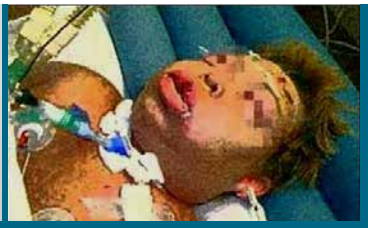
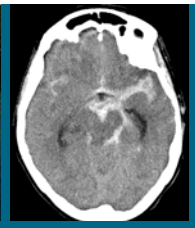
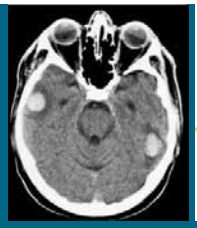




wachkoma coma vigile apallisches syndrom vegetative state minimally conscious state unresponsive wakefulness syndrome

Das schwere Schädel-Hirn-Trauma:

Die Rolle der Notfalls- und Neuro-Intensivmedizin

Univ.Prof. Dr. Erich Schmutzhard
Ass.-Prof. Priv.-Doz. Dr. Ronny Beer

Neurologische Intensivstation
Universitätsklinik für Neurologie
Medizinische Universität Innsbruck

Interessenskonflikte in Bezug auf **diese** Präsentation:
ES: Berater-Honorar von Vasopharm (NOSTRA), **Forschungsunterstützung** von BHR (SyNAPSE)
RB: keine

Tiroler Tageszeitung Montag, 6.10.2014

- **Schwerer Unfall von Bianchi überschattet Hamiltons Triumph**
- Nach dem Chaos-Rennen von Suzuka und dem Sieg von Lewis Hamilton wollte niemand feiern. Das Rennen endete nach 44 Runden vorzeitig mit einem Schock, als der Franzose Jules Bianchi schwer verunglückte. Er wurde bewusstlos ins Krankenhaus gebracht

Tiroler Tageszeitung Montag, 6.10.2014

- **Schw hattet Hami**
- Nach und dem emand feierr unden vorze nzose Jules wurde bewu

Tiroler Tageszeitung, Montag 6.10.2014

- Nach Angaben der französischen Fachzeitung „L‘Equipe“ muss der 25-Jährige nach dem Eingriff nicht mehr künstlich beatmet werden. Bianchi könne wieder selbstständig atmen…..

- Suzuka – Formel-1-Pilot Jules Bianchi befindet sich weiter in **Lebensgefahr**. Sein Gesundheitszustand sei **„kritisch, aber stabil“ und weiter „sehr, sehr ernst“,** erklärte FIA-Sprecher Matteo Bonciani am Montagabend vor dem Krankenhaus in Yokkaichi mit. Die Eltern von Bianchi hatten den Internationalen Automobil-Verband (FIA) um diese Mitteilung gebeten.
- Bianchi war am Sonntag im Grand Prix von Japan in Suzuka in Runde 43 von der regennassen Strecke abgekommen und in der Auslaufzone ins Heck eines Bergungsfahrzeugs gekracht. Dieses war gerade dabei, den ebenfalls in dieser Kurve von der Piste gerutschten Boliden des deutschen Sauber-Fahrers Adrian Sutil zu entfernen. Bianchi erlitt bei dem Unfall schwere Kopfverletzungen und wurde noch am Sonntag in Yokkaichi operiert.

- Suzuka – Formel-1-Pilot Jules Bianchi befindet sich weiter in **Lebensgefahr**. Sein Gesundheitszustand sei **„kritisch, aber stabil“ und weiter „sehr, sehr ernst“,** erklärte FIA-Sprecher Matteo Bonciani am Montagabend vor dem Krankenhaus in Yokkaichi mit. Die Eltern von Bianchi hatten den Internationalen Automobil-Verband (FIA) um diese Mitteilung gebeten.
- Bianchi war am Sonntag im Grand Prix von Japan in Suzuka in Runde 43 von der regennassen Strecke abgekommen und in der Auslaufzone ins Heck eines Bergungsfahrzeugs gekracht.

Tiroler Tageszeitung 6.10.2014

- Nach Angaben der französischen Fachzeitung „L‘Equipe“ muss der 25-Jährige nach dem Eingriff nicht mehr künstlich beatmet werden. Bianchi **könne wieder selbstständig atmen** …

survival

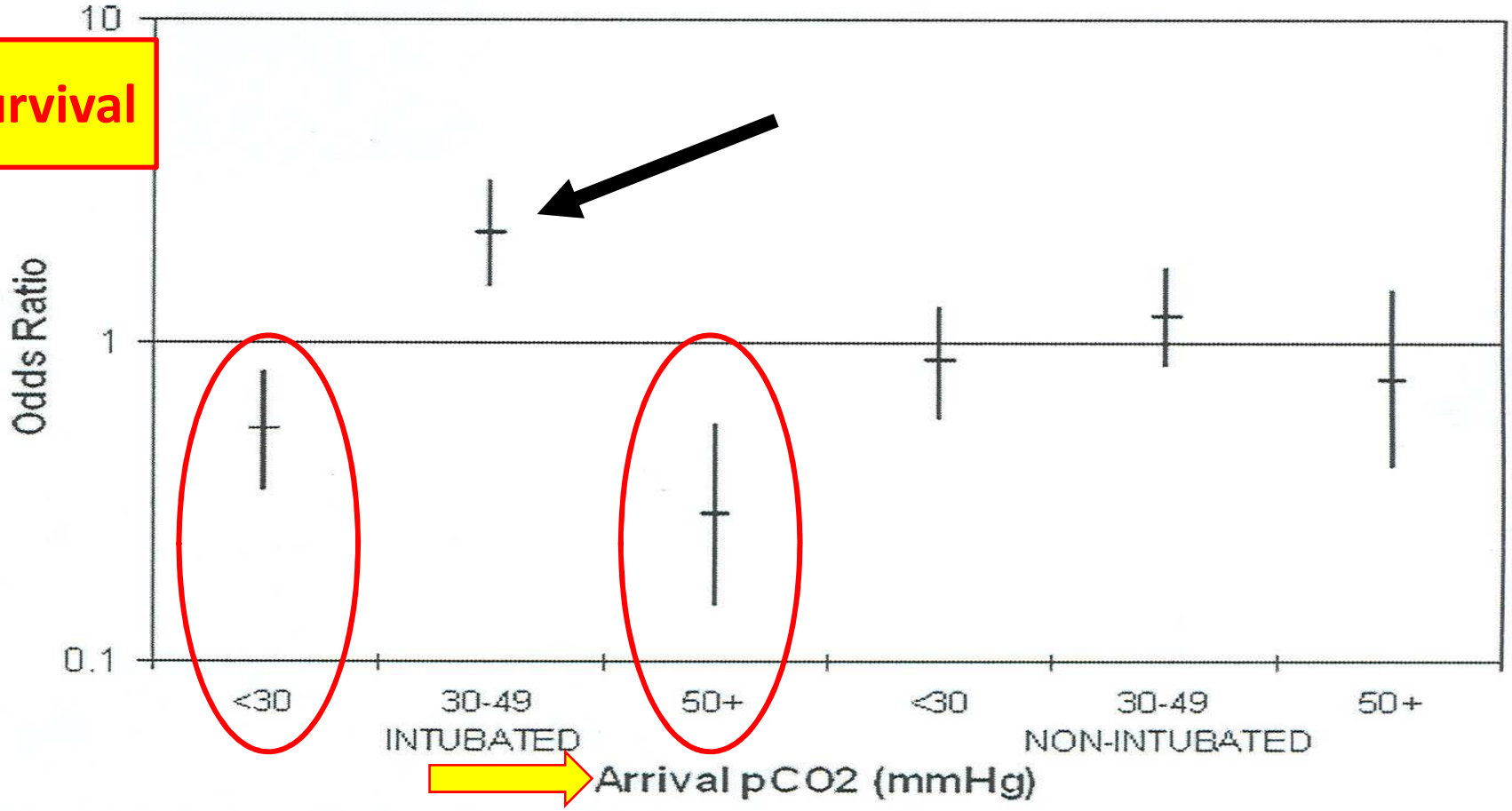


Figure 2. Adjusted odds ratio of survival and a good outcome for patients within and outside the target range for arrival Pco_2 (30–49 mm Hg). Odds ratios are adjusted for age, gender, mechanism of injury, year of injury, preadmission Glasgow Coma Scale, Head Abbreviated Injury Score, Injury Severity Score, preadmission hypotension, arrival Po_2, and base deficit. Adjusted odds ratio of survival and good outcomes for intubated and nonintubated patients with hyperventilation (arrival Pco_2 values <30 mm Hg), euventilation (arrival Pco_2 30–49 mm Hg), and hypoventilation (arrival Pco_2 ≥50 mm Hg). Intubated patients within the optimal range were compared with other intubated patients below and above this range, whereas nonintubated patients within this range were compared with other nonintubated patients outside this range.

Davis, 2006

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Mortality Related to Severe Sepsis and Septic Shock Among Critically Ill Patients in Australia and New Zealand, 2000-2012

Kirsi-Maija Kaukonen, MD, PhD, EDIC; Michael Bailey, PhD; Satoshi Suzuki, MD; David Pilcher, FCICM; Rinaldo Bellomo, MD, PhD

CONCLUSIONS AND RELEVANCE In critically ill patients in Australia and New Zealand with severe sepsis with and without shock, there was a decrease in mortality from 2000 to 2012. These findings were accompanied by changes in the patterns of discharge to home, rehabilitation, and other hospitals.

JAMA. 2014;311(13):1308-1316. doi:10.1001/jama.2014.2637

Figure 1. Mean Annual Mortality in Patients With Severe Sepsis

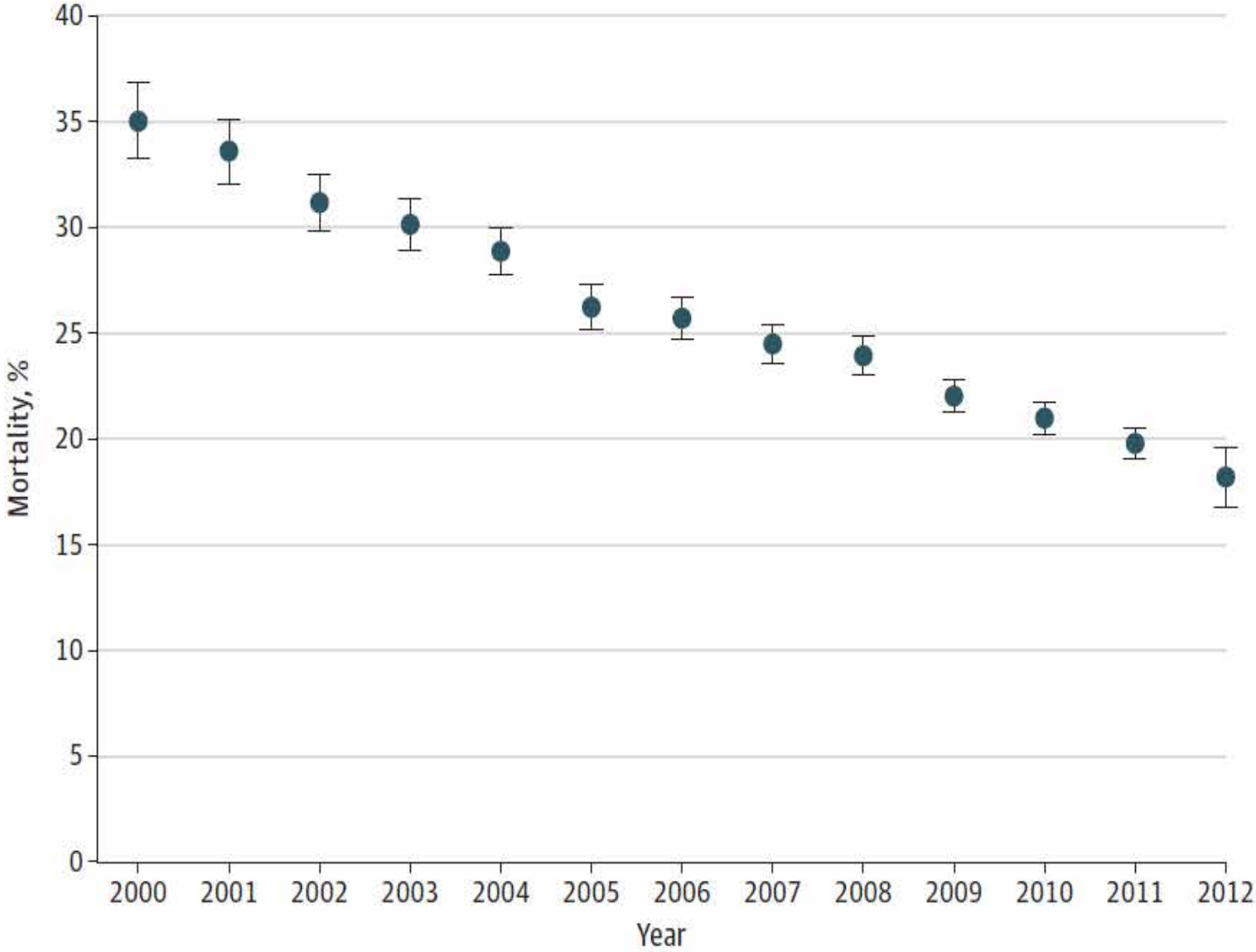


Table 2. Mortality Rate Among Severe Sepsis Patients Overall and Within Subgroups in 2000 and 2012[a]

	2000			2012			Risk Reduction	
	No. of Events	No. of Patients	Mortality, % (95% CI)	No. of Events	No. of Patients	Mortality, % (95% CI)	Absolute	Relative
All patients with severe sepsis	949	2708	35.0 (33.2-36.8)	2300	12 512	18.4 (17.8-19.0)	16.7 (14.8-18.6)	47.5 (44.1-50.8)
Without comorbidities[b]	529	1800	29.4 (27.2-31.6)	1136	8110	14.0 (13.2-14.8)	15.4 (13.2-17.7)	52.3 (47.9-56.4)
With comorbidities[b]	420	908	46.3 (43.0-49.6)	1164	4402	26.4 (25.0-27.8)	19.8 (16.3-23.3)	42.8 (37.7-47.5)
Severe sepsis without shock	426	1411	30.2 (27.8-32.6)	815	5755	14.2 (13.2-15.2)	16.0 (13.5-18.6)	53.1 (48.1-57.6)
Septic shock	523	1297	40.3 (37.6-43.0)	1485	6757	22.0 (21.0-23.0)	18.3 (15.5-21.2)	45.5 (41.0-49.7)
Medical admissions	784	2052	38.2 (36.0-40.4)	1959	9824	19.9 (19.1-20.7)	18.3 (16.0-20.5)	47.8 (44.1-51.2)
Surgical admissions	165	656	25.2 (21.9-28.5)	341	2688	12.7 (11.5-13.9)	12.5 (9.0-16.1)	49.6 (40.5-57.2)
Respiratory failure[c]	652	1642	39.7 (37.3-42.1)	1106	4603	24.0 (22.8-25.2)	15.7 (13.0-18.4)	39.5 (34.5-44.1)
Acute renal failure[d]	445	805	55.3 (51.8-58.8)	1069	3100	34.5 (32.7-36.3)	20.8 (17.0-24.6)	37.6 (32.5-42.3)
APACHE score								
II <25	370	1679	22.0 (20.0-24.0)	1079	9537	11.3 (10.7-11.9)	10.7 (8.7-12.9)	48.7 (42.9-53.8)
II ≥25	554	942	58.8 (55.7-61.9)	1177	2732	43.1 (41.3-44.9)	15.7 (12.0-19.3)	26.7 (21.5-31.6)
III Q1	47	498	9.4 (6.9-11.9)	77	3486	2.2 (1.8-2.6)	7.2 (4.9-10.1)	76.6 (66.8-83.5)
III Q2	103	544	18.9 (15.6-22.2)	317	3254	9.7 (8.7-10.7)	9.2 (5.9-12.8)	48.5 (37.0-58.0)
III Q3	215	607	35.4 (31.7-39.1)	634	3149	20.1 (18.7-21.5)	15.3 (11.3-19.4)	43.2 (35.4-50.0)
III Q4	498	819	60.8 (57.5-64.1)	1258	2591	48.6 (46.6-50.6)	12.3 (8.4-16.1)	20.2 (14.6-25.4)
Age, y								
≤44	98	443	22.1 (18.2-26.0)	130	1778	7.3 (6.1-8.5)	14.8 (11.0-19.1)	66.9 (58.0-74.0)
45-64	226	742	30.5 (27.2-33.8)	524	3660	14.3 (13.1-15.5)	16.1 (12.7-19.7)	53.0 (46.2-58.9)
65-84	537	1326	40.5 (38.0-43.0)	1260	5806	21.7 (20.7-22.7)	18.8 (16.0-21.7)	46.4 (41.9-50.6)
≥85	88	197	44.7 (37.6-51.8)	386	1268	30.4 (27.9-32.9)	14.2 (7.0-21.6)	31.9 (18.7-42.9)

Schädel-Hirn-Trauma (SHT) – In den Schlagzeilen

tirol ORF.at Innsbruck: 15.7 °C Live: ▶ Radio Tirol

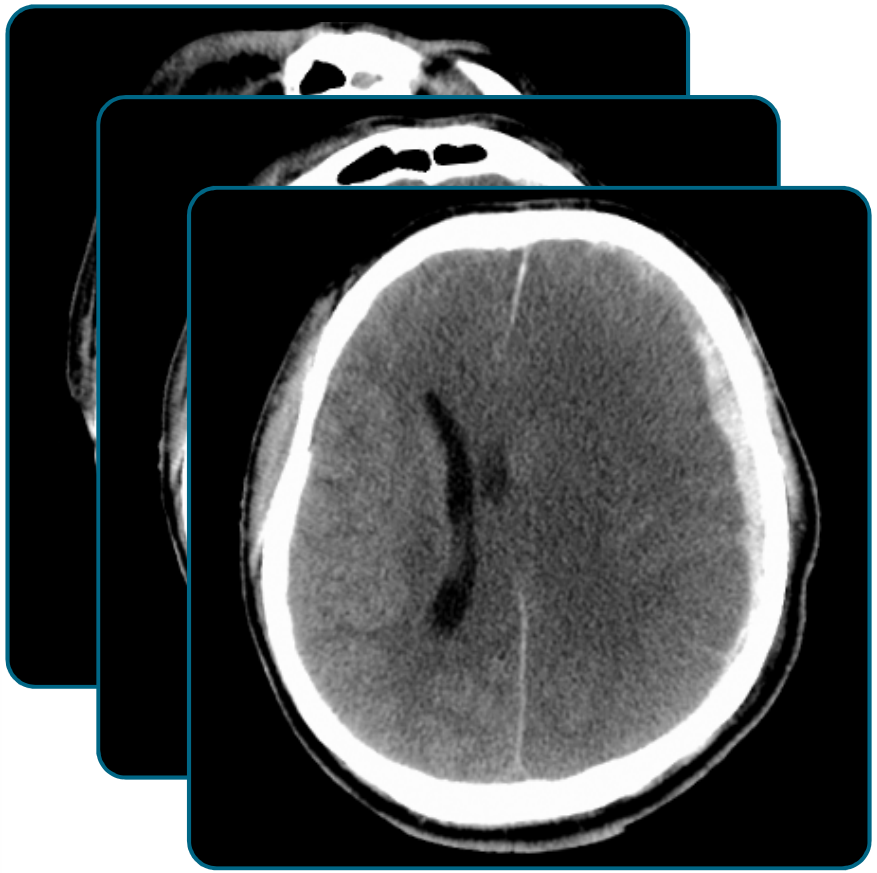
Fernsehen TVthek Radio Debatte Österreich Wetter IPTV Sport News ORF.at im Überblick

Mann ringt nach Absturz mit dem Tod

Im Gemeindegebiet von Finkenberg ist am Dienstag ein deutsches Paar über ein Schneefeld 200 Meter abgestürzt. Die Bergung der teils lebensbedrohlich Verletzten gestaltete sich schwierig. Beide Urlauber liegen an der Klinik auf der Intensivstation.

Der 55-Jährige und die 52-Jährige waren laut Polizei im Bereich des Schönbichler Horns unterwegs. Sie hatten zuvor auf dem Furtschaglhaus übernachtet und wollten zur Berliner Hütte. Auf etwa 2.800 Meter Seehöhe rutschten beide - unabhängig voneinander - auf einem Schneefeld rund 200 Meter ab und blieben an der Schneeoberfläche liegen.

Einer der Verletzten in dem Schneefeld.



http://tirol.orf.at/news/stories/2654419/ (25.06.2014)

SHT – Epidemiologie

- **Inzidenz** in Mitteleuropa **ca. 150–300 pro 100 000** Personen pro Jahr
- In Europa unter den drei häufigsten Diagnosen hinsichtlich **Verletzungs-bedingter medizinischer Folgekosten**
- **Hohe Morbidität** und **Mortalität** (ca. 15 pro 100 000 Personen pro Jahr)

Parameter	Place				
	Europe[1]	U.S.[2]	Australia[3]	Asia[4]	India[5]
Incidence rate[6,7]	235	103	226	344	160
Prevalence rate[6]	NR	1893	NR	709	97
Mortality rate[6]	15.4	18.1	NR	38	20
Severity (% Mi/Mo/Sev)	79/12/9	80/10/10	76/12/11	78/9/13	71/15/13
Case fatality rate[8]	2.7[a]	6.2	2.4	11	6
External cause (% Fall/MVC/Vio)	37/40/7	21/25/6	49/25/9	23/65/7	59/25/14
Outcomes[9] (% GOS unfavor)	50[b]	64[c]	NR	27	9

[1] Source: this report, [2] source: aggregate data from references 24, 23, 47, [3] source: aggregate data from references 42, 16, 5, [4] source: Chiu, [8], [5] source: Gururaj, [14], [6] per 100,000 population, [7] includes hospitalized & deaths, [8] rate per 100 hospitalized, [9] unfavorable includes deaths, PVS, and severe disability.

[a] Excludes outlier rates of 46.5, 30, and 52/100 from Table 2.

[b] Source: EBIC [29] includes moderate/severe TBI.

[c] Source: U.S. Traumatic Coma Data Bank [47] severe cases.

NR not reported.

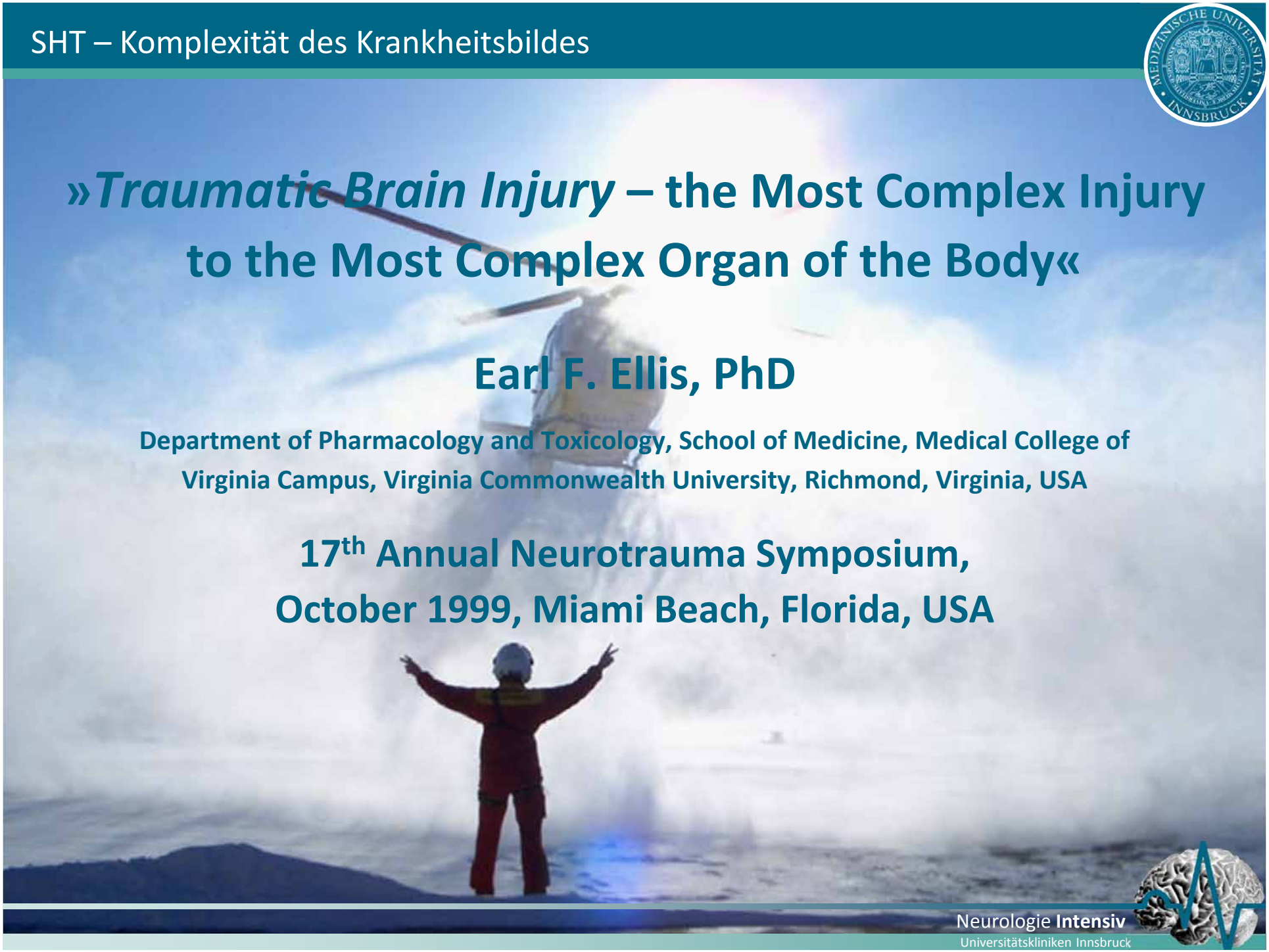
Modifiziert nach Tagliaferri et al., Acta Neurochir 2006; 148: 255–268

….. **road traffic accidents** constitute constitute a vast majority of cases of traumatic brain injury in **Southern** Europe……

(Tagliaferri et al 2006, Servadei et al, 2002)

……**falls,** partially related to alcohol consumption, are the leading cause of trauma in **Central** and **Northern** Europe…..

(Ingebrigtsen et al, 1998; Hukkelhoven et al 2002, Kleiven et al 2003, Steudel et al 2005)



»*Traumatic Brain Injury* – the Most Complex Injury to the Most Complex Organ of the Body«

Earl F. Ellis, PhD

Department of Pharmacology and Toxicology, School of Medicine, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, Virginia, USA

17th Annual Neurotrauma Symposium,
October 1999, Miami Beach, Florida, USA

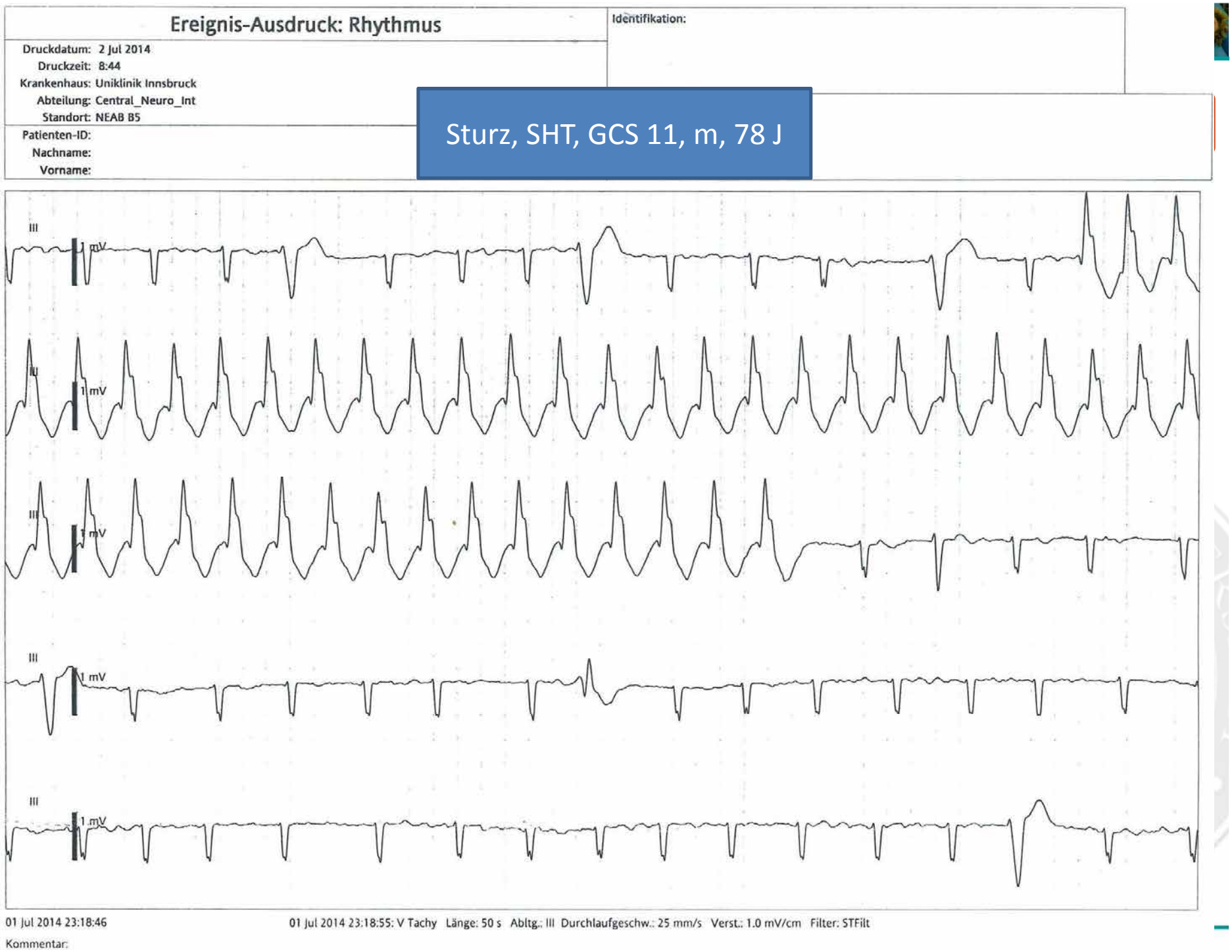
»*Traumatic Brain Injury* – the Most Complex Injury to the Most Complex Organ of the Body«

Earl F. Ellis, PhD

Department of Pharmacology and Toxicology, School of Medicine, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, Virginia, USA

17th Annual Neurotrauma Symposium,
October 1999, Miami Beach, Florida, USA

… und in den letzten Jahren zunehmend häufiger bei alten/älteren Menschen mit mehr und mehr Comorbiditäten …


Ereignis-Ausdruck: Rhythmus
Druckdatum: 2 Jul 2014
Druckzeit: 8:44
Krankenhaus: Uniklinik Innsbruck
Abteilung: Central_Neuro_Int
Standort: NEAB B5
Patienten-ID:
Nachname:
Vorname:
Identifikation:
Sturz, SHT, GCS 11, m, 78 J
III
1 mV
II
1 mV
III
1 mV
III
1 mV
III
1 mV
01 Jul 2014 23:18:46
01 Jul 2014 23:18:55: V Tachy Länge: 50 s Abltg.: III Durchlaufgeschw.: 25 mm/s Verst.: 1.0 mV/cm Filter: STFilt
Kommentar:


Ereignis-Ausdruck: Rhythmus
Druckdatum: 2 Jul 2014
Druckzeit: 8:44
Krankenhaus: Uniklinik Innsbruck
Abteilung: Central_Neuro_Int
Standort: NEAB B5
Patienten-ID:
Nachname:
Vorname:
Identifikation:
Sturz, SHT, GCS 11, m, 78 J
III
1 mV
II
1 mV
III
1 mV
III
1 mV
III
1 mV
01 Jul 2014 23:18:46
01 Jul 2014 23:18:55: V Tachy Länge: 50 s Abltg.: III Durchlaufgeschw.: 25 mm/s Verst.: 1.0 mV/cm Filter: STFilt
Kommentar:

High-volume trauma centers have better outcomes treating traumatic brain injury

Survival and discharge status from severe traumatic brain injury (TBI) patients treated during the past 11 years in seven state-designated Level I trauma centers was analyzed to test for a relationship between patient volume and outcome.
Data for patients age 16 years to 64 years were aggregated by quarter for years 2000 to 2010. TBI patients were identified using DRG International Classification of Diseases—9th Rev.—Clinical Modification codes: 800 to 804 and 850.1 to 854. Severity was defined using the International Classification Injury Severity Score (ICISS) less than 0.85 (risk of death > 15%). Using a

After controlling for severity, demographics, and insurance status, highest-volume centers demonstrated a 9% lower mortality risk ($p < 0.001$). Lower-volume hospitals discharged a significantly larger proportion of TBI patients to skilled nursing facilities and fewer patients to home or rehabilitation facilities ($p < 0.01$).

Two high-volume hospitals consistently treated more TBI patients (>40 patients per quarter). Four treated less than 40 patients per quarter, and one transitioned to high-volume midway through the study period. After controlling for severity, demographics, and insurance status, highest-volume centers demonstrated a 9% lower mortality risk ($p < 0.001$). Lower-volume

High volume (>40 patients per quarter) is associated with improved severe TBI patient survival and, probably, improved quality of life.

of life. Efforts to identify best practices and implement educational interventions to improve compliance with best-practice standards will benefit patients with severe traumatic brain injury.

Modifiziert nach Tepas et al., J Trauma Acute Care Surg 2013; 74: 143–148

High-volume trauma centers have better outcomes treating traumatic brain injury

Survival and discharge status from severe traumatic brain injury (TBI) patients treated during the past 11 years in seven state-designated Level I trauma centers was analyzed to test for a relationship between patient volume and outcome.
Data for patients age 16 years to 64 years were aggregated by quarter for years 2000 to 2010. TBI patients were identified using DRG International Classification of Diseases—9th Rev.—Clinical Modification codes: 800 to 804 and 850.1 to 854. Severity was defined using the International Classification Injury Severity Score (ICISS) less than 0.85 (risk of death > 15%). Using a

After controlling for severity, demographics, and insurance status, highest-volume centers demonstrated a 9% lower mortality risk ($p < 0.001$). Lower-volume hospitals discharged a significantly larger proportion of TBI patients to skilled nursing facilities and fewer patients to home or rehabilitation facilities ($p < 0.01$).

Two high-volume hospitals consistently treated more TBI patients (>40 patients per quarter). Four treated less than 40 patients per quarter, and one transitioned to high-volume midway through the study period. After controlling for severity, demographics, and insurance status, highest-volume centers demonstrated a 9% lower mortality risk ($p < 0.001$). Lower-volume

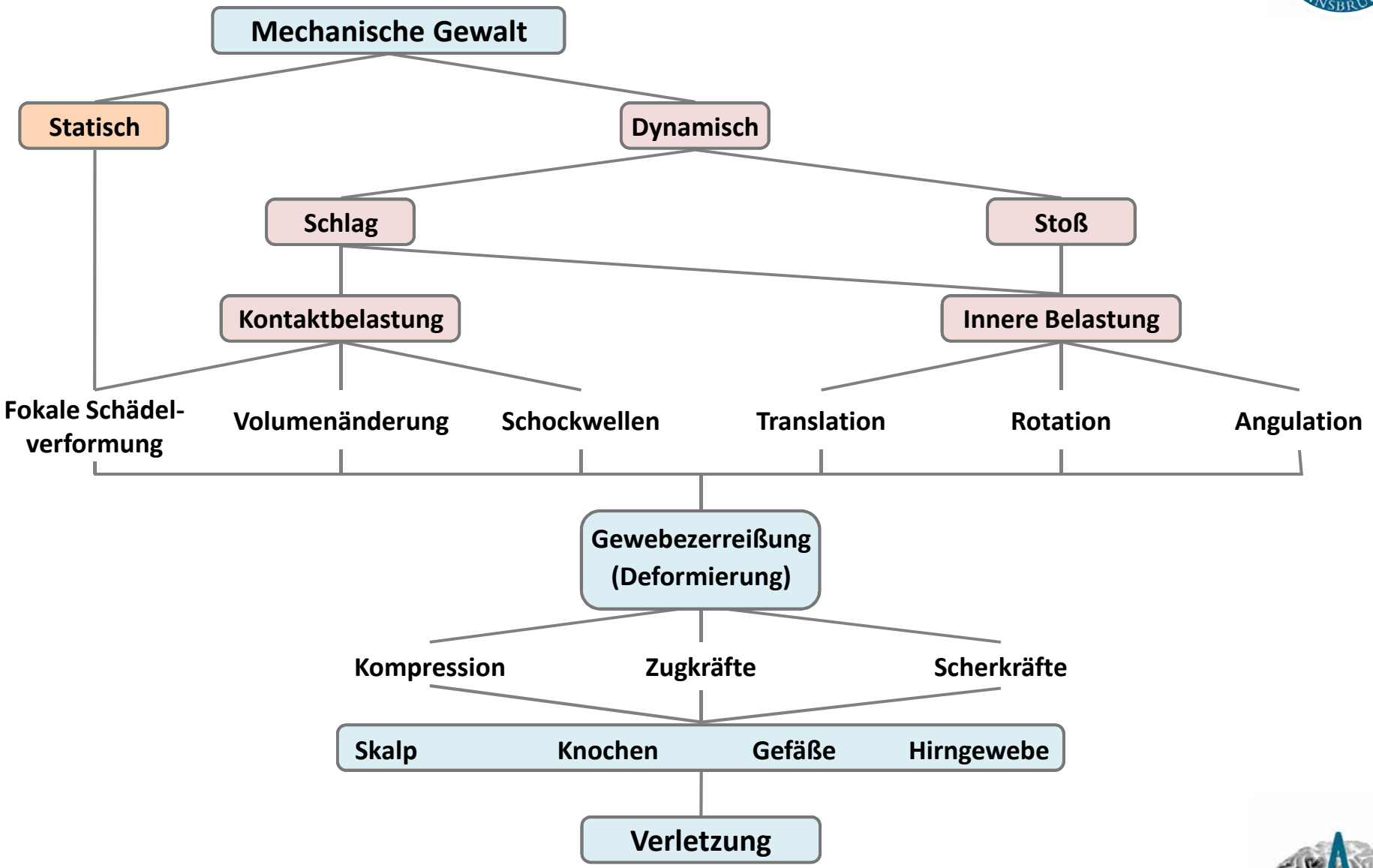
High volume (>40 patients per quarter) is associated with improved severe TBI patient survival and, probably, improved quality of life.

of life. Efforts to identify best practices and implement educational interventions to improve compliance with best-practice standar

High volume centres, with specialised critical care medicine

Modifiziert nach Tepas et al., J Trauma Acute Care Surg 2013; 74: 143–148

SHT – Patho(physio)logie



- **Verletzungsmuster**
  - Läsionen der **Weichteile**, des **Knochens**, der **Gefäße** und des **Hirnparenchyms**
  - **Primäre** (mechanische Gewalteinwirkung) versus **sekundäre** Schädigung
  - **Fokale** versus **diffuse** Verletzungen

Fokale Verletzungen

- Schädelfrakturen
- Traumatische intrakranielle Blutungen
- Kontusionen
- Andere Verletzungen
  - Hirnnervenläsionen, traumatische Gefäßverletzungen etc.

Diffuse Verletzungen

- Hirnschwellung und traumatisches Hirnödem
- Diffuse axonale Verletzung (DAI)
- Diffuse vaskuläre Schädigung (DVI)
  - Zerebrale Mikroblutungen
  - Globale zerebrale Ischämie

- **Sekundäre Schädigungen** nach SHT
  - **Häufigkeit** von sekundären Schädigungen wird in Autopsiestudien mit **70–90%** angegeben

Extrakranielle Ursachen	**Intrakranielle** Ursachen
Hypotension	Intrakranielle Hämatome
Hypox(äm)ie	Hirnschwellung und Hirnödem
Hyperkapnie und Hypokapnie	Vasospasmus nach traumatischer SAB
Fieber	Posttraumatische epileptische Anfälle
Hyperglykämie und Hypoglykämie	(Nosokomiale) Infektionen

  - **Intrakranielle Hypertension** als gemeinsame Endstrecke
  - Teils **potentiell behandelbare** Ursachen
  - Monitoring **systemischer** und **zerebraler Parameter**

SHT – »Nicht-neurologische« Sekundärfolgen

- Auch das **isolierte schwere SHT** stellt eine **Multisystem-Erkrankung** dar
  - **Systemische**, **nicht-neurologische Komplikationen** sind häufig und repräsentieren wesentliche, **potenziell modifizierbare Risikofaktoren** für erhöhte **Morbidität** und **Mortalität**

Non-neurologic organ dysfunction in severe traumatic brain injury*

Objective: To
dysfunction and
severe traumatic

Design: Obse

Patients: Pati
traumatic brain

Measurement
function was me
dysfunction scor
ponent score of
unit stay. One hu
dysfunction of at

six organ system failures were identified in 74 patients (35%). Respiratory failure was the most common non-neurologic organ system failure, occurring in 23% of patients, whereas cardiovas-

Table 4. No. of organ system failures and mortality rate

No. of Organ System Failures	Proportion of Patients Not Surviving to Hospital Discharge	No. of Patients
0	0.26	135
1	0.40	55
2	0.47	17
3	1.0	1
4	1.0	1

Conclusions: Non-neurologic organ dysfunction is common in patients with severe traumatic brain injury and is independently associated with worse outcome.

Modifiziert nach Zygun et al., Crit Care Med 2005; 33: 654–660

Schweres SHT – Hyperadrenerges Stress-Syndrom

A Review of Paroxysmal Sympathetic Hyperactivity after Acquired Brain Injury

Iain Perkes, BMedSc,[1,2,3] Ian J. Baguley, MBBS, PhD,[1,4]
Melissa T. Nott, BAppSc, PhD,[1] and David K. Menon, MD, PhD[2]

TABLE 1: Features of Paroxysmal Sympathetic Hyperactivity and Mixed Autonomic Hyperactivity

Category	Clinical Features	Paroxysmal Sympathetic Hyperactivity	Mixed Autonomic Hyperactivity
Sympathetic	Increases in HR, RR, BP, temperature, sweating, and pupillary dilation	Yes	Yes
Parasympathetic	Decreases in HR, RR, BP, temperature, and pupillary contraction	No	Yes
Motor features	Decerebrate posturing, decorticate posturing, spasticity, hypertonia and/or dystonia, teeth-grinding, agitation	Yes	Variable
Other	Hiccups, lacrimation, sighing, yawning	No	Yes

TABLE 3: Sample Characteristics of Paroxysmal Sympathetic Hyperactivity Cases

Characteristic	Value
Age, mean yr ± SD	24.2 ± 11.8
Sex, No. (%)	
Male	112 (78)
Female	31 (22)
GCS severe injury [<9], No. (%)	199 (100)
GOS, No. (%)	
1: Death	22 (18)
2: PVS	37 (30)
3: Severe disability	56 (45)
4: Moderate disability	7 (5)
5: Good recovery	3 (2)
Clinical setting, No. (%)	
ICU	139 (45)
Rehabilitation	119 (39)
Combined	48 (16)

Severe excessive autonomic overactivity occurs in a subgroup of people surviving acquired brain injury, the majority of whom show paroxysmal sympathetic and motor overactivity. Delayed recognition of paroxysmal sympathetic hyperactivity (PSH) after brain injury may increase morbidity and long-term disability.

Modifiziert nach Perkes et al., Ann Neurol 2010; 68: 126–135

Schweres SHT – Hyperadrenerges Stress-Syndrom

Contemporary Reviews in Cardiovascular Medicine

The Brain–Heart Connection

Martin A. Samuels, MD

Sympathetic Storm

1

Adrenal Catecholamines

Neurally Released Catecholamines

Exogenous Catecholamines

Cardiac Receptor Operated Calcium Channel

2

3

ECG Changes
Wall Motion Disorders
Contraction Bands

Sudden Death
»Takotsubo«
Cardiomyopathy

Free Radical Release

4

5

Calcium Entry
Enzyme Leak
Contraction Band Necrosis

Possible therapeutic approaches
to prevent neurocardiac damage:

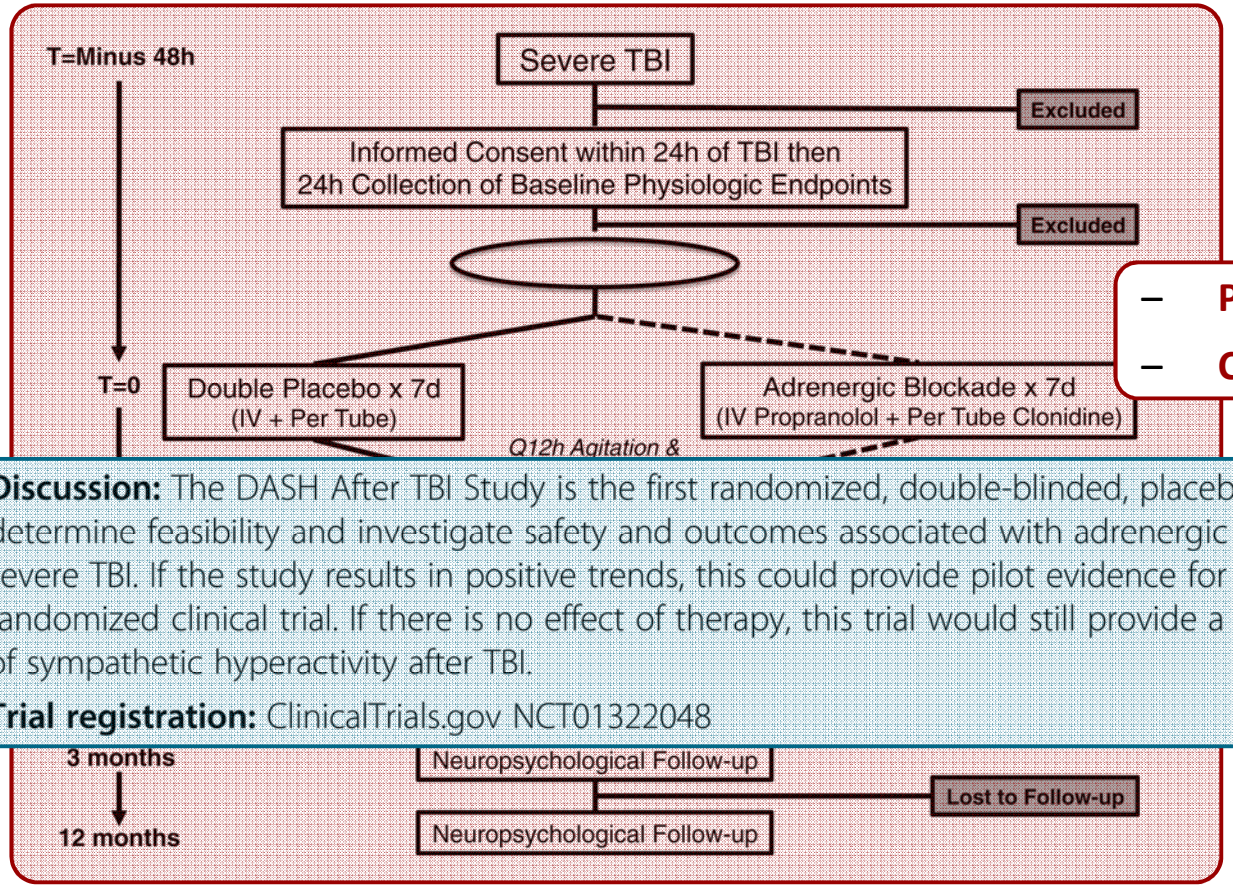
1. **GABA Agonists**
2. **Beta-Blockers**
3. **Calcium Channel Blockers**
4. **Free Radical Scavengers**
5. **Anti-Oxidants**

Modifiziert nach Samuels, Circulation 2007; 116: 77–84

Schweres SHT – Hyperadrenerges Stress-Syndrom als therapeutisches Ziel

Decreasing adrenergic or sympathetic hyperactivity after severe traumatic brain injury using propranolol and clonidine (DASH After TBI Study): study protocol for a randomized controlled trial

DASH trial



- **Propranolol** 1 mg IV qid
- **Clonidin** 0,1 mg PO bid

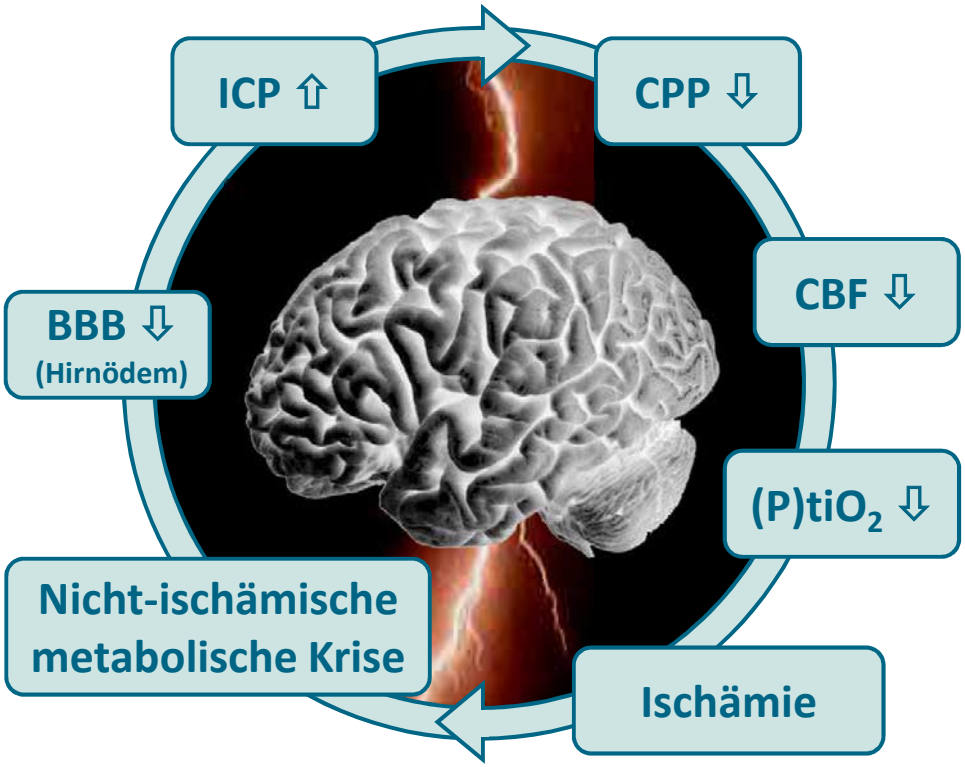
Discussion: The DASH After TBI Study is the first randomized, double-blinded, placebo-controlled trial powered to determine feasibility and investigate safety and outcomes associated with adrenergic blockade in patients with severe TBI. If the study results in positive trends, this could provide pilot evidence for a larger multicenter randomized clinical trial. If there is no effect of therapy, this trial would still provide a robust prospective description of sympathetic hyperactivity after TBI.

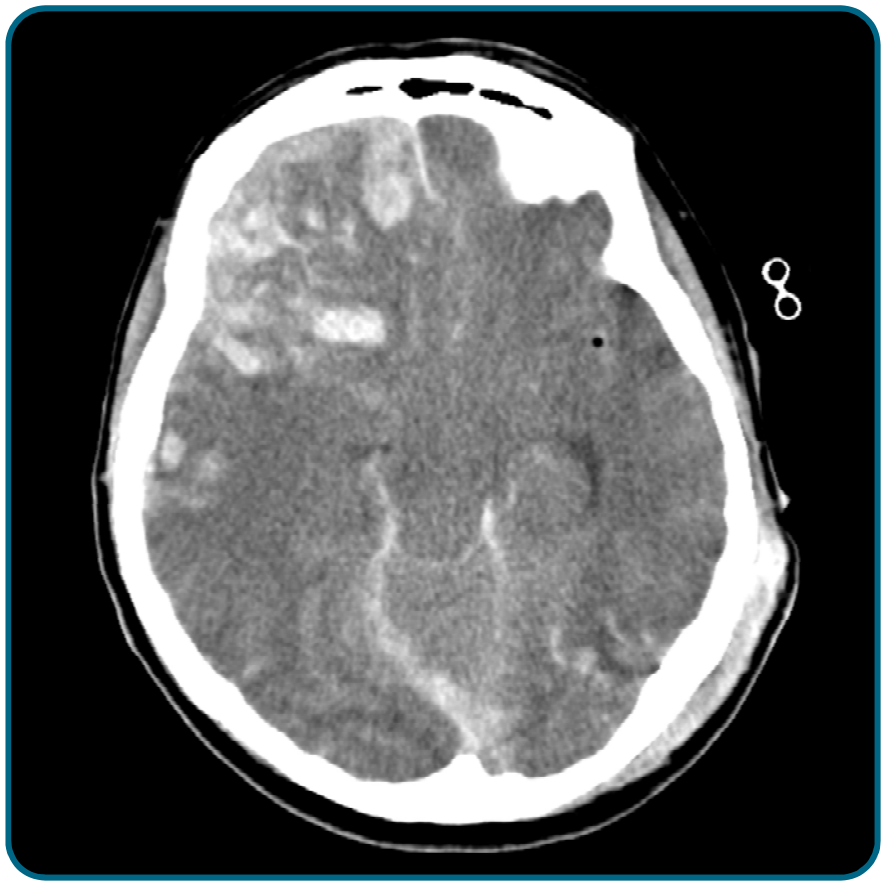
Trial registration: ClinicalTrials.gov NCT01322048

Modifiziert nach Patel et al., Trials 2012; 13: 177

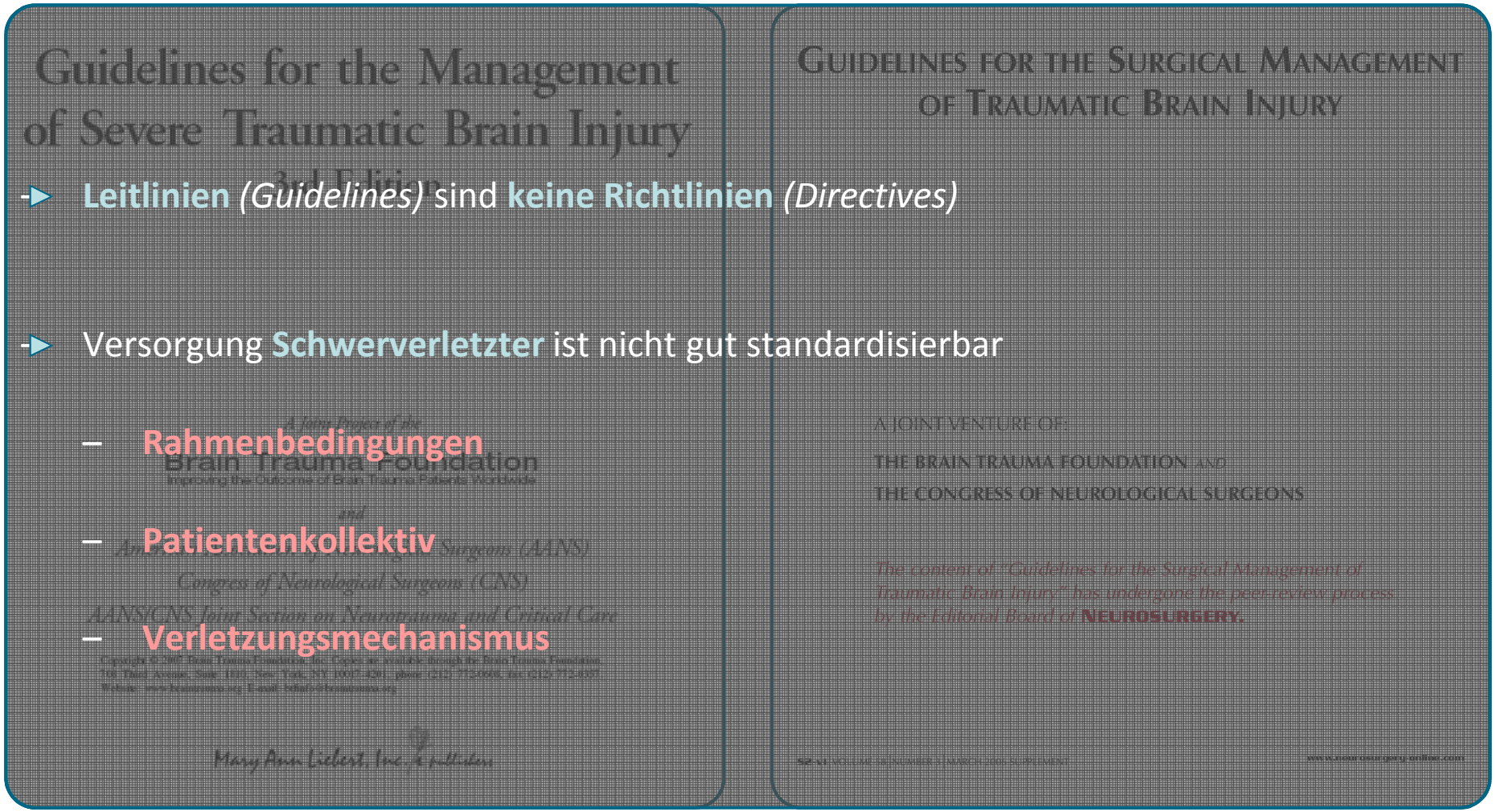
SHT – Patho(physio)logie

- **Circulus vitiosus** nach traumatischer ZNS-Schädigung





SHT – »*Evidence-Based Medicine*«



- **Leitlinien** *(Guidelines)* sind **keine Richtlinien** *(Directives)*

- Versorgung **Schwerverletzter** ist nicht gut standardisierbar
  - **Rahmenbedingungen**
  - **Patientenkollektiv**
  - **Verletzungsmechanismus**

SHT – »*Evidence-Based Medicine*«

SHT – Internationale Leitlinien-Empfehlung (BTF, 2007) zum ICP-Monitoring

- **Indikation zur Anlage einer ICP-Sonde** bei Patienten mit einem **schweren SHT** ist ein **pathologisches CT** mit Nachweis eines intrakraniellen Hämatoms, einer Kontusion, eines Hirnödems bzw. von komprimierten basalen Zisternen

- Bei **unauffälligem CT-Befund** ist die Anlage einer **ICP-Sonde indiziert**, wenn zumindest zwei der folgenden Kriterien zutreffen:
  - Uni- oder bilaterale **Beuge- und/ oder Strecktendenzen** am Unfallort
  - (Therapierefraktäre) **arterielle Hypotension**
  - Lebensalter **über 40 Jahre**

- Die ICP-Messung sollte **intraventrikulär** über eine EVD vorgenommen werden (Druck-messung mittels »Tip-Transducer« wünschenswert), da dann die Möglichkeit besteht, durch Ablassen von Liquor zumindest kurzfristig den ICP zu senken

- Alternativer Messort ist das **Hirnparenchym**, in Ausnahmefällen der Epiduralraum (sehr artefaktanfällig)

Monitoring of intracranial pressure in patients with severe traumatic brain injury: an Austrian prospective multicenter study

Parameter	Group "noICP"	Group "ICP"	Significance (p)
No. of patients	825 (44%)	1,031 (56%)	
Age (years)	53 (34–74)	46 (29–63)	<0.0001
Gender (% male patients)	74	73	n.s.
Injury Severity Score	25 (16–32.5)	25 (16–29)	n.s.
Isolated TBI (%)	63	70	0.0023
AIS head score			
TISS 28 per day (first week)			
TISS 28/day without ICP (first week)			
Mechanical ventilation (first week, % patients)			
Catecholamines used (first week, % patients)			
Length of ICU stay (days)			
SAPS II score			
SAPS II predicted mortality (%)			
ICU mortality (%)	34	35	n.s.
Hospital mortality (%)	38	39	n.s.

In conclusion, the decision to use ICP monitoring seems to be based on neurological status as well as trauma severity.

The "worst" and the "best" cases were both less likely to receive ICP monitoring, whereas patients with an uncertain prognosis were most likely to receive ICP monitoring.

The ICP monitoring may possibly have some beneficial effects, as the lowest hospital mortality rates were found in the group with the highest percentage of ICP monitoring.

Modifiziert nach Mauritz et al., Intensive Care Med 2008; 34: 1208–1215

A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury

BACKGROUND

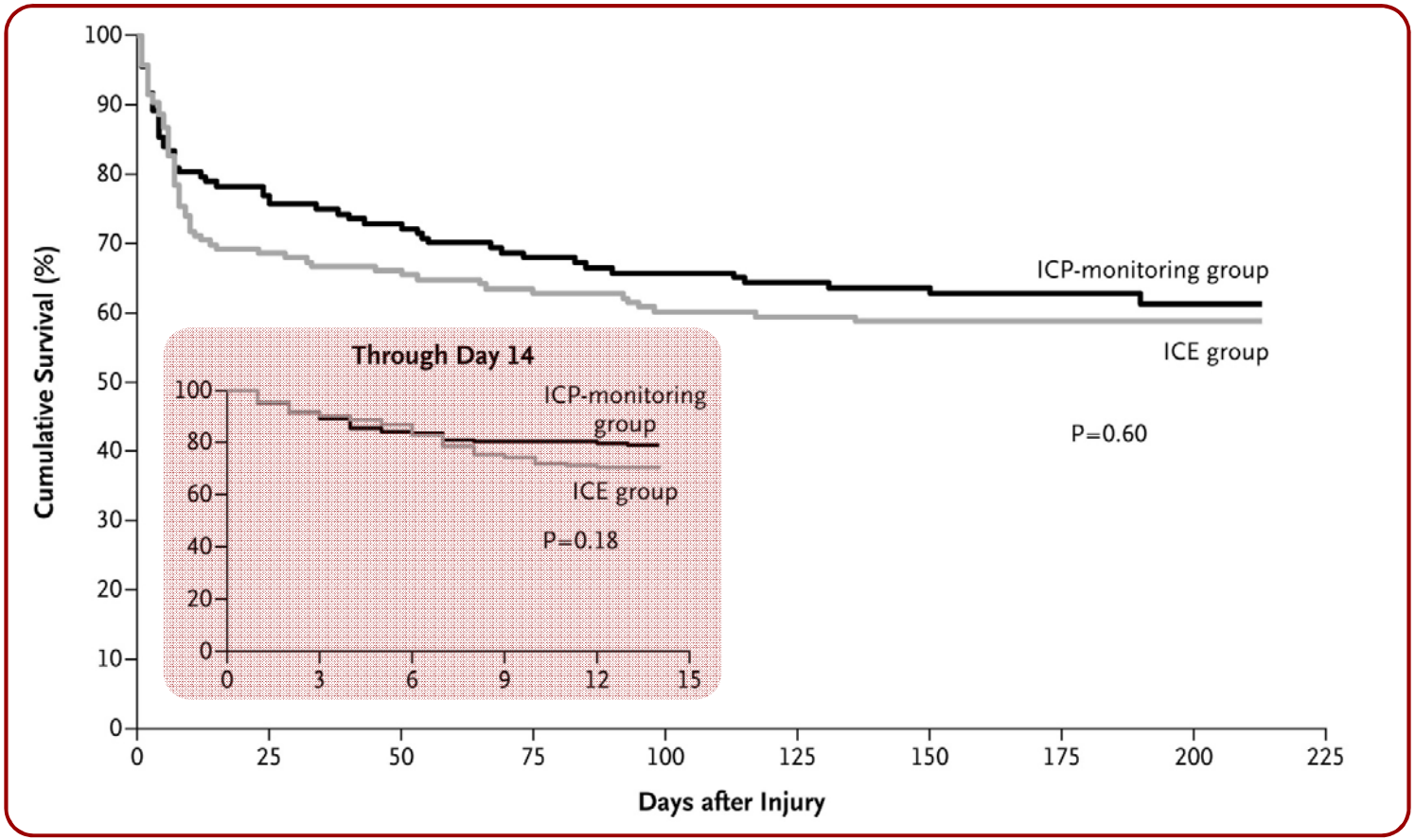
Intracranial-pressure monitoring is considered the standard of care for severe traumatic brain injury and is used frequently, but the efficacy of treatment based on monitoring in improving the outcome has not been rigorously assessed.

METHODS

We conducted a multicenter, controlled trial in which 324 patients 13 years of age or older who had severe traumatic brain injury and were being treated in intensive care units (ICUs) in Bolivia or Ecuador were randomly assigned to one of two specific protocols: guidelines-based management in which a protocol for monitoring intraparenchymal intracranial pressure was used (pressure-monitoring group) or a protocol in which treatment was based on imaging and clinical examination (imaging–clinical examination group). The primary outcome was a composite of survival time, impaired consciousness, and functional status at 3 months and 6 months and neuropsychological status at 6 months; neuropsychological status was assessed by an examiner who was unaware of protocol assignment.

Modifiziert nach Chesnut et al., N Engl J Med 2012; 367: 2471–2481

A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury



Modifiziert nach Chesnut et al., N Engl J Med 2012; 367: 2471–2481

A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury

ICP und **nicht CPP**

Variable	Pressure-Monitoring Group (N=157)	Imaging–Clinical Examination Group (N=167)	P Value†	Proportional Odds Ratio (95% CI)‡
Post hoc comparisons¶				
Integrated brain-specific treatment intensity			<0.001	2.36 (1.60–3.47)
Median	69	125		
Interquartile range	13–181	45–233		
Individual treatments — no./total no. (%)				
Mannitol	80/157 (51)	94/166 (57)	0.25	1.32 (0.82–2.13)
Hypertonic saline	90/156 (58)	119/166 (72)	0.008	1.95 (1.19–3.22)
Furosemide	6 (4)	13 (8)	0.11	2.53 (0.82–7.81)
Hyperventilation	93 (60)	122 (73)	0.003	2.16 (1.29–3.61)
Cerebrospinal fluid drainage	1 (1)	3 (2)	0.37	2.84 (0.29–27.78)
Barbiturates	38 (24)	22 (13)	0.02	0.46 (0.25–0.83)

CONCLUSIONS

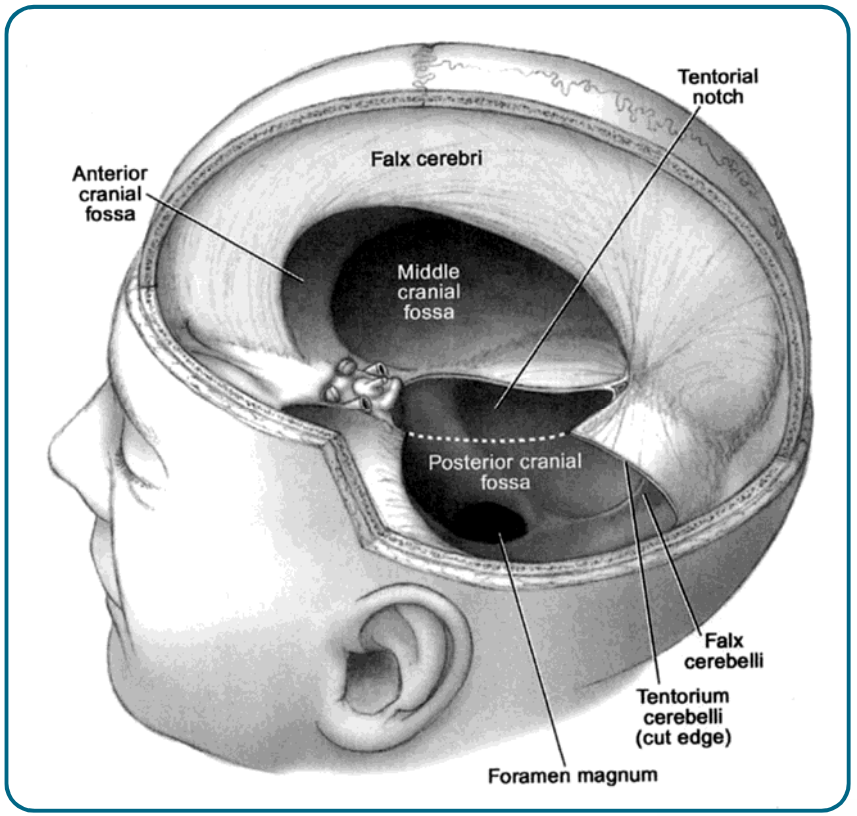
For patients with severe traumatic brain injury, care focused on maintaining monitored intracranial pressure at 20 mm Hg or less was not shown to be superior to care based on imaging and clinical examination.

Modifiziert nach Chesnut et al., N Engl J Med 2012; 367: 2471–2481

ICP-Monitoring bei SHT – Wichtige Überlegungen

- Innerhalb des ZNS können erhebliche **Druckgradienten** auftreten
  - Bei **unilateraler** Raumforderung sind **Druckunterschiede bis zu 20–40 mmHg** möglich
  - **Supra-/ infratentorielle Druckgradienten bis zu 80 mmHg** sind beschrieben

- Gemessene **ICP-Werte** müssen daher **nicht für das gesamte ZNS repräsentativ** sein, sondern können **u. U. nur regional aussagekräftig** sein
  - **Supratentoriell** gemessene ICP-Werte sind bezüglich der Druckverhältnisse im Bereich der **hinteren Schädelgrube** nur bedingt verwertbar



Increased mortality in patients with severe traumatic brain injury treated without intracranial pressure monitoring

Object. Evidence-based guidelines recommend intracranial pressure (ICP) monitoring for patients with severe traumatic brain injury (TBI), but there is limited evidence that monitoring and treating intracranial hypertension reduces mortality. This study uses a large, prospectively collected database to examine the effect on 2-week mortality of ICP reduction therapies administered to patients with severe TBI treated either with or without an ICP monitor.

Methods. From a population of 2134 patients with severe TBI (Glasgow Coma Scale [GCS] Score < 9), 1446 patients were treated with ICP-lowering therapies. Of those, 1202 had an ICP monitor inserted and 244 were treated without monitoring. Patients were admitted to one of 20 Level I and two Level II trauma centers, part of a New York State quality improvement program administered by the Brain Trauma Foundation between 2000 and 2009. This database also contains information on known independent early prognostic indicators of mortality, including age, admission GCS score, pupillary status, CT scanning findings, and hypotension.

Results. Age, initial GCS score, hypotension, and CT scan findings were associated with 2-week mortality. In addition, patients of all ages treated with an ICP monitor in place had lower mortality at 2 weeks ($p = 0.02$) than those treated without an ICP monitor, after adjusting for parameters that independently affect mortality.

Conclusions. In patients with severe TBI treated for intracranial hypertension, the use of an ICP monitor is associated with significantly lower mortality when compared with patients treated without an ICP monitor. Based on these findings, the authors conclude that ICP-directed therapy in patients with severe TBI should be guided by ICP monitoring.

Modifiziert nach Farahvar et al., J Neurosurg 2012; 117: 729–734

Increased mortality in patients with severe traumatic brain injury treated without intracranial pressure monitoring

Characteristic	No ICP Monitoring (%)	ICP Monitoring (%)	p Value
no. of pts	223	1084	
age (yrs)			
mean ± SD	45.9 ± 21.8	38.3 ± 17.5	<0.0001
range	16–89	16–93	
age			
<60	158 (70.9)	943 (87.0)	<0.0001
≥60	65 (29.1)	141 (13.0)	
sex			
male	164 (73.5)	843 (77.8)	0.17
female	59 (26.5)	241 (22.2)	
initial GCS score			
6–8	96 (48.5)	449 (43.5)	0.20
3–5	102 (51.5)	583 (56.5)	

Characteristic	No ICP Monitoring (%)	ICP Monitoring (%)	p Value
no. of pts	223	1084	
hypotension present on Day 1			
yes	38 (17.0)	170 (15.8)	0.63
no	185 (83.0)	909 (84.2)	
CT scan findings			
normal	9 (4.1)	35 (3.3)	0.52
abnormal	209 (95.9)	1037 (96.7)	
pupillary abnormalities			
yes	72 (32.6)	245 (23.0)	0.003
no	149 (67.4)	821 (87.0)	
2-wk outcome			
alive	149 (66.8)	872 (80.4)	<0.0001
dead	74 (33.2)	212 (19.6)	

Conclusions. In patients with severe TBI treated for intracranial hypertension, the use of an ICP monitor is associated with significantly lower mortality when compared with patients treated without an ICP monitor. Based on these findings, the authors conclude that ICP-directed therapy in patients with severe TBI should be guided by ICP monitoring.

Modifiziert nach Farahvar et al., J Neurosurg 2012; 117: 729–734

ICP-Monitoring bei SHT – *TBI-Trac Database* Analyse (Pro)

Increased mortality in patients with severe traumatic brain injury treated without intracranial pressure monitoring

Predictor Variable	Adults		All Ages	
	Adjusted OR (95% CI)	p Value	Adjusted OR (95% CI)	p Value
ICP monitoring				
yes	0.64 (0.41–1.00)	0.05	0.63 (0.41–0.94)	0.02
no	reference		reference	
age (yrs)				
≥60	2.43 (1.56–3.79)	<0.0001	2.50 (1.65–3.78)	<0.0001
<60	reference		reference	
initial GCS score				
6–8	0.46 (0.37–0.57)	<0.0001	0.44 (0.36–0.53)	<0.0001
3–5	reference		reference	
hypotension present on Day 1				
yes	2.08 (1.48–2.92)	<0.0001	2.08 (1.54–2.82)	<0.0001
no	reference		reference	
CT scan findings				
abnormal	2.45 (1.05–5.75)	0.04	2.71 (1.11–6.60)	0.03
normal	reference		reference	
pupil abnormalities on Day 1				
yes	1.38 (0.99–1.91)	0.05	1.40 (0.98–2.00)	0.07
no	reference		reference	

Modifiziert nach Farahvar et al., J Neurosurg 2012; 117: 729–734

A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury

CONCLUSIONS

For patients with severe traumatic brain injury, care focused on maintaining monitored intracranial pressure at 20 mm Hg or less was not shown to be superior to care based on imaging and clinical examination.

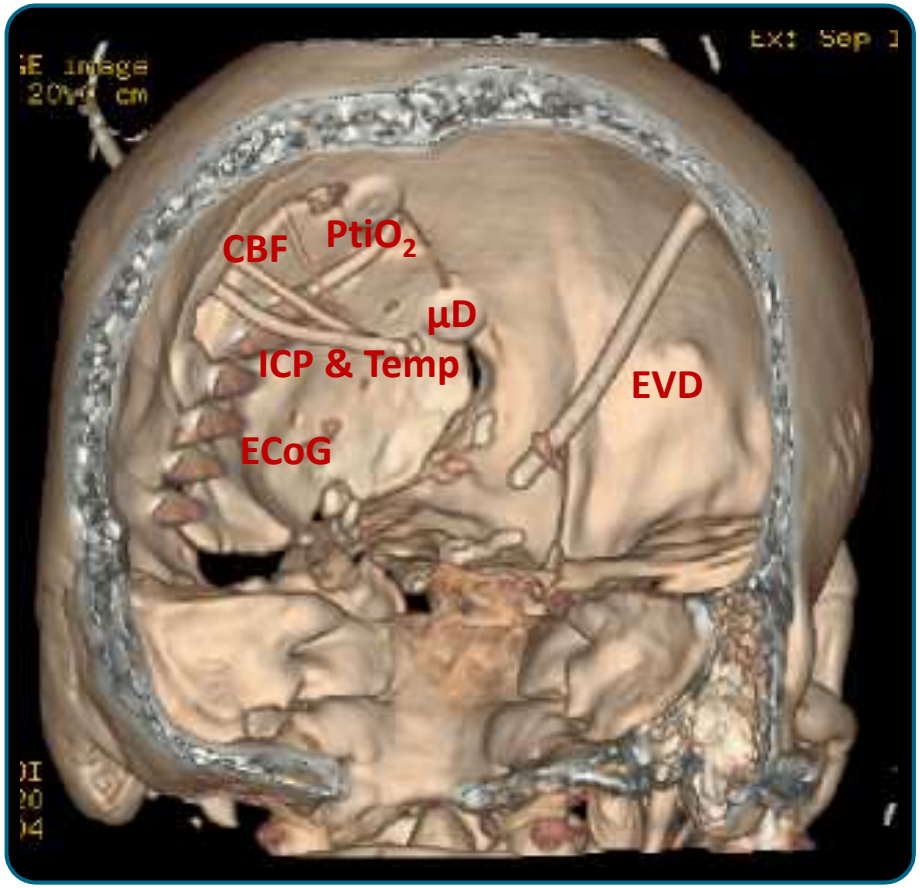
Increased mortality in patients with severe traumatic brain injury treated without intracranial pressure monitoring

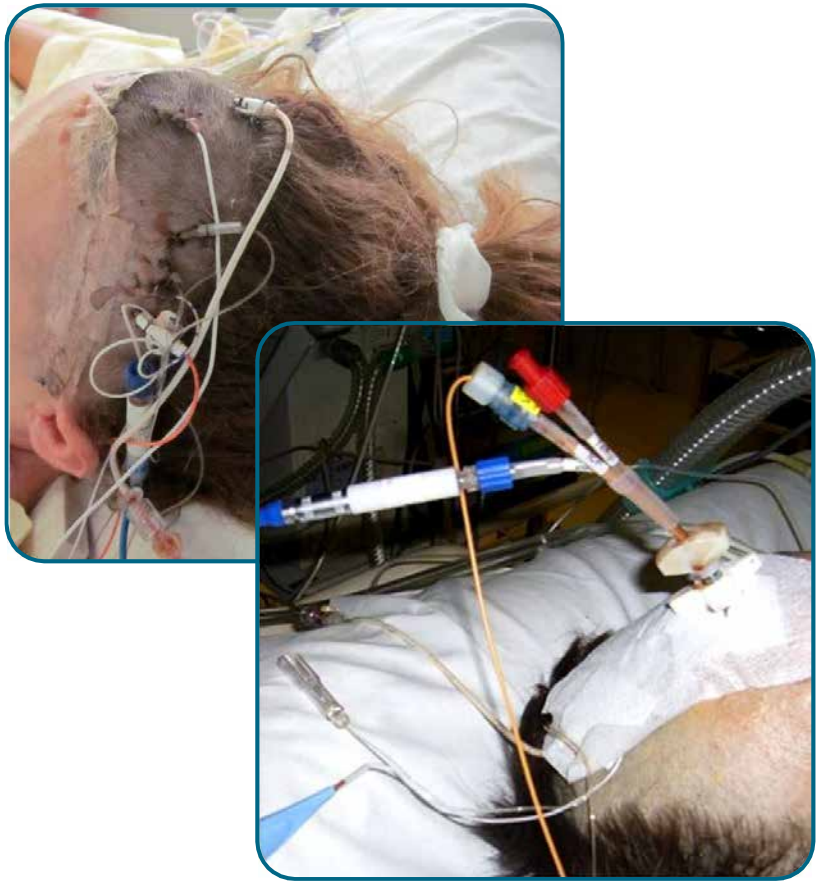
Conclusions. In patients with severe TBI treated for intracranial hypertension, the use of an ICP monitor is associated with significantly lower mortality when compared with patients treated without an ICP monitor. Based on these findings, the authors conclude that ICP-directed therapy in patients with severe TBI should be guided by ICP monitoring.

Chesnut et al., N Engl J Med 2012; 367: 2471–2481 sowie Farahvar et al., J Neurosurg 2012; 117: 729–734

Plädoyer für »Multimodales Neuromonitoring« bei SHT

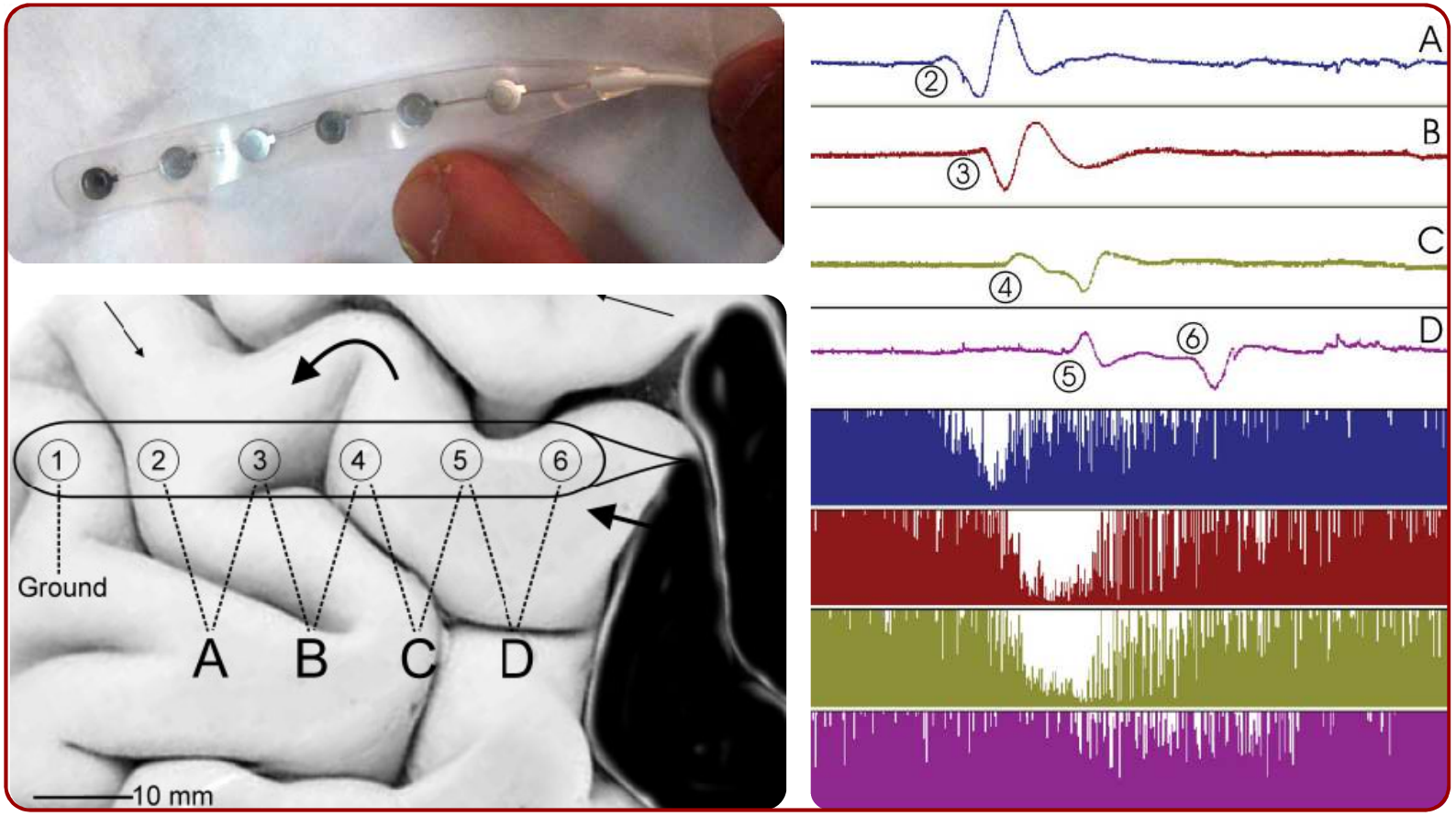
- **»Neuromonitoring-Bündel«** an der **Neurologischen Intensivstation Innsbruck**





Schweres SHT – »Multimodales Neuromonitoring« im Fokus

- **Elektrocorticographie** (ECoG) als MNM-Erweiterung



Modifiziert nach Fabricius et al., Brain 2006; 129: 778–790

Spreading depolarisations and outcome after traumatic brain injury: a prospective observational study

Outcome prediction (multivariate ordinal regression analysis)

	Common odds ratio (95% CI)	p
Prognostic score	1·76 (1·26–2·46)	0·0009
Depolarisation		0·0008
None	1·0	..
CSD	1·56 (0·72–3·37)	0·26
ISD	7·58 (2·64–21·8)	0·0002

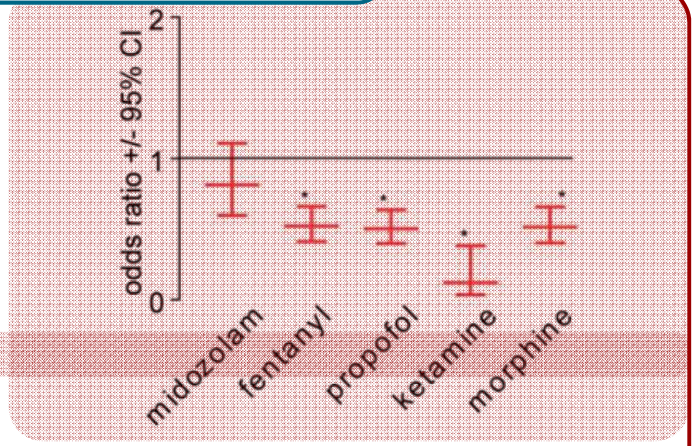
CSD=cortical spreading depression. ISD=isoelectric spreading depolarisation

By multivariate analysis, both prognostic score (p=0·0009) and spreading depolarisation category (p=0·0008) were significant predictors of neurological outcome. CSD and ISD were associated with an increased risk of unfavourable outcome (common odds ratios 1·56 [95% CI 0·72–3·37] and 7·58 [2·64–21·8], respectively). Addition of depolarisation category to the regression model increased the proportion of variance in outcome that could be attributed to predictors from 9% to 22%, compared with the prognostic score alone.

Jed Hartings et al., Lancet Neurol 2011; 10: 1058–1064

Effect of analgesics and sedatives on the occurrence of spreading depolarizations accompanying acute brain injury

	Odds ratio for spreading depolarization occurrence (95% CI)
Midazolam	1.28 (0.93–1.75)
Fentanyl	0.97 (0.68–1.38)
Propofol	0.89 (0.68–1.16)
Sufentanil	1.06 (0.64–1.76)
Ketamine	0.38 (0.18–0.79)
Morphine	0.93 (0.65–1.3)



We found that administration of ketamine was associated with a reduction of spreading depolarizations and spreading depolarization clusters ($P < 0.05$). Midazolam anaesthesia, in contrast, was associated with an increased number of spreading depolarization clusters ($P < 0.05$). By using a univariate odds ratio analysis, we also found a significant association between ketamine administration and reduced occurrence of isoelectric spreading depolarizations in patients suffering from traumatic brain injury, subarachnoid haemorrhage and malignant hemispheric stroke ($P < 0.05$). Our findings suggest that ketamine—or another *N*-methyl-D-aspartate receptor antagonist—may represent a viable treatment for patients at risk for spreading depolarizations. This hypothesis will be tested in a prospective study.

Modifiziert nach Hertle et al., Brain 2012; 135:2390–2398

Peter Le Roux
David K. Menon
Giuseppe Citerio
Paul Vespa
Mary Kay Bader
Gretchen M. Brophy
Michael N. Diringer
Nino Stocchetti
Walter Videtta
Rocco Armonda
Neeraj Badjatia
Julian Böesel
Randall Chesnut
Sherry Chou
Jan Claassen
Marek Czosnyka
Michael De Georgia
Anthony Figaji
Jennifer Fugate
Raimund Helbok
David Horowitz
Peter Hutchinson
Monisha Kumar
Molly McNett
Chad Miller
Andrew Naidech
Mauro Oddo
DaiWai Olson
Kristine O'Phelan
J. Javier Provencio
Corinna Puppo
Richard Riker
Claudia Robertson
Michael Schmidt
Fabio Taccone

Intensive Care Med (2014) 40:1189–1209
DOI 10.1007/s00134-014-3369-6

CONFERENCE REPORTS AND EXPERT PANEL

Consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care

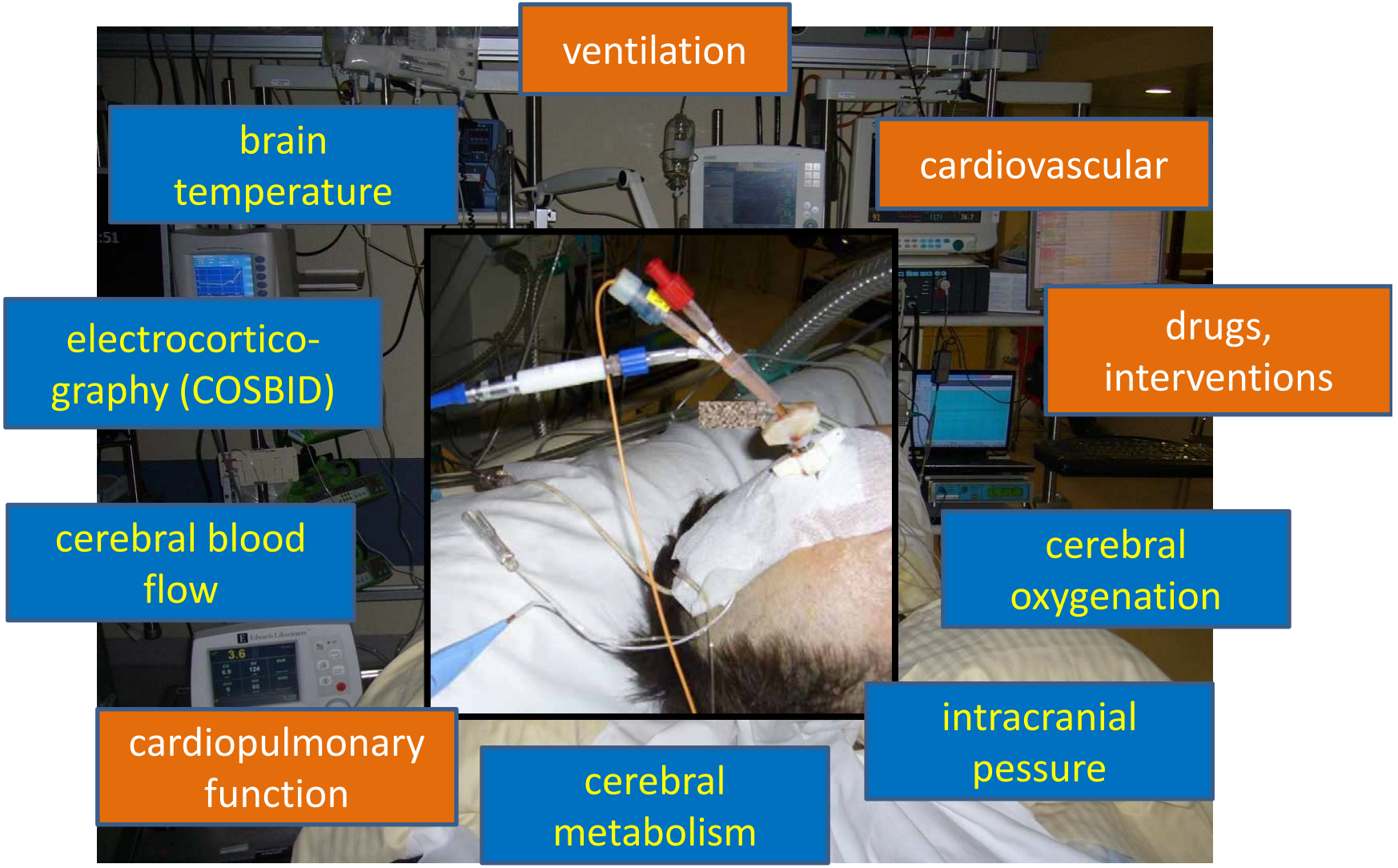
A statement for healthcare professionals from the Neurocritical Care Society and the European Society of Intensive Care Medicine

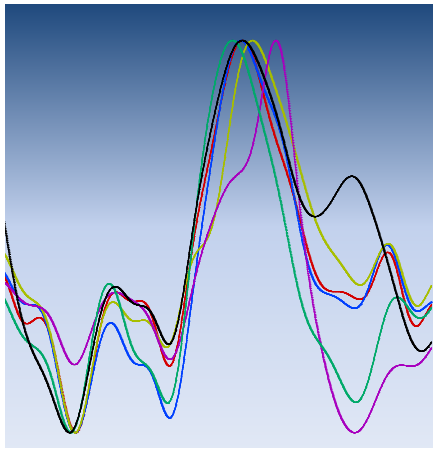
Received: 26 May 2014
Accepted: 7 June 2014
Published online: 20 August 2014

Table 2 Physiological processes that are important to neurocritical care clinicians that were selected for review in the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care

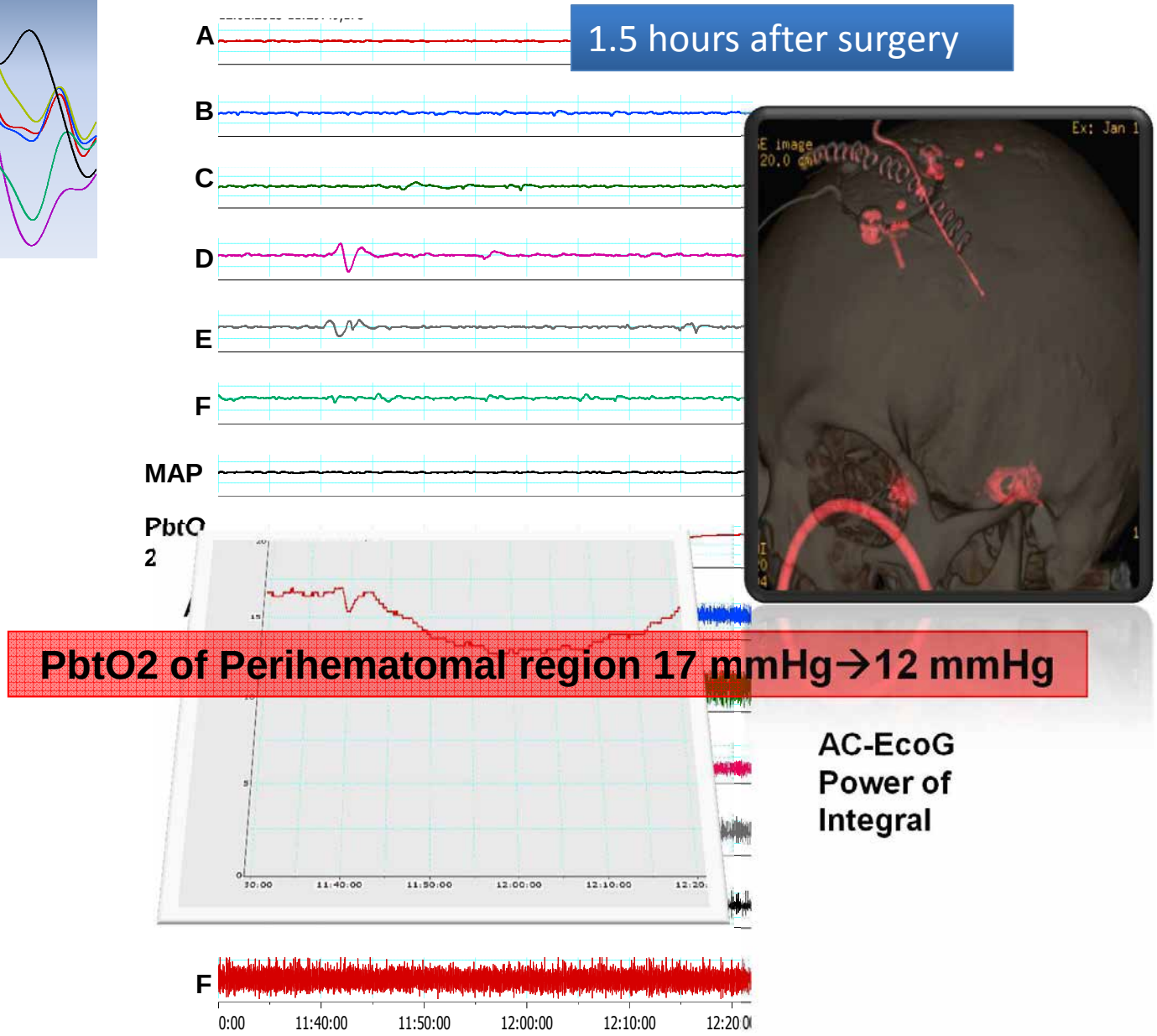
Topic section
Clinical evaluation
Systemic hemodynamics
Intracranial pressure and cerebral perfusion pressure
Cerebrovascular autoregulation
Systemic and brain oxygenation
Cerebral blood flow and ischemia
Electrophysiology
Cerebral metabolism
Glucose and nutrition
Hemostasis and hemoglobin
Temperature and inflammation
Biomarkers of cellular damage and degeneration
ICU processes of care
Multimodality monitoring informatics integration, display and analysis
Monitoring in emerging economies
Future directions and emerging technologies

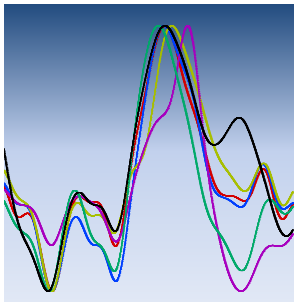
Invasives multimodales Neuromonitoring Innsbruck 2014





COSBID – *Case - **#4***





COSBID - preliminary Innsbruck

CSDs and $P_{bt}O_2$

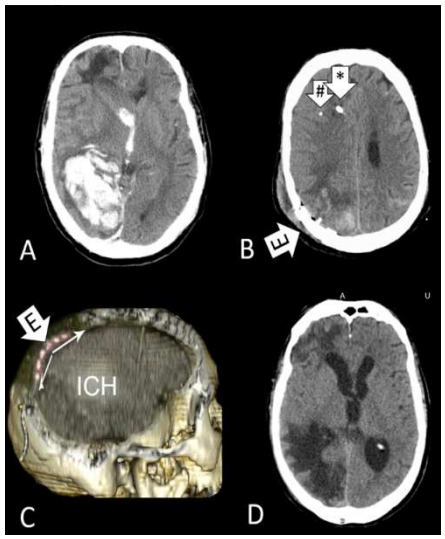
Patient	EcoG	ECoG depressions			Duration	Perihematomal Physiology			
#		CSD fast recovery	CSD prolonged recovery	Synchronous		**$P_{bt}O_2$ Change** (mmHg)	**CBF Change** (mmHg)	Duration (min)	**LPR change**
1	162			2	28 (21-28)	2/2 ↓ 9 (9-13)	2/2 ↑ 29 (23-29)	15 (7-15)	2/2
3	372	1	10		19 (17-23)	NA	NA		8/11
4	214		4	1	14 (14-19)	4/4 ↓ 4 (3-6)	NA	20 (11-29)	NA
9	299	1		6	22 (5-31)	6/7↓ 8 (11-4)	NA	4 (1-14)	No
10	123	1	4		18(12;20)	5/5↓ 5 (8-4)	3/3↓ 2/3↑	2 (1-2)	Yes

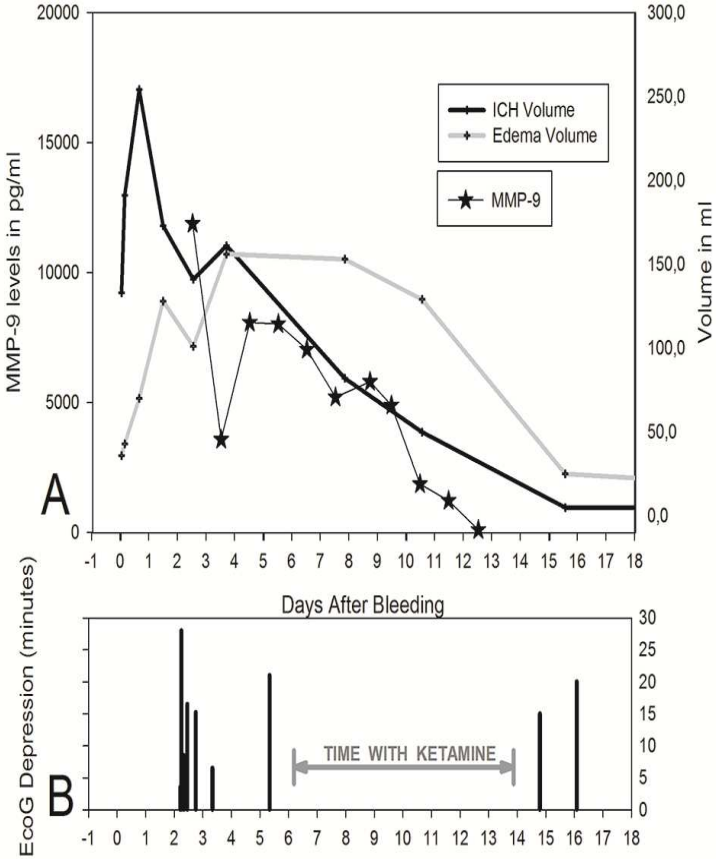
neurocritical care society Neurocrit Care
DOI 10.1007/s12028-014-0050-4

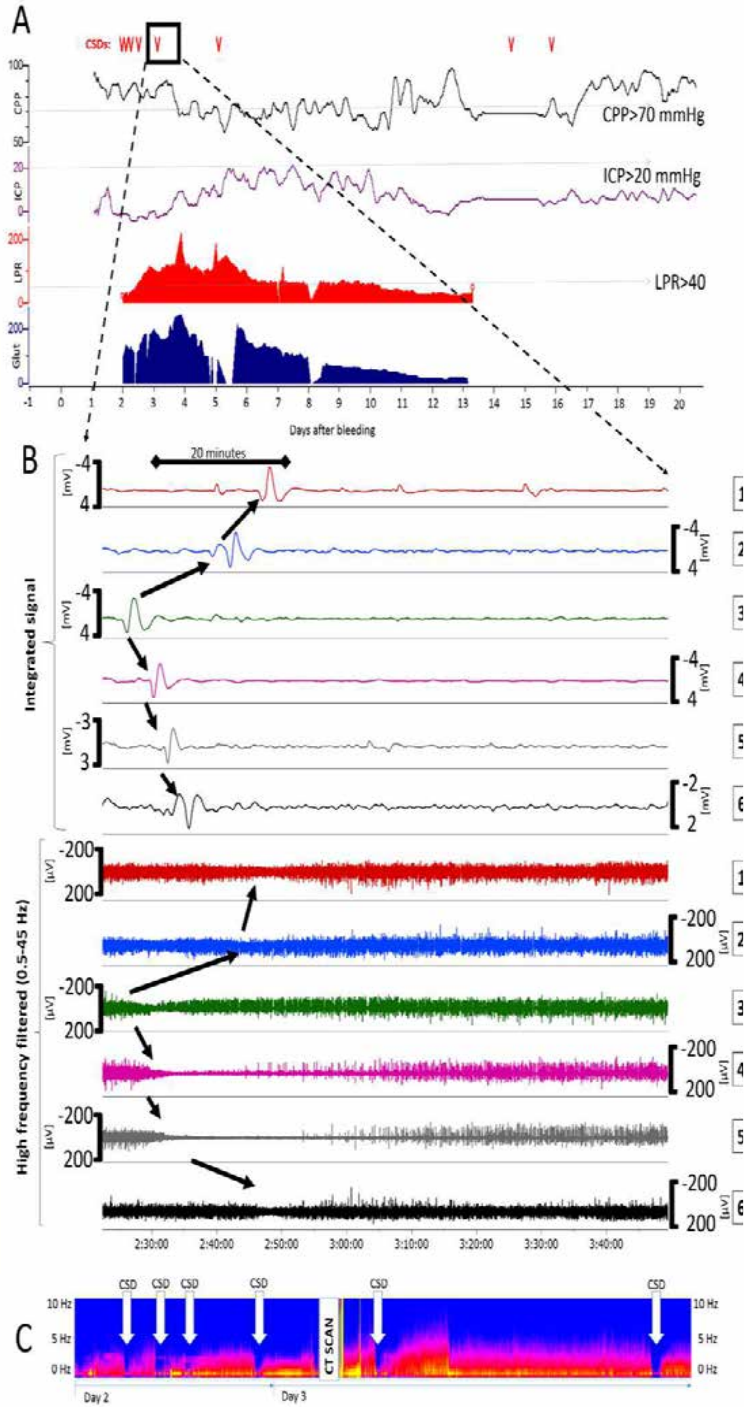
PRACTICAL PEARL

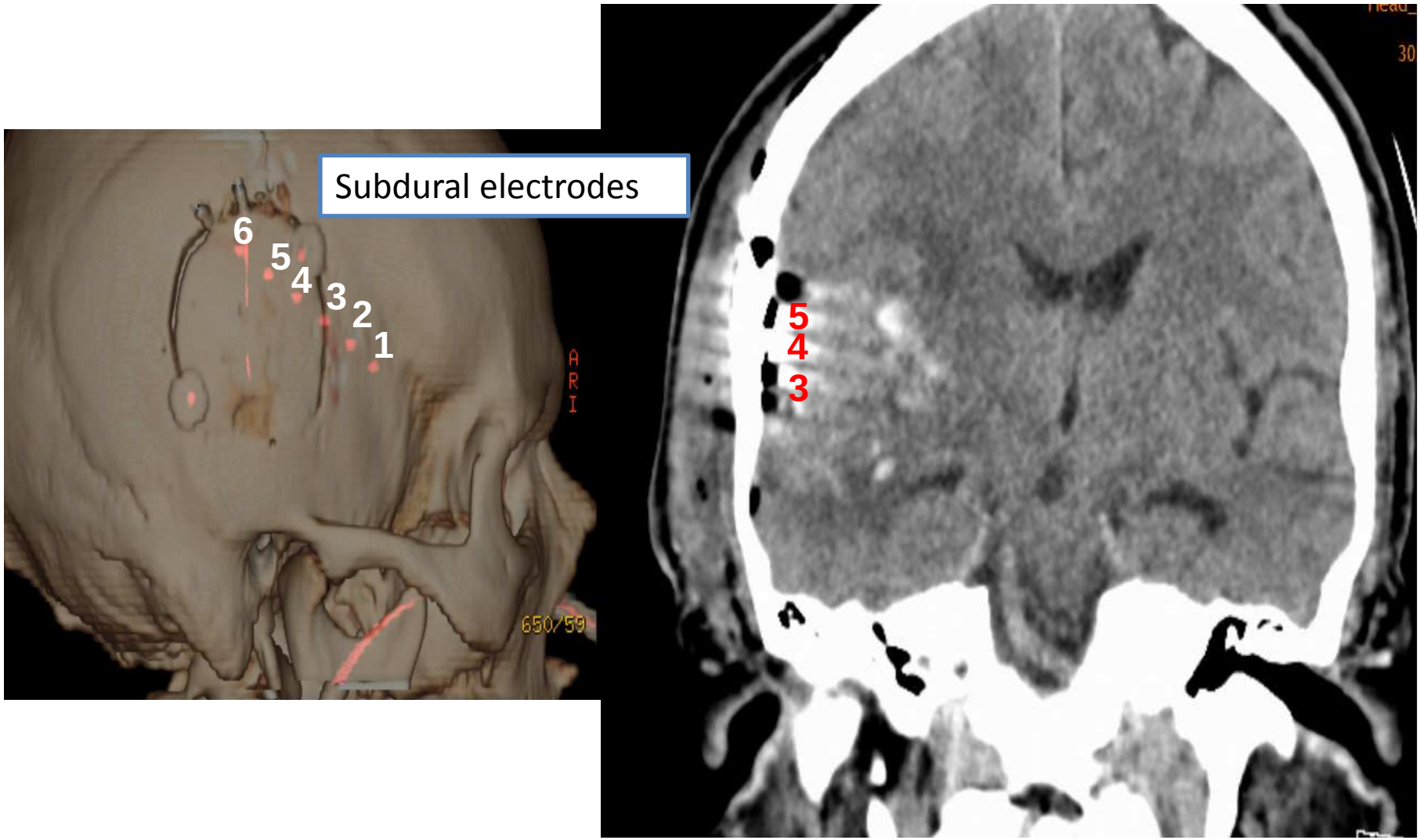
Clusters of Cortical Spreading Depolarizations in a Patient with Intracerebral Hemorrhage: A Multimodal Neuromonitoring Study

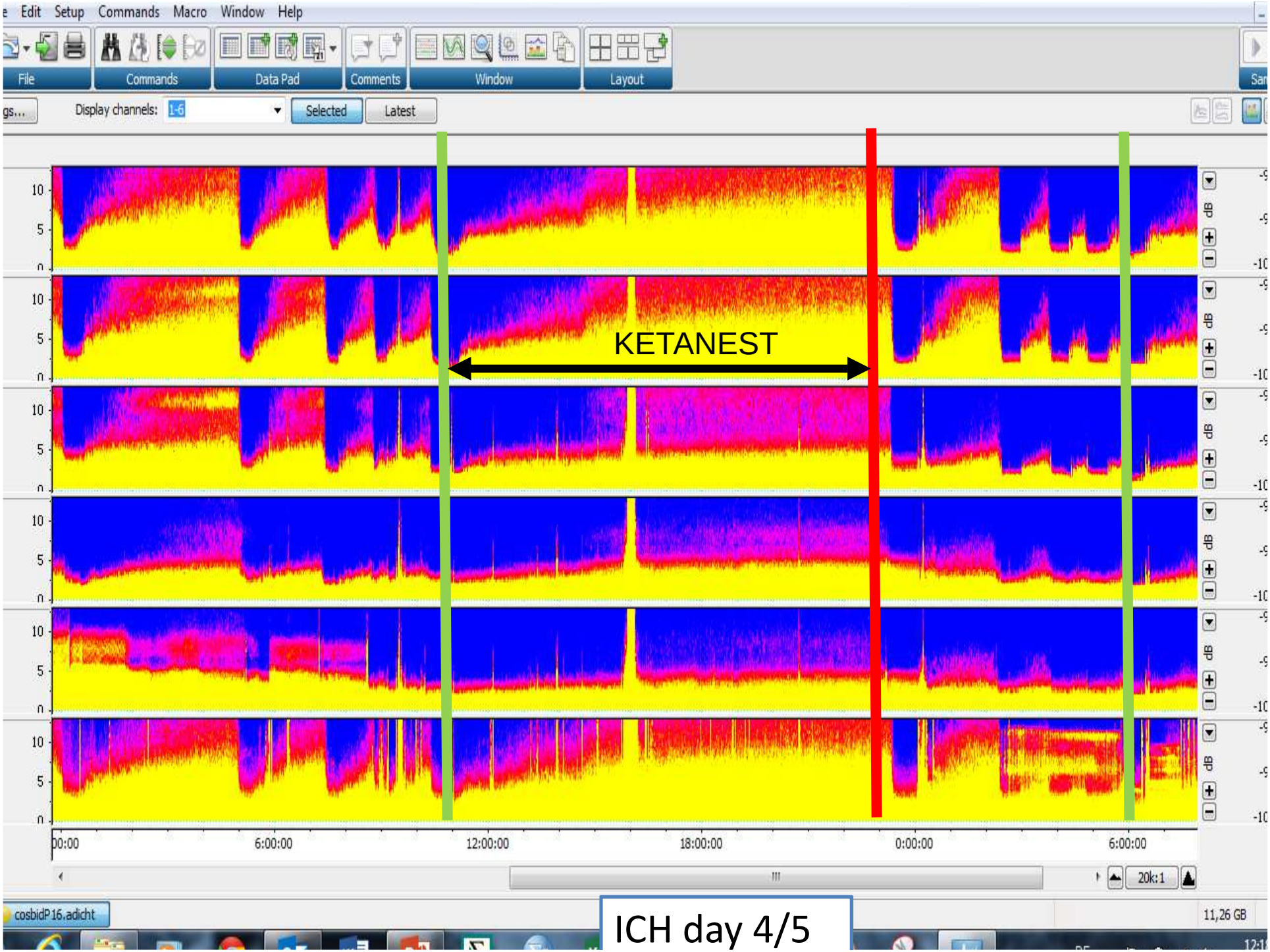
A. J. Schiefecker · R. Beer · B. Pfausler · P. Lackner · G. Broessner · I. Unterberger · F. Sohm · M. Mulino · C. Thome · C. Humpel · E. Schmutzhard · R. Helbok








Subdural electrodes
6
5
4
3
2
1
5
4
3


Edit Setup Commands Macro Window Help
File
Commands
Data Pad
Comments
Window
Layout
Display channels: 1-6
Selected
Latest
KETANEST
10
5
0
dB
-10
0:00
6:00:00
12:00:00
18:00:00
0:00:00
6:00:00
20k:1
cosbidP16.adicht
11,26 GB
ICH day 4/5

Ketamineffekt

CSD-Clusters in der Elektrokortikographie

- **Ohne** Ketamin → **6 CSDs / 6 Stunden**
- **Mit** Ketamin (25mg/ml) **1-4 ml/h** → **0 CSDs / 6 Stunden**
- **Mit** Ketamin (25mg/ml) **0,5 ml/h** → **2-3 CSDs / 6 Stunden**

neurocritical care society Neurocrit Care
DOI 10.1007/s12028-014-0050-4

PRACTICAL PEARL

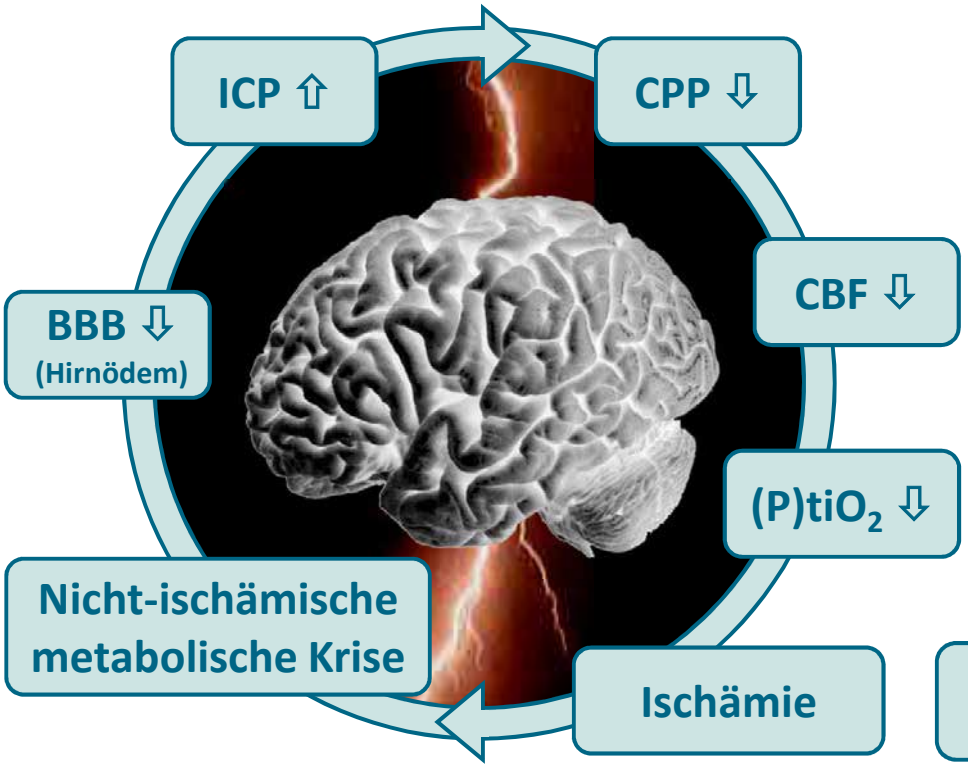
Clusters of Cortical Spreading Depolarizations in a Patient with Intracerebral Hemorrhage: A Multimodal Neuromonitoring Study

A. J. Schiefecker · R. Beer · B. Pfausler · P. Lackner · G. Broessner · I. Unterberger · F. Sohm · M. Mulino · C. Thome · C. Humpel · E. Schmutzhard · R. Helbok

SHT – Überlegungen zum Eingriff in den Circulus vitiosus

- **Circulus vitiosus** nach traumatischer ZNS-Schädigung

Sicherstellung **adäquater Kreislauffunktion**



- **Primäre Schädigung**
  »*Primary Injury*«
- **Sekundärschaden**
  »*Secondary Injury*«
- **Sekundärkomplikationen**
  »*Secondary Insults*«

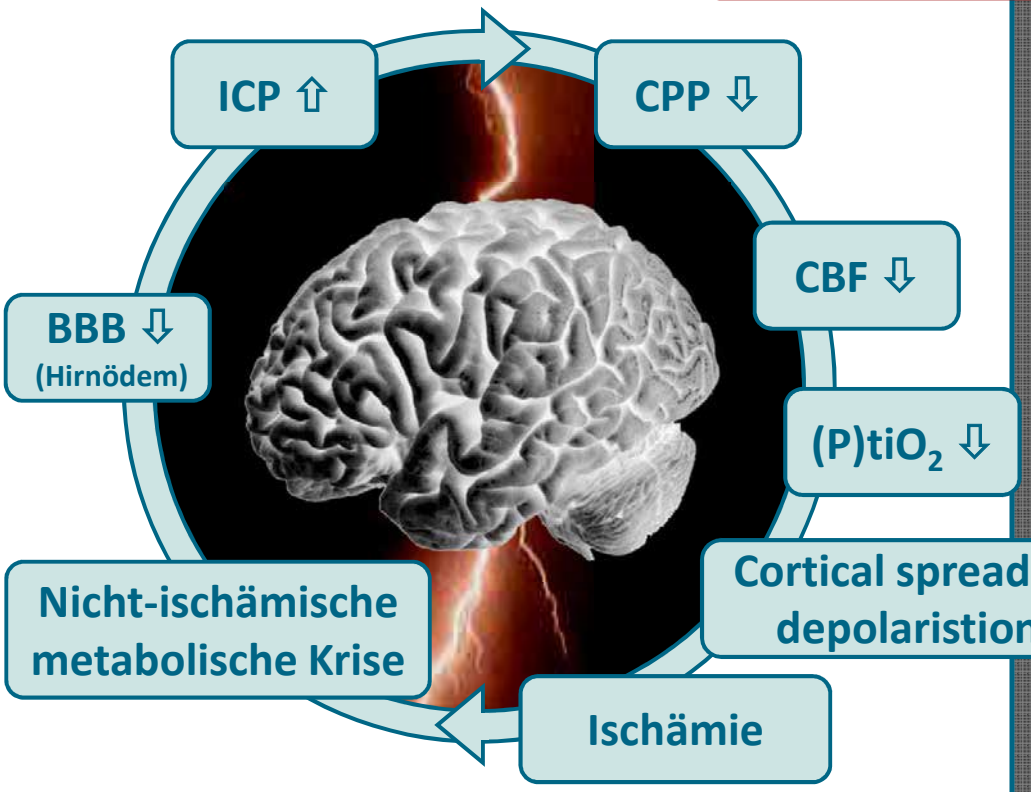
Cortical spreading depolaristions

Atemwegsicherung und **Oxygenierung**

SHT – Überlegungen zum Eingriff in den Circulus vitiosus

- **Circulus vitiosus** nach traumatischer ZNS-Schädigung

Sicherstellung **adäquater Kreislauffunktion**

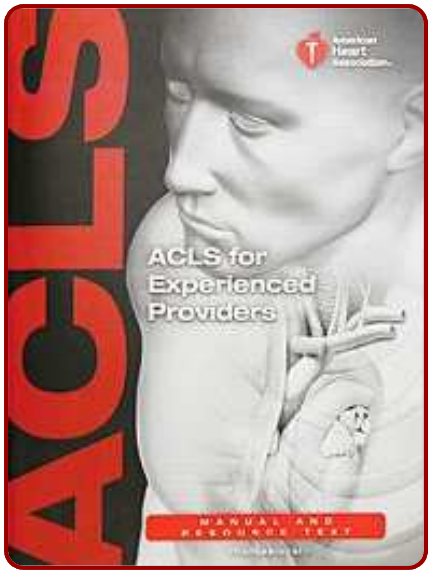


- **Primäre Schädigung**
  »Primary Injury«
- **Sekundärschaden**
  »Secondary Injury«

Sekundärkomplikationen
»Secondary Insults«

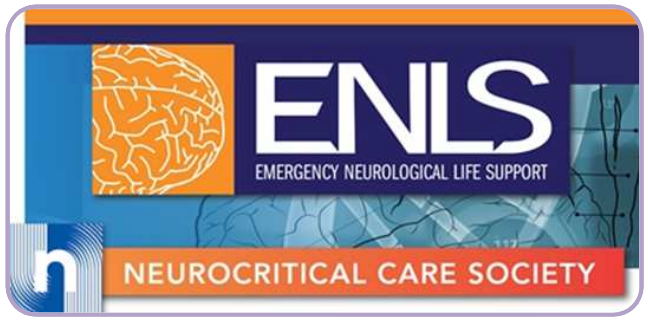
Atemwegsicherung und **Oxygenierung**

NeuroIntensivmedizin – »*The First or Golden Hour*«



Advanced CARDIOVASCULAR Life Support | AHA/ERC

Advanced TRAUMA Life Support | ACS



Emergency NEUROLOGICAL Life Support | NCS

- »***Improve brain perfusion and thereby outcomes***«
- **Kritische neurologische Krankheit** betrifft **sämtliche Organsysteme** (vgl. »neurogene« Organfunktions-störungen)

Hypoxia and hypotension, the "lethal duo" in traumatic brain injury: implications for prehospital care

- **Hypox(äm)ie** und **Hypotension** sind **starke Prädiktoren** für ein **ungünstiges** Outcome
  - **Arterielle Entsättigungen** (SaO_2 < 90%) bzw. **Hypox(äm)ie** (PaO_2 < 60 mmHg) sind mit einem **Letalitätsrisiko** bzw. einem **Risiko** für **schwere Behinderung** assoziiert
  - Eine **einzelne hypotensive Episode** (SBP < 90 mmHg) in der Prähospitalphase bedingt ein **höheres Letalitätsrisiko**

Modifiziert nach Stahel et al., Intensive Care Med 2008; 34: 402–404

Prehospital Hypoxia Affects Outcome in Patients With Traumatic Brain Injury: A Prospective Multicenter Study

Results: We enrolled 150 patients into the study. Fifty-seven patients had at least one secondary insult; 37 had only hypoxic episodes, 14 had only hypotensive episodes, and 6 patients had both. Demographics and injury characteristics did not differ between those with and those without secondary insults. The mortality for patients without secondary insults was 20%, compared with 37% for patients with hypoxic episodes, 8% for patients with hypotensive episodes, and 24% for patients with both. The Disability Rating Scale score at discharge was significantly higher in patients with secondary insults. Using multivariate analysis, the calculated odds ratio of mortality caused by prehospital hypoxia after head injury was 2.66 ($p < 0.05$).

Conclusions: Secondary insults after TBI are common, and these insults are associated with disability. Hypoxia in the prehospital setting significantly increases the odds of mortality after brain injury controlled for multiple variables.

Table 4 Injury Characteristics and Mortality

Injury Variables	No. Alive	No. Dead	*p* Value (univariate)	Mortality Odds Ratio	OR *p* Value (multivariate)
Hypoxia	28 (65.1%)	15 (34.9%)	0.05	2.66	0.043
Hypotension	17 (85%)	3 (15)	0.41	0.41	0.24
Age >65	7 (46.7%)	8 (53.3%)	0.018	26.6	0.010
GCS ≤8	28 (87.5%)	4 (12.5%)	0.023	4.63	0.048

Injury characteristic differences with univariate *p* values ≤0.21 were considered as potential mortality predictors for multivariate analysis. Odds ratios were then calculated for each candidate variable and multivariate logistic regression analysis performed for test of significance. Only presence of hypoxia, age >65 and GCS ≤8 were significant predictors of death after multivariate modeling.

Modifiziert nach Chi et al., J Trauma 2006; 61: 1134–1141

Schweres SHT – Therapieeskalation bei intrakranieller Hypertension

Traumatic Intracranial Hypertension

Nino Stocchetti, M.D., and Andrew I.R. Maas, M.D., Ph.D.

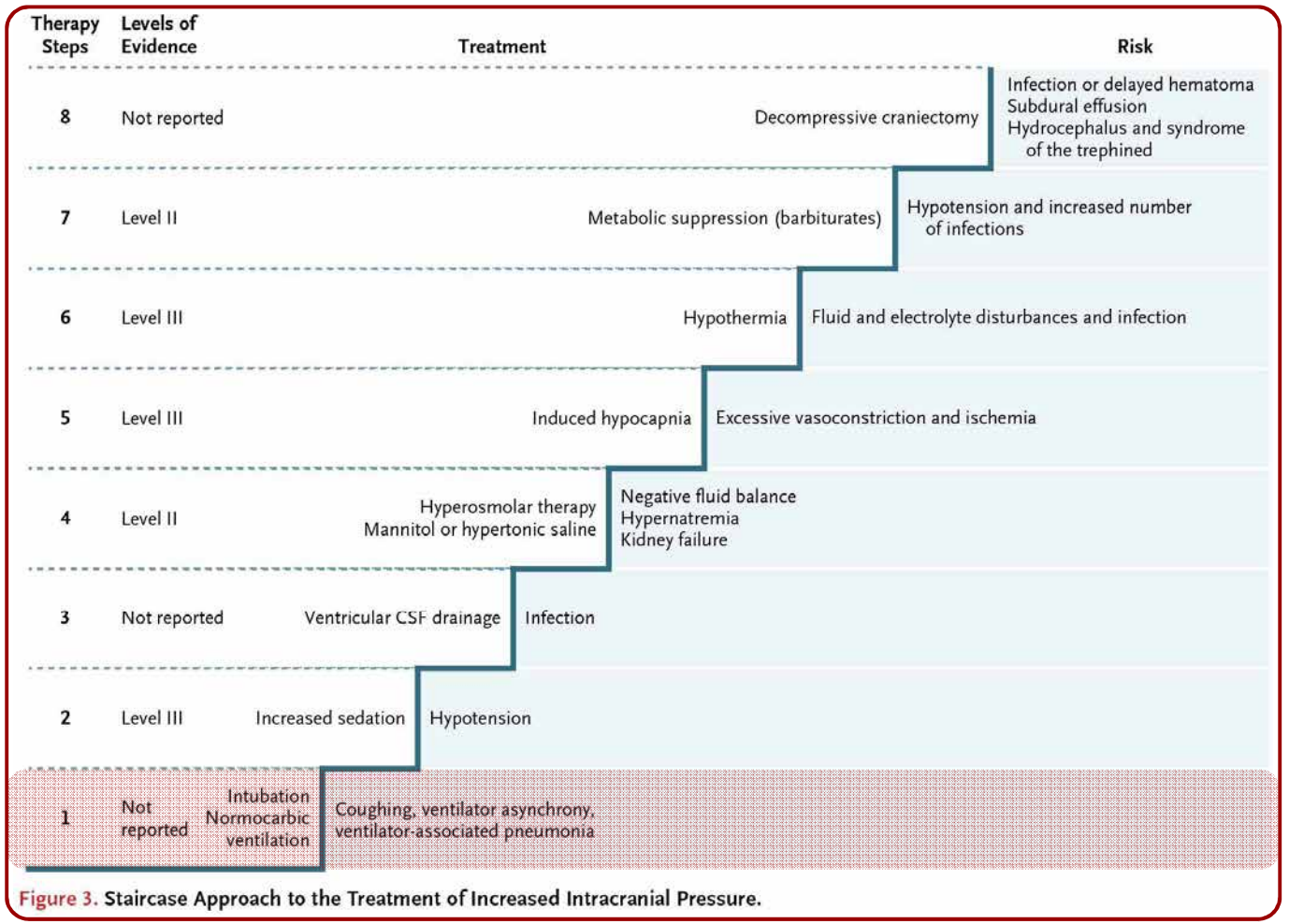


Figure 3. Staircase Approach to the Treatment of Increased Intracranial Pressure.

Modifiziert nach Stocchetti und Maas, N Engl J Med 2014; 370: 2121–2130

Schweres SHT – Therapieeskalation bei intrakranieller Hypertension

Traumatic Intracranial Hypertension

Nino Stocchetti, M.D., and Andrew I.R. Maas, M.D., Ph.D.

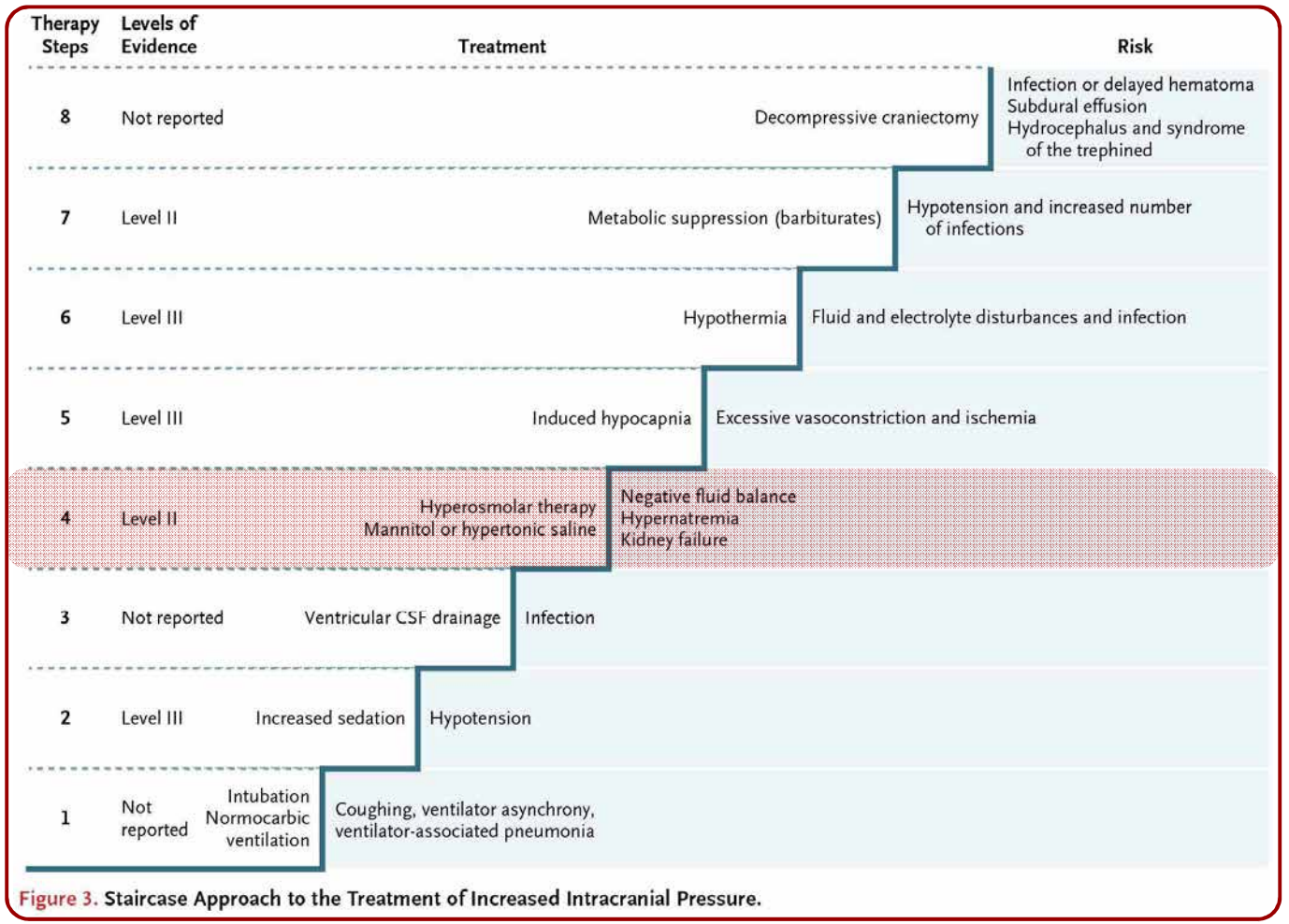


Figure 3. Staircase Approach to the Treatment of Increased Intracranial Pressure.

Modifiziert nach Stocchetti und Maas, N Engl J Med 2014; 370: 2121–2130

Schweres SHT – Therapieeskalation bei intrakranieller Hypertension

Traumatic Intracranial Hypertension

Nino Stocchetti, M.D., and Andrew I.R. Maas, M.D., Ph.D.

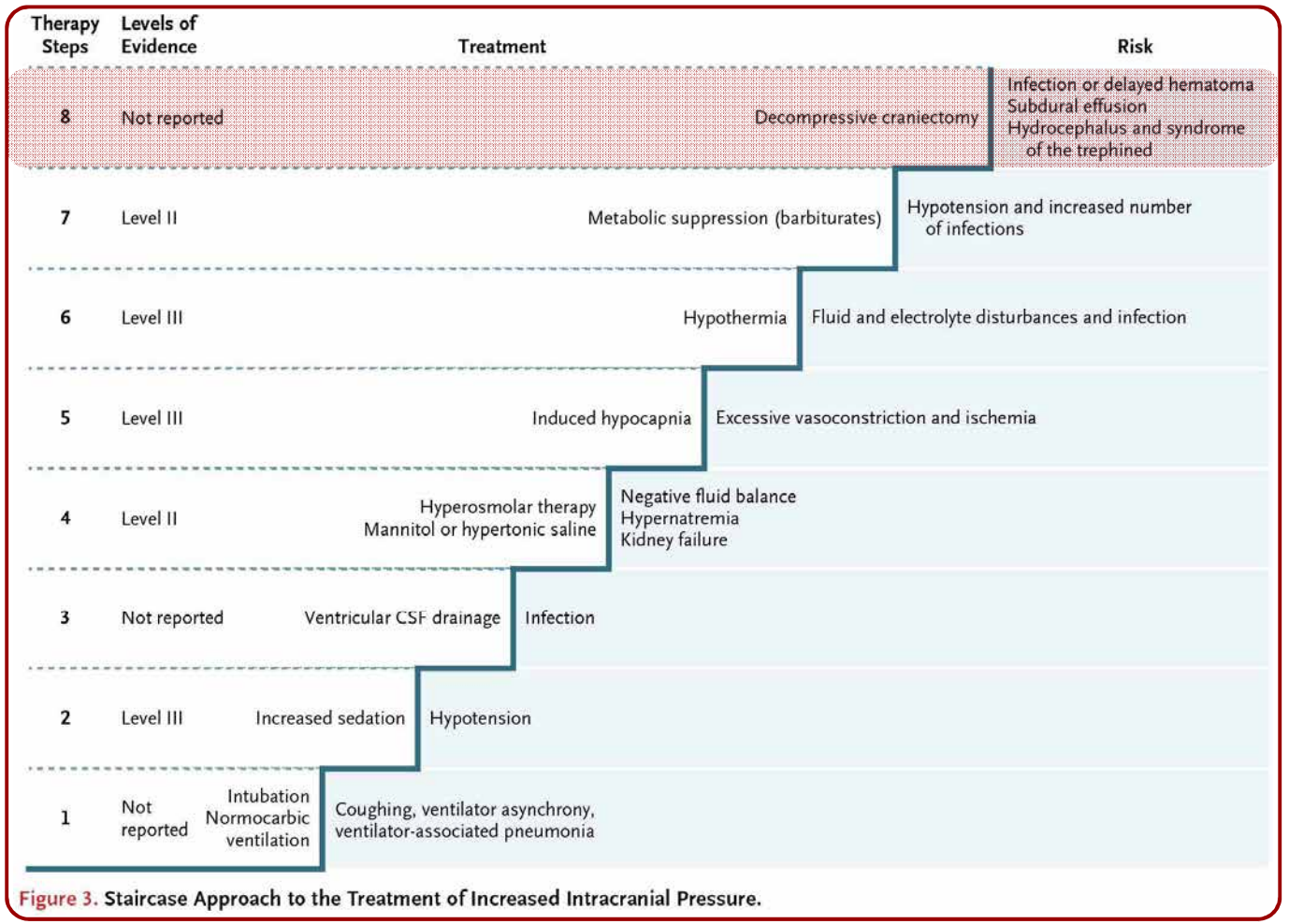


Figure 3. Staircase Approach to the Treatment of Increased Intracranial Pressure.

Modifiziert nach Stocchetti und Maas, N Engl J Med 2014; 370: 2121–2130

Schweres SHT – Therapieeskalation bei intrakranieller Hypertension

Traumatic Intracranial Hypertension

Nino Stocchetti, M.D., and Andrew I.R. Maas, M.D., Ph.D.

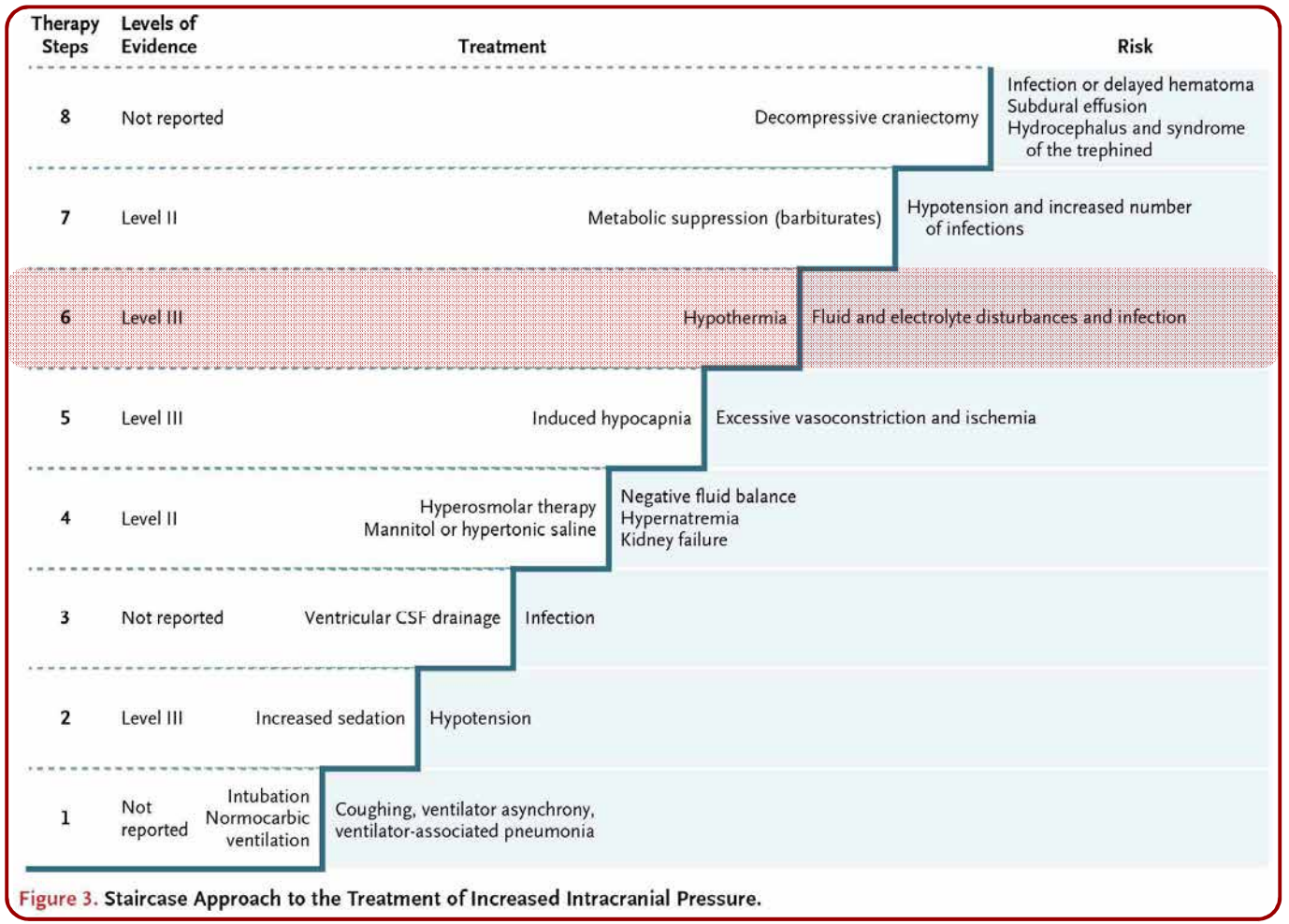


Figure 3. Staircase Approach to the Treatment of Increased Intracranial Pressure.

Modifiziert nach Stocchetti und Maas, N Engl J Med 2014; 370: 2121–2130

Therapeutic Hypothermia on Its 10th Anniversary

Is it Time to Turn the Thermostat Down?

Tomas Drabek, MD; Patrick M. Kochanek, MD

Modifiziert nach Drabek und Kochanek, Circulation 2012; 126: 2803–2805

The NEW ENGLAND JOURNAL of MEDICINE

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

Modifiziert nach Hypothermia after Cardiac Arrest Study Group, N Engl J Med 2002; 346: 549–556

The NEW ENGLAND JOURNAL of MEDICINE

TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA

STEPHEN A. BERNARD, M.B., B.S., TIMOTHY W. GRAY, M.B., B.S., MICHAEL D. BUIST, M.B., B.S., BRUCE M. JONES, M.B., B.S., WILLIAM SILVESTER, M.B., B.S., GEOFF GUTTERIDGE, M.B., B.S., AND KAREN SMITH, B.SC.

Modifiziert nach Bernard et al., N Engl J Med 2002; 346: 557–563

The NEW ENGLAND JOURNAL of MEDICINE

LACK OF EFFECT OF INDUCTION OF HYPOTHERMIA AFTER ACUTE BRAIN INJURY

GUY L. CLIFTON, M.D., EMMY R. MILLER, PH.D., R.N., SUNG C. CHOI, PH.D., HARVEY S. LEVIN, PH.D., STEPHEN MCCAULEY, PH.D., KENNETH R. SMITH, JR., M.D., J. PAUL MUIZELAAR, M.D., PH.D., FRANKLIN C. WAGNER, JR., M.D., DONALD W. MARION, M.D., THOMAS G. LUERSSEN, M.D., RANDALL M. CHESNUT, M.D., AND MICHAEL SCHWARTZ, M.D.

Modifiziert nach Clifton et al., N Engl J Med 2001; 344: 556–563

Induced hypothermia and fever control for prevention and treatment of neurological injuries

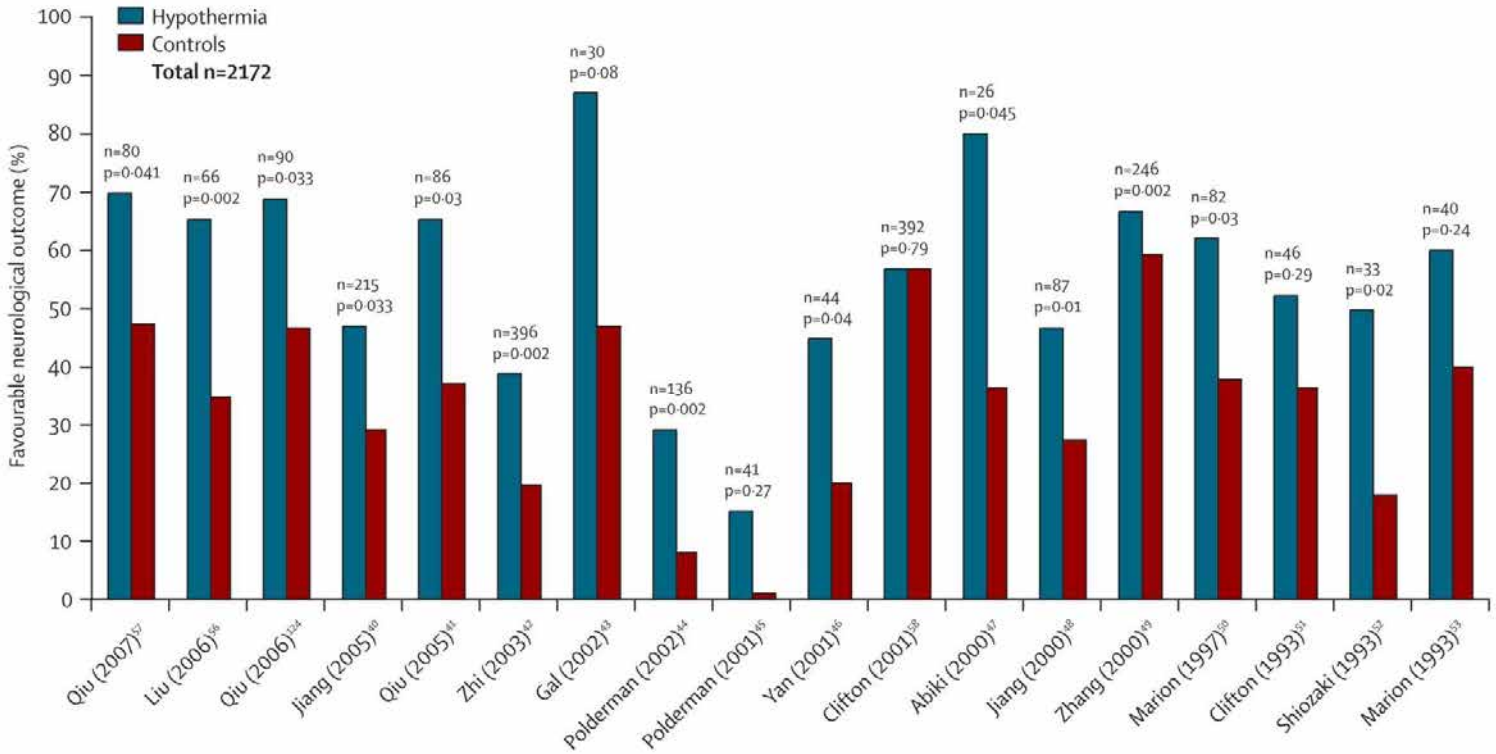


Figure 4: Clinical trials assessing the effects of hypothermia on neurological outcome in patients with traumatic brain injury and intracranial hypertension

Modifiziert nach Polderman, Lancet 2008; 371: 1955–1967

Hypothermia Treatment for Traumatic Brain Injury: A Systematic Review and Meta-Analysis

Consequently, main analyses were conducted based on eight trials that demonstrated the lowest potential for bias ($n = 781$).

Reductions in risk of mortality were greatest (RR 0.51; 95% CI 0.33, 0.79) and favorable neurologic outcomes much more common (RR 1.91; 95% CI 1.28, 2.85) when hypothermia was maintained for more than 48 h. However, this evidence comes with the suggestion that the potential benefits of hypothermia may likely be offset by a significant increase in risk of pneumonia (RR 2.37; 95% CI 1.37, 4.10).

In sum, the present study's updated meta-analysis supports previous findings that hypothermic therapy constitutes a beneficial treatment of TBI in specific circumstances. Accordingly, the BTF/AANS guidelines task force has issued a Level III recommendation for optional and cautious use of hypothermia for adults with TBI.

Modifiziert nach Peterson et al., J Neurotrauma 2008; 25: 62–71

Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial

Methods The National Acute Brain Injury Study: Hypothermia II (NABIS: H II) was a randomised, multicentre clinical trial of patients with severe brain injury who were enrolled within 2·5 h of injury at six sites in the USA and Canada. Patients with non-penetrating brain injury who were 16–45 years old and were not responsive to instructions were randomly assigned (1:1) by a random number generator to hypothermia or normothermia. Patients randomly assigned to hypothermia were cooled to 35°C until their trauma assessment was completed. Patients who had none of a second set of exclusion criteria were either cooled to 33°C for 48 h and then gradually rewarmed or treated at normothermia, depending upon their initial treatment assignment.

Interpretation This trial did not confirm the utility of hypothermia as a primary neuroprotective strategy in patients with severe traumatic brain injury.

Modifiziert nach Clifton et al., Lancet Neurol 2011; 10: 131–139

Early induction of hypothermia for evacuated intracranial hematomas: a post hoc analysis of two clinical trials

Guy L. Clifton, M.D.,[1] Christopher S. Coffey, Ph.D.,[2] Sierra Fourwinds,[3]
David Zygun, M.D., Ph.D.,[4] Alex Valadka, M.D.,[1] Kenneth R. Smith Jr., M.D.,[5]
Melisa L. Frisby, M.S.N., R.N.,[6] Richard D. Bucholz, M.D.,[5] Elisabeth A. Wilde, Ph.D.,[6]
Harvey S. Levin, Ph.D.,[6] and David O. Okonkwo, M.D., Ph.D.[7]

TABLE 1: Relationship of outcome to hypothermia and normothermia treatment assignment and to the time of reaching 35°C relative to surgery start time

Trial	No. of Patients	% Poor Outcomes	p Value	RR (95% CI)	Time From Surgery Start to Temp ≤ 35°C (hrs)	Mean Temp For 24-Hr Period After Surgery Start (°C)	p Value
NABIS:H I*	112		0.16	0.74 (0.49–1.13)			<0.001
≤35°C w/in 1.5 hrs	31	45			0.5 ± 0.5	32.9 ± 0.8	
>35°C w/in 1.5 hrs	23	61			4.0 ± 2.0	33.5 ± 0.8	
normothermia	58	60				36.7 ± 0.9	
NABIS:H II†	28		0.02	0.44 (0.22–0.88)			<0.001
hypothermia	15	33			0.4 ± 0.9	33.0 ± 0.3	
normothermia	13	69				37.3 ± 0.6	

Results. A meta-analysis of 46 patients with hematomas in both trials who reached 35°C within 1.5 hours of surgery start showed a significantly reduced rate of poor outcomes (41%) compared with 94 patients treated with hypothermia who did not reach 35°C within that time and patients treated at normothermia (62%, p = 0.009).

Conclusions. Induction of hypothermia to 35°C before or soon after craniotomy with maintenance at 33°C for 48 hours thereafter may improve outcome of patients with hematomas and severe traumatic brain injury.

Modifiziert nach Clifton et al., J Neurosurg 2012; 117: 714–720

Therapeutische **Hypo**thermie bei SHT – Studien mit laufender Rekrutierung

anzic research centre

The POLAR-RCT

The Prophylactic hypOthermia trial to Lessen trAumatic bRain injury-Randomised Controlled Trial

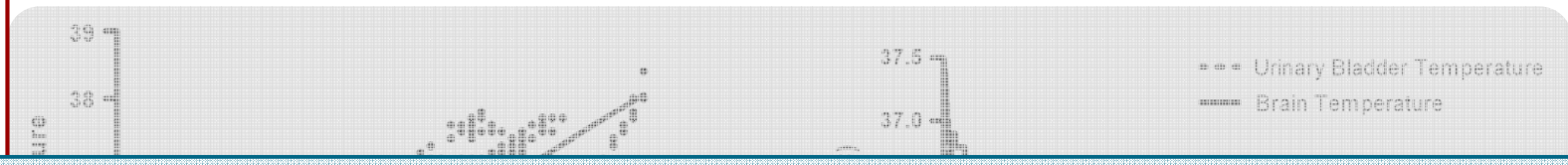
(ACTRN12605000009617)

Prospective randomised controlled multi-centre trial of early and sustained prophylactic hypothermia in 500 patients with severe TBI

polar

Keep the Brain Cool—Endovascular Cooling in Patients With Severe Traumatic Brain Injury: A Case Series Study

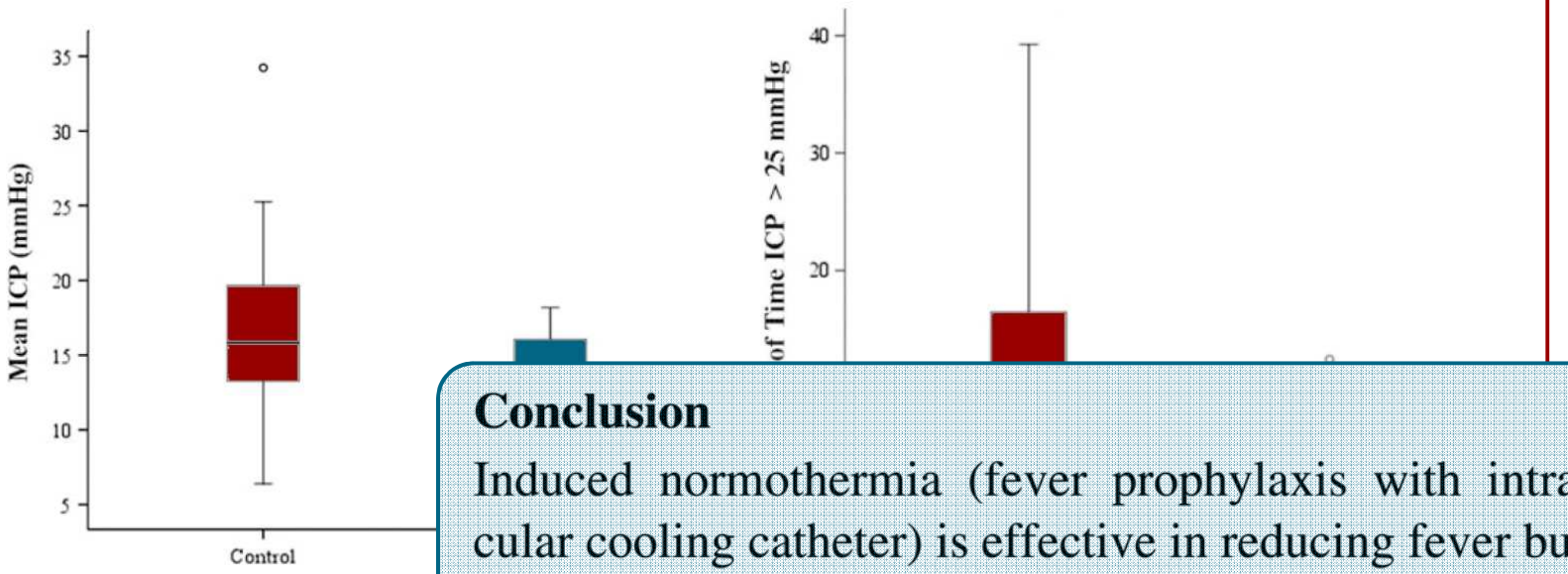
OBJECTIVE: To study the influence of prophylactic normothermia on brain temperature and the temperature gradient between brain and core body in patients with severe TBI using an intravascular cooling system and to assess the relationship between brain temperature and intracranial pressure (ICP) under endovascular temperature control.



CONCLUSION: Intravascular temperature management stabilizes both brain and body core temperature; prophylactic normothermia reduces the otherwise extreme increase of intracerebral temperature in patients with severe TBI. The intravascular cooling management proved to be an efficacious and feasible method to control brain temperature and to avoid hyperthermia in the injured brain. We could not find a statistically significant correlation between brain temperature and ICP.

Modifiziert nach Fischer et al., Neurosurgery 2011; 68: 867–873

Induced Normothermia Attenuates Intracranial Hypertension and Reduces Fever Burden after Severe Traumatic Brain Injury



Conclusion

Induced normothermia (fever prophylaxis with intravascular cooling catheter) is effective in reducing fever burden and may offer a means to attenuate secondary injury, as evidenced by a reduction in intracranial hypertension and fever burden in an adult population with severe TBI.

Modifiziert nach Puccio et al., Neurocrit Care 2009; 11: 82–87

Brain Injury, December 2012; 26(13–14): 1523–1548

informa
healthcare

REVIEW

Randomized controlled trials in adult traumatic brain injury

JUAN LU[1,2], KELLI W. GARY[3], JANET P. NEIMEIER[4], JOHN WARD[2], & KATE L. LAPANE[1]

[1]*Department of Epidemiology and Community Health, Virginia Commonwealth University, Richmond, VA, USA,* [2]*Department of Neurosurgery, Virginia Commonwealth University, Richmond, VA, USA,* [3]*Department of Occupational Therapy, Virginia Commonwealth University, Richmond, VA, USA, and* [4]*Department of Physical Medicine and Rehabilitation and Psychiatry, Virginia Commonwealth University, Richmond, VA, USA*

Table I. Results of 100 randomized controlled clinical trials in adults with traumatic brain injury.

	Intervention effectiveness[a]						
	Positive effect		Adverse effect		No effect		
Types of intervention	*n*	%	*n*	%	*n*	%	Total, *n*
Acute phase post-TBI							
Pharmacological drug trials	4	13	4	13	24	75	32
Published trials	4	20	3	12	18	72	25
Unpublished Phase III trials[b]			1	14	6	86	7
Non-pharmacological trials	11	48	2	10	10	43	23
Decompressive craniectomy	2	67	1	33			3
Early nutritional supplement	2	100					2
Hyperbaric oxygen therapy					2	100	2
Hyperventilation			1	100			1
Osmotic therapy	2	40			3	60	5
Therapeutic hypothermia	4	44			5	56	9
Pre-hospital rapid sequence intubation	1	100					1
Post-acute phase following TBI							
Cognitive rehabilitation	22[c]	92			2	8	24
Comprehensive interdisciplinary models	8	89			1	11	9
Cognitive or academic exercises and communication skill training	3	100					3
Compensatory technique and computer-assisted training	4	100					4
Education	4	80			1	20	5
Psychotherapy and behaviour modification	3	100					3
Physical rehabilitation	6[c]	75			2	25	8
Pharmacotherapy	6	55	1	9	4	36	11
Nutrition therapy	1	100					1
Alternative therapy	1	100					1

[a]Based on the study primary outcome defined by the original authors.
[b]The information is based on the review article by Maas et al. [6] (six trials) and all seven trials were completed before 2008.
[c]The positive effect is reported as that observed from the study intervention only, as well as from both study intervention and controls (four cognitive and three physical rehabilitation trials). The latter condition is commonly due to the study design, such as repeated measures (e.g. outcome measures are compared with the measures at baseline or before treatment) or both study arms are interventions (e.g. supervised fitness centre based exercise *vs.* unsupervised home-based exercise programme).

Table I. Results of 100 randomized controlled clinical trials in adults with traumatic brain injury.

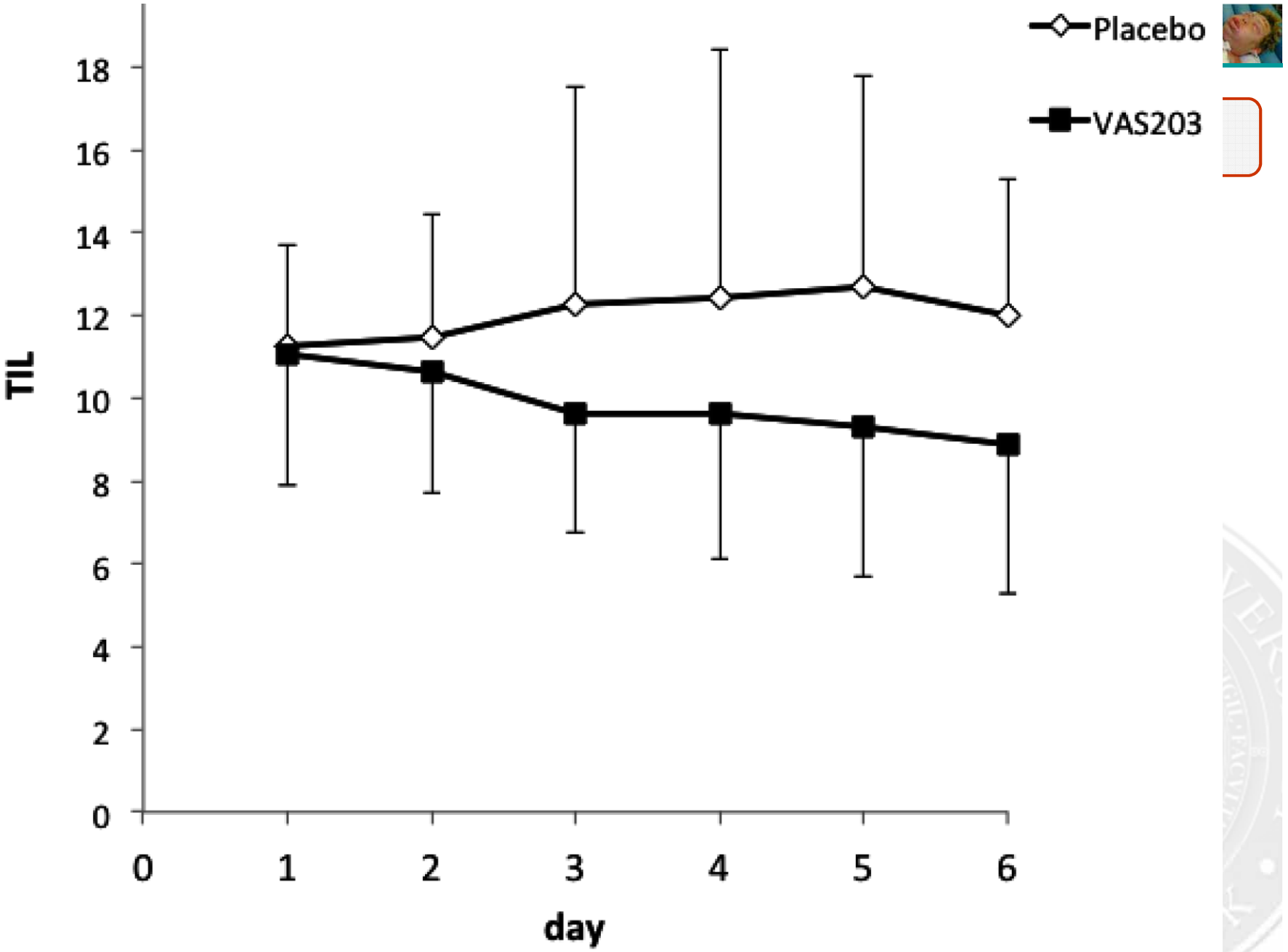
Types of intervention	Intervention effectiveness[a]						
	Positive effect		Adverse effect		No effect		
	n	%	*n*	%	*n*	%	Total, *n*
Acute phase post-TBI							
Pharmacological drug trials	4	13	4	13	24	75	32
Published trials	4	20	3	12	18	72	25
Unpublished Phase III trials[b]			1	14	6	86	7
Non-pharmacological trials	11	48	2	10	10	43	23
Decompressive craniectomy	2	67	1	33			3
Early nutritional supplement	2	100					2
Hyperbaric oxygen therapy					2	100	2
Hyperventilation			1	100			1
Osmotic therapy	2	40			3	60	5
Therapeutic hypothermia	4	44			5	56	9
Pre-hospital rapid sequence intubation	1	100					1
Post-acute phase following TBI							
Cognitive rehabilitation	22[c]	92			2	8	24
Comprehensive interdisciplinary models	8	89			1	11	9
Cognitive or academic exercises and communication skill training	3	100					3
Compensatory technique and computer-assisted training	4	100					4
Education	4	80			1	20	5
Psychotherapy and behaviour modification	3	100					3
Physical rehabilitation	6[c]	75			2	25	8
Pharmacotherapy	6	55	1	9	4	36	11
Nutrition therapy	1	100					1
Alternative therapy	1	100					1

[a]Based on the study primary outcome defined by the original authors.
[b]The information is based on the review article by Maas et al. [6] (six trials) and all seven trials were completed before 2008.
[c]The positive effect is reported as that observed from the study intervention only, as well as from both study intervention and controls (four cognitive and three physical rehabilitation trials). The latter condition is commonly due to the study design, such as repeated measures (e.g. outcome measures are compared with the measures at baseline or before treatment) or both study arms are interventions (e.g. supervised fitness centre based exercise *vs.* unsupervised home-based exercise programme).

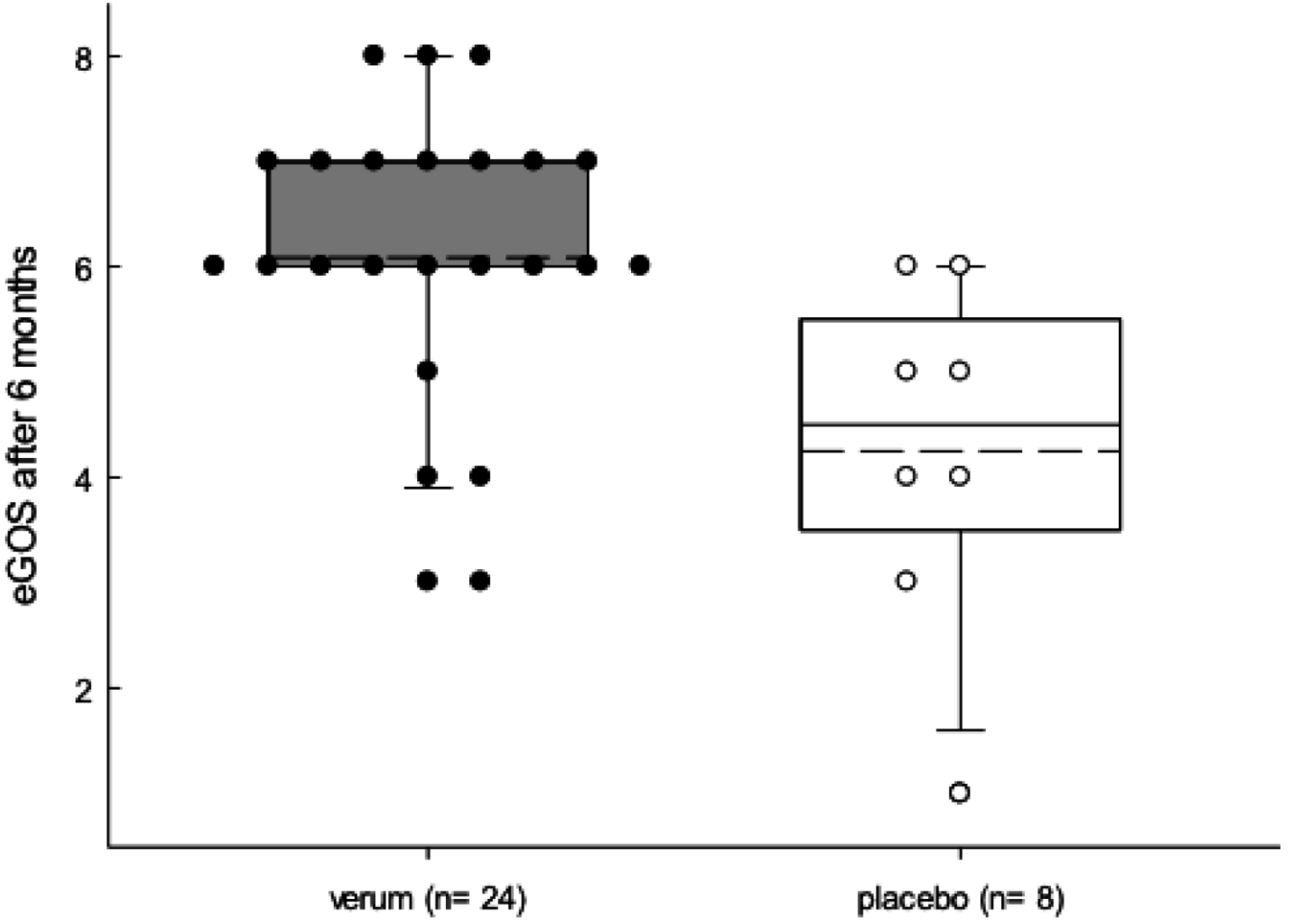
Nitric Oxide Synthase Inhibition with Antipterin VAS203 improves Neuropsychological Outcome following **Moderate and Severe Traumatic Brain Injury**: a Placebo-Controlled randomised **Phase II** Trial **(NOSTRA)**

20. 5. 2014
Journal of Neurotrauma

John F. Stover , Antonio Belli, Diederik Bulters, Henry Boret, Juan Sahuquillo, Erich Schmutzhard, Elisabeth Zavalla, Urban Ungerstedt, Reinhard Schinzel, Frank Tegtmeier; on behalf of the NOSTRA investigators


Placebo
VAS203
TIL
18
16
14
12
10
8
6
4
2
0
0
1
2
3
4
5
6
day

3



Interpretation:

VAS203 is safe at a total dose of up to 20 mg/kg infused intravenously at a constant rate for 48 hours.

…. the significant **improvement in clinical outcome parameters** is indicative of VAS203-mediated **neuroprotection** following TBI ….

J. Stover et al 2014, J Neurotrauma

SHT – Collaborative European **NeuroTrauma Effectiveness Research** in TBI

CENTER-TBI has received funding from the European Union Seventh Framework Programme (FP7/2007–2013) under grant agreement n°602150

Prioritized Research Targets → **Evidence Generation** → **Research Outputs**

- Better characterization of initial severity, disease process and outcome
- Effectiveness of care and treatment
- Evidence to underpin guidelines
- Knowledge transfer

International comparisons (EU, USA, Canada, Australia, China)

National/regional registries (e.g., TARN)

Study registry (n ~ 20,000)

Core data (n ~ 5,400; ICU = 1,800)

Enhanced datasets (n ~ 200–400)
HR ICU MRI EEG Coagulation

Clinical data | Neuroimaging | Genomics | Biomarkers | High resolution ICU data | Clinical and patient assessed outcomes

Evidence communication
- Pathophysiological insights
- Multidimensional classification
- Effective stratification
- Novel biomarkers
- Intermediate endpoints
- Improved prognostication

Evidence synthesis
- Advanced statistical analysis
- Machine learning approaches

Evidence translation
- Guidelines
- Improved Training
- Efficient care pathways

Research Legacy: Data & Sample Repositories

SHT – Collaborative European **NeuroTrauma Effectiveness Research** in TBI

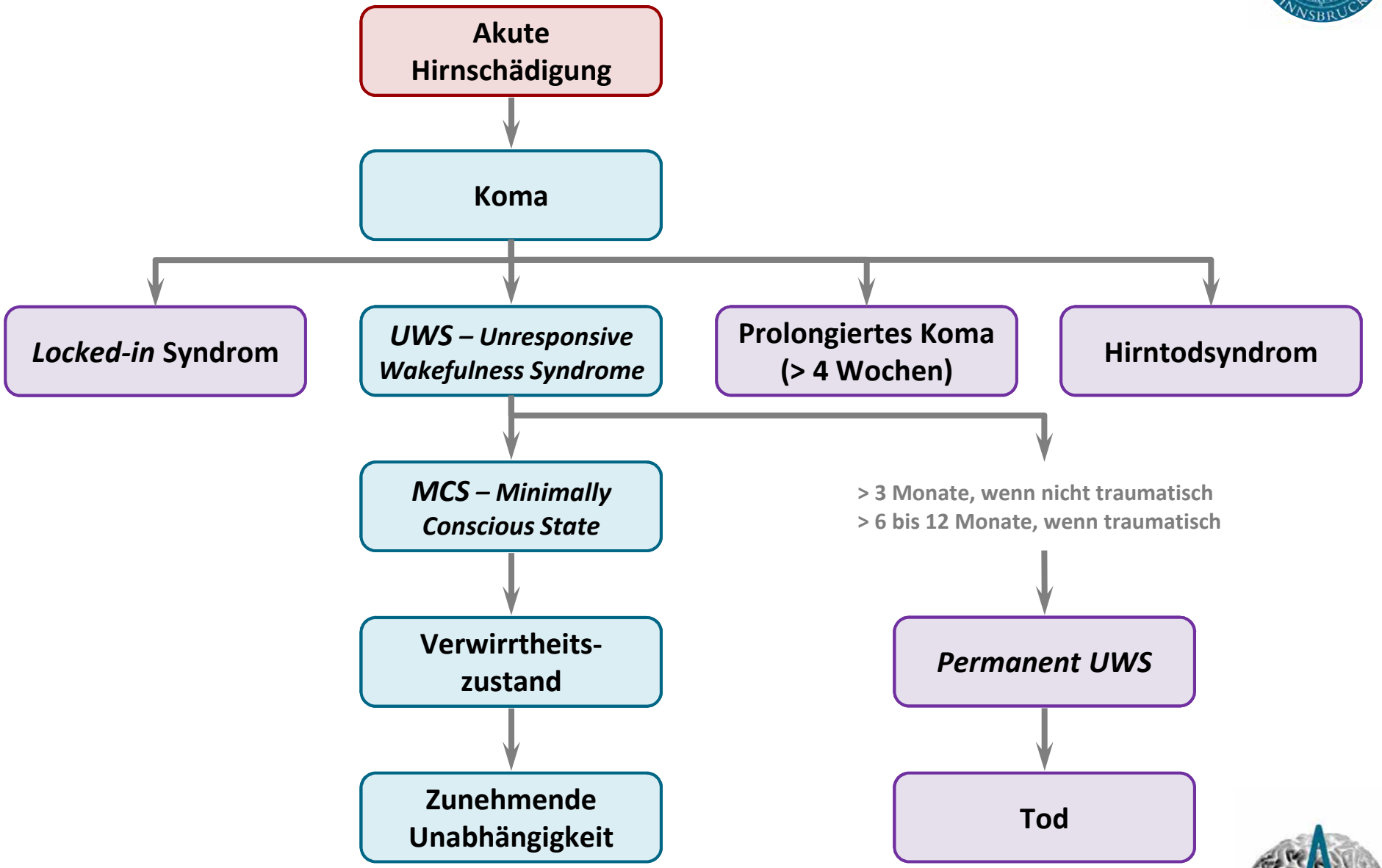
CENTER-TBI
Collaborative European NeuroTrauma Effectiveness Research in TBI
A 2020 vision: Generating knowledge for improving TBI outcomes

European Commission

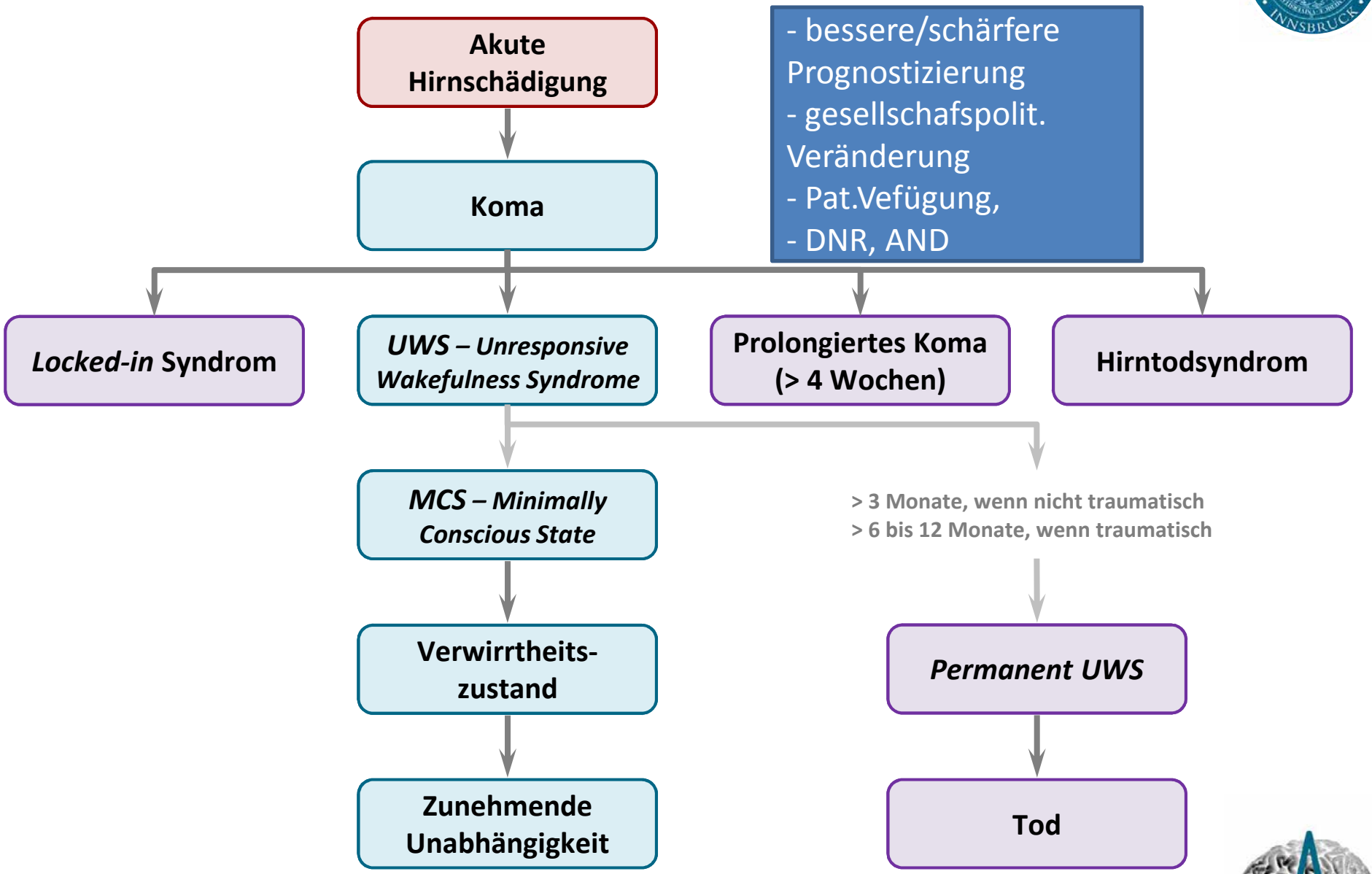
CENTER-TBI has received funding from the European Union Seventh Framework Programme (FP7/2007–2013) under grant agreement n°602150

SEVENTH FRAMEWORK PROGRAMME

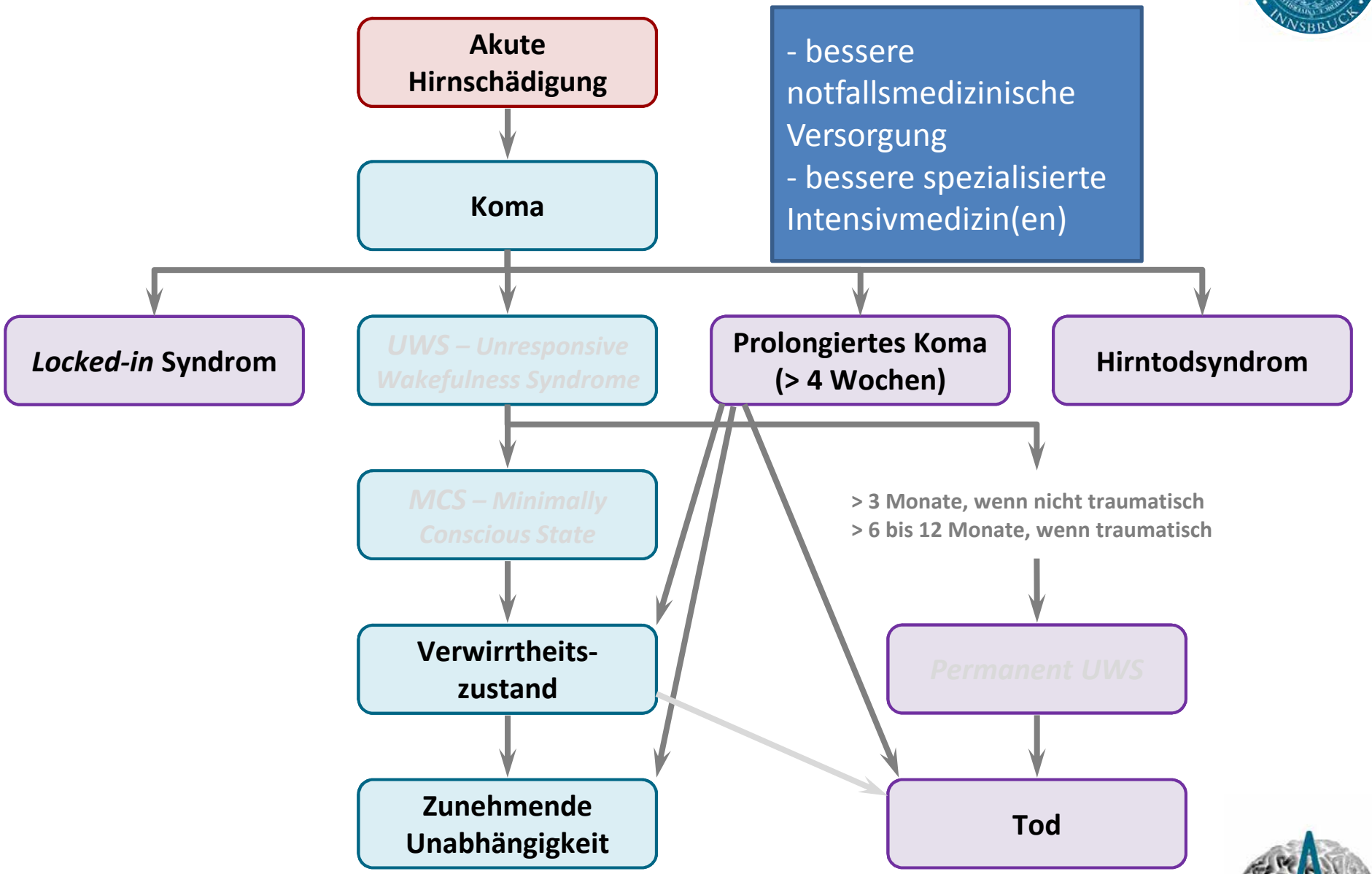
(Möglicher) Verlauf von schweren Hirnschädigungen

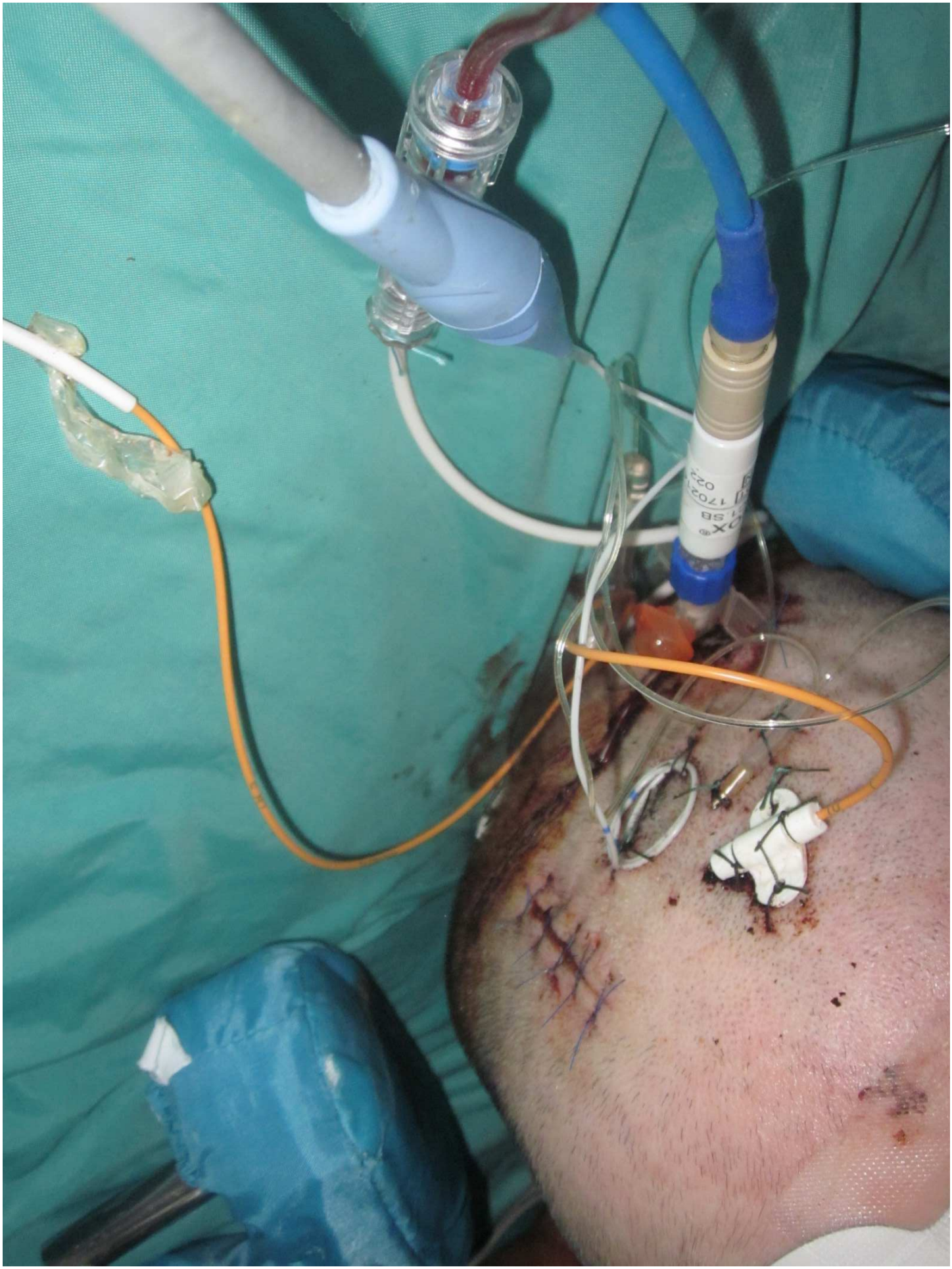


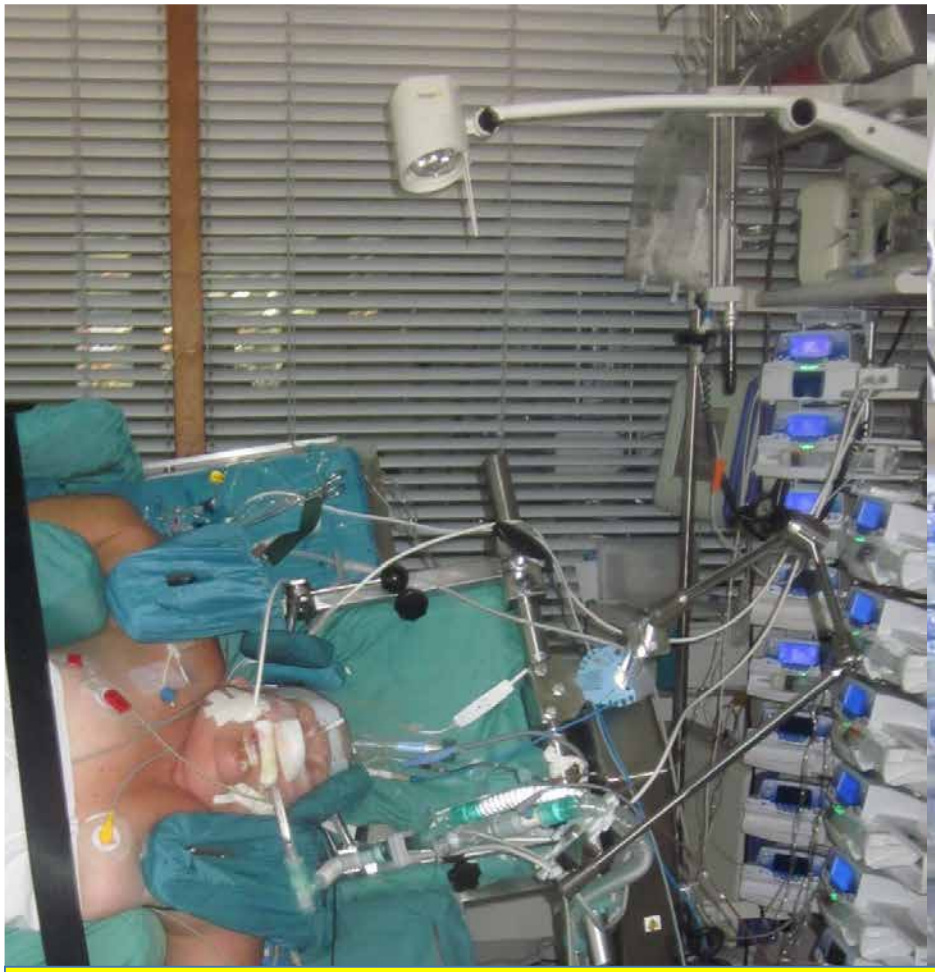
(Möglicher) Verlauf von schweren Hirnschädigungen

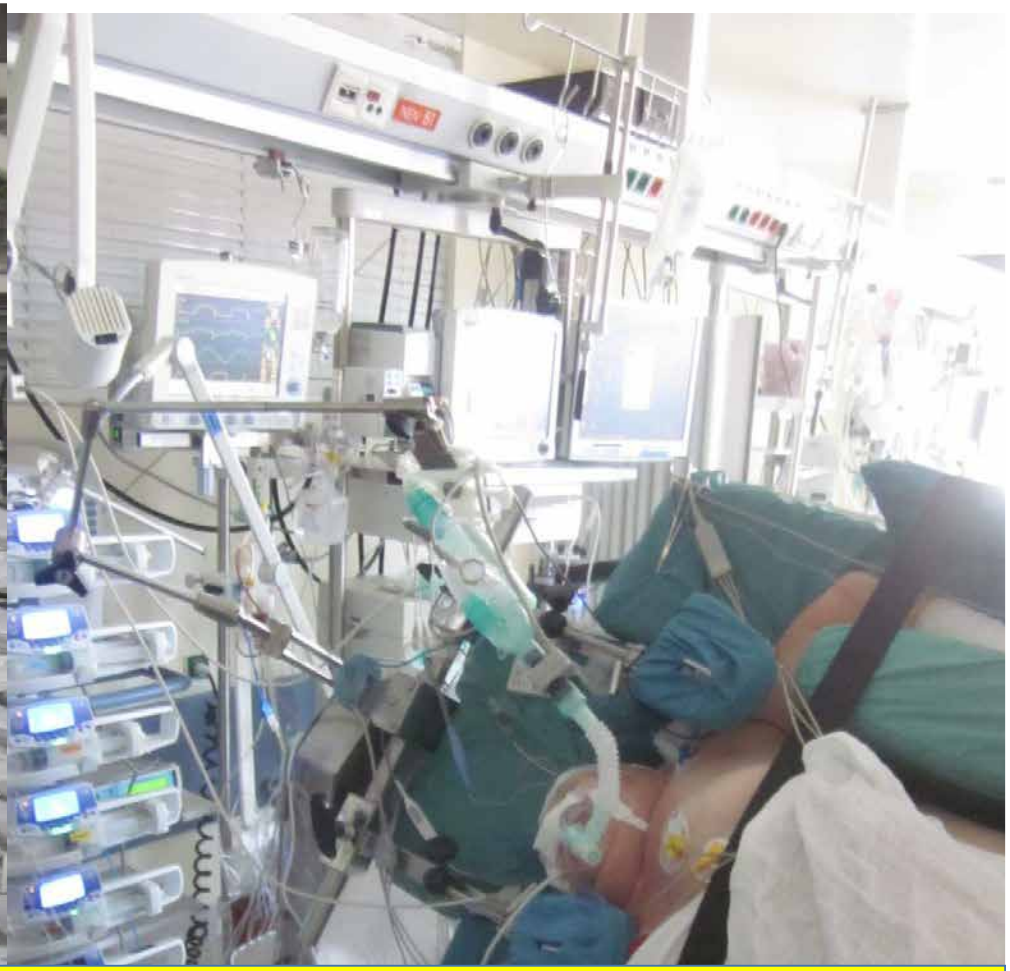


(Möglicher) Verlauf von schweren Hirnschädigungen/schwerem SHT

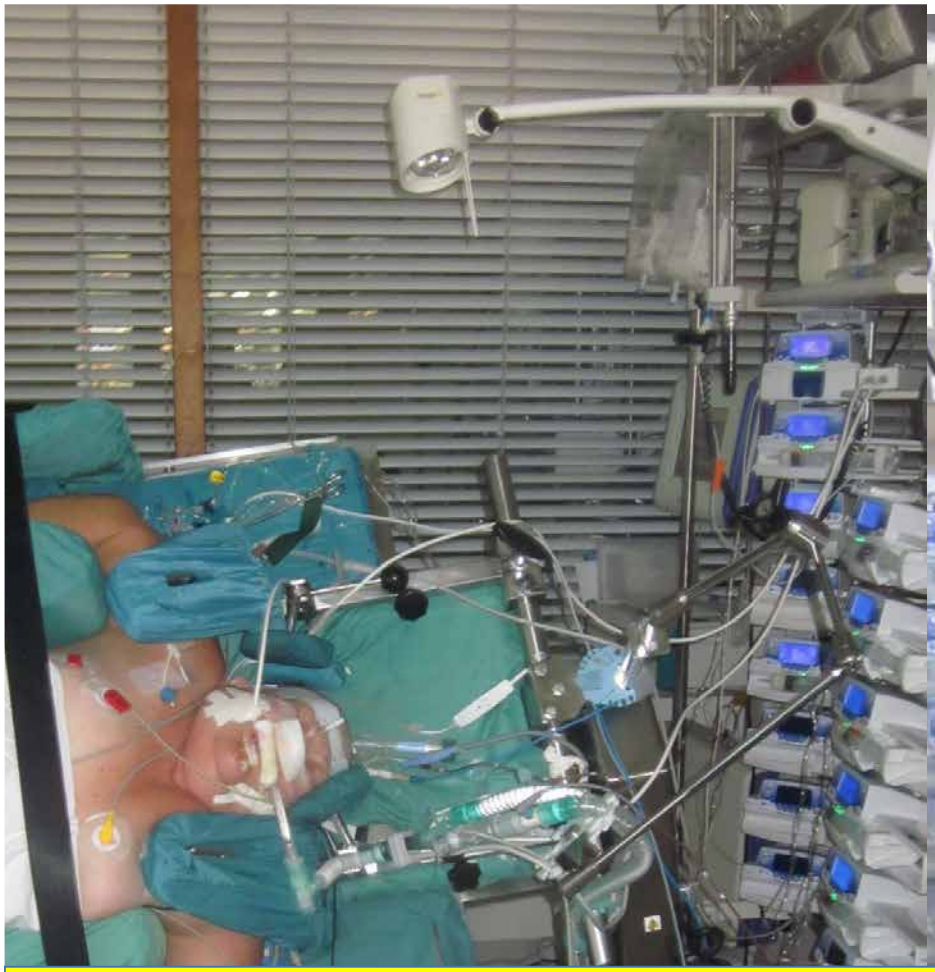


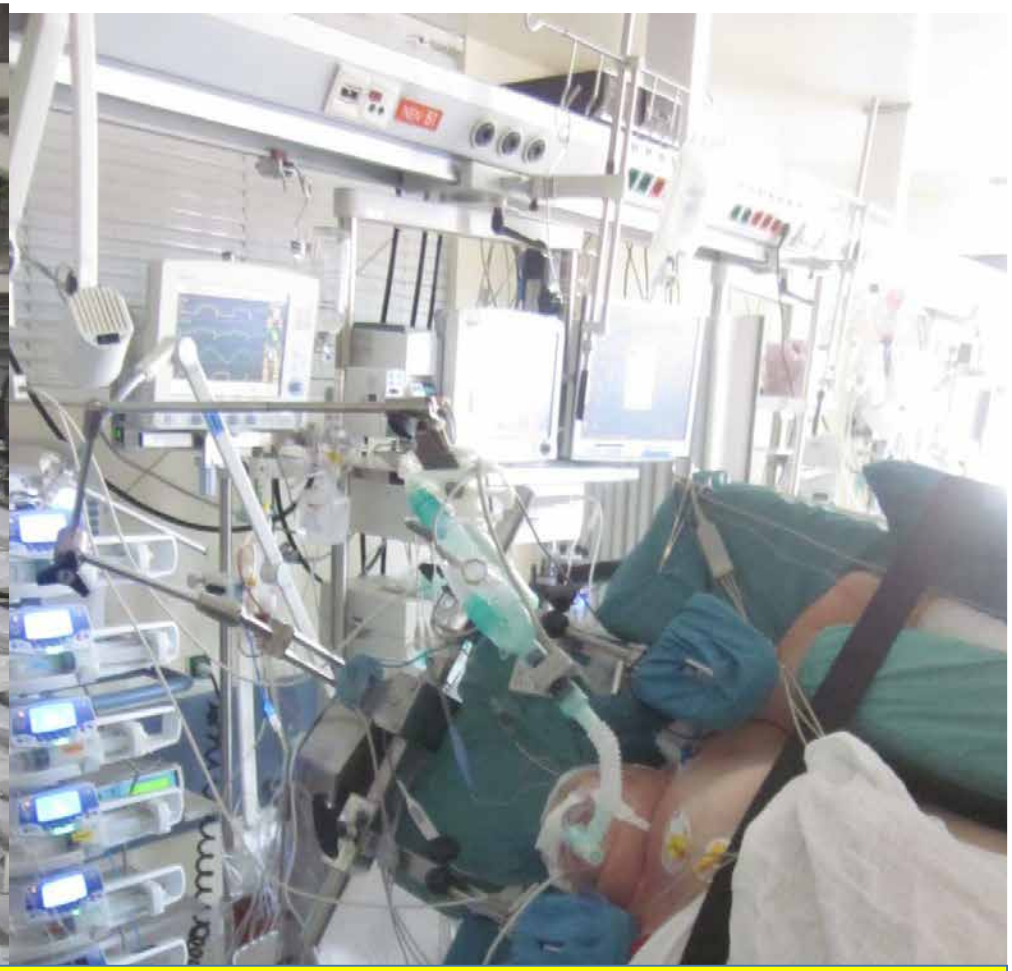




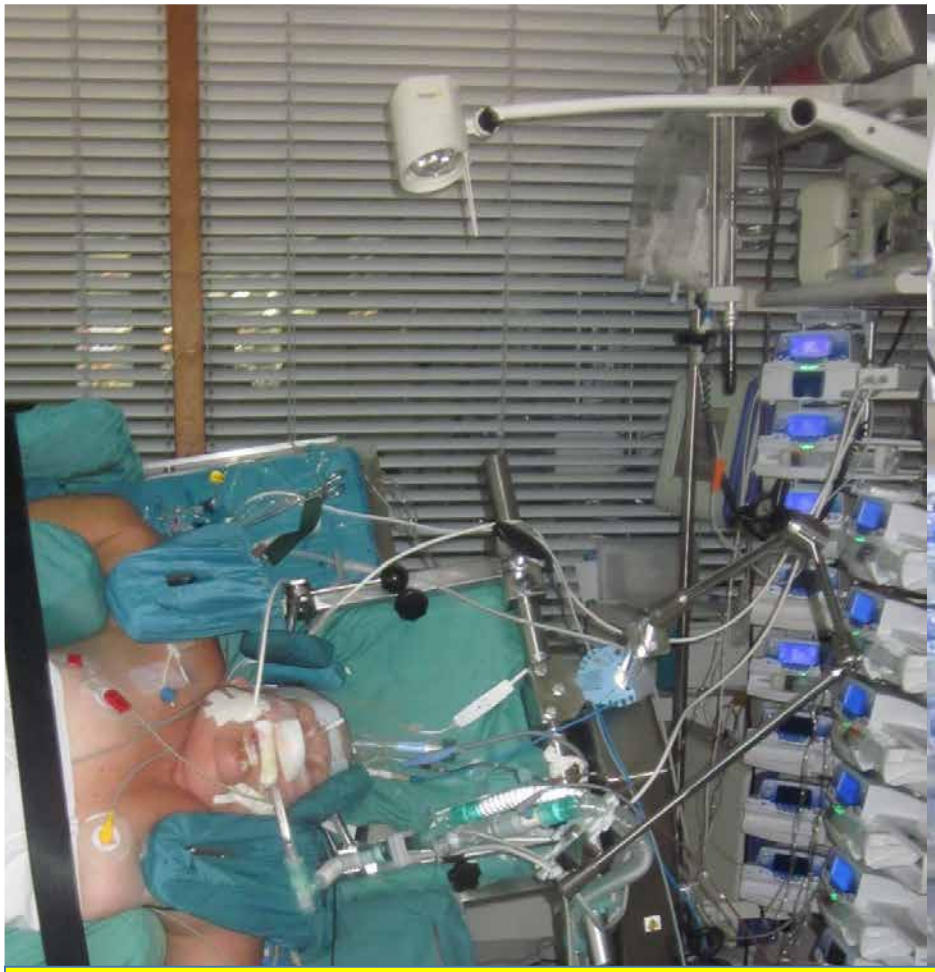


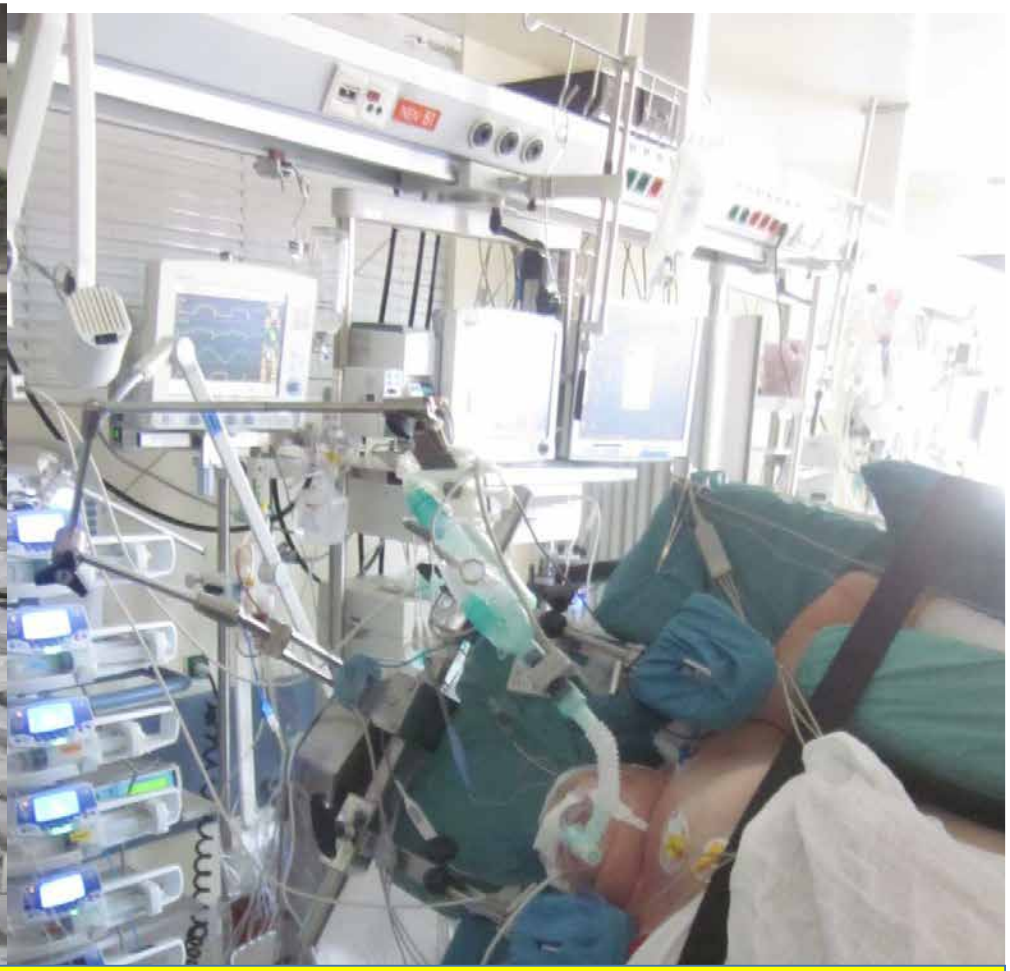
Notfallsmedizin und Neuro-Intensivmedizin/Intensivneurologie ist für die Neurologie eine Herausforderung





Notfallsmedizin und Neuro-Intensivmedizin/Intensivneurologie ist Voraussetzung, die Chance zu wahren





.... und die Chance ist realistisch ....

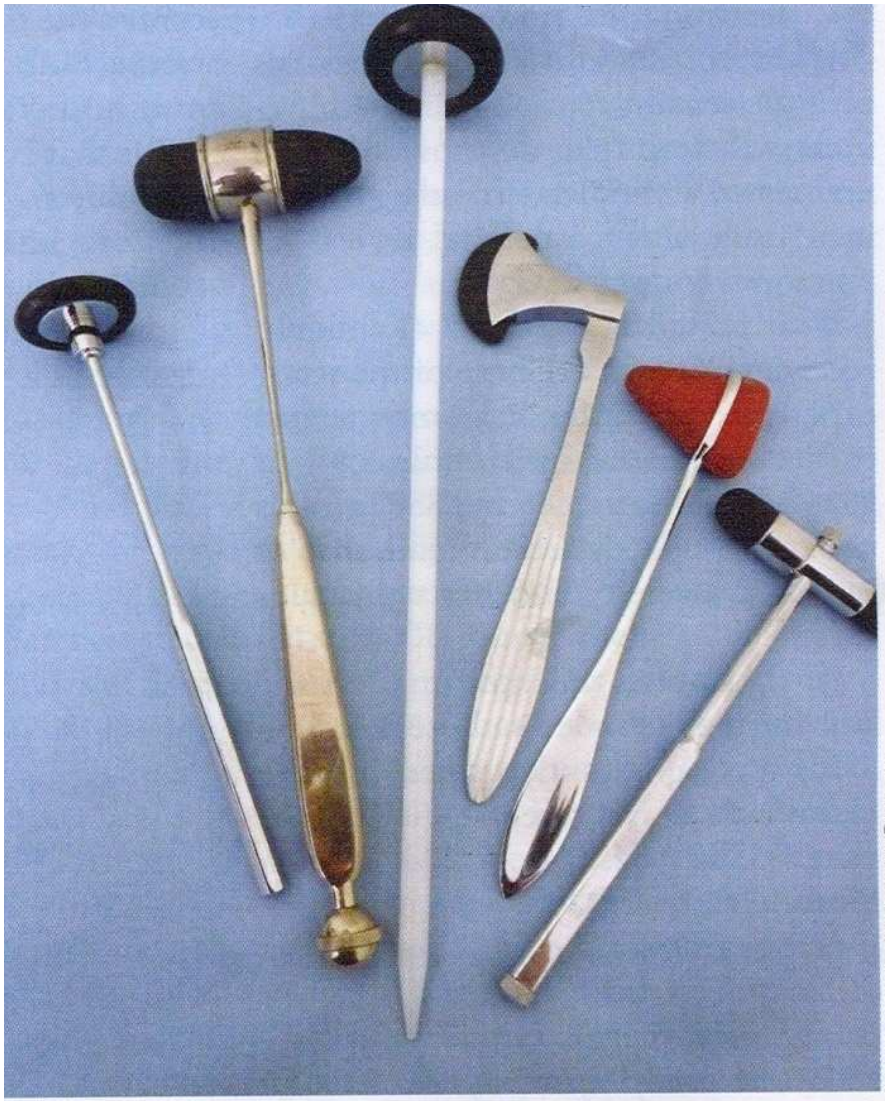
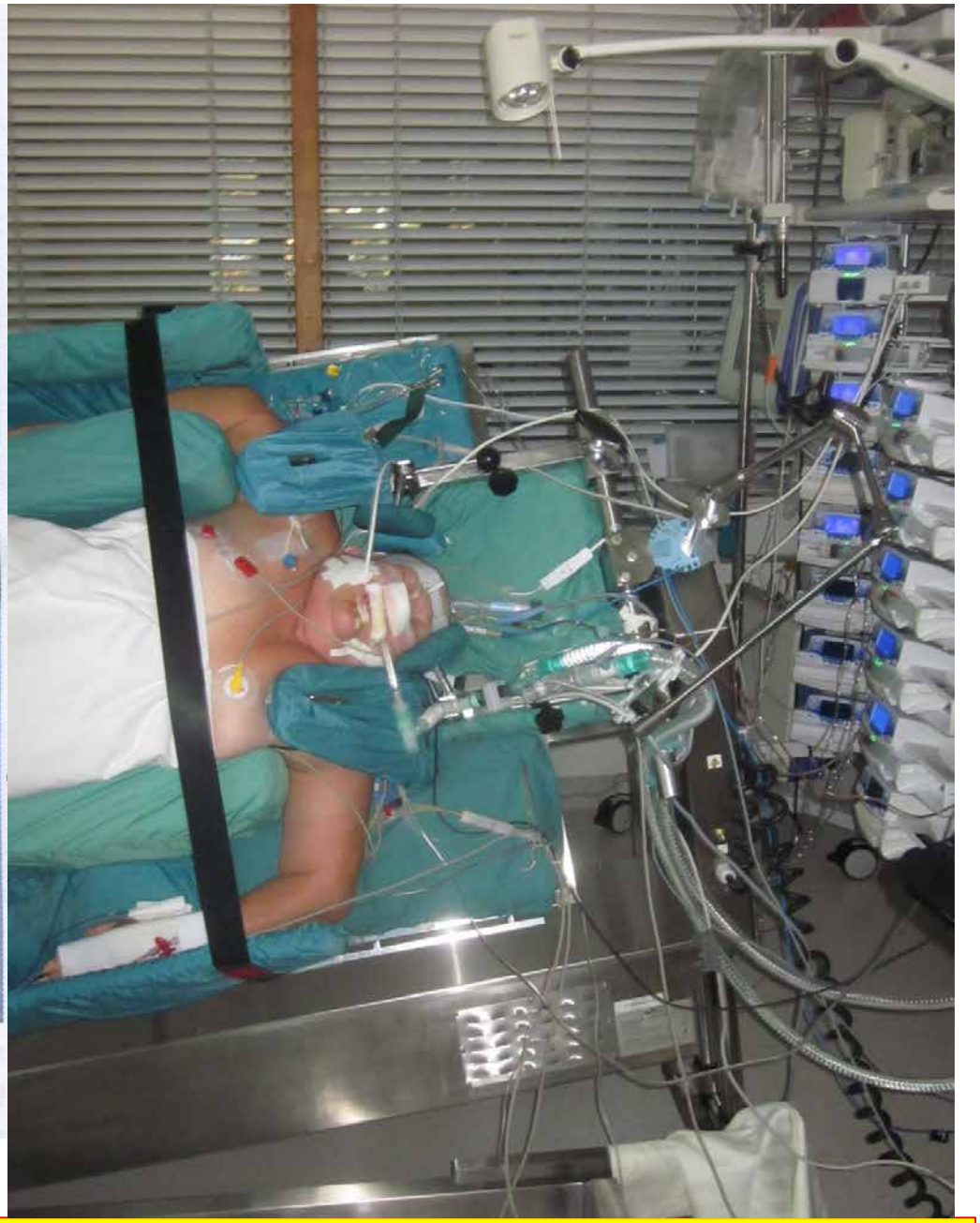
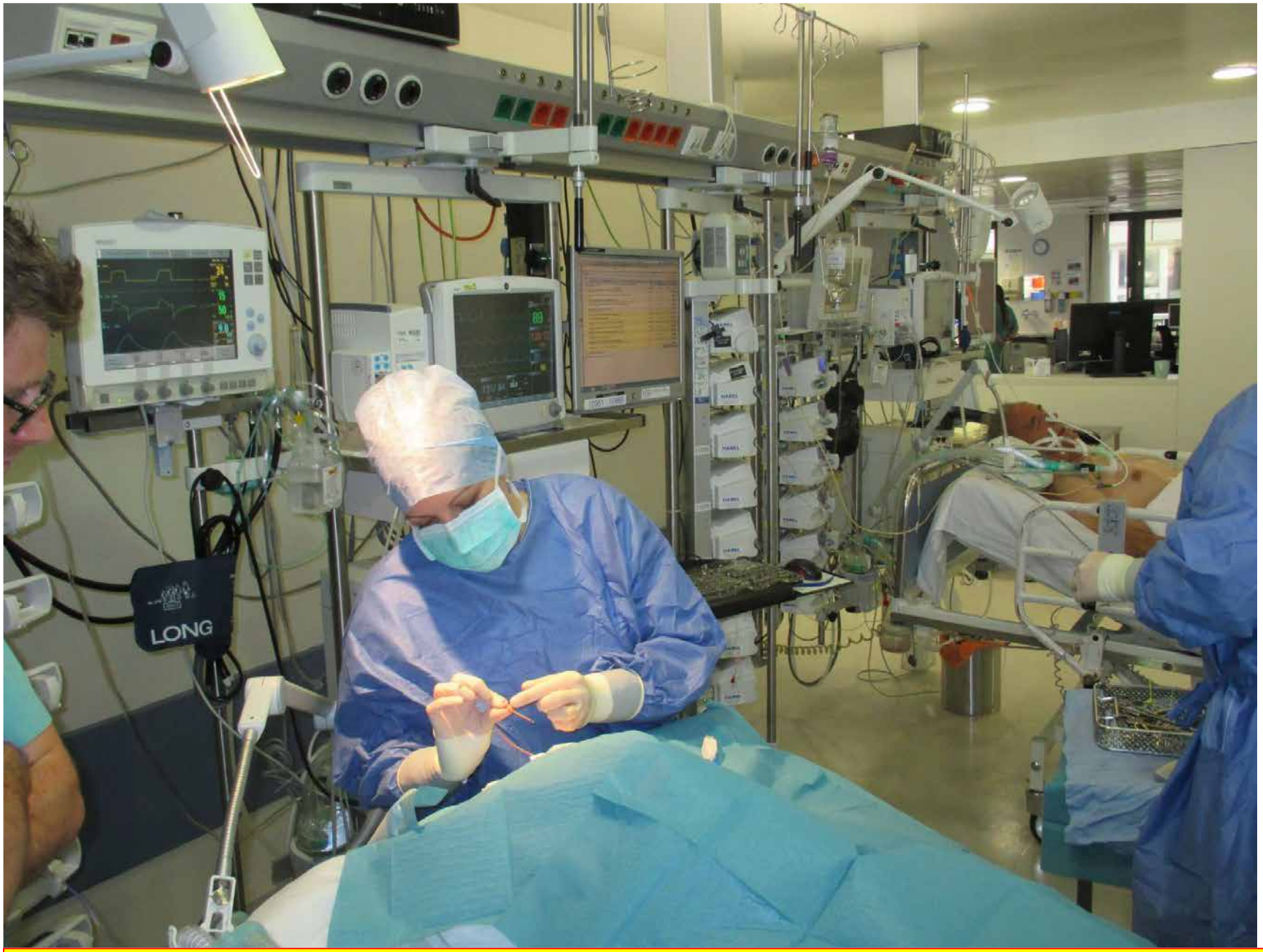


Figure 2. Hammers are, from left, the Babinski, Hurst, Queen Square (modern), Berliner, Taylor, and Buck.

Courtesy: Catherine Storey



Besten Dank für Ihre Aufmerksamkeit



und allen meinen MitarbeiterInnen

und allen meinen MitarbeiterInnen

Bettina Pfausler: **ZNS Infektionen**, **Prognose und Komplikationen in Intensivneurologie, Hirntod, Ethik** in der Intensivneurologie, Ernährung, Nodding Syndrome

Ronny Beer: SHT, zerebrale Hypoxie, Biomarker, **AB PK/PD,** SyNAPSE, INTERACT 2,3, CINCH, NOSTRA, **Centre TBI**, **Ernährung - Metabolismus**

Raimund Helbok: **Multimodales Monitoring, Mikrodialyse, COSBID,** NOSTRA, Neurorobotics, **nichtinvasive ICP Messung, Centre TBI,** Ernährung

Gregor Broessner: **Targeted Temp.Management,** prophylaktische **Normothermie,** CINCH, IcTUS 2

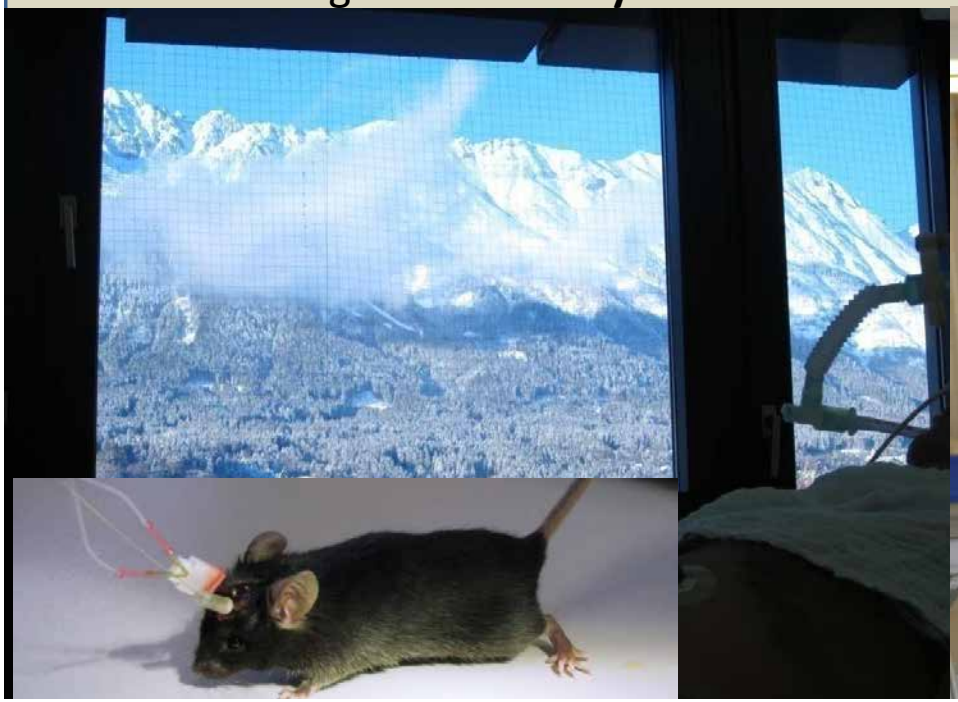
Peter Lackner: **Translationale** Intensivneurologie: murine zerebrale Malaria, Sepsisenzephalopathie, -Otopathie, Mikrodialyse in muriner Malaria, Sepsis und SAB, murine SAB

Marlene Fischer: **Neurovaskuläres Kompartment** und Hirn-Temperatur, IcTUS 2

Alois Schiefecker: **Multimodales Neuro-Monitoring,** COSBID, **nichtinvasive ICP Messung;** TCD

Mario Kofler: **Multimodales Neuro-Monitoring,** COSBID, nichtinvasive ICP Messung

Susanne Böttinger: **Mikrodialyse in** muriner Malaria, Sepsis und SAB, **murine SAB**



SHT – Globales Forschungsinteresse