-established</td>
</tr>
<tr>
<td>Class III</td>
<td>Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful</td>
</tr>
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</table>

*From the American Heart Association Evidence-Based Scoring System.*
Clinical Utility of SPECT Neuroimaging in the Diagnosis and Treatment of Traumatic Brain Injury: A Systematic Review
Cyrus A. Raji1, Robert Tarzwell3, Dan Pavel4, Howard Schneider5, Michael Uszler6, John Thornton7, Muriel van Lierop8, Phil Cohen9, Daniel G. Amen10, Theodore Henderson"2*

Received September 3, 2013; Accepted February 10, 2014; Published March 19, 2014

Review spanned 30 years of publications
Figure 2. This figure outlines a flowchart of article selection in this study from the initial 1600 that were identified to the final 71 manuscripts that were included in the systematic review.
Conclusions: This review demonstrates Level IIA evidence (at least one non-randomized controlled trial) for the value of SPECT in TBI. Given its advantages over CT and MRI in the detection of mild TBI in numerous studies of adequate quality, and given its excellent negative predictive value, it may be an important second test in settings where CT or MRI are negative after a closed head injury with post-injury neurological or psychiatric symptoms.
What is the Strength of Evidence for All Advanced Neuroimaging Techniques

Imaging Evidence and Recommendations for Traumatic Brain Injury: Advanced Neuro- and Neurovascular Imaging Techniques

M. Wintermark, P.C. Sanelli, Y. Anzai, A.J. Tsiouris, and C.T. Whitlow, on behalf of the American College of Radiology Head Injury Institute
Advanced neuroimaging techniques, including MR imaging, DTI, blood oxygen level–dependent (BOLD) fMRI, MR spectroscopy, perfusion imaging, PET/SPECT, and magnetoencephalography (MEG), are of particular interest in identifying further injury in patients with TBI when conventional NCCT and MR imaging findings are normal, as well as for prognostication in patients with persistent symptoms. Based on the National Insti-
Article was a very thorough position paper

Reviewed in detail all of the literature for each modality based on Oxford evidence based criteria
**Summary**

1) Advanced neuroimaging techniques, including MR imaging DTI, BOLD fMRI, MR spectroscopy, perfusion imaging, PET/SPECT, and MEG, are of particular interest for patients with mild TBI when conventional NCCT and MR imaging findings are negative. These advanced neuroimaging techniques have shown promising results in group comparison analyses.
2) At the time of writing, there is insufficient evidence supporting the routine clinical use of advanced neuroimaging for diagnosis and/or prognostication at the individual patient level (class IIb recommendation).
We have reviewed a broad range of neuroimaging methodology focused on those techniques that are helpful under the new guidelines. The greatest level of evidence is with CT and MRI scanning. Unfortunately, they may be normal in mTBI.
We have reviewed selective Advanced Neuroimaging techniques

- Discussed pros and cons
- While current evidence gives these techniques an over
  - Class IIb recommendation
- They are very very promising techniques
- Moving toward more RCT trials which will ultimately solve the uncertainty issue
- This will make these tests standard accepted imaging tools
- Best guess
Thank you for your time and consideration