Neurotelemetry: Clinical Application for Therapeutic Hypothermia Treatment in Cardiac Arrest Patients

Ryan R. Lau, MS,

R.EEG/EP T., CNIM, CLTM

Supervisor, Neurophysiology

Sara Brown, BSBME

Research Liaison, Neurophysiology

IU Health Neuroscience Center

Methodist Hospital
Indiana University Health
Indianapolis, IN

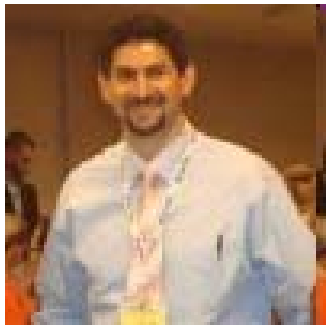
About Me

- 10 years experience in Neurodiagnostics

  -EEG, LTME, Neurotelemetry

  -EP

  -IONM (Neuro, Ortho, CV, & Periph)



- AAS in Neurodiagnostics
- BA in Exercise Science
- MS in Psychology
- Over 60 slides and hope to be done in 60 mins! ☺

What You Will Learn Today

- What is Neurotelemetry (NT)?
- Benefits of NT vs. Routine EEG
- Uses for NT
- Utility of NT for Therapeutic Hypothermia
- Therapeutic Hypothermia and Theory/Mechanisms of Neuroprotection
- Cardiac Arrest and Return of Spontaneous Circulation
- Case Studies
- Our Protocol for NT during Therapeutic Hypothermia

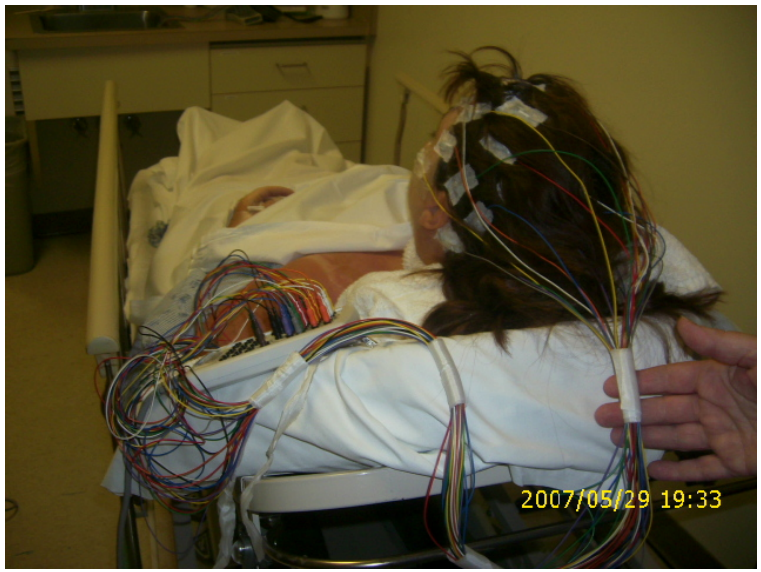
What are NT and LTM?

- Continuous EEG Monitoring
  - With or without Video
  - Recording is done continuously 24 hours a day
  - Can be 1, 2, 3, 4…, 10… days

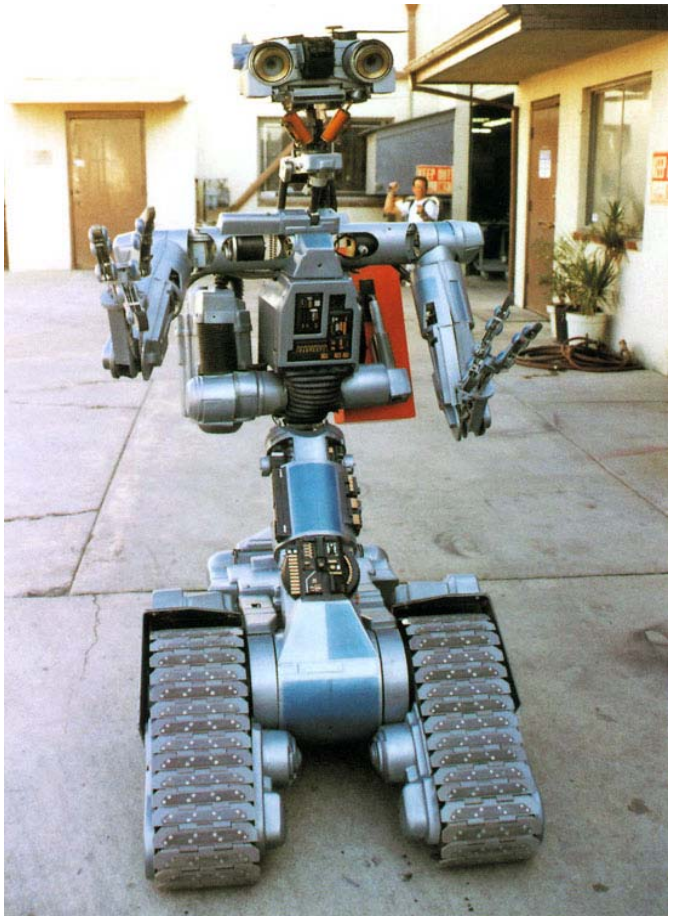
    unlimited in theory…
  - Soooo, it is not a routine 20-30 minute EEG

Neurotelemetry vs. Long Term Monitoring

- What's the difference?
- Different names sometimes mean the same thing
  - cEEG
  - vEEG
  - cVEEG
  - Long Term Monitoring (LTM)
  - Neurotelemetry (NT)
  - CLTM
  - LTME
  - Video Unit
  - EMU, NMU
  - There are certainly more out there!



Nicolet ICU/LTM Monitor a.k.a : Johnny 5



findmearobot.com/.../Johnny%205.html

Lets Separate them even Further

- Different centers have differing names for their long term EEG units
- Can be specific as well
- We (Methodist Hospital) have coined the Larry Hirsch term

“Neurotelemetry!”

for Real-Time Long-Term Video EEG in the ICU and other areas of the hospital by R.EEG Ts or CLTMs

Lets get specific now: Neurotelemetry

- It was put in place specifically for our critically ill patients (ICU)
- What makes these patient populations different from our typical IP/OP's?
- Are they higher risk patients?

Why Monitor the Brain Continuously?

- Seizures
- Status
- Sedation
- Subclinical Seizures or no clinical signs
- ALOC or mental status change
- Burst-Suppression Monitoring
- Cerebral Metabolism (ischemic events)
- Detection of reversible abnormalities
- Ability to sometimes tell the effectiveness of interventions or no intervention
- Characterize unknown movements or behavior changes

Vespa, Nenov, Nuwer, J. Clin Neurophys 1999

Neurotelemetry

What is the peer reviewed literature saying or suggesting???

NCSE in Comatose Patients

- (n = 610 patients)
- 33% (40/110) of comatose children were in NCSE
- 22% (108/491) of comatose adults were in NCSE

Hosain SA, American Epilepsy Society Meeting 2002

NCSE in Comatose Patients

- (n = 236 patients)
- 8% (19/236) of unexplained comatose patients were in NCSE

Towne, et. Al (2000)

Neurotelemetry

What is the peer reviewed literature saying or suggesting???

Seizures detected by Neurotelemetry in the ICU

- (n = 570)
- 110/570 (19%)
- 101/110 (92%) Sz's were non-convulsive
- Needed at least 72 Hrs of NT monitoring to r/o NCSE in comatose patients
- Video also assisted /c interpreting the data

Based on Claasen J. et al. Neurology 2004; 62: 1743-1748

Neurotelemetry

What is the peer reviewed literature saying or suggesting???

NCSE in Intracerebral Hemorrhage

- 16/63 (25%) had NCSE on NT
- NT detected four times as many Sz's as occurred clinically
- NCSE was associated with progressive cerebral edema
- Early detection and control of Sz's may improve clinical outcome by reducing edema by stopping the Sz's

Vespa PM., et al., Neurology 2003; 60: 1441-1446

Neurotelemetry

Other Physiological Factors of Importance: What do Sz's do?
NCSE in TBI: Effect on ICP

	Mean ICP (mmHg)	% time ICP >20mmHg
Seizure (ictal) (n=10)	17.6 +/-6.5	32% +/-28
No Seizure (Inter-ictal) (n=10)	12.2 +/-4.2	6% +/-8.4
	p<.04	p<.02

Vespa, Crit Care Med, 2007

Neurotelemetry

Other Physiological Factors of Importance: What do Sz's do?
NCSE in TBI: Effect on ICP and Cerbral Metabolism

	ICP (mm Hg)	Lactate/Pyruvate Ratio (LPR) (measure of neuronal stress)	Glutamate (increased amounts can propagate Sz's)
No Seizure (inter-ictal mean)	9.6 +/-5	23.8	2.6
Seizure (ictal mean)	22.4 +/-7	49.4	13.1
	p<.002	p<.02	p<.001

Vespa, Crit Care Med, 2007

NCSE and Growing Evidence that NCSE and Sz's are Harmful

- Sz's can increase glutamate to neurotoxic levels
- NCSE and Periodic Discharges have been independent predictors of declining outcomes in multiple Pt populations
- Prolonged NCSE can lead to permanent neurological injury (Vespa, 2007)
- NCSE has been independently related to death in cardiac arrest victims (Koenig, 2006)
- NT can detect NCSE with real-time intervention to eliminate or lessen Sz's to improve Pt outcomes

What is Therapeutic Hypothermia?

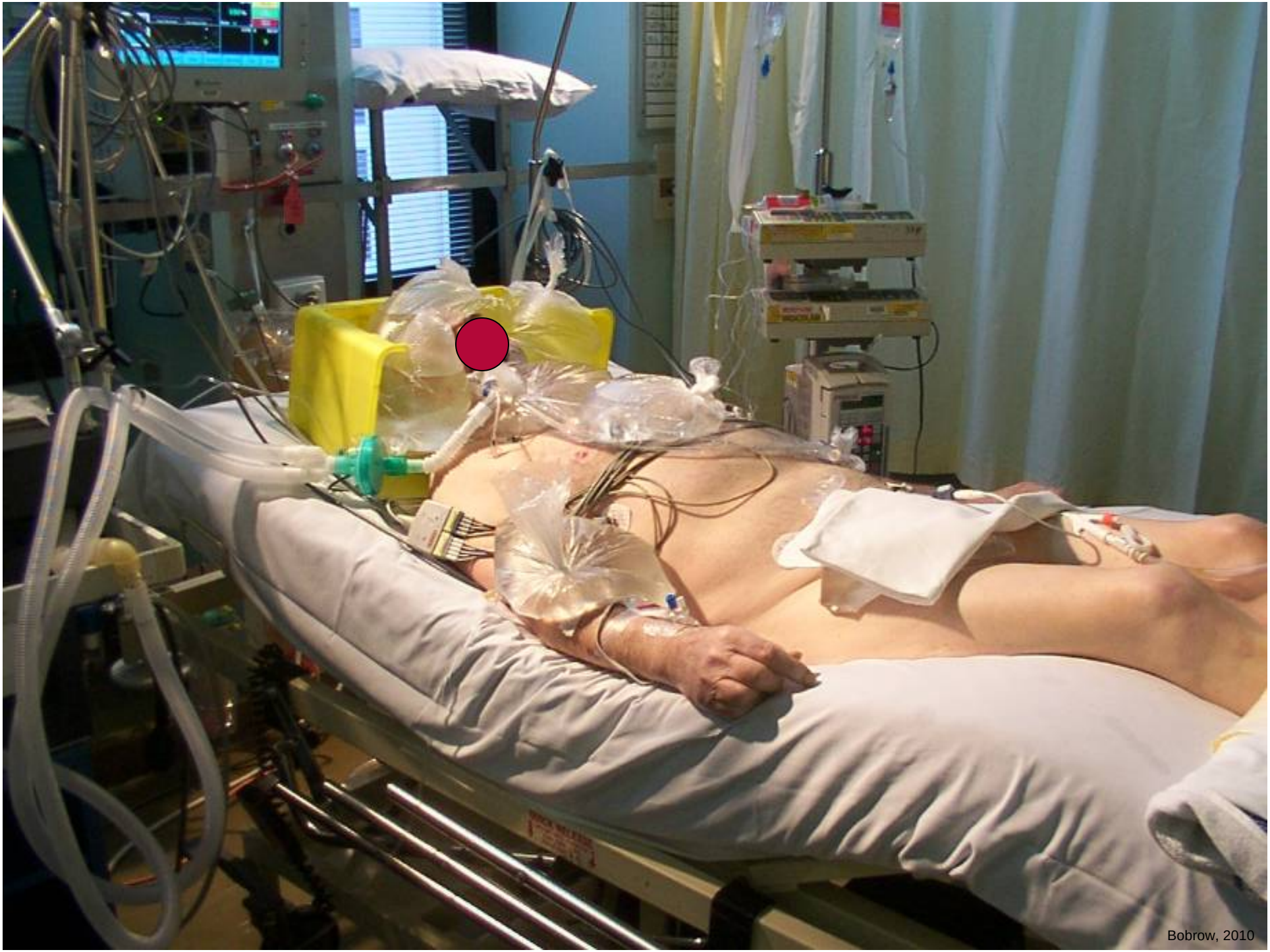
- Controlled cooling of the body down to 32-34 degrees C for 12-24 hrs with a controlled re-warming period of 12-24 hrs
- Can be done via: ice packs to head and torso, cold air mattress or blanket, cold IV saline, and cooling gel pads /c water tubing


Cramer
Flex-i-Cold
all out
all the time

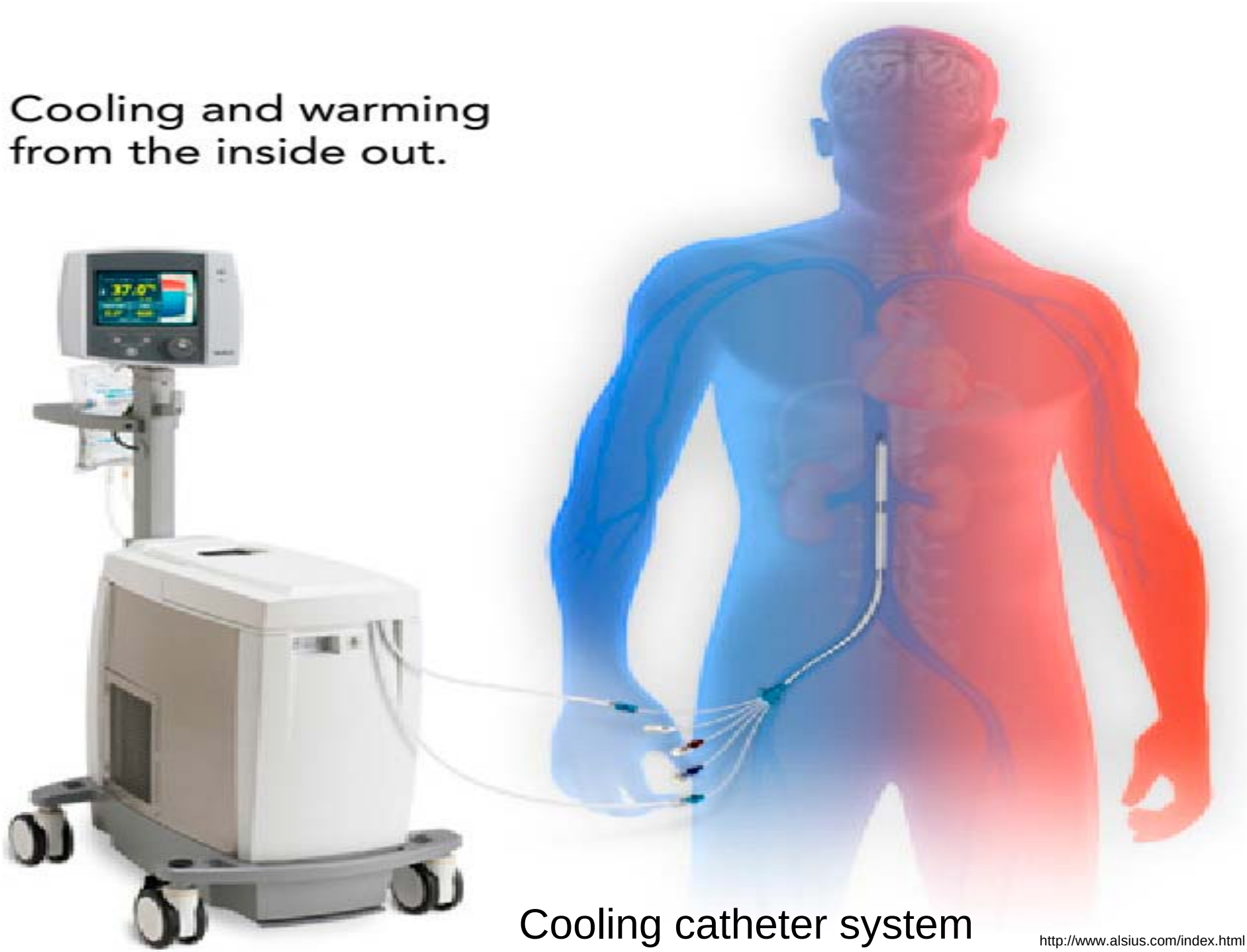

COLD-HOT PACK
REUSABLE
FOR COLD USE:
FOR WARM USE:
CAUTION:
Mueller


RAPID
RELIEF

Bobrow, 2010


Bobrow, 2010


Bobrow, 2010



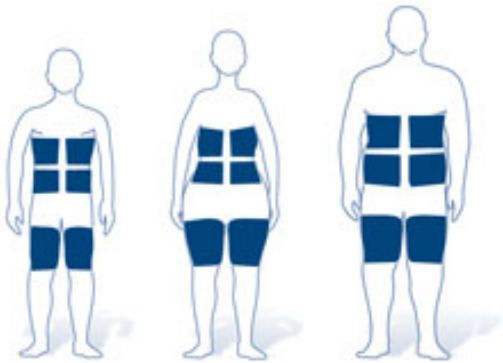
Cooling catheter system

http://www.alsius.com/index.html

http://www.life-recovery.com/Life_Recovery_Systems/Home.html

Used in our Institution and considered the current "Gold Standard"

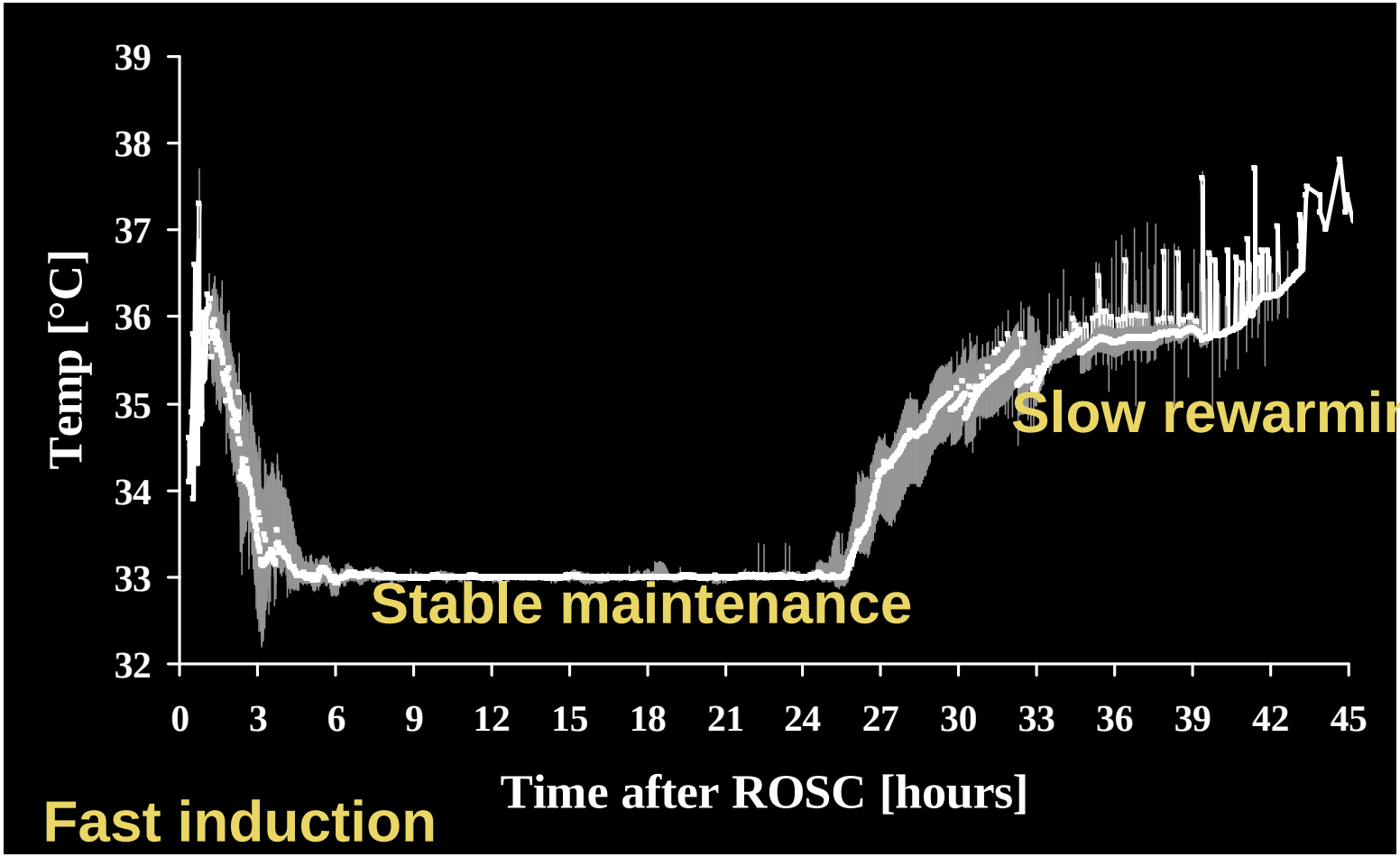
Arctic Sun Energy Transfer Pads



http://www.medivance.com/html/products_arcticgel.htm

Bobrow, 2010

Why is TH or Cooling Important?



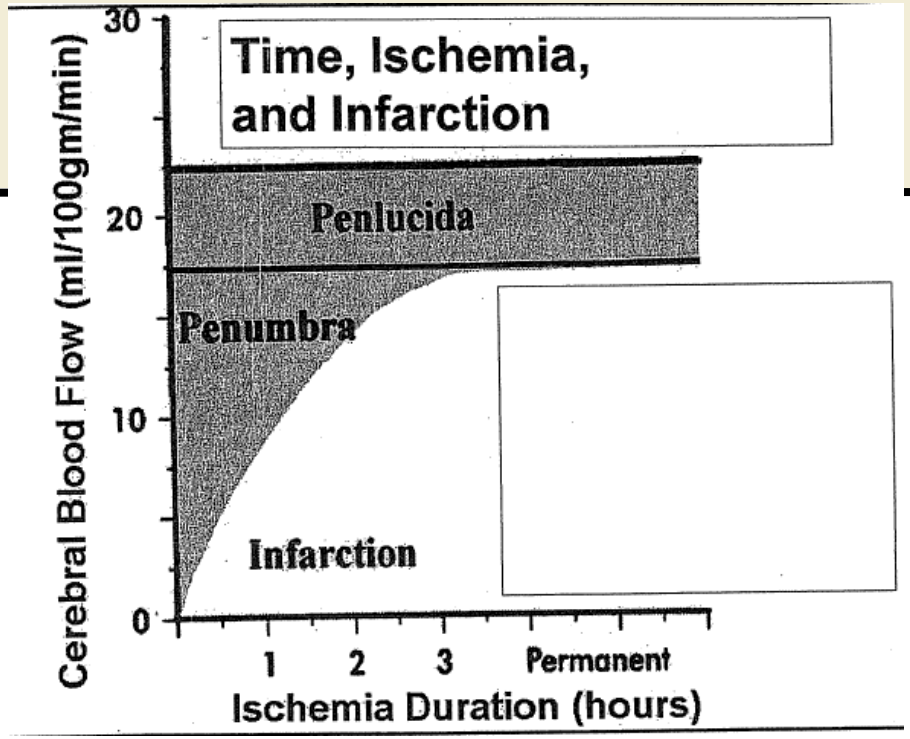
Bobrow, 2010

NEUROPROTECTION

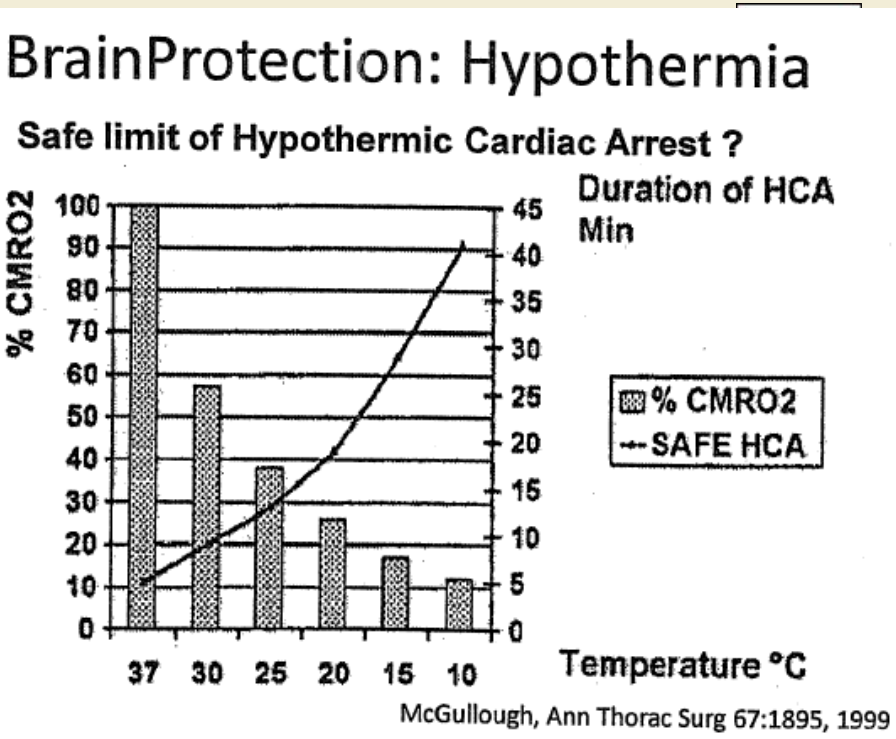
- Goal is to cool vital organs (Brain) to a point where metabolism is slower and requires less oxygen and reduction of risk by ischemic injury
- Decrease in cerebral metabolism
  - 6% reduction for every 1^0C drop in temperature
  - $32\text{-}34^0C$ = 18% – 30% decrease in cerebral metabolism
- Decreases speed of neuronal transmission
- Suppression of reperfusion injury
  - Decreased free radical production
  - Reduction in excitatory neurotransmitters
  - Suppression of Ca^{+2} mediated cell death
  - Reduce apoptosis (programmed cell death due to biochemical negative fluctuations)
  - This specific function can be welcomed (Tadpole – Frog) however not in Neuronal Death
  - Anti-inflammatory effects

    Nolan et al. (2003) Circulation

    Froehler and Geocadin (2007) J of Neuro Sci



Sloan, ASNM Meeting 2009

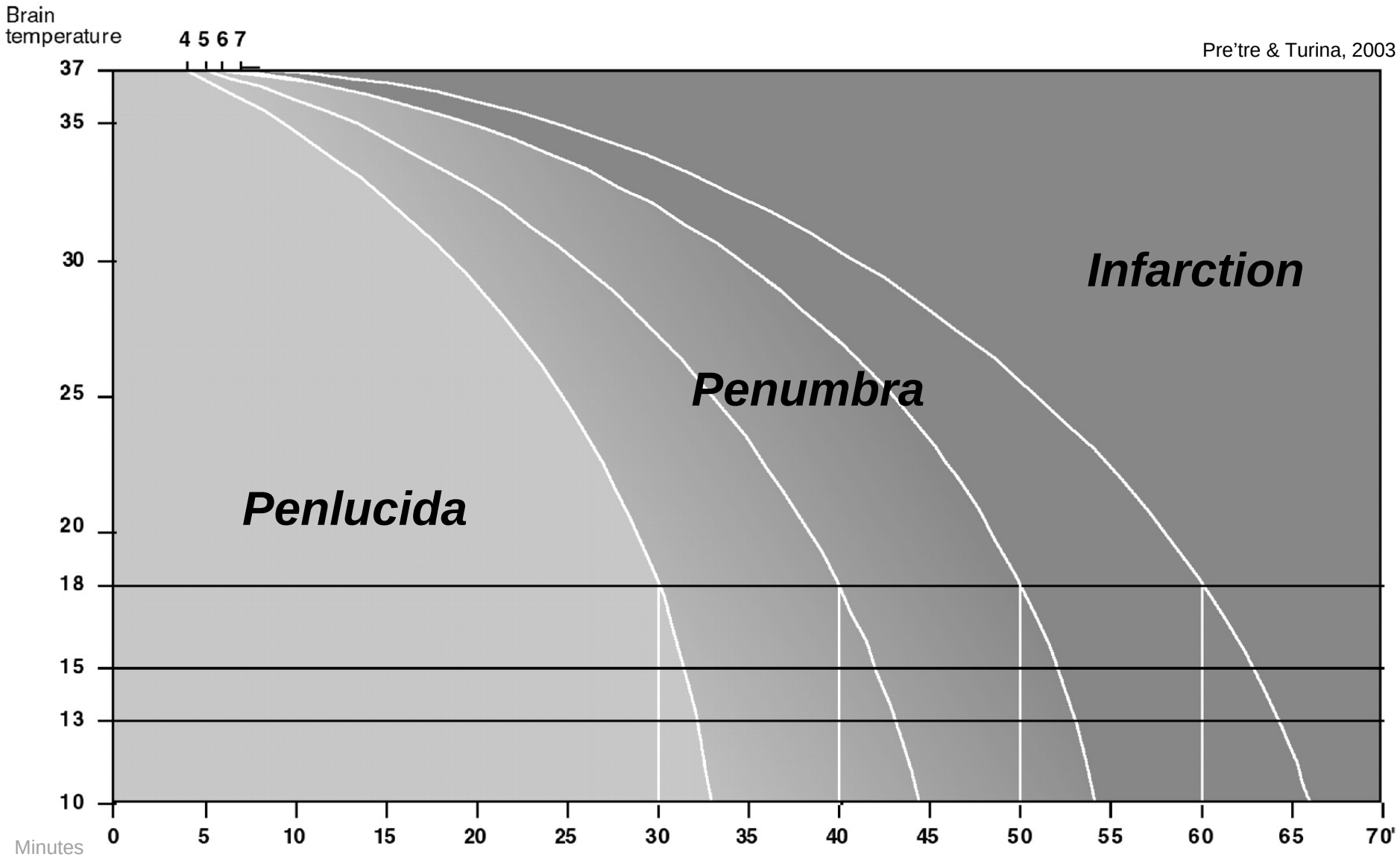


CMRO2 – Cerebral Metabolic Rate of Oxygen

- Human Brain requires 5.5 mg of glucose per 100 grams of neuronal tissue per minute at 37 degrees C and unfortunately has no glucose reserve
- 32-34 degrees C, CMRO2 drops approx. 40% as well as glucose needs
- Penlucida – point at which CBF can no longer support neuronal tissue enough oxygen and glucose to function at normal levels, however infarction does not occur
- Penumbra – point at which cell death begins to occur from too low of CBF correlating to not enough oxygen or glucose to maintain cell viability or Infarction

Bruno, 2004

- Circulatory arrest in relation to temperature and duration of cerebral ischemia
- The light color depicts the periods of safe circulatory arrest
- The dark color depicts the periods of obligatory harmful circulatory arrest
- The transitional area depicts the periods where the risk and extent of brain damage are dependent on the conduct of surgery and pharmacological intervention
- The light gray area is compatible with reversible deficits, while the dark gray area is associated with irreversible injuries.

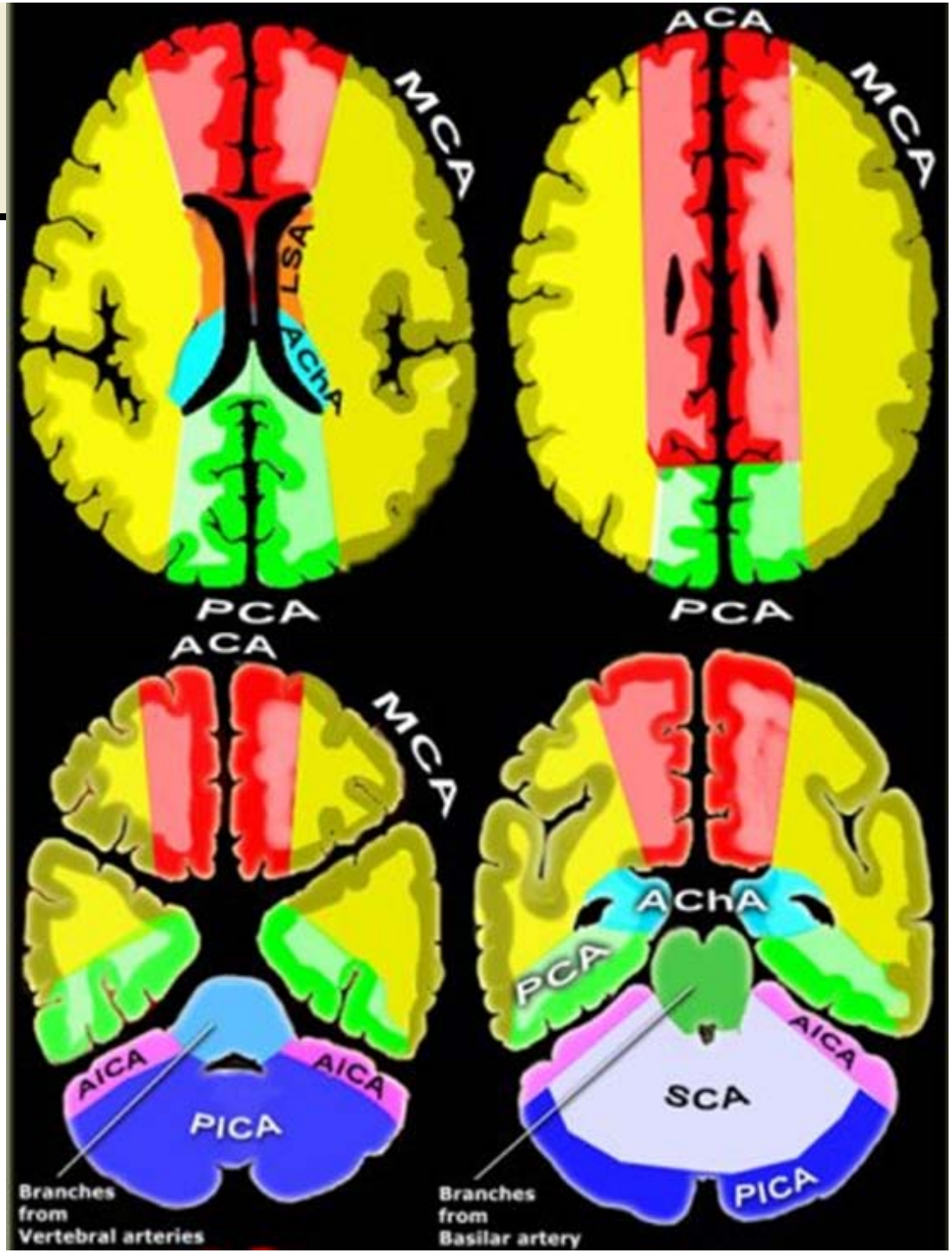


We Favor Mild TH, Risks of Deeper TH in Post Cardiac Arrest Pts

- Temp below 32^0C can introduce added complications such as:
- Arrhythmias (do not want to add one heart problem on top of another!)
- Infection
- Coagulopathy or inability to form blood clots
- Risk of increased focal cerebral deficits due to decreased oxygenation to watershed areas aka “watershed lesions.”

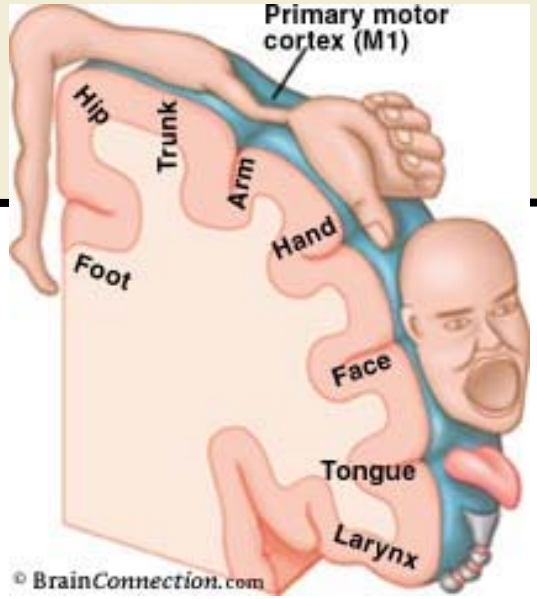
Cerebral Arterial Territories

- MCA – Middle Cerebral Artery
- ACA – Anterior Cerebral Artery
- PCA - Posterior Cerebral Artery
- SCA – Superior Cerebellar Artery
- AICA – Anterior Inferior Cerebellar Artery
- PICA – Posterior Inferior Cerebellar Artery
- AchA – Anterior Choroideal Artery
- LSA – Lenticulo-Striate Arteries

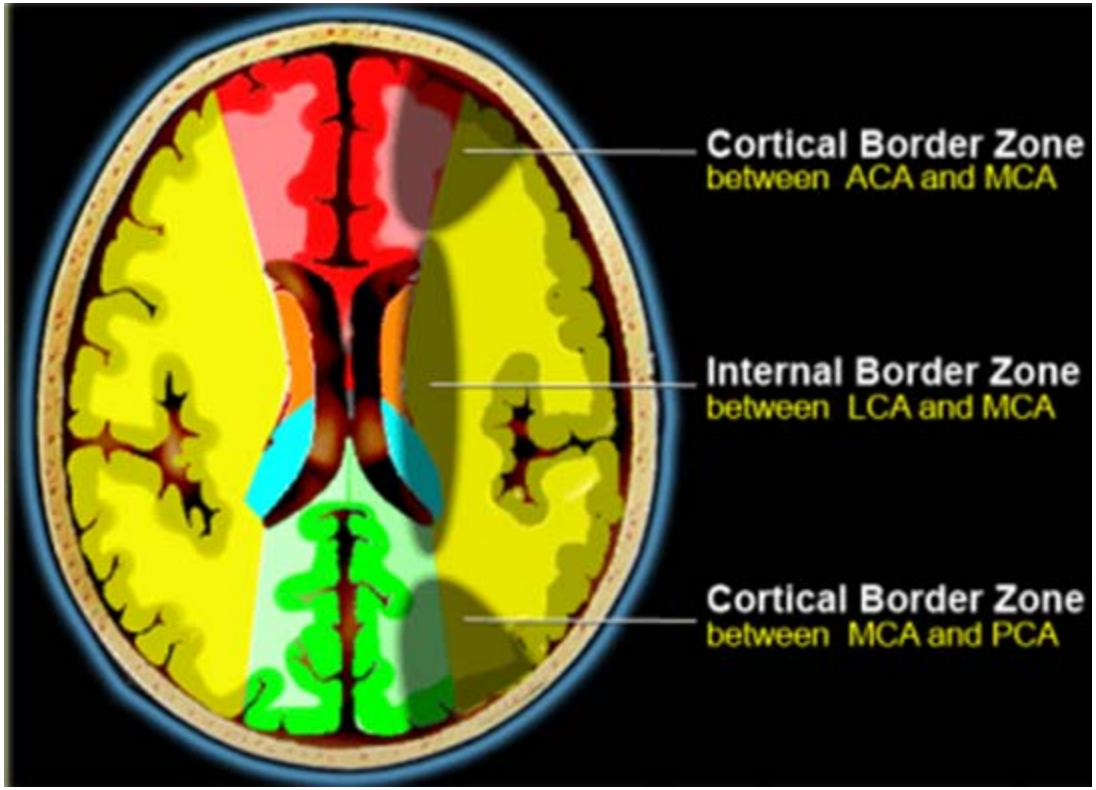


http://www.radiologyassistant.nl/en/484b8328cb6b2

Watershed Areas



- Border zones between major arterial territories
- Lesions/Infarcts can occur due to hypoperfusion
- What functional areas are at risk?



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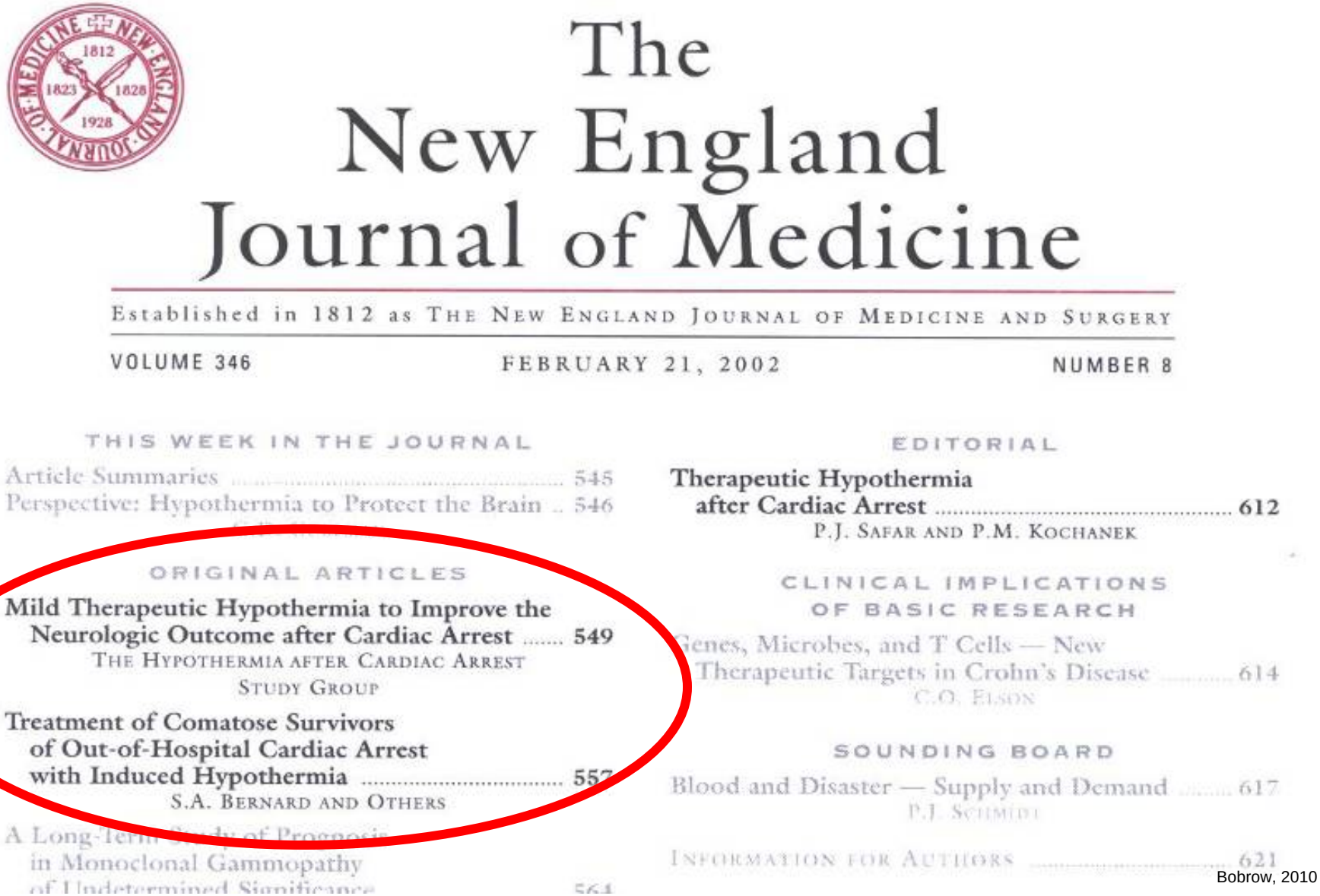
Evidence of The Theory



The New England Journal of Medicine

Established in 1812 as The New England Journal of Medicine and Surgery

VOLUME 346 FEBRUARY 21, 2002 NUMBER 8

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Bobrow, 2010

Mild Therapeutic Hypothermia to Improve the Neurologic Outcome After Cardiac Arrest (**HACA**):

Vienna, Austria

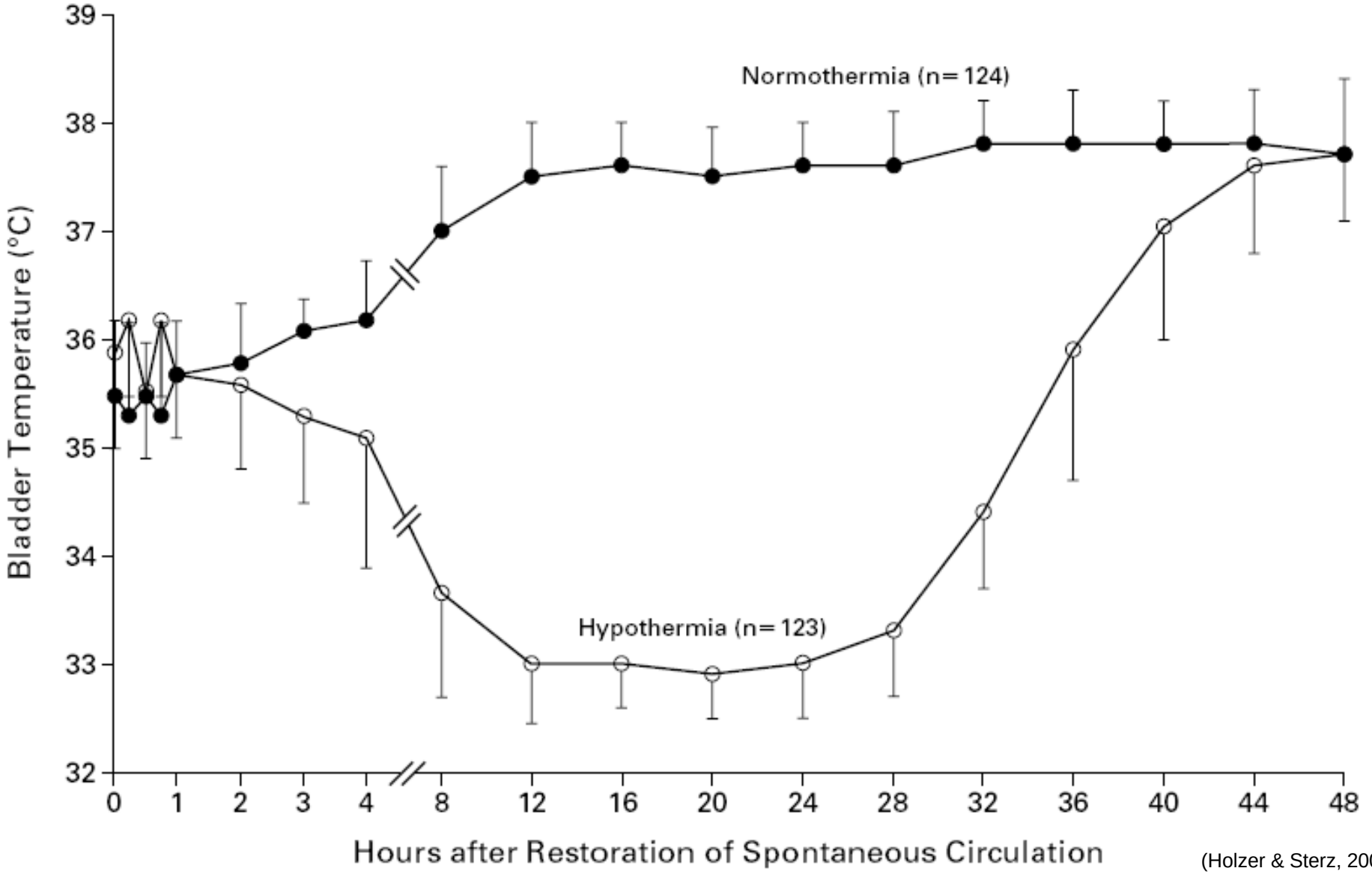
- Patients with witnessed cardiac arrest from VF or pulseless VT, 18-75 years of age, estimated 5-15 minutes to attempted resuscitation, and less than 60 minutes from collapse to restoration of spontaneous circulation
- 275 patients of 3,551 cardiac arrests studied
- 137 patients received hypothermia

(Holzer & Sterz, 2002)

TH and Cardiac Arrest

- Normothermia pts had target temperature of 37° C
- Pts assigned to hypothermia had target temp of 32-34° C by use of an air cooled tent and mattress
- hypothermia was maintained for 24 hrs followed by passive rewarming over 8 hrs

Bladder Temperature



(Holzer & Sterz, 2002)

TH and Cardiac Arrest

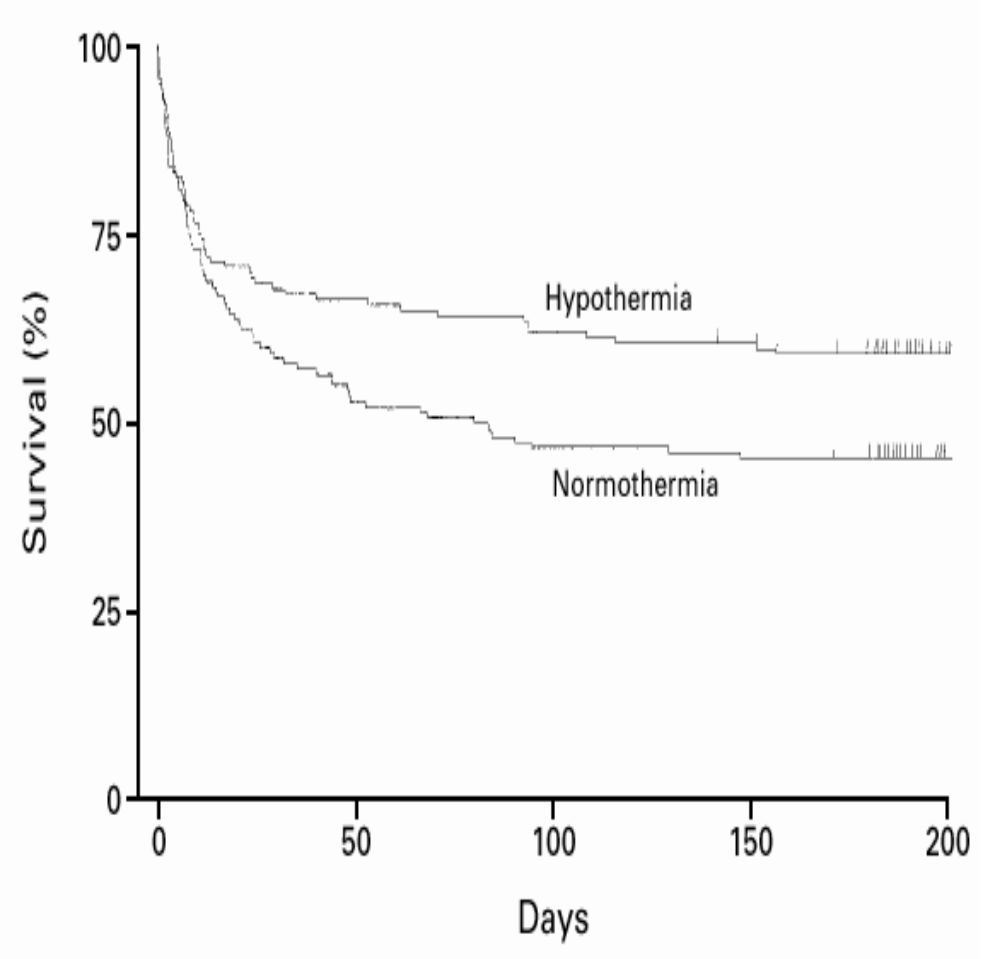
Outcomes (at 6 mo):

- 55% of the TH group had a *"favorable outcome"* compared to 39% in the NTh group, p = 0.009
- mortality was 41% in the TH group compared to 55% in the NTh group,

  p= 0.02

Favorable Outcome =

"Good Recovery or Moderate Disability"



(Holzer & Sterz, 2002)

Complications Which Were All NS

	NTh	Hypothermia
• Bleeding	19%	26%
• Pneumonia	29%	37%
• Sepsis	7%	13%
• Pulmonary Edema	4%	7%
• Renal Failure / HD	10% / 4%	10% / 4%
• Seizure	8%	7%
• Serious Arrhythmia	32%	36%
• Pancreatitis	1%	1%

(Holzer & Sterz, 2002)

Tx of Comatose Survivors Out of Hospital Cardiac Arrest /c TH:

Melbourne, Australia

- NTh pts had target temperature of 37º C
- HT pts had target temp of 33ºC by extensive application of ice packs
- 43 pts were randomized to HT, 34 to NTh
- Hypothermia was maintained for 12 hours then were actively rewarmed at 18 hours for the next 6 hours

Bernard, et al., 2002

Hypothermia in Cardiac Arrest

- Outcomes:
  - 49% of the HT group had a *"good outcome"* compared with 26% in the NTh group, ($p<0.05$)
  - mortality was 51% in the HT group and 68% in the NTh group, (p=NS)
- Good Outcome Defined =

  "Discharged to home or rehab facility."

Conclusions from Studies

"In patients who have been successfully resuscitated after cardiac arrest due to ventricular fibrillation, therapeutic mild hypothermia increased the rate of a favorable neurologic outcome and reduced mortality."

Holzer & Sterz, 2002

"…treatment with moderate hypothermia appears to improve outcomes in patients with coma after resuscitation from out-of-hospital cardiac arrest."

Bernard et al., 2002

Modified from Bobrow, 2010

Recommendations

- Unconscious adult patients with return of spontaneous circulation (ROSC) after out-of hospital cardiac arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12 to 24 hours when the initial rhythm was ventricular fibrillation. *Class IIa*
- Similar therapy may be beneficial for patients with non-VF arrest out of hospital or for in-hospital arrest. *Class IIb*

American Heart Association 2005 Guidelines

Further Needs from AHA

- Sz's or myoclonus occur in 5-15% of adult ROSC Pt's and 10-40% of those remain comatose
- Sz's increase metabolism up to 3-fold!
- Can be viewed as a Double Whammy… in these Pt's that needs to cease when identified
- "Prospective studies are needed to determine the benefit of continuous EEG monitoring."

Neumar et al., 2008 ILCOR AHA Circulation Journal

Int'l Liaison Committee on Resuscitation

Use of NT in Therapeutic Hypothermia

- Routine/Intermittent (30 min. recordings) EEG's have a high probability of missing subclinical Sz's
- 1440 minutes in a day
- Routine EEG is 30 minutes long or 2% of the day, if 2 or 3 EEG's are run, this only increases to 6%
- The use of Neurotelemetry to detect seizures during this time is specifically recommended (100% of 1440 min's of EEG is recorded /c Video)
  - SE has been independently related to death in cardiac arrest survivors (Rosetti et al., 2007).
- For patients treated with therapeutic hypothermia, neuromuscular blockade (NMB) must be used frequently to prevent shivering
- Shivering is a normal physiological function and will occur with less than 1°C drop
- NMB can mask the clinical Sz's, another reason why NT is IMPORTANT in this patient population

What Else have We Found?
Anecdotally:

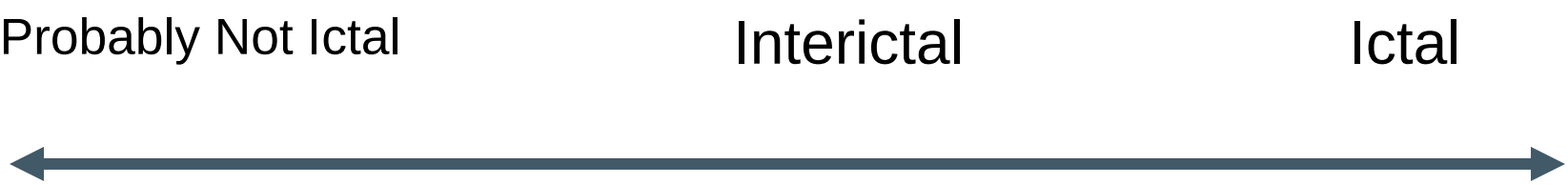
- After the rewarming period, some Pt's do not wake up due to over use of sedation and have increased length of stay
- Sedation is given because we do not want the Pt to be aware of the TH (very cold!)
- Feelings of worry/empathy can lead to over-sedated Pts
- If Pt is in a suppression or burst suppression pattern, does regular sedation need to be given? Can we unequivocally say that these patterns are unconscious?
- After discussion with our Medical Director who also reads these studies, he felt it was safe to say that these are unconscious patterns and there would not be a need to continually sedate with them
- We can also see waking patterns that may deem sedation is needed

What Else have We Found? Anecdotally:

- Before shivering clinically presents
- What do you think we see on EEG?
- Increased EMG artifact
- We can also be clinically useful with alerting nursing that increased NMB may be needed (microshivering)

Neurotelemetry

The Rich Admixture of EEG Activity



FIRDA

Monomorphic Delta

PLEDS

GPEDS

IEDS

Triphasics

TIRDA

GIRDA

SIRPIDS

Rhythmic Spikes

PDA

BiPLEDS

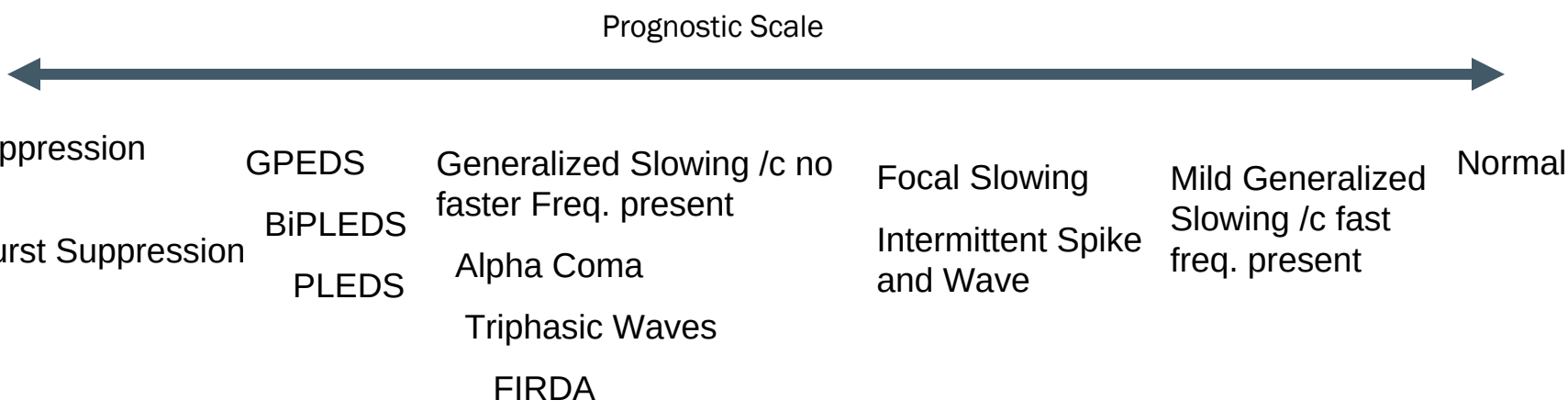
OIRDA

Intermittent Spikes

Burst-Suppression

Modified from S. LaRoche PPT

Organizing the Brain Wave Continuum



- Brain patterns can transition up or down the scale and seizure patterns can arise from any pattern on the Prognostic Continuum

- Significant doses of the following drugs can artificially induce suppression or burst suppression and mask any of the patterns. Propofol; pentobarbital; etc.

Organizing the Brain Wave Continuum

Seizure Frequency

Status Epilepticus (Continuous seizures)	Frequent Seizures Convulsive and Non-convulsive ~1 or more every 2 hours	Intermittent Seizures ~6 per day	Sporadic Seizures < 6 per day

Modified from presentation of L. Hirsch, MD

NT Protocol for Hypothermia Pts

- Cooling
  - Initiate with ER as soon as patient is on the floor
  - From start of EEG to start of Day 1 of normothermia, call nurse every 6 hours
  - Cooling takes 2-4 hrs to 33 degree C
  - Maintain at 24 hrs
  - Re-warmed at 24 hrs
  - Once at 36 degrees C, they are considered Normothermic

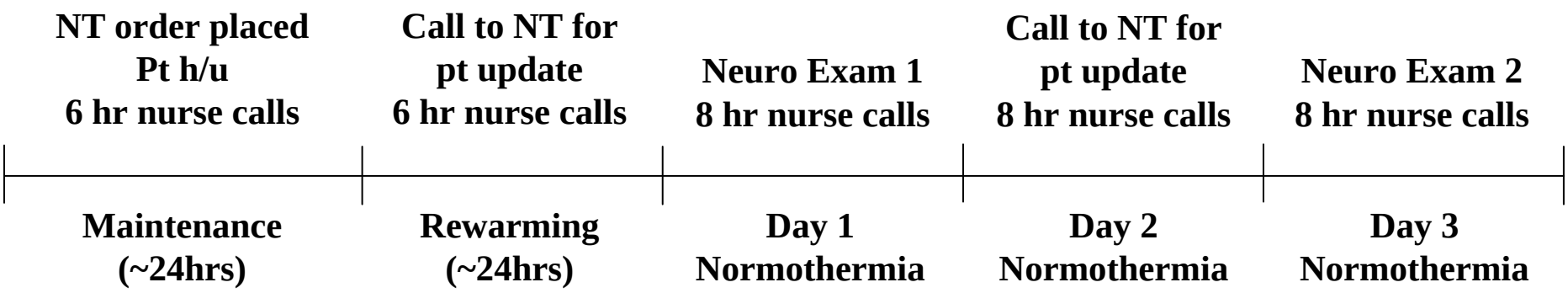
NT Protocol

- Maintenance
  - Notify the nurse that no additional sedation is needed if the patient is in burst suppression or suppression
  - Tech will check temp and MAP levels and then call to verify drugs and dosages
  - 18-24 hrs into maintenance, the tech will ask what time rewarming will begin

NT Protocol

- Rewarming
  - Continue nurse calls every 6 hours
  - At 12 hours, tech will begin checking temp and note when pt returns to normothermia
  - Tech will populate dates/times for normothermia days 1-3 in Patient Event Log
- Normothermia Days 1-3
  - Return to normal nurse calls every 8 hours with status reports

Patient Timeline



Neuro Exams

- Performed by a neurologist blinded to the Neurotelemetry data on Day 1 and 3 of Normothermia
- When performed, they give their subjective opinion of “Liklihood of Survival” by only knowing the Neuro Exam results
- GCS and FOUR Score exams are used for this study

Neuro Exam Flow Sheet

Date: _____ Time: _____

Patient Name: _____ MRN: _____

	Day 1 (Post-hypothermia) Circle choice	Day 3 (Post-hypothermia) Circle choice
Cranial nerves		
Pupillary reflex (circle all that apply)	E: Equal Unequal R: Round RL: Reactive/Sluggish reaction/Nonreactive A: Present Absent	E: Equal Unequal R: Round RL: Reactive/Sluggish reaction/Nonreactive A: Present Absent
Corneal reflex	Left: Present Absent Right: Present Absent	Left: Present Absent Right: Present Absent
Gag reflex	Present Absent	Present Absent
Oculocephalic reflex (Doll's eyes)	Positive Negative Abnormal	Positive Negative Abnormal
If Doll's eye cannot be performed then use:		
Oculovestibular reflex (cold calorics)	Present Absent	Present Absent
Reflexes		
Tendon reflexes	0 1+ 2+ 3+ 4+	0 1+ 2+ 3+ 4+
Babinski reflex	Present Absent	Present Absent
Decorticate posturing (see diagram)	Present Absent	Present Absent
Decerebrate posturing (see diagram)	Present Absent	Present Absent
Seizures		
Seizure activity	Present Absent	Present Absent
Sedation		
List agents used	Dose	Dose
GCS		
Eye response (1-4)	1 2 3 4	1 2 3 4
4 = Eyes open spontaneously 3 = Eye opening to verbal command 2 = Eye opening to pain 1 = No eye opening		
Motor response (1-6)	1 2 3 4 5 6	1 2 3 4 5 6
6 = Obeys commands 5 = Localizing pain 4 = Withdrawal from pain 3 = Flexion response to pain 2 = Extension response to pain 1 = No motor response		

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page 1 of 2

Verbal response (1-5)	1 2 3 4 5	1 2 3 4 5
5 = Oriented 4 = Confused 3 = Inappropriate words 2 = Incomprehensible sounds 1 = No verbal response		
	GCS score:_____	GCS score:_____
FOUR Score (see diagram)		
Eye response (0-4):	0 1 2 3 4	0 1 2 3 4
4 = Eyelids open or opened, tracking, or blinking to commmand 3 = Eyelids open but not tracking 2 = Eyelids closed but open to loud voice 1 = Eyelids closed but open to pain 0 = Eyelids remain closed with pain		
Motor response (0-4):	0 1 2 3 4	0 1 2 3 4
4 = Thumbs-up, fist, or peace sign 3 = Localizing to pain 2 = Flexion response to pain 1 = Extension reponse to pain 0 = No response to pain or generalized myoclonus status		
Brainstem reflexes (0-4)	0 1 2 3 4	0 1 2 3 4
4 = Pupil and corneal reflexes present 3 = One pupil wide and fixed 2 = Pupil or corneal reflexes absent 1 = Pupil and corneal reflexes absent 0 = Absent pupil, corneal, and cough reflex		
Respiration (0-4)	0 1 2 3 4	0 1 2 3 4
4 = Not intubated, regular breathing pattern 3 = Not intubated, Cheyne-Stokes breathing pattern 2 = Not intubated, irregular breathing 1 = Breathes above ventilator rate 0 = Breathes at ventilator rate or apnea		
	FOUR score:_____	FOUR score:_____
Likelihood of Survival	CBD 0 1 2 3 4 5	CBD 0 1 2 3 4 5
Physician's prediction based on patient history and exam. CBD = Cannot be determined 0 = Will not survive 1 = Highly unlikely 2 = Not likely, but possible 3 = Survive with significant deficit 4 = Survive with some quality of life 5 = Survive with significant quality of life		

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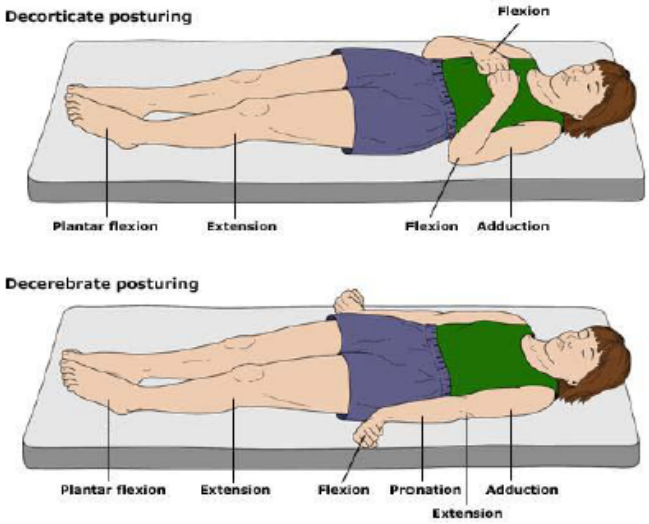
Neuro Exam Figures

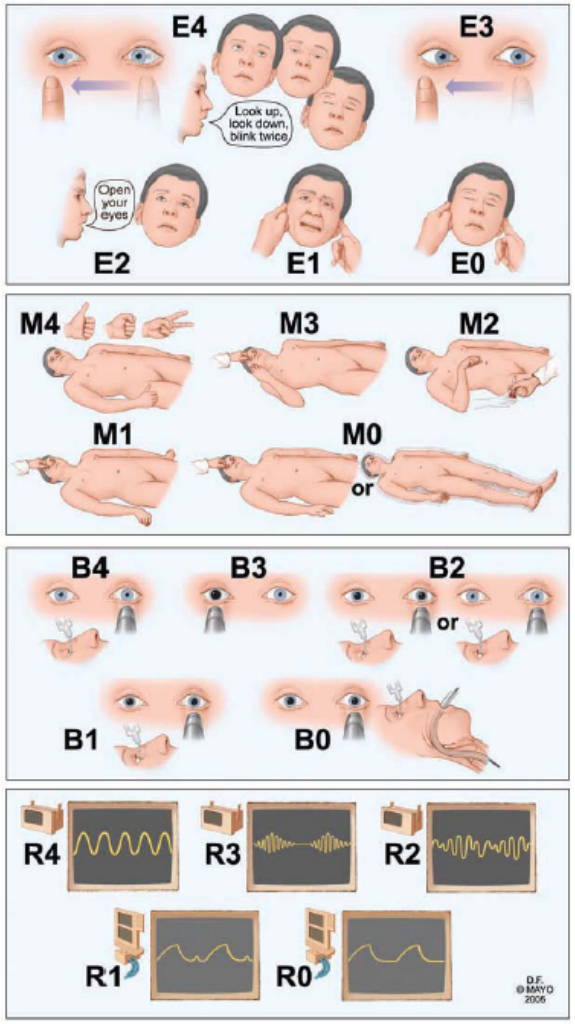
Decorticate and Decerebrate Posturing

Decorticate posturing - semi-flexion, adduction and internal rotation at the shoulders and semi-flexion or flexion at the elbows.

Decerebrate posturing - extension of upper limbs, adduction and internal rotation of the shoulders, with pronation of the forearms.



Description of Full Outline of UnResponsivenes (FOUR) score



Eye response:
E4 = eyelids open or opened, tracking, or blinking to command;
E3 = eyelids open but not tracking;
E2 = eyelids closed but open to loud voice;
E1 = eyelids closed but open to pain;
E0 = eyelids remain closed with pain.

Motor response:
M4 = thumbs-up, fist, or peace sign;
M3 = localizing to pain;
M2 = flexion response to pain;
M1 = extension response to pain;
M0 = no response to pain or generalized myoclonus status.

Brainstem reflexes:
B4 = pupil and corneal reflexes present;
B3 = one pupil wide and fixed;
B2 = pupil or corneal reflexes absent;
B1 = pupil and corneal reflexes absent;
B0 = absent pupil, corneal, and cough reflex.

Respiration pattern:
R4 = not intubated, regular breathing pattern;
R3 = not intubated, Cheyne-Stokes breathing pattern;
R2 = not intubated, irregular breathing;
R1 = breathes above ventilator rate;
R0 = breathes at ventilator rate or apnea.

Additional NT Application

- Early studies suggest that continuous EEG appears more accurate and valid as a prognostic tool than intermittent monitoring, but it remains to be adequately tested
- Continuous EEG with the addition of trending and quantitative analyses has reportedly shown an even stronger prognostic value for this patient population

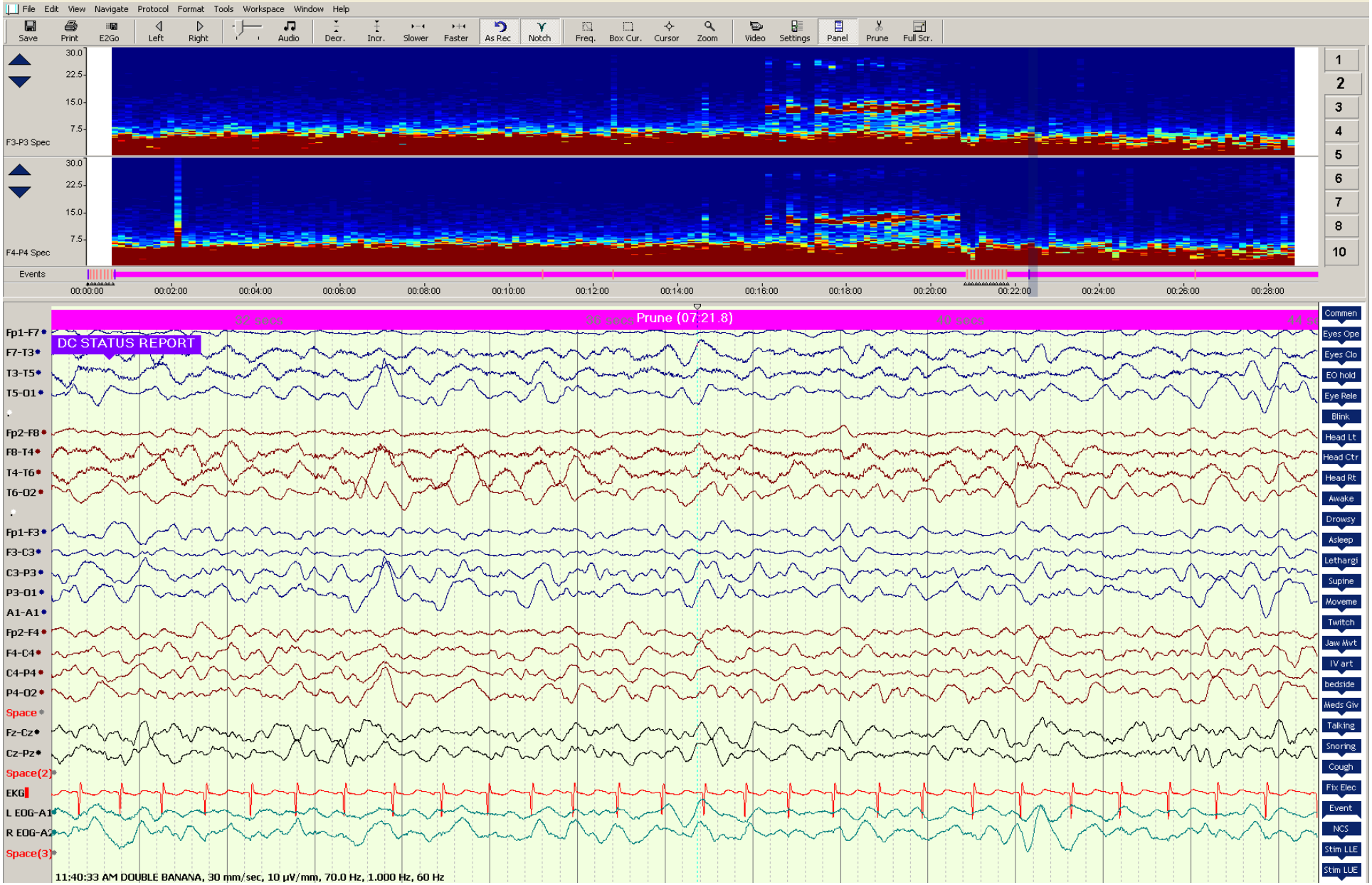
Trending

- Trending is a tool that digitally analyzes continuous EEG data
- Large amounts of data can be compressed to see the “big picture”
- Types of trending
  - Amplitude-based trends
    - Envelope, Amplitude Integrated EEG, Total Power
  - Frequency-based trends
    - Spectrogram, Band Power, Alpha Variability

Trending

- Clinical advantages:
  - Detects subclinical seizures, changes in pattern amplitude and frequency
  - Filters out transient events emphasizing rhythmic events, artifact
  - Helps neurologist make changes to treatment in real-time

Frequency Trending example: Spectogram



Pilot Study

- This study includes patients undergoing hypothermia with Neurotelemetry following cardiac arrest to determine the additional benefits of NT monitoring in this population as related to prognosis
- Each subject currently receives NT monitoring for up to 3-5 days after admission following cardiac arrest as a standard part of their care

Short-term Study Goals

- The data will be used to identify data clusters and prognostic indicators that allow for differentiation of subject outcomes
- This early pilot data will be used to develop our prospective prognostic algorithm which will be tested in the next phase of the study

Long-term NT & Study Goals

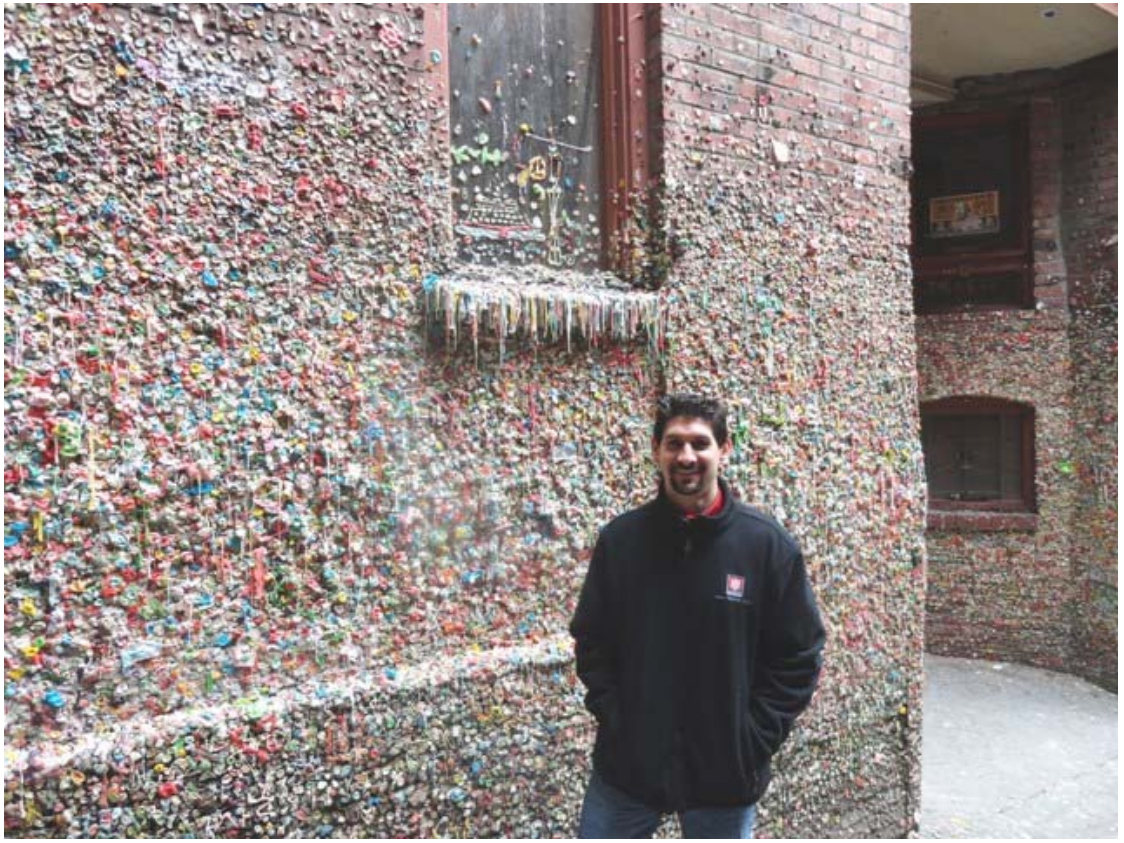
- Improve outcomes through treatment of previously undetected subclinical seizures
- Improve outcomes through better prognostic ability determine when aggressive treatments are indicated
- Improve ability to prepare family members for end of life decision making
- Preserve resources that could be potentially spent in a futile fashion on patients with non-survivable outcomes

We don’t know what we don’t know. -Donald Rumsfeld

Modified from S. LaRoche PPT

Thank You!!! Questions/Comments???

The “Gum Wall” in Seattle



Ryan Lau

RLau2@IUHealth.org