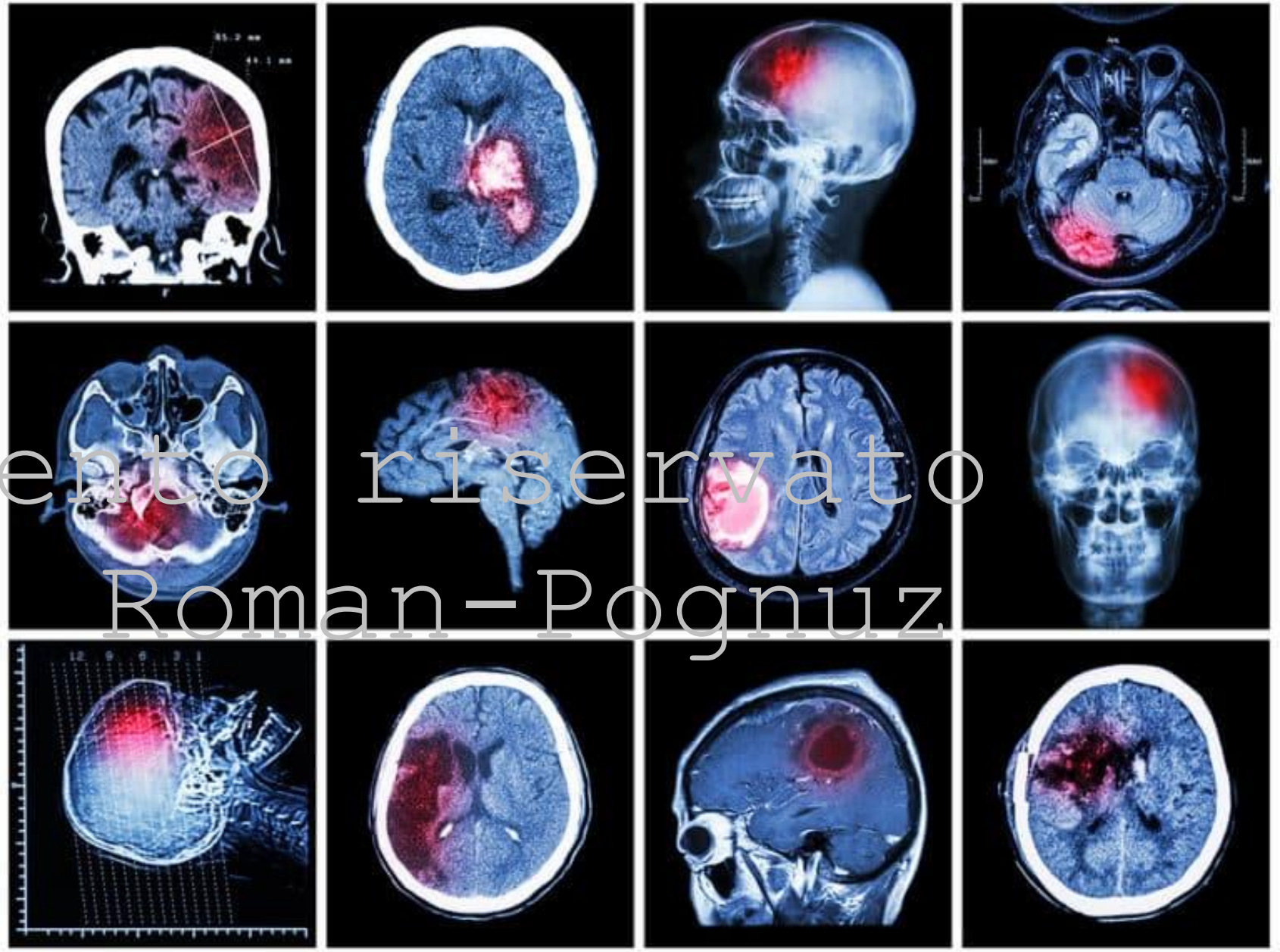
Traumatic brain injury



Prof. Erik Roman-Pognuz MD, PhD
Intensive care Unit
University of Trieste

Epidemiology

Global and Regional Burden

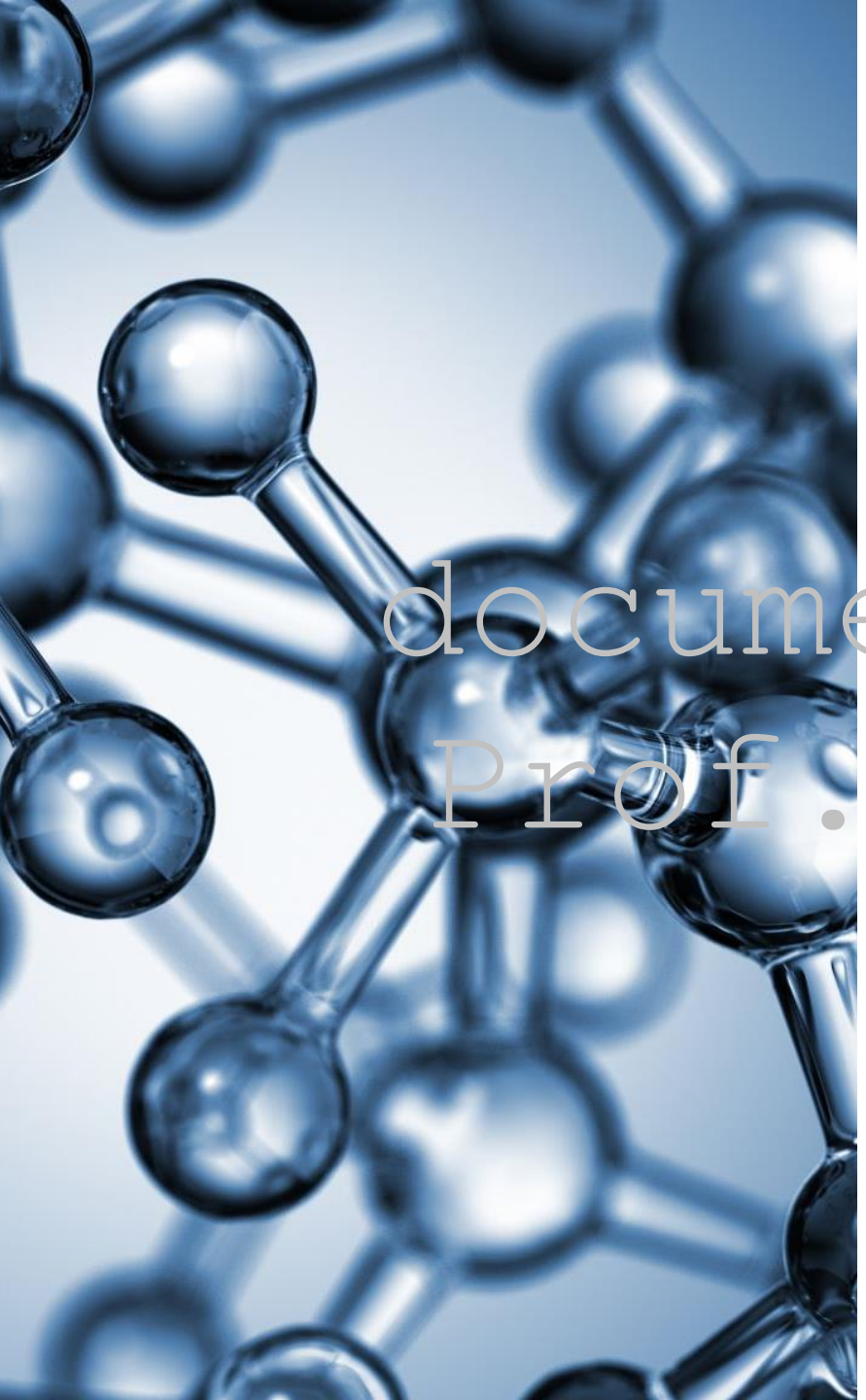
- Incidence: 69 million people/year globally.
- Common causes: Road traffic accidents, falls, violence, and sports injuries.
- Age groups: High incidence in children, adolescents, and elderly.
- Mortality and morbidity: Leading cause of death and disability among young adults.

Economic Impact

- Healthcare costs: Hospitalization, rehabilitation, and long-term care.
- Societal burden: Loss of productivity and quality of life.

Healthcare Costs

- **United States**:
  - **Annual Direct Medical Costs**: Approximately $76.5 billion, encompassing hospitalization, rehabilitation, and long-term care. Cambridge University Press
  - **Per Patient Lifetime Costs**:
    - **Mild TBI**: Up to $85,000.
    - **Severe TBI**: Can exceed $3 million.
- **United Kingdom**:
  - **Annual Economic Burden**: Estimated at £15 billion, representing 0.8% of the GDP.



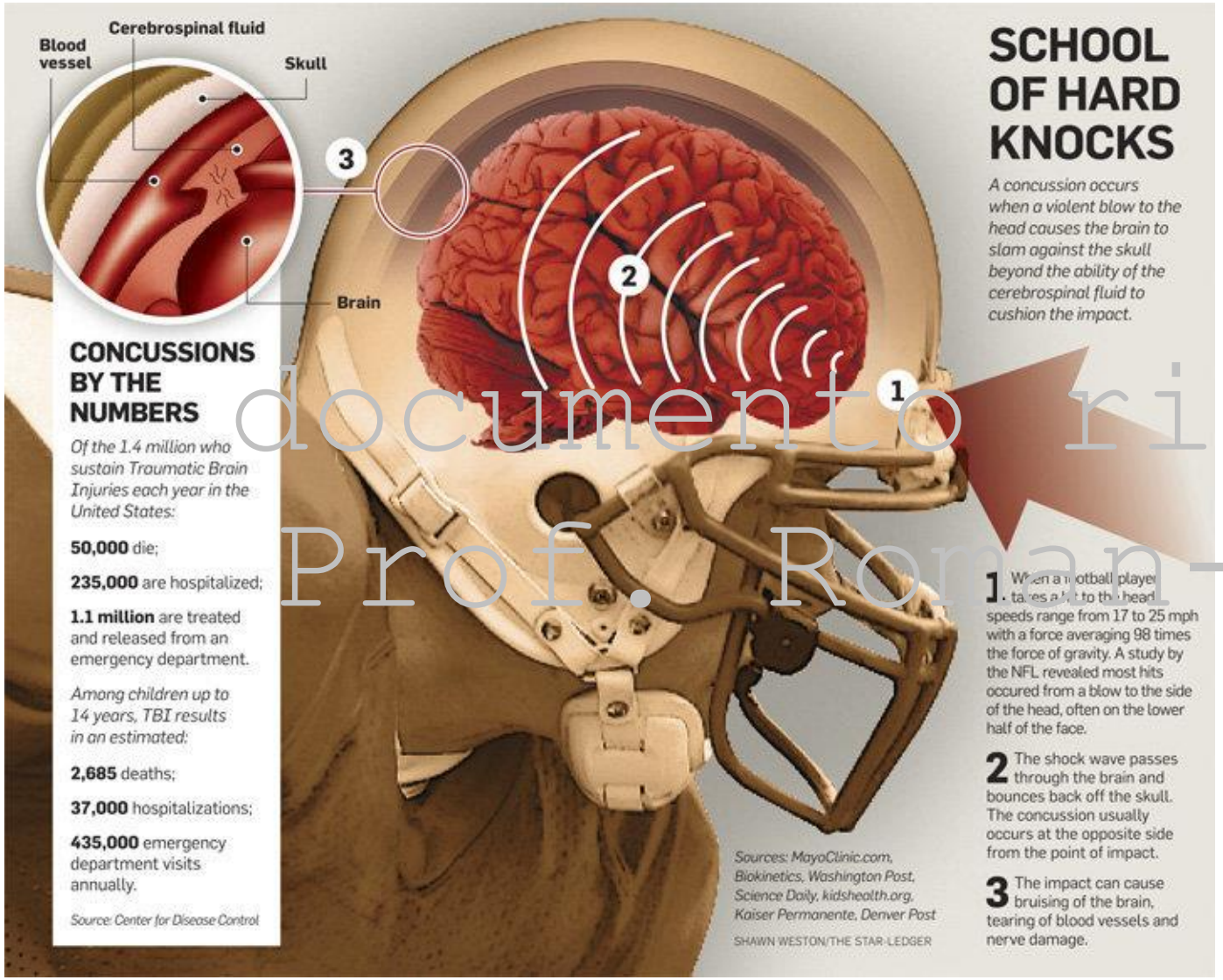
Societal Burden

Loss of Productivity:

- **Global Perspective**: TBI contributes to a significant reduction in workforce participation, with many individuals unable to return to pre-injury employment levels.
- **United States**: Annual productivity losses are estimated at $33 billion.

Quality of Life:

- **Disability**: Approximately 5.3 million Americans live with TBI-related disabilities, impacting daily functioning and independence.
- **Caregiver Burden**: Families often face emotional and financial strain, with caregiving costs contributing to the overall economic impact.



Sport Injury

Retirements

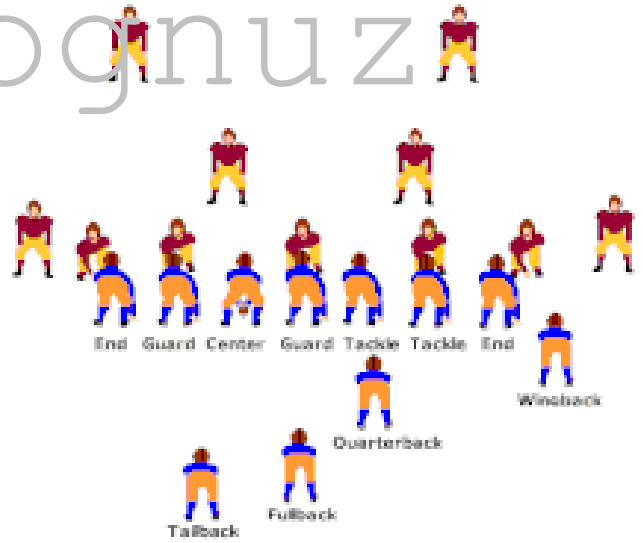
- **Jack Tuttle**: In October 2024, Michigan quarterback Jack Tuttle announced his retirement after experiencing his fifth concussion and ongoing issues from a UCL repair in his throwing arm. He emphasized the need to prioritize his health.
- **Grayson McCall**: Also in October 2024, North Carolina State quarterback Grayson McCall retired following multiple concussions, including a significant injury during a game against Wake Forest. After consulting with brain specialists and his family, he decided to step away from football to focus on his long-term well-being.

Michigan QB Jack Tuttle, 25, Retires from Football After 5 Concussions: 'Need to Start Prioritizing My Health'

The seventh-year senior previously played at Utah and Indiana before backing up J.J. McCarthy during the 2023 championship season

By Anna Lazarus Caplan | Published on October 29, 2024 11:53AM EDT

1 COMMENTS



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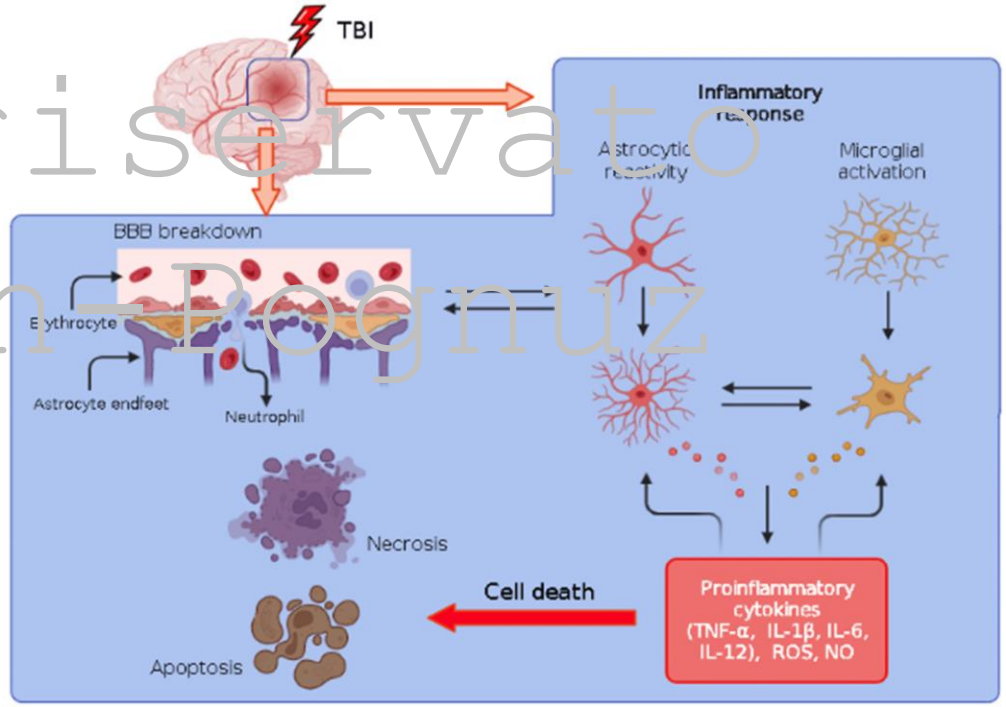
March 20, 2024

Definition and Pathophysiology

- **Definition**
  - Traumatic brain injury (TBI): Disruption of normal brain function caused by external mechanical force.
  - Categorized as mild, moderate, or severe based on clinical and imaging criteria.
- **Pathophysiology**
  - Primary injury: Direct mechanical damage at the time of trauma.
  - Secondary injury: Ongoing cellular damage from hypoxia, ischemia, inflammation, and oxidative stress.



Primary Injury

Definition: The immediate physical damage to the brain caused by external mechanical forces at the time of trauma.

- **Mechanisms of Primary Injury**

1. **Focal Injuries**:
    1. Localized damage due to direct impact or penetrating trauma.
    2. Examples:
        1. **Contusions**: Brain bruising at the site of impact.
        2. **Hematomas**: Epidural, subdural, or intracerebral bleeding.
    3. Typical Imaging Findings: Hemorrhage, fractures, or skull deformities.
2. **Diffuse Injuries**:
    1. Widespread damage due to inertial forces (e.g., rotational or shear stress).
    2. Examples:
        1. **Diffuse Axonal Injury (DAI)**: Stretching or tearing of axons.
        2. Common in high-velocity accidents.

Mechanical Forces:

1. Compression: Localized pressure on brain tissue.
2. Acceleration/Deceleration: Rapid movement changes causing axonal stretching.

Pathological Outcomes

•Disruption of neuronal, glial, and vascular structures.

•Immediate loss of cellular homeostasis.

•Mechanical disruption of the blood-brain barrier (BBB).

Clinical Significance

•Severity of primary injury influences the onset and magnitude of secondary injury.

Secondary Injury

Definition: Progressive, delayed damage initiated by cellular and molecular cascades following the primary insult.

- **Mechanisms of Secondary Injury**

1. **Hypoxia and Ischemia**:
    1. Reduced oxygen delivery and impaired cerebral perfusion.
    2. Mechanisms:
        1. Cerebral edema leading to increased intracranial pressure (ICP).
        2. Hypoperfusion due to vascular compromise or systemic hypotension.
2. **Inflammatory Cascade**:
    1. Activation of microglia and astrocytes.
    2. Release of pro-inflammatory cytokines (e.g., TNF-α, IL-6).
    3. Blood-brain barrier disruption exacerbates leukocyte infiltration.
3. **Oxidative Stress**:
    1. Overproduction of reactive oxygen species (ROS) and reactive nitrogen species (RNS).
    2. Causes lipid peroxidation, protein degradation, and DNA damage.

Secondary Injury

1. **Excitotoxicity**:
    1. Excessive release of glutamate leading to sustained neuronal depolarization.
    2. Results in intracellular calcium overload and activation of destructive enzymes.
2. **Mitochondrial Dysfunction**:
    1. Impaired ATP production exacerbates energy failure.
    2. Contributes to cell death via necrosis or apoptosis.

- **Pathological Outcomes**
- Cytotoxic and vasogenic edema.
- Progression to neuronal and glial cell death.
- Secondary ischemia and delayed hemorrhage.
- **Clinical Implications**
- Targeted interventions (e.g., hyperosmolar therapy, neuroprotective agents) aim to mitigate secondary injury and improve outcomes.

Injury Scales

- **Glasgow Coma Scale (GCS)**
  - Scoring system: Eye opening (E), verbal response (V), motor response (M).
  - Categories:
    - Mild TBI: GCS 13–15
    - Moderate TBI: GCS 9–12
    - Severe TBI: GCS ≤8
- **Other Scales**
  - Abbreviated Injury Scale (AIS): Focused on the severity of anatomical injuries.
  - Marshall CT Classification: Imaging-based classification for structural damage.

AIS code	Injury Level	Fatality Range
0	No injury	0.0 %
1	Minor	0.0 - 0.1 %
2	Moderate	0.1 - 0.4 %
3	Serious	0.8 - 2.1 %
4	Severe	7.9 - 10.6 %
5	Critical	53.1 - 58.4 %
6	Maximum	Virtually unsurvivable

Marshall Scoring of TBI

	MLS	Cisterns	High or mixed-density lesion	Notes
I	None	Present	None	No visible pathology on CT scan
II	0-5mm	Present	None	
III	0-5mm	Compressed or absent	None	Swelling
IV	>5mm		None	
V	Any	Any	Any	Any lesion surgically evacuated
VI			>25cm3	Not surgically evacuated

*MLS-midline shift

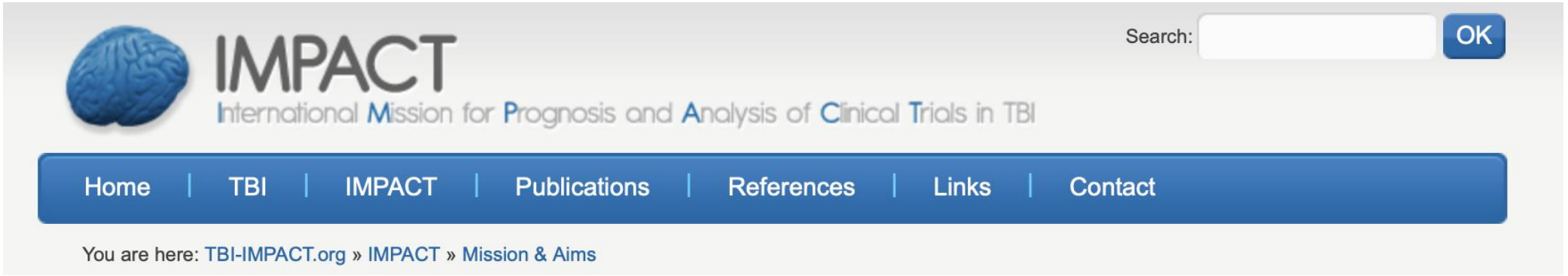
Extended Glasgow Outcome Scale (GOSE)

Purpose: Provides a more detailed assessment compared to GOS.

- **Expanded Categories**:
  - Adds subcategories (e.g., upper/lower severe disability) for granular evaluation.
- **Advantages**: Greater sensitivity to subtle functional improvements or declines.

Table 2: GOSE Score

Score	Performance
1	Dead
2	Vegetative State
3	Lower Severe Disability (completely dependent on others)
4	Upper Severe Disability (dependent on others for some activities)
5	Lower Moderate Disability (unable to return to work or participate in social activities)
6	Upper Moderate Disability (return to work at reduced capacity, reduced social function)
7	Lower Good Recovery (minor social or mental deficits)
8	Upper Good Recovery



Prognostic Models

IMPACT (International Mission for Prognosis and Analysis of Clinical Trials in TBI):

- Uses data from GCS, CT findings, and age to predict outcomes.

Diagnosis

Clinical Evaluation

- Initial assessment: Airway, breathing, circulation (ABC).
- Neurological examination: GCS, pupil reactivity, motor function.

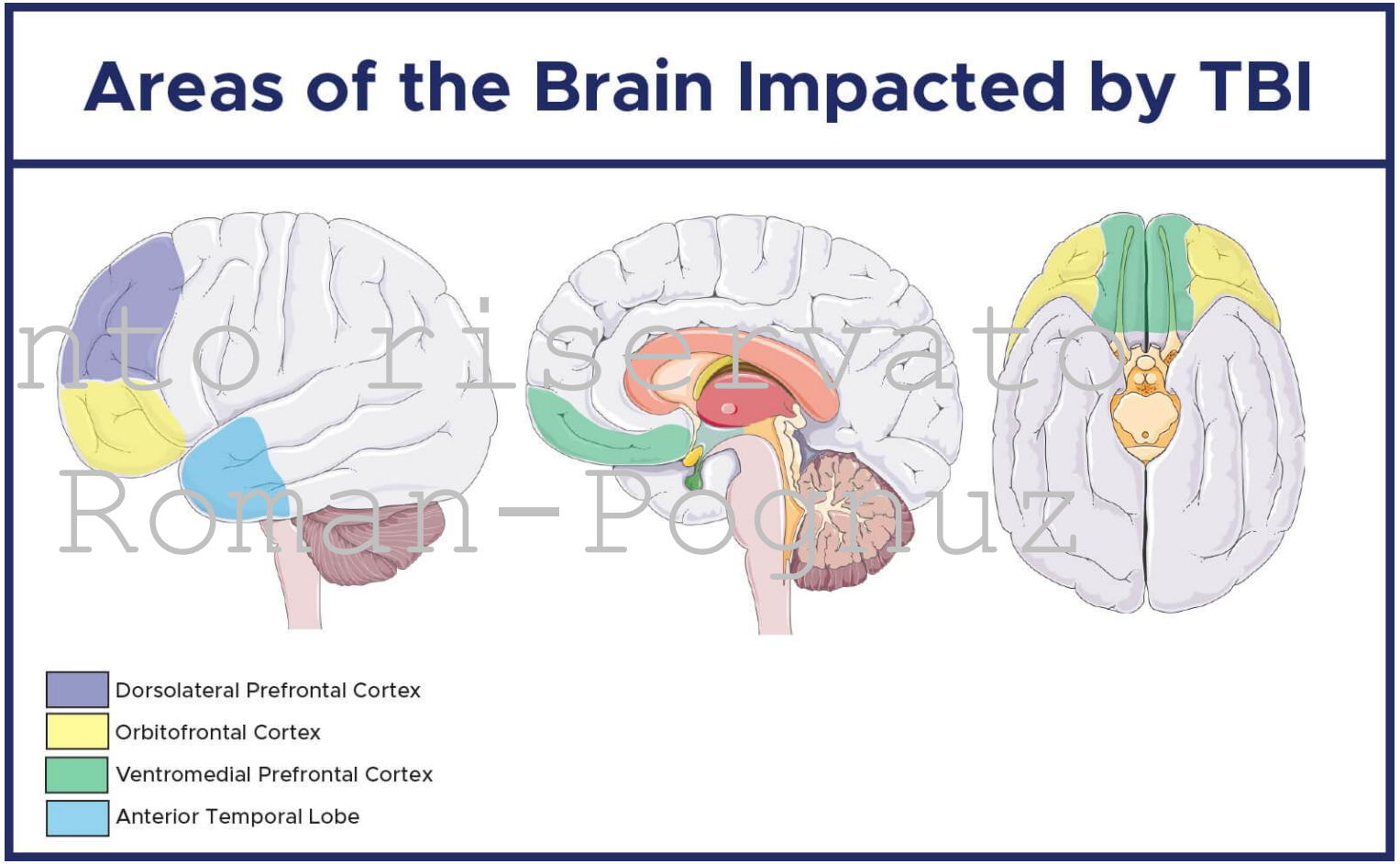
Imaging Modalities

- CT scan: First-line imaging for detecting hemorrhage, edema, and fractures.
- MRI: Superior for detecting diffuse axonal injury and posterior fossa lesions.

Biomarkers

- Emerging role of serum biomarkers (e.g., S100B, GFAP) for injury severity and prognosis.

Clinical evaluation



Clinical Evaluation of TBI (Primary Survey)

Purpose: Identify and manage life-threatening conditions quickly.

1. **Airway**:
    1. Assess for airway obstruction (e.g., blood, foreign objects).
    2. Ensure cervical spine stabilization during airway management.
2. **Breathing**:
    1. Check respiratory rate, effort, and oxygen saturation.
    2. Identify pneumothorax, hemothorax, or inadequate ventilation.
3. **Circulation**:
    1. Assess hemodynamic status (pulse, blood pressure, capillary refill).
    2. Look for signs of shock due to external or internal bleeding.
4. **Disability (Neurological Assessment)**:
    1. Perform **Glasgow Coma Scale (GCS)** evaluation.
    2. Assess pupil size, reactivity, and lateralizing signs.
5. **Exposure and Environmental Control**:
    1. Fully expose the patient to assess for other injuries.
    2. Prevent hypothermia by covering the patient once evaluation is complete.

Secondary Survey: Detailed and Comprehensive Examination

Purpose: Detect less obvious injuries and assess the extent of brain and systemic damage.

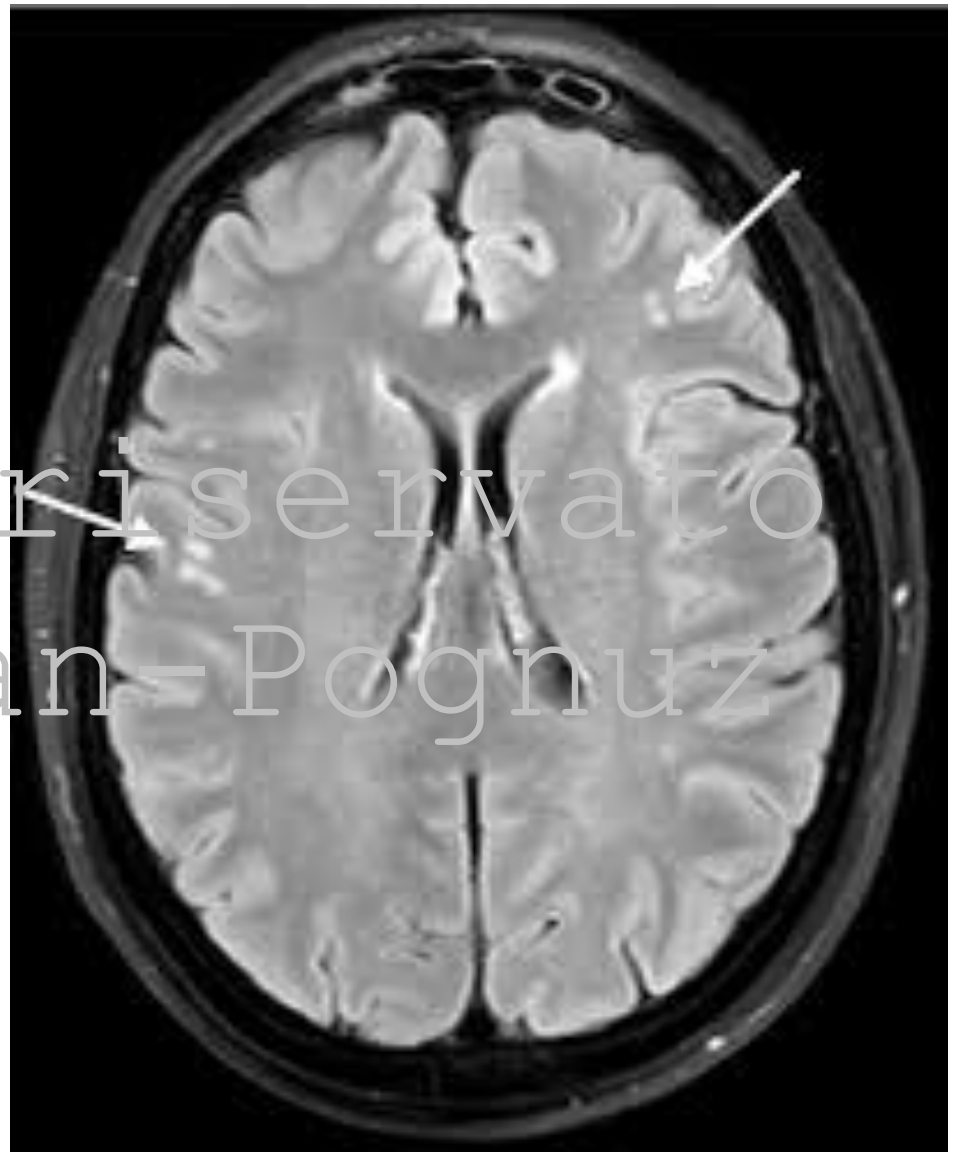
1. **History (AMPLE)**:
    1. **A**: Allergies.
    2. **M**: Medications.
    3. **P**: Past medical history.
    4. **L**: Last meal or drink.
    5. **E**: Events leading to injury.
2. **Head-to-Toe Examination**:
    1. **Head**: Check for scalp lacerations, skull fractures, or facial injuries.
    2. **Neck**: Evaluate for cervical spine injuries and neck vein distension.
    3. **Chest/Abdomen**: Identify concurrent thoracic or abdominal trauma.
3. **Focused Neurological Examination**:
    1. Reassess **GCS** for changes in mental status.
    2. Monitor cranial nerve function and extremity motor/sensory responses.
4. **Imaging Studies**:
    1. Obtain **non-contrast CT scan** for intracranial injuries.
    2. Consider MRI for diffuse axonal injury or posterior fossa lesions.
5. **Monitoring**:
    1. Place patient on continuous ECG, pulse oximetry, and blood pressure monitoring.

Key Takeaway

The **primary survey** prioritizes life-threatening conditions, while the **secondary survey** ensures a comprehensive evaluation of injuries.

Early and systematic evaluation improves outcomes in TBI patients.

Imaging



Initial Imaging: Non-Contrast CT Scan

First-Line Modality: Non-contrast computed tomography (CT) is the gold standard for acute TBI.

- Rapid assessment of hemorrhage, fractures, edema, midline shift, and mass effect.

Indications for Immediate CT:

- GCS ≤13 on admission.
- Focal neurological deficits.
- Persistent vomiting (>2 episodes).
- Severe headache or signs of skull fracture.
- Post-traumatic seizures.
- Suspected penetrating head injury.

Magnetic Resonance Imaging (MRI)

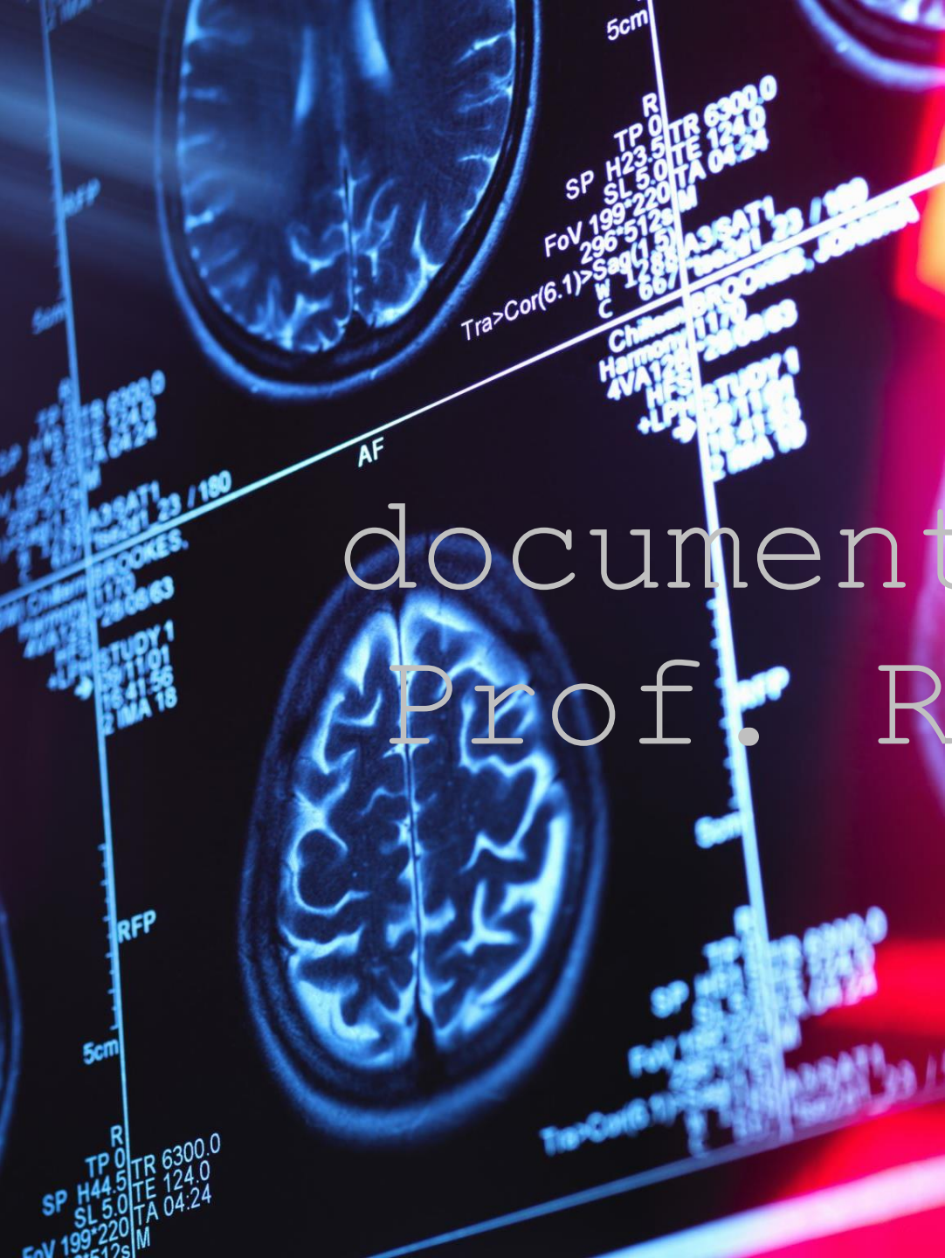
Second-Line Modality: Used when CT findings are inconclusive or for detailed evaluation of brain parenchyma.

Indications:

- Suspected diffuse axonal injury (DAI).
- Posterior fossa or brainstem lesions.
- Prolonged post-traumatic amnesia or cognitive deficits.
- Delayed deterioration with a normal CT.

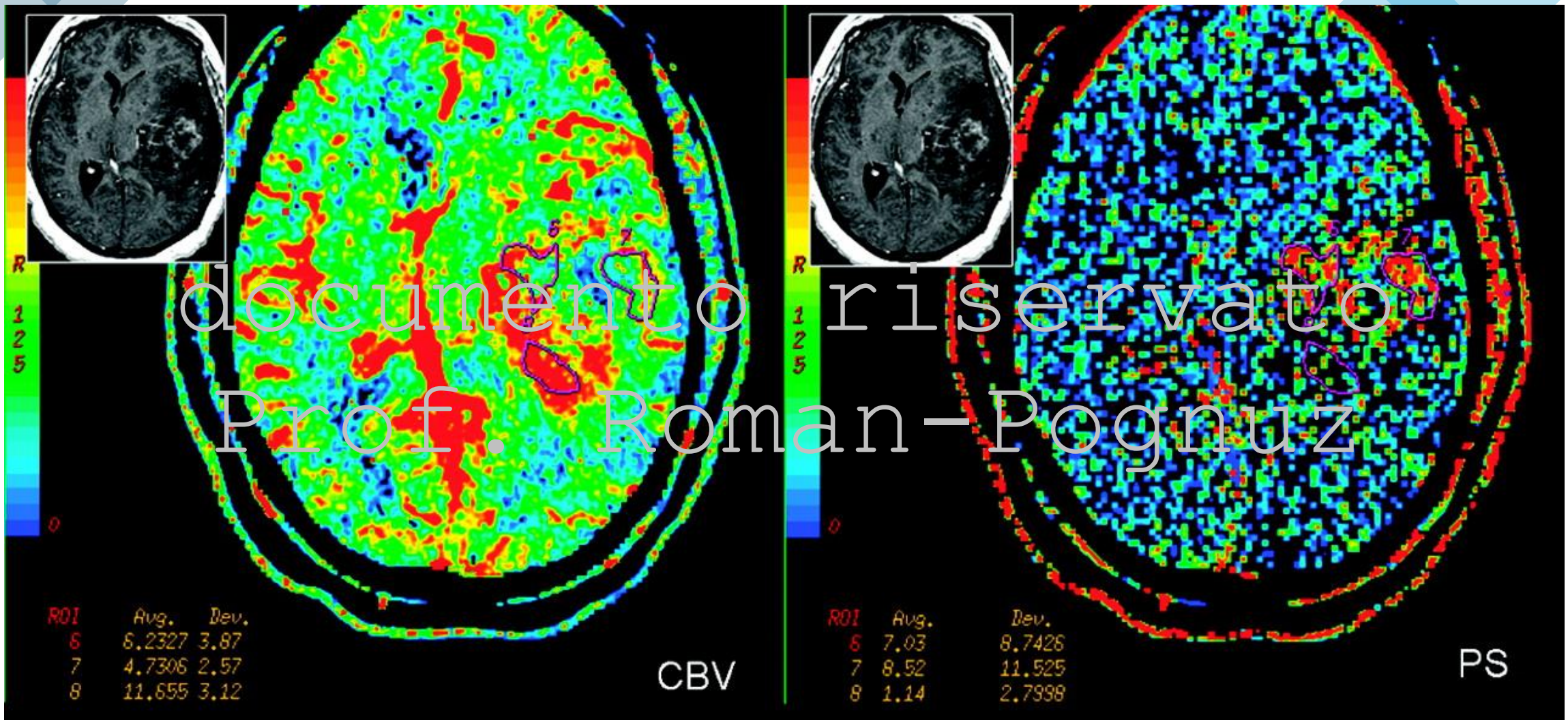
Preferred MRI Sequences:

- Gradient echo (GRE) or susceptibility-weighted imaging (SWI): Detect microhemorrhages.
- Diffusion-weighted imaging (DWI): Evaluate ischemic changes and axonal injury.

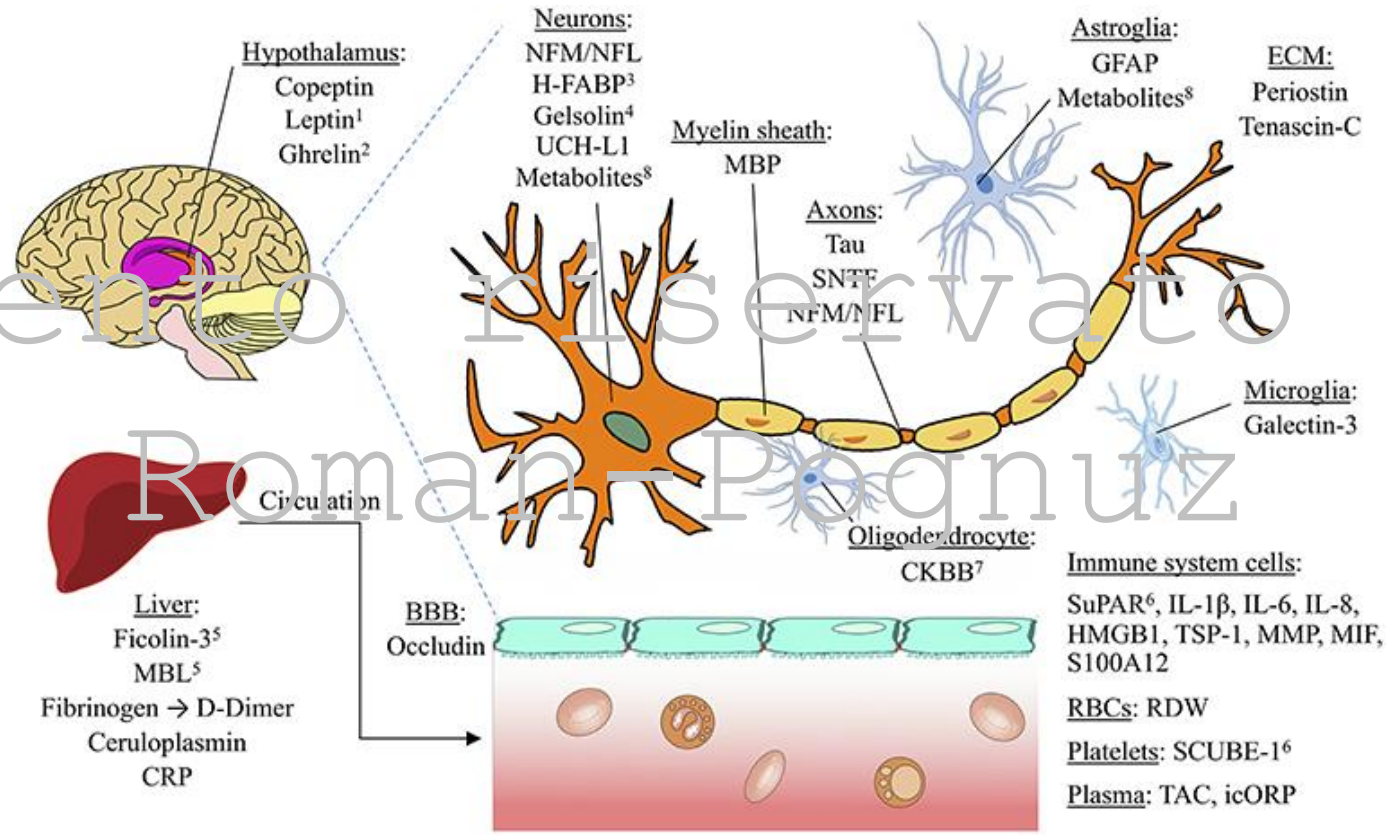


Advanced Imaging Techniques

- **CT Angiography (CTA) and Venography (CTV)**:
  - Indicated for suspected vascular injuries (e.g., dissection, aneurysm, or dural sinus thrombosis).
- **Perfusion CT/MRI**:
  - To assess cerebral blood flow in secondary injury and monitor ischemia.
- **Emerging Modalities**
  - **Positron Emission Tomography (PET)**: Used in research to study brain metabolism.
  - **Magnetoencephalography (MEG)**: Evaluates functional brain disturbances post-TBI.

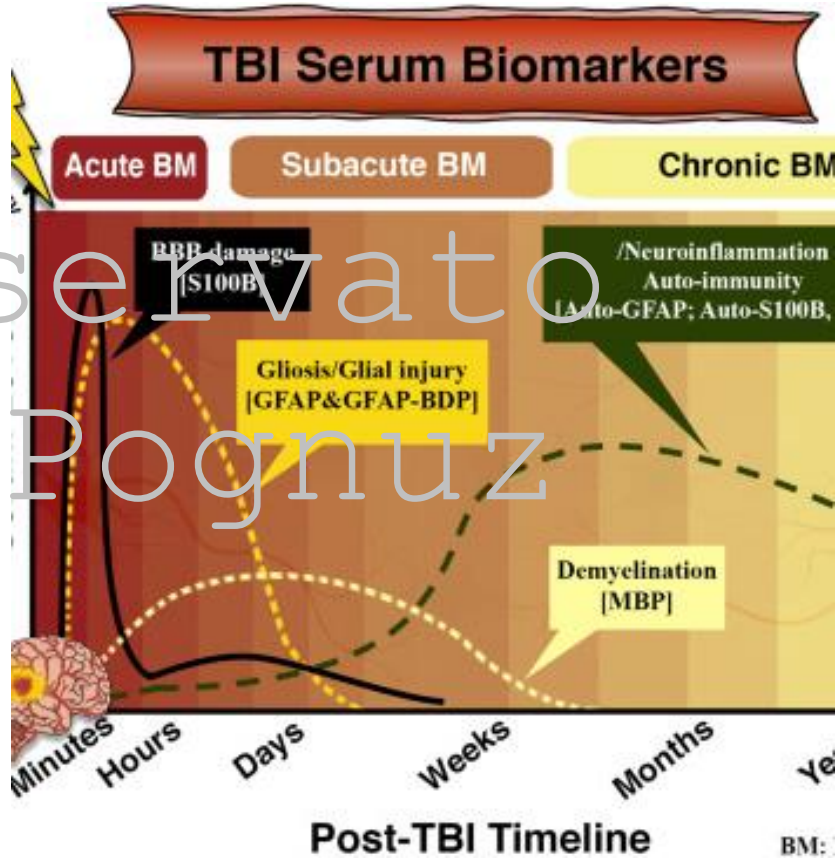


Biomarker

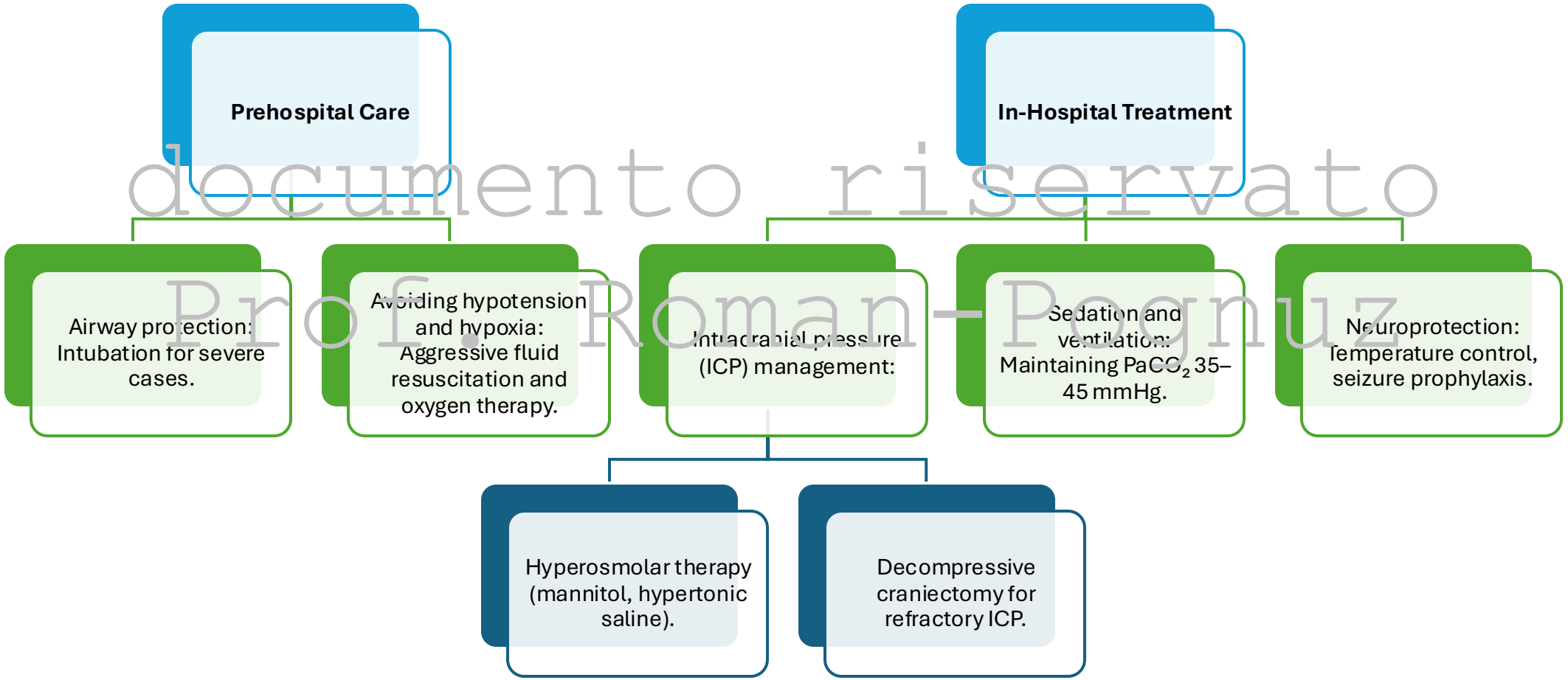


Biomarkers

- **S100B (S100 Calcium-Binding Protein B)**
  - **Source**: Primarily released from astrocytes in the central nervous system (CNS).
  - **Utility**:
    - Elevated levels correlate with **blood-brain barrier disruption**.
    - High sensitivity for detecting **mild TBI**, especially in ruling out significant injuries.
  - **Clinical Use**:
    - Widely used in Europe as part of the Scandinavian Neurotrauma Guidelines.
    - Reduces unnecessary CT scans in mild TBI.
- **2. GFAP (Glial Fibrillary Acidic Protein)**
  - **Source**: Released from astrocytes during structural CNS damage.
  - **Utility**:
    - Highly specific for **moderate-to-severe TBI**.
    - Associated with **intracranial lesions** visible on CT/MRI.
  - **Clinical Use**:
    - FDA-approved in conjunction with UCH-L1 (ubiquitin carboxyl-terminal hydrolase-L1) for assessing mild TBI.



Management: Acute Phase



Prehospital Care in TBI

1. Airway Protection

Objective: Ensure adequate oxygenation and ventilation while preventing secondary injury.

Indications for Intubation:

- GCS ≤ 8 (inability to protect airway)
- Severe facial trauma or compromised airway.
- Respiratory failure or apnea.

Methods:

- **Endotracheal Intubation**: Preferred in severe cases, with cervical spine immobilization.
- **Supraglottic Devices**: Used as temporary alternatives when intubation is delayed.

Precautions:

- Employ rapid sequence intubation (RSI) with minimal interruptions to oxygenation.
- Avoid hyperventilation ($PaCO_2$ <35 mmHg) to prevent cerebral vasoconstriction.

Avoiding Hypotension and Hypoxia

Objective: Minimize secondary brain injury by maintaining adequate perfusion and oxygen delivery.

- **Hypoxia Management**
- **Oxygen Therapy**:
  - Administer 100% oxygen via a non-rebreather mask for all suspected TBI patients.
  - Intubated patients: Target PaO_2 ≥100 mmHg and SpO_2 >94%.
- **Key Considerations**:
  - Hypoxia (SpO_2 <90%) doubles the risk of mortality in TBI patients.
- **Hypotension Management**
- **Fluid Resuscitation**:
  - Use **isotonic crystalloids** (e.g., normal saline or lactated Ringer's) to maintain systolic BP ≥100 mmHg (adults).
  - Avoid hypotonic solutions (e.g., D5W) to prevent cerebral edema.
- **Blood Pressure Targets**:
  - Adults: SBP ≥110 mmHg in older patients (>50 years).
  - Pediatrics: Age-appropriate norms for SBP.
- **Avoid Over-Resuscitation**:
  - Monitor for signs of fluid overload or increased ICP.

Immobilization and Transport

Maintain cervical spine stabilization with a collar during airway and resuscitation procedures.

Prioritize rapid transfer to a **trauma center** equipped for neurosurgical intervention.

Prehospital Monitoring

Continuous pulse oximetry and capnography during transport.

Monitor Glasgow Coma Scale (GCS) regularly to assess neurological deterioration.

In-Hospital Treatment

1. Initial Stabilization

- **Goal**: Prevent secondary injury through airway, breathing, circulation management.
- **Airway and Ventilation**:
  - Secure airway if GCS ≤8 using endotracheal intubation.
  - Maintain **PaO_2 ≥100 mmHg** and **$PaCO_2$ 35-45 mmHg** to ensure adequate oxygenation and cerebral perfusion.
- **Hemodynamic Stabilization**:
  - **Target Blood Pressure**: Maintain systolic BP ≥110 mmHg in adults.
  - Use isotonic crystalloids or vasopressors (e.g., norepinephrine) if needed.

Neurological Monitoring

- **Intracranial Pressure (ICP)** Monitoring:
  - Indicated in severe TBI (GCS ≤8 with abnormal CT).
  - **Normal ICP**: 5–15 mmHg; aim to keep ICP <22 mmHg.
- **Cerebral Perfusion Pressure (CPP)**:
  - Calculate: CPP = MAP - ICP.
  - Target CPP: **60–70 mmHg**.
- **Neurological Assessments**:
  - Frequent monitoring of **Glasgow Coma Scale (GCS)**, pupil reactivity, and motor responses.

Management of Intracranial Pressure (ICP)

Medical Interventions:

- **Hyperosmolar Therapy**:
  - Mannitol (0.25–1 g/kg IV) or hypertonic saline to reduce cerebral edema.
- **Sedation and Analgesia**:
  - Propofol or midazolam for sedation; fentanyl or morphine for pain control.

Surgical Interventions:

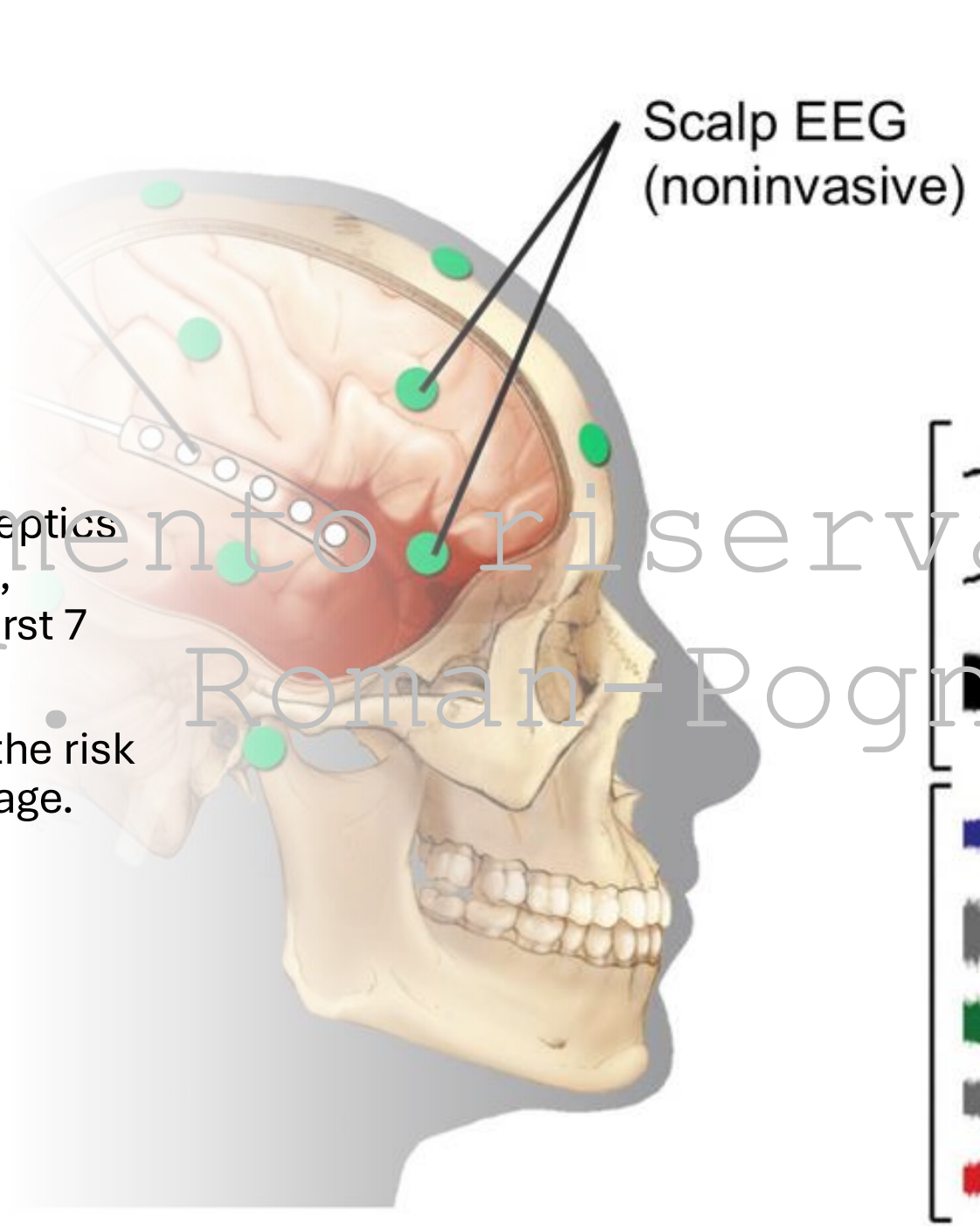
- **Decompressive Craniectomy**: For refractory elevated ICP.
- Evacuation of hematomas or contusions if causing mass effect.

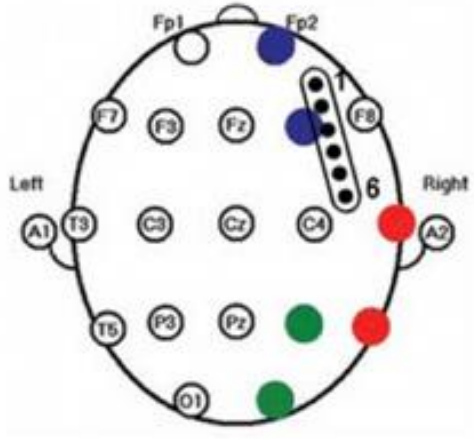
Positioning and Ventilation:

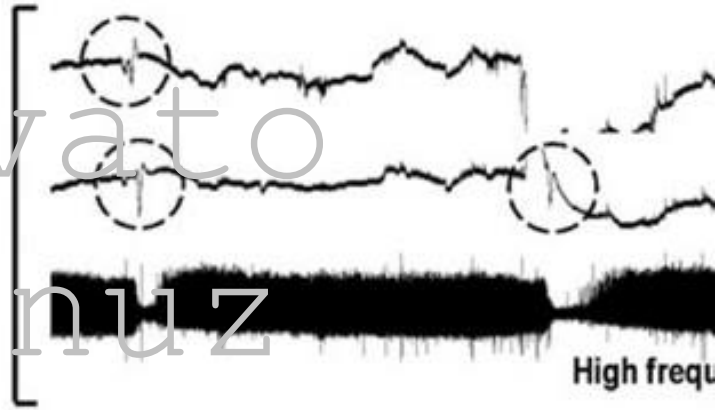
- Elevate head of bed to 30° to facilitate venous drainage.
- Avoid hyperventilation unless there are signs of impending herniation.

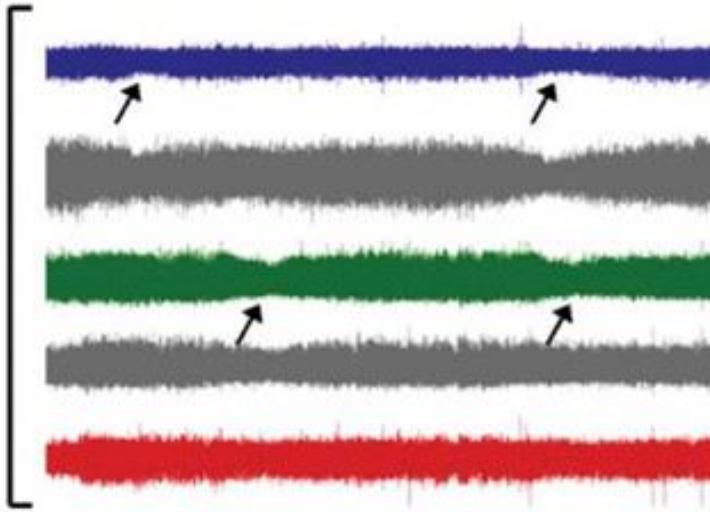
Seizure Prophylaxis

- **Medications**:
  - Administer antiepileptics (e.g., levetiracetam, phenytoin) for the first 7 days post-TBI.
- Early seizures increase the risk of secondary brain damage.









Temperature and Glycemic Control

Temperature:	Avoid hyperthermia; maintain normothermia (36–37°C).
	Consider targeted temperature management (TTM) if required.
Blood Glucose:	Maintain glucose levels between **140–180 mg/dL**.
	Avoid hypoglycemia (<70 mg/dL) as it worsens outcomes.

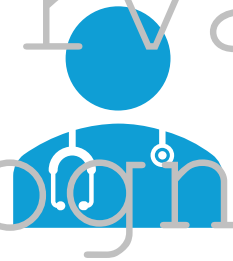
Advanced Neuroprotection and Monitoring

- **Advanced Modalities**:
  - Jugular bulb oximetry or brain tissue oxygen monitoring ($PbtO_2$).
  - Multimodal monitoring of cerebral metabolism.
- **Neuroprotective Agents**:
  - No definitive neuroprotective drugs proven effective yet; ongoing research is exploring options.

Rehabilitation Planning

Early Mobilization:

Initiate physical and occupational therapy as soon as the patient stabilizes.



Multidisciplinary Team:

Include neurology, physiotherapy, and social support in post-acute care planning.

Management: Rehabilitation and Long-term Care

- **Early Rehabilitation**
  - Physical, occupational, and speech therapy.
  - Cognitive rehabilitation programs.
- **Long-term Strategies**
  - Addressing post-traumatic epilepsy, mood disorders, and cognitive decline.
  - Multidisciplinary team involvement: Neurologists, psychologists, social workers.

Outcomes and Prognosis

Outcome Predictors

- Severity of injury (GCS, CT findings).
- Age and pre-existing comorbidities.

Functional Outcomes

- Return to baseline: Possible in mild TBI.
- Long-term disability: Frequent in moderate to severe TBI (physical, cognitive, psychological).

Mortality

- Higher in severe cases despite advances in care.

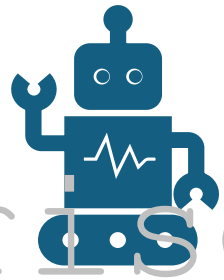
Future Directions and Improvements

Research Areas

Novel neuroprotective agents: Anti-inflammatory, antioxidant therapies.

Advanced monitoring: Multimodal monitoring including ICP, brain oxygenation, and metabolism.

Precision medicine: Biomarker-guided individualized therapy.



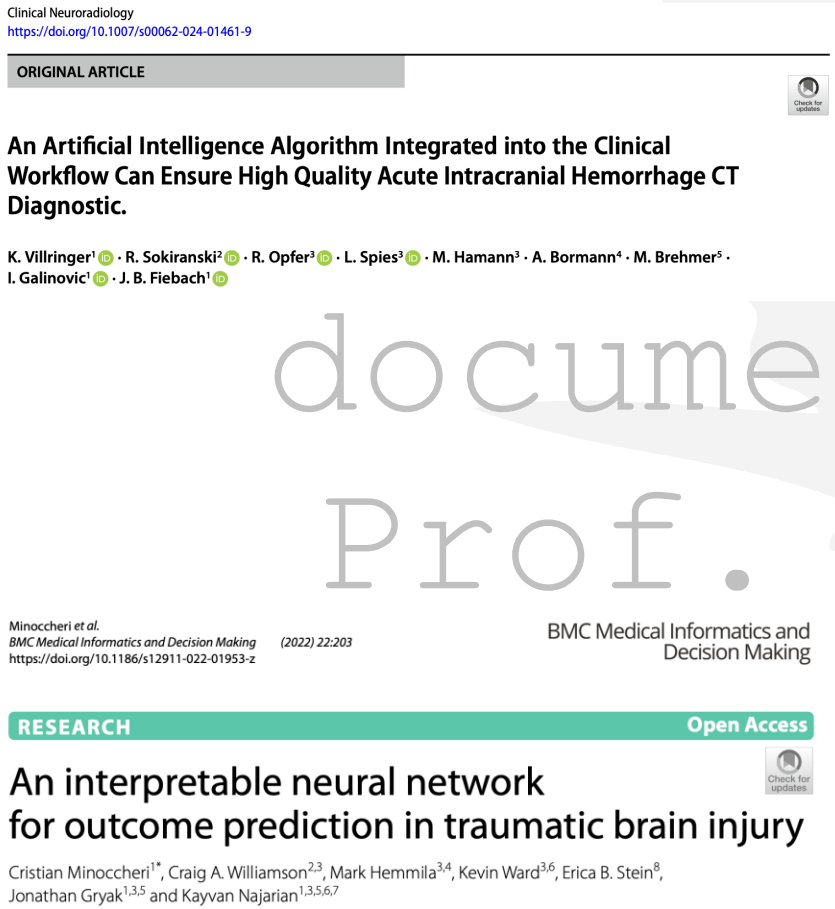
Technology Integration

Artificial intelligence for imaging and outcome prediction.

Virtual reality and robotics in rehabilitation.

Technology Integration in TBI Management

- **Artificial Intelligence (AI) for Imaging and Outcome Prediction**
- **Role in Imaging**
- **AI-Powered Image Analysis**:
  - AI tools assist in **rapid detection of intracranial hemorrhages**, midline shifts, and fractures on CT and MRI.
  - Example: Deep learning algorithms like those used in Aidoc and Viz.ai for automated radiology assessments (Chang et al., Radiology, 2021).
- **Precision Diagnosis**:
  - AI enhances sensitivity and specificity, reducing diagnostic errors.
  - Predicts lesion evolution, guiding intervention timing (Geis et al., Radiology: AI, 2022).



Clinical Neuroradiology
https://doi.org/10.1007/s00062-024-01461-9

ORIGINAL ARTICLE

An Artificial Intelligence Algorithm Integrated into the Clinical Workflow Can Ensure High Quality Acute Intracranial Hemorrhage CT Diagnostic.

K. Villringer[1] · R. Sokiranski[2] · R. Opfer[3] · L. Spies[3] · M. Hamann[3] · A. Bormann[4] · M. Brehmer[5] · I. Galinovic[1] · J. B. Fiebach[1]

Minoccheri *et al.*
BMC Medical Informatics and Decision Making (2022) 22:203
https://doi.org/10.1186/s12911-022-01953-z

BMC Medical Informatics and Decision Making

RESEARCH Open Access

An interpretable neural network for outcome prediction in traumatic brain injury

Cristian Minoccheri[1*], Craig A. Williamson[2,3], Mark Hemmila[3,4], Kevin Ward[3,6], Erica B. Stein[8], Jonathan Gryak[1,3,5] and Kayvan Najarian[1,3,5,6,7]

Technology Integration in TBI Management

- **Artificial Intelligence (AI) for Imaging and Outcome Prediction**
  - **Outcome Prediction**
  - AI models analyze **multimodal data** (imaging, biomarkers, clinical parameters) to forecast:
    - Functional outcomes (e.g., Glasgow Outcome Scale scores).
    - Risk of secondary complications like seizures or cognitive decline.
    - Example: Predictive models like XGBoost and neural networks have shown high accuracy in stratifying patients (Raj et al., PLOS One, 2021).

Technology Integration in TBI Management

Clinical Neuroradiology
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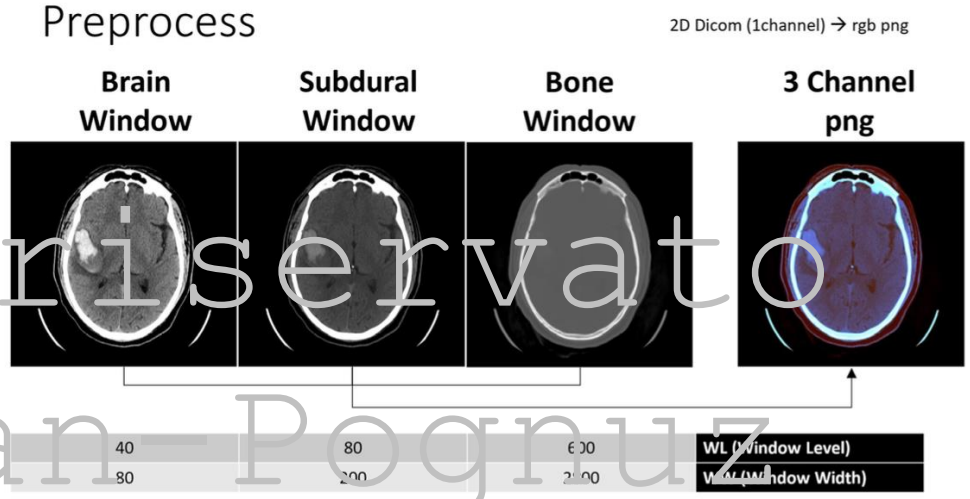
ORIGINAL ARTICLE

An Artificial Intelligence Algorithm Integrated into the Clinical Workflow Can Ensure High Quality Acute Intracranial Hemorrhage CT Diagnostic.

K. Villringer[1] · R. Sokiranski[2] · R. Opfer[3] · L. Spies[3] · M. Hamann[3] · A. Bormann[4] · M. Brehmer[5] · I. Galinovic[1] · J. B. Fiebach[1]



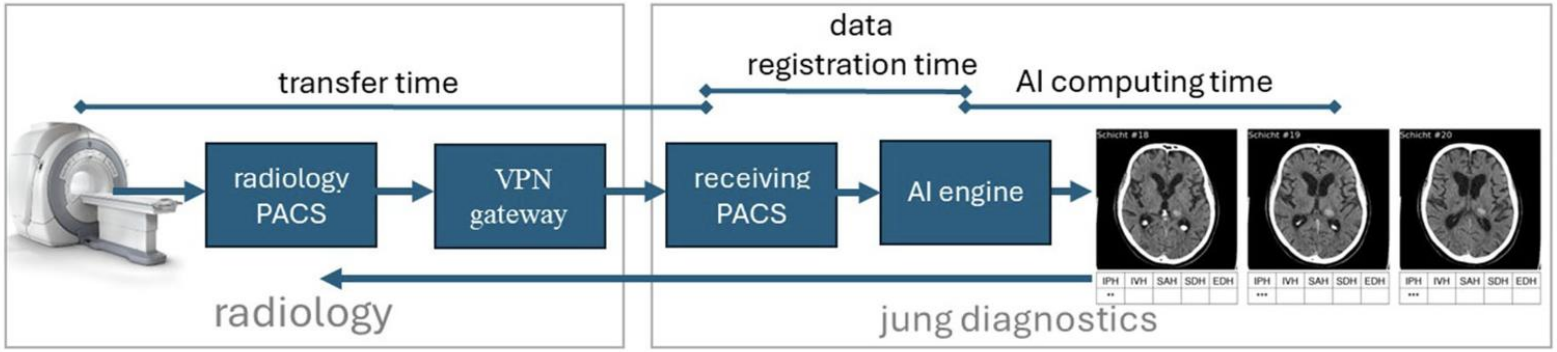
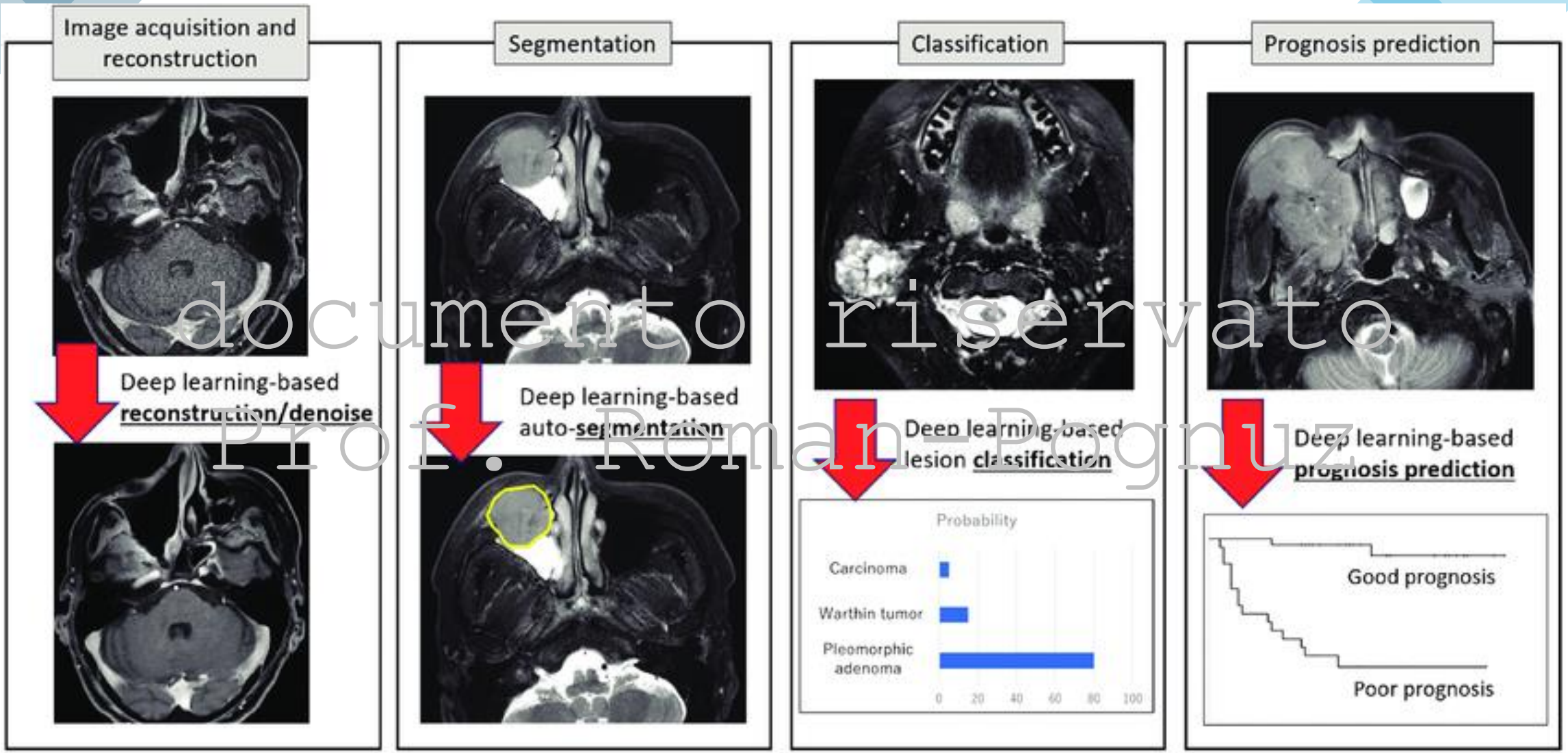


Fig. 3 Schematic representation of the workflow and associated time intervals



After discharge?

How is the QoL?

Standardized Quality of Life Assessment Tools

Health-Related Quality of Life (HRQoL) Scales

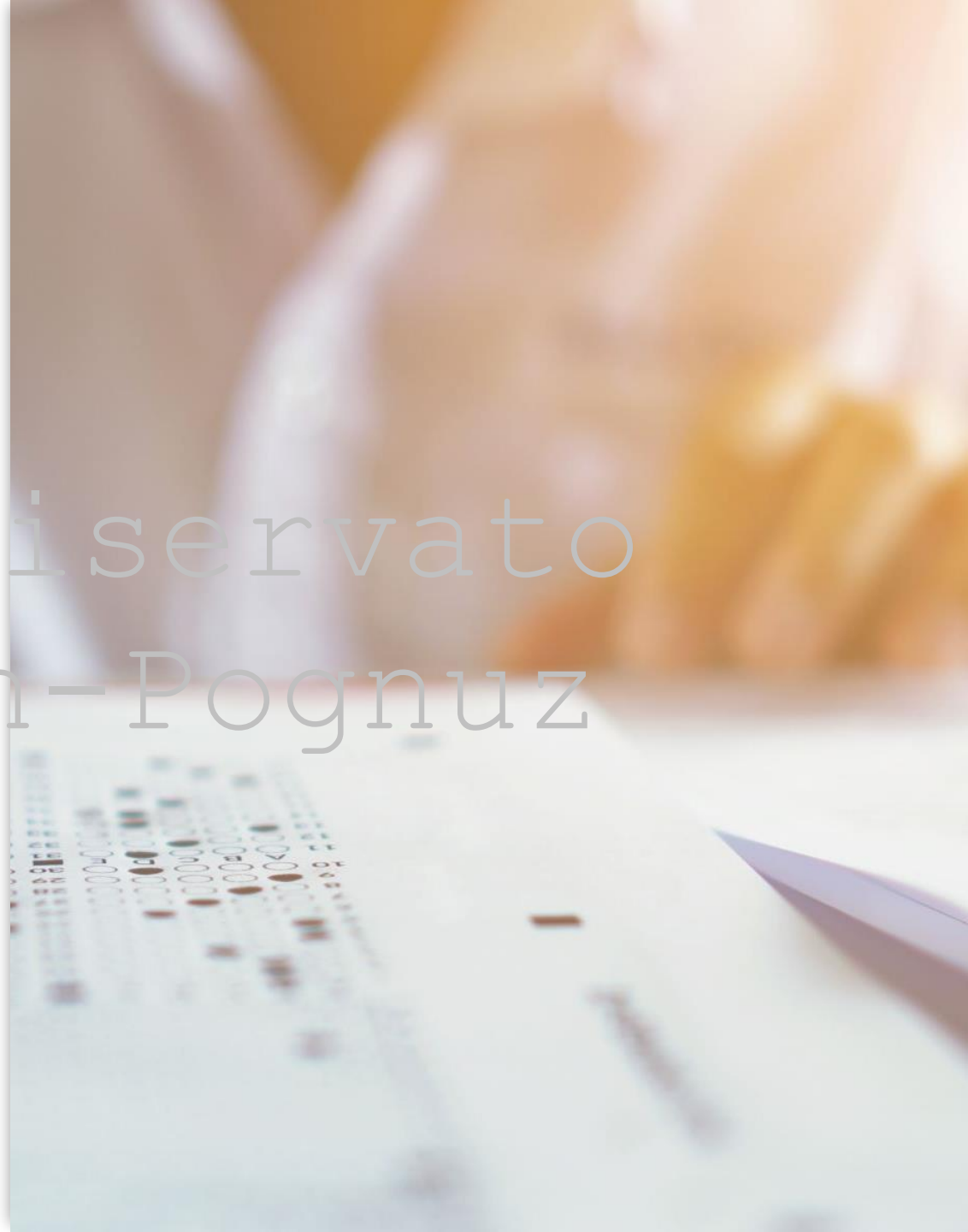
- **SF-36 (Short Form Health Survey)**:
  - Measures physical and mental health domains.
  - Subdomains: Physical functioning, role limitations, pain, general health, vitality, social functioning, emotional well-being.
  - Provides a holistic understanding of QoL post-TBI.
- **EQ-5D (EuroQol Five-Dimensional Questionnaire)**:
  - Measures mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.
  - Includes a visual analog scale (VAS) for overall health.

TBI-Specific Scales

- **Quality of Life after Brain Injury (QOLIBRI)**:
  - Designed specifically for TBI patients.
  - Domains: Cognition, self-perception, daily life, social relationships, emotions.
  - Provides insights into TBI-specific challenges and recovery.
- **Glasgow Outcome Scale-Extended (GOSE)**:
  - Assesses functional outcomes with specific attention to independence and disability.

Cognitive and Psychological Assessments

- **Neuropsychological Testing**:
  - Focuses on memory, attention, executive function, and processing speed.
- **Mental Health Screening**:
  - Depression: Use tools like PHQ-9 (Patient Health Questionnaire).
  - Anxiety: Generalized Anxiety Disorder-7 (GAD-7) scale.
  - Post-Traumatic Stress Disorder (PTSD): Impact of Events Scale-Revised (IES-R).



Physical Health Evaluation

Motor Function:

Assess mobility and balance using tools like the Berg Balance Scale or the Timed Up and Go Test (TUG).

Pain Management:

Evaluate chronic pain using the Visual Analog Scale (VAS) or Numerical Pain Rating Scale.

Sleep Quality:

Use sleep diaries or scales like the Pittsburgh Sleep Quality Index (PSQI).

Social and Vocational Outcomes

Social Reintegration:

Tools like the Community Integration Questionnaire (CIQ) evaluate social interaction, community mobility, and productivity.

Vocational Assessments:

Determine the ability to return to work or school.

Consider ongoing cognitive or physical challenges impacting employment.

Longitudinal Follow-Up

Regular Monitoring:	Periodic reassessment of QoL using the same tools to track progress and adjust interventions.
Caregiver Feedback:	Include caregivers' perspectives on patient well-being and challenges.
Telemedicine Options:	Facilitate remote monitoring and support, especially for rural or mobility-restricted patients.