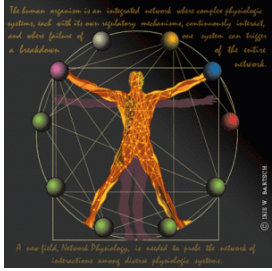
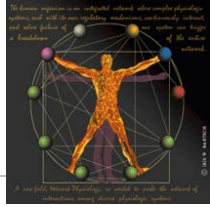


The Mysteries of the Injured Brain: Can they be solved with network physiology?

Dick Moberg
Moberg ICU Solutions

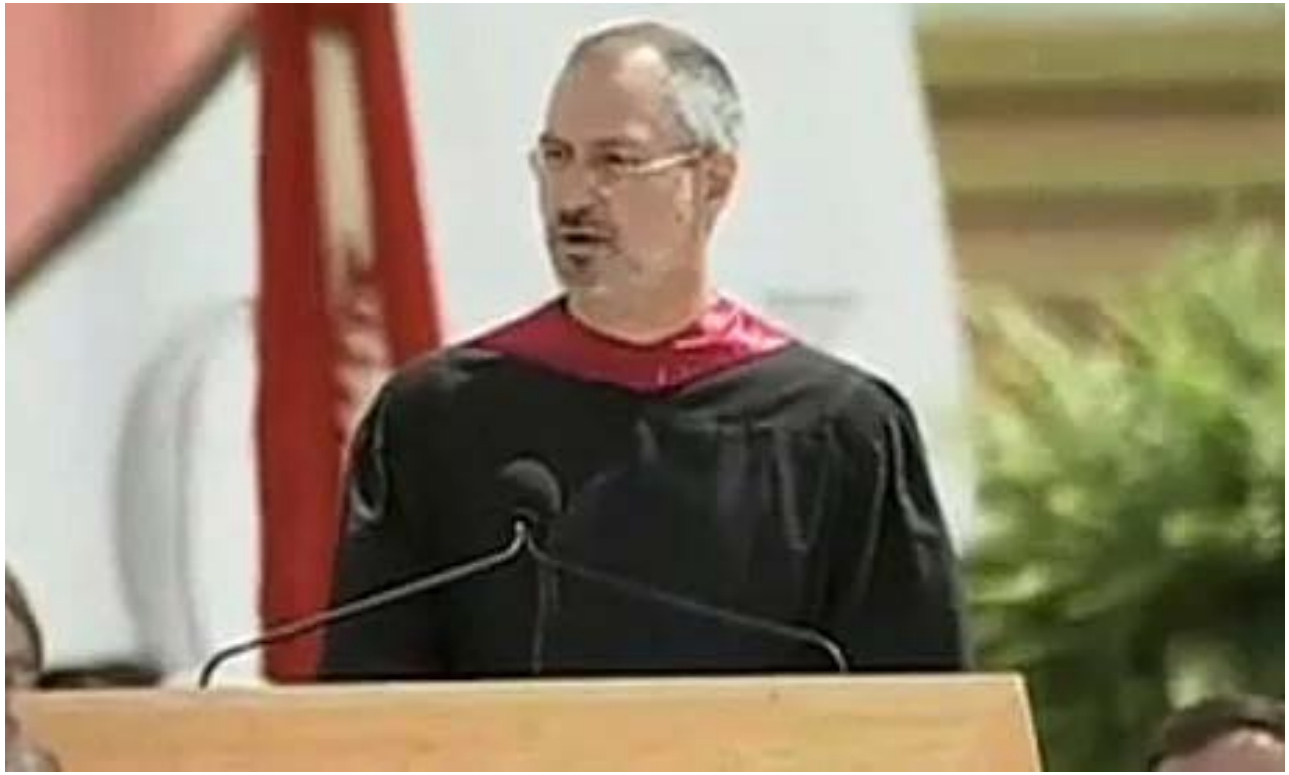
Traumatic Brain Injury (U.S.)



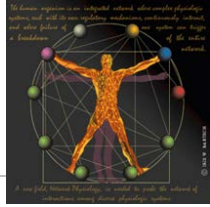
- Incidence:
  - 2.5 million/year
  - 250,000 hospitalized
  - 50,000 deaths
- Cost of TBI:
  - 76 billion dollars
  - 5 million people living with a TBI-related disability
- Conclusion
  - Small improvement in management/outcome can have a high impact on quality of life and cost of disease

Connecting the Dots

Steve Jobs Commencement Speech
Stanford - 2005



Two Parallel Stories

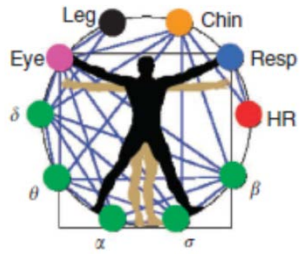


1970s

Traumatic Brain Injury

Brain Monitoring

Remaining Work



CNS Injury – 1970s

Injury

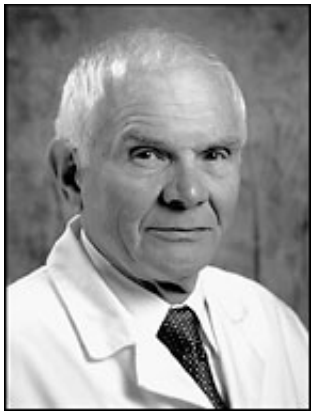
Brain

Damage is done, nothing we can do

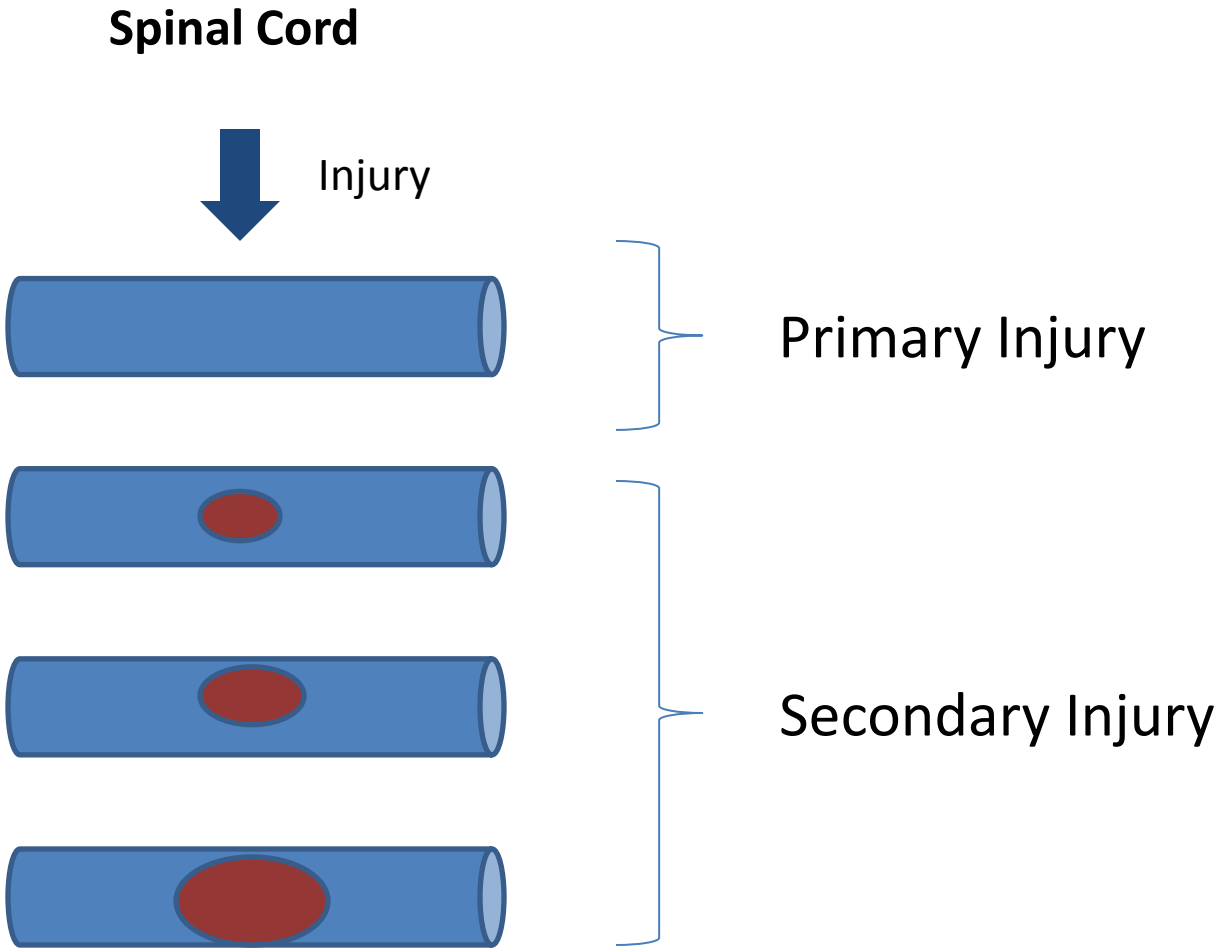
Spinal Cord

Impact + Secondary Injury

Spine Injury – 1970s

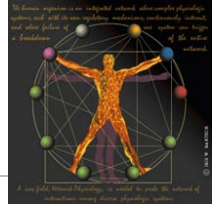


Jewell Osterholm



The pathophysiological response to spinal cord injury
Jewell L. Osterholm, Journal of Neurosurgery, *January 1974* / Vol. 40 / No. 1 : Pages 3-33

Brain Injury – 1970s



Monitoring

Very crude metrics

- GCS (1974)
- ICP (Richmond bolt)
- Pupils

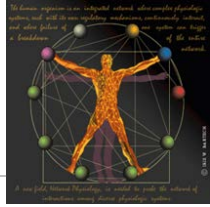
Imaging

- None

Secondary Injury

- “None”
- <u>There is nothing we can do for these patients</u>

Two Parallel Stories



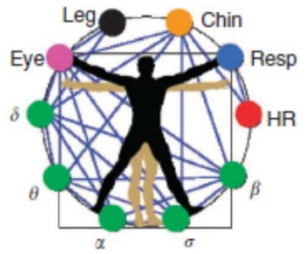
1970s

Secondary Injury in Spinal Cord

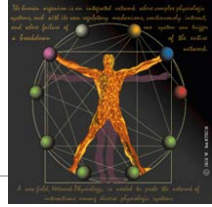
Traumatic Brain Injury

Brain Monitoring

Remaining Work

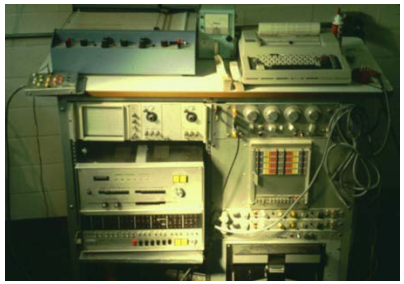


Brain Monitoring 1970s – 1980s



1970 1980s 1990 2000

Nicolet
Med-80

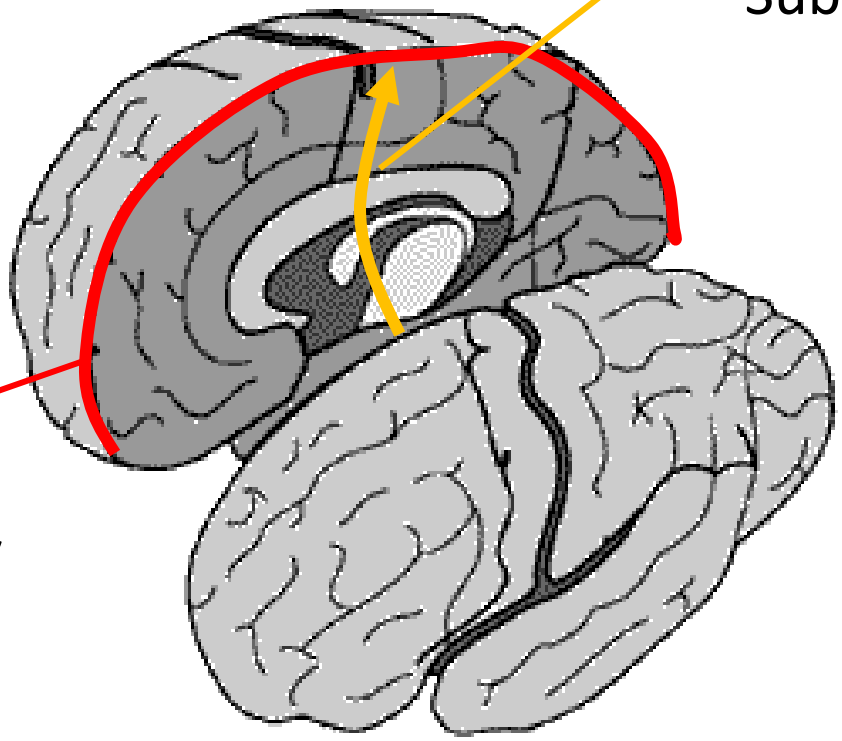


Jefferson
Hospital

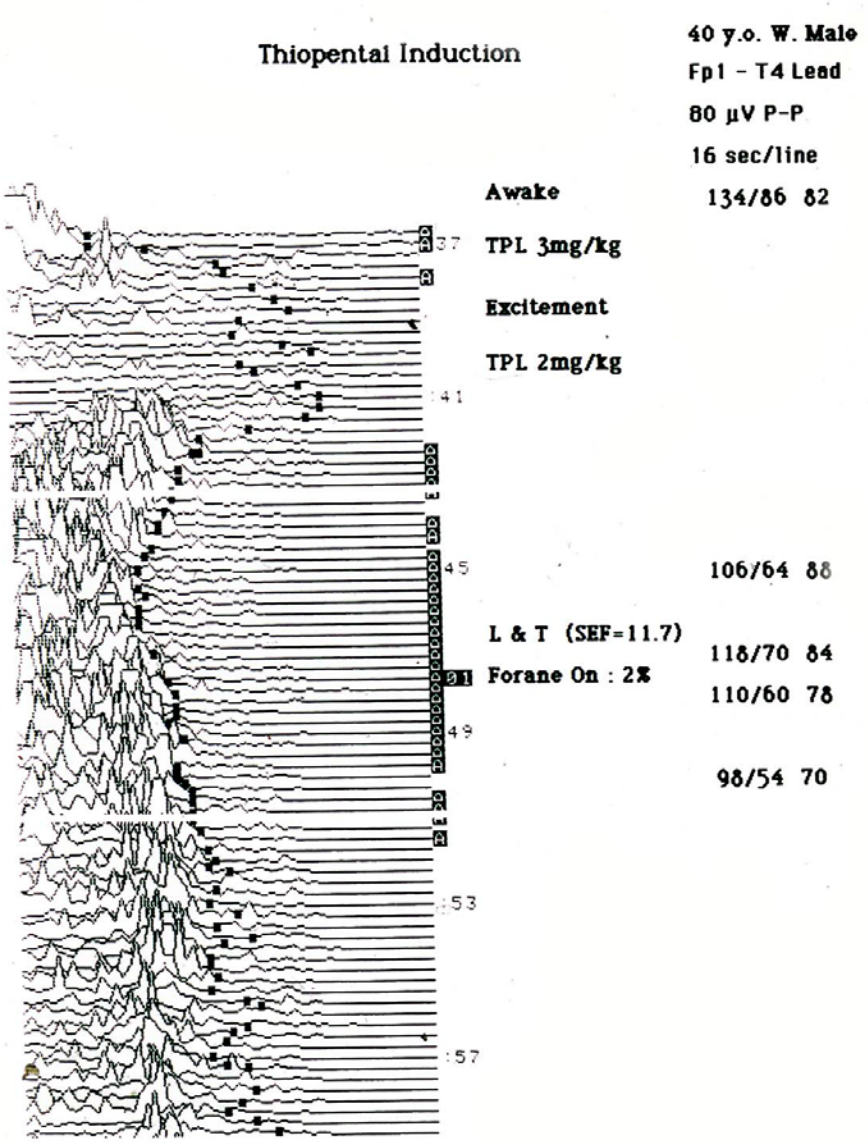
Neurotrac

Interspec

Brain Monitoring 1970s – 1980s



Brain Monitoring 1970s – 1980s



Spectral Edge Frequency
1st EEG Metric
Used for Monitoring

Brain Monitoring 1990s

1989

Experimental Device

NIH/NINDS Funding

HEWLETT® PACKARD

1994

Neurotrac II

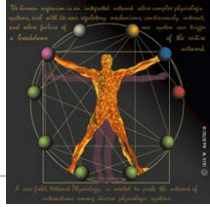
Continuous Monitoring

EEG + EP + TCD

EEG Metrics

- Power Bands (Absolute, Percent)
- Mean Dominant Frequency
- Median Power Frequency
- Peak Power Frequency
- Spectral Edge Frequency

Two Parallel Stories



1970s

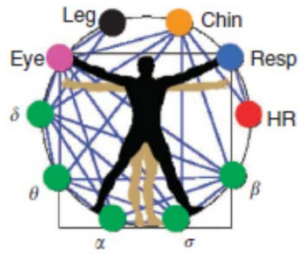
Secondary Injury in Spinal Cord

Traumatic Brain Injury

Brain Monitoring

Single Metrics
- ICP
- EEG
- GCS

Remaining Work



CNS Injury – 1980s – 1990s

Injury

Brain

Impact + Secondary Injury

Spinal Cord

Impact + Secondary Injury

Brain Injury – 1990s

Monitoring

Very crude metrics

- GCS (1974)
- ICP (Richmond bolt)
- Pupils

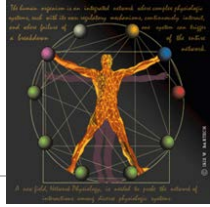
Imaging

- CT (early 1980s)

Secondary Injury

- Apoptosis
- Many trials started
  - **All failed**

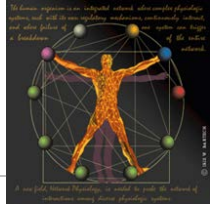
Why All the Failures?



- Complexity of the brain
- Too much variability in TBI patients

- Narayan et. al. - 2002

Two Parallel Stories



1970s

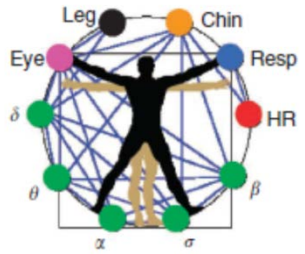
Secondary Injury in Spinal Cord	Secondary Injury In Brain but No Successful Trials

Traumatic Brain Injury

Brain Monitoring

Single Metrics
- ICP
- EEG
- GCS

Remaining Work



Multimodal Monitoring

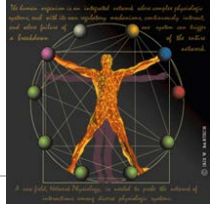
Gert Pfurtscheller

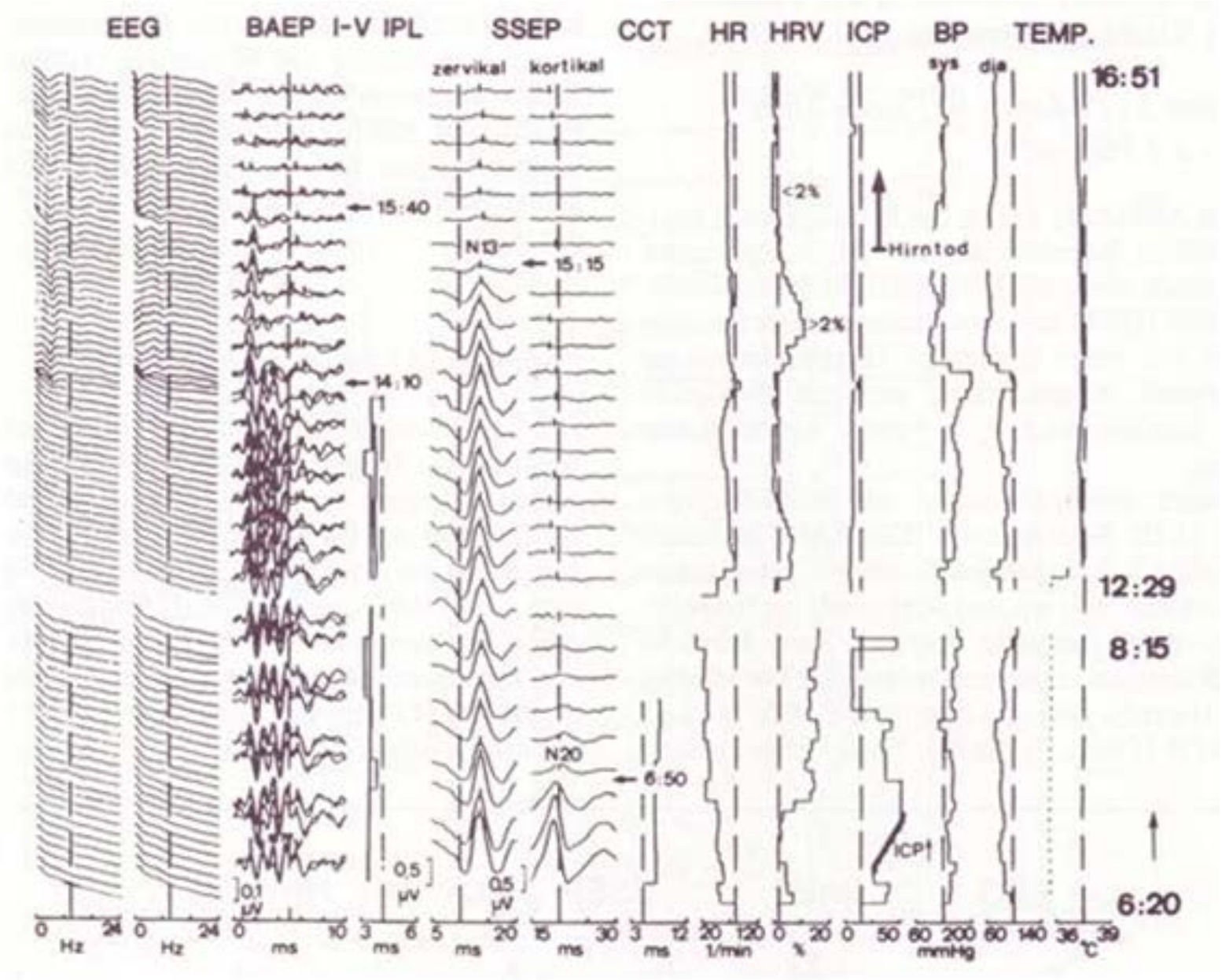
Graz

Karin

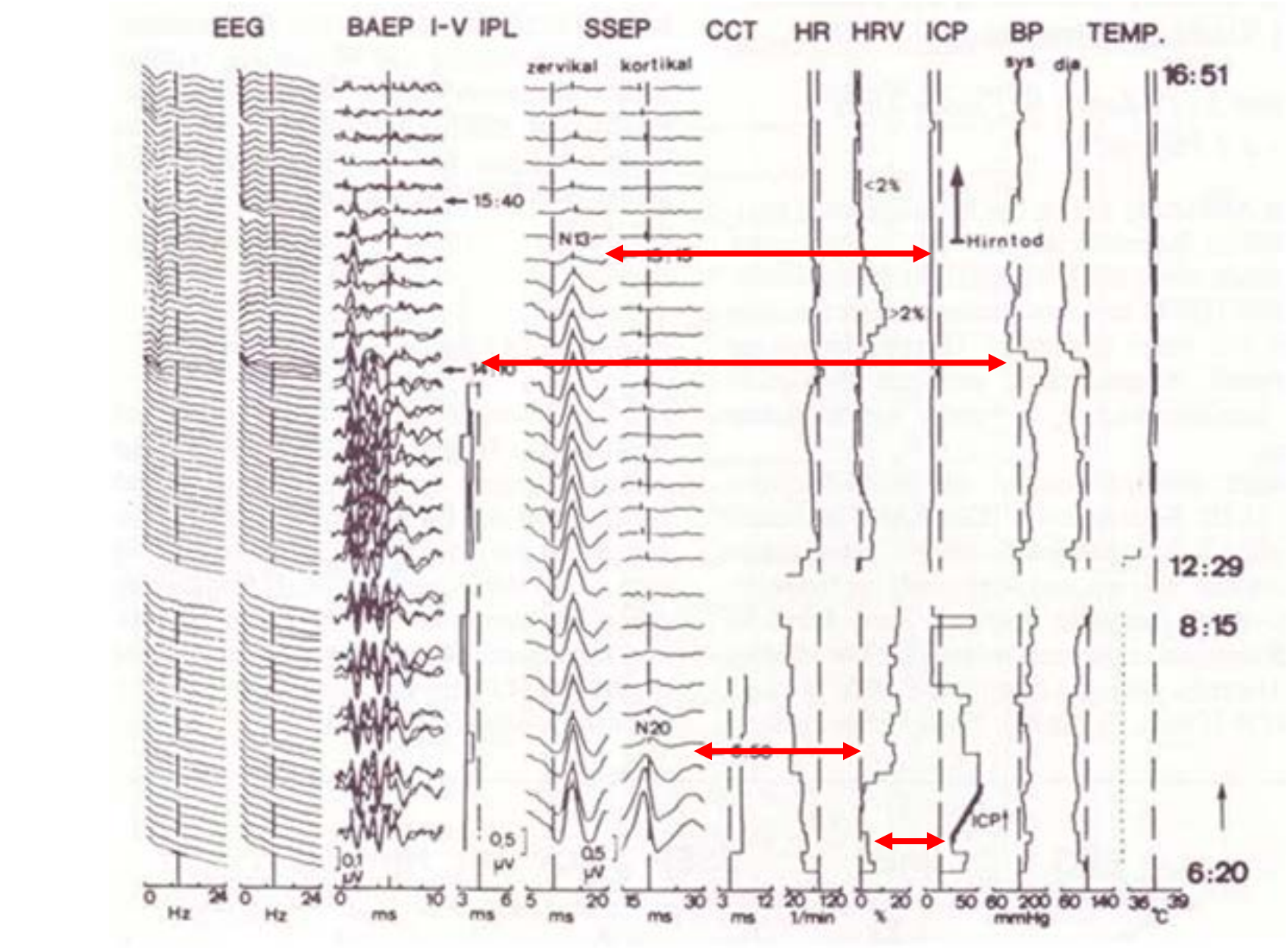
Gerhard Litscher

Brain Roadmap – Dr. Gerhard Litscher





Brain Roadmap – System Connections

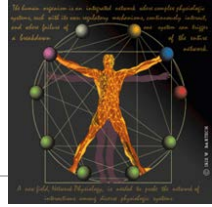


Multimodal Monitoring - 1996

Multimodal Monitoring

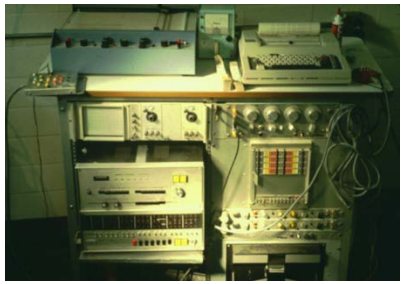
- Grant from NIH
- Developed computer architecture for gathering data from multiple products

Brain Monitoring 1970s – 2000s



1970 | 1980s | 1990 | 2000

Nicolet Med-80



Jefferson Hospital

Neurotrac

Interspec

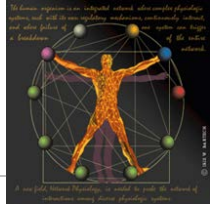
Neurotrac II

Moberg Medical

CNS Monitor

Moberg Research

The Product

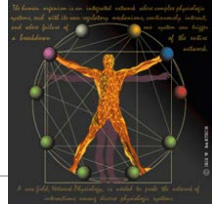


The Component Neuromonitoring System (CNS)

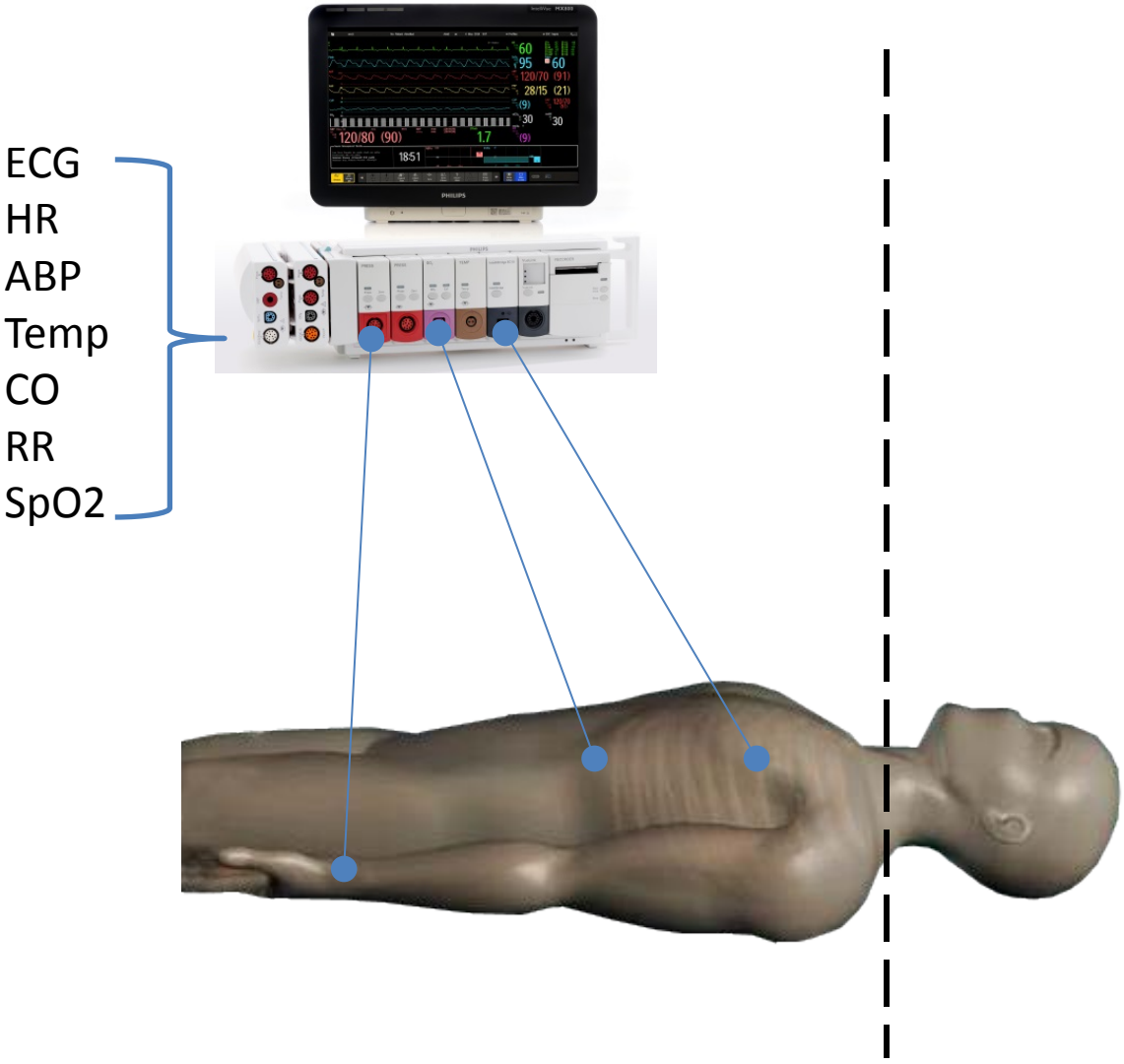
A System of Components for Managing Data in Neurocritical Care

The Smart Neuro ICU

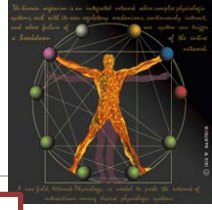
Traditional Vital Signs Monitoring



Vital Signs Monitoring



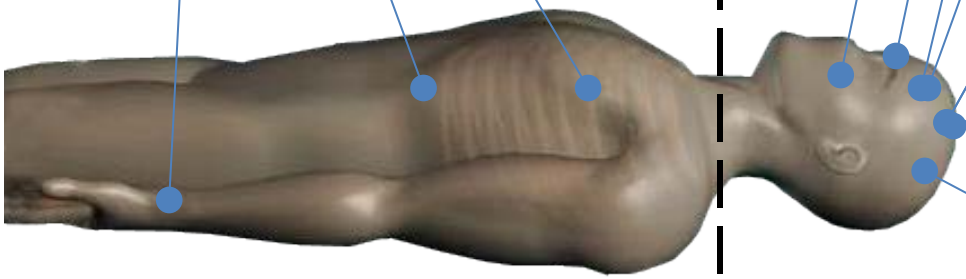
Challenge: Current Neuromonitoring



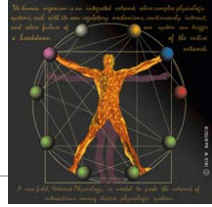
Vital Signs Monitoring

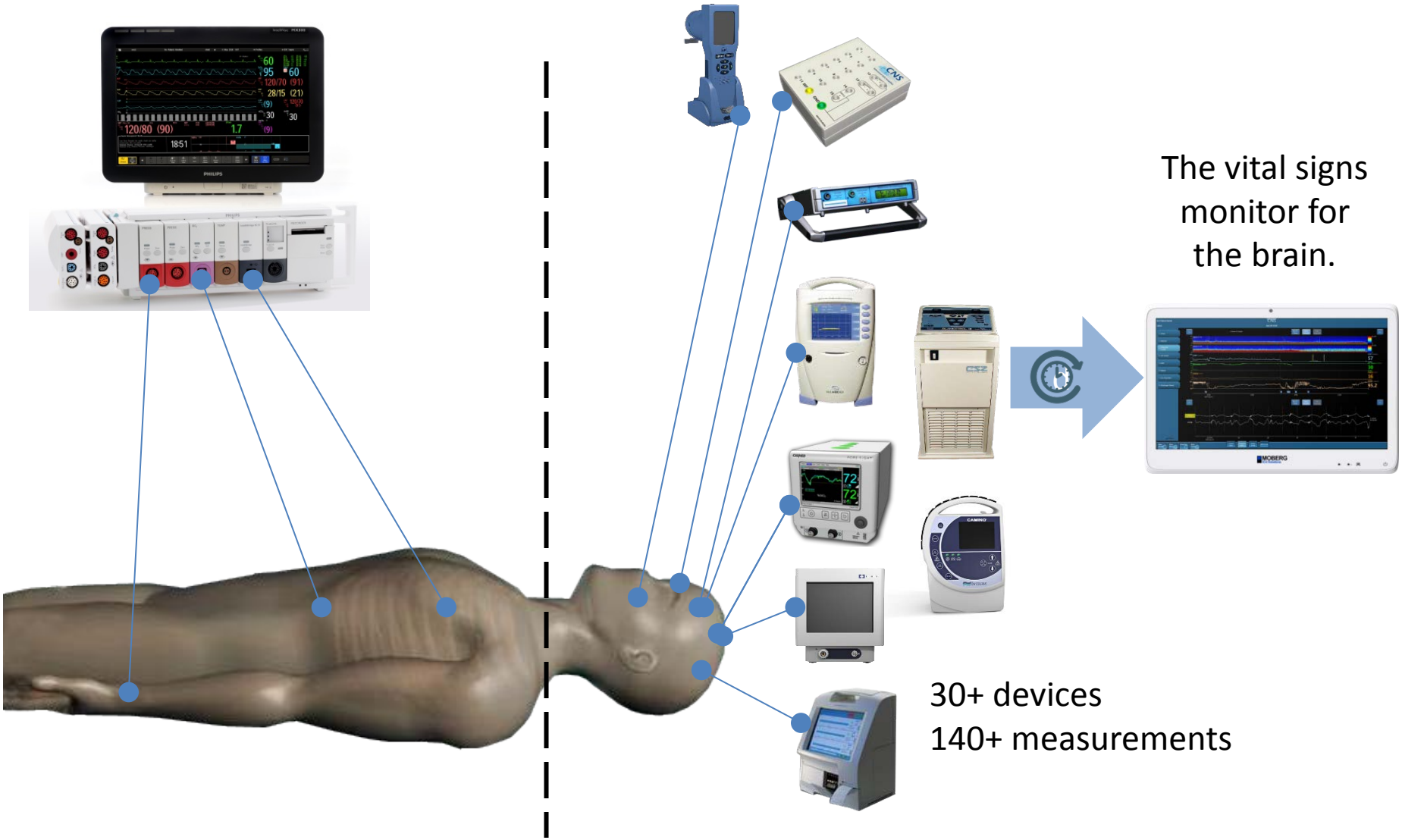
Neuromonitoring: Today

ECG
HR
ABP
Temp
CO
RR
SpO2

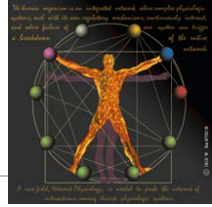


Solution




The vital signs monitor for the brain.
30+ devices
140+ measurements

Collect Data from Brain/Body Systems



Metabolism

Brain Oxygen

EEG

Perfusion

TCD

Temperature

Vital Signs

Pupils

Sedation

ICP

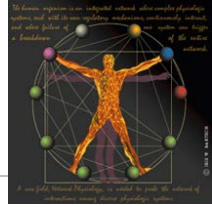
Video

Hemodynamics

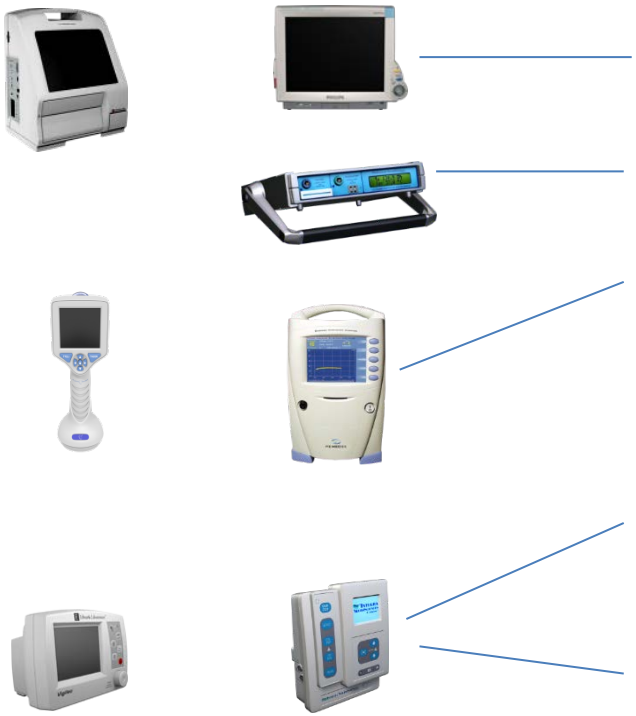
CO2

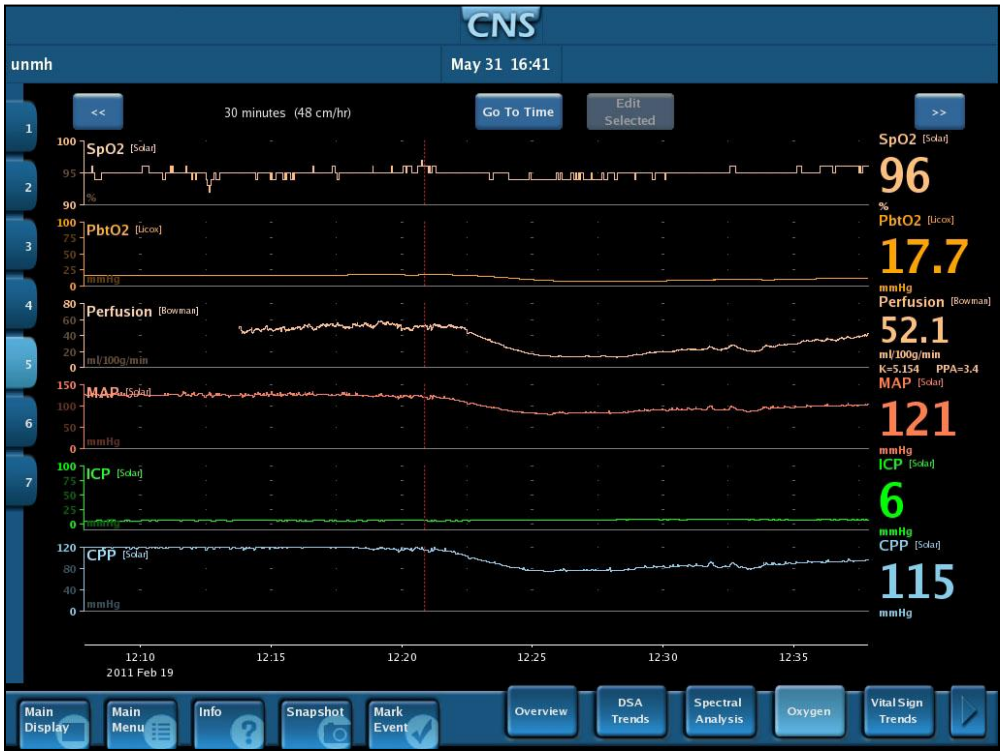
Device - Pupilometer

Data Recording and Display



30+ Devices → **Time-Synchronized Data**

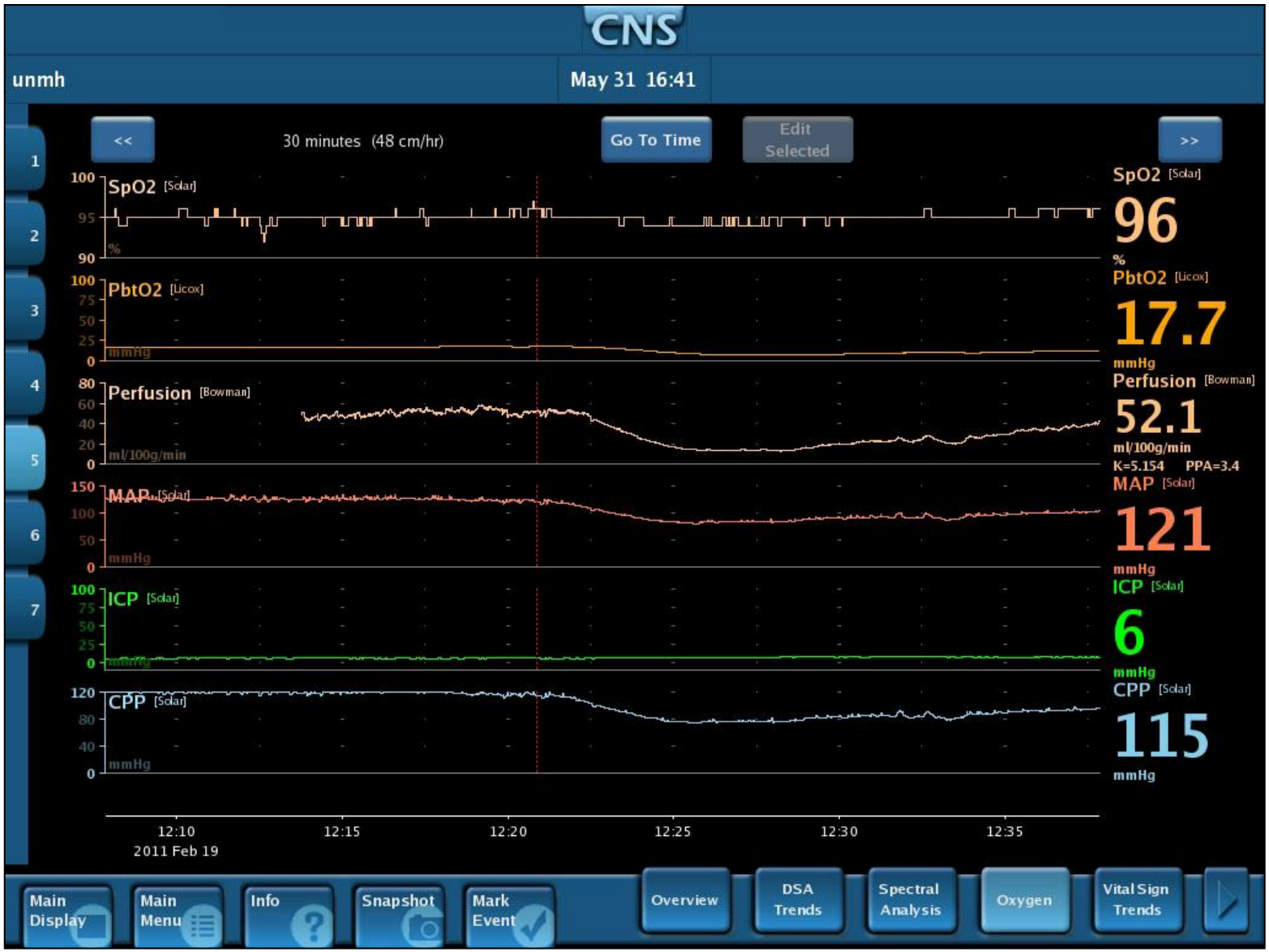




Typical CNS Installation

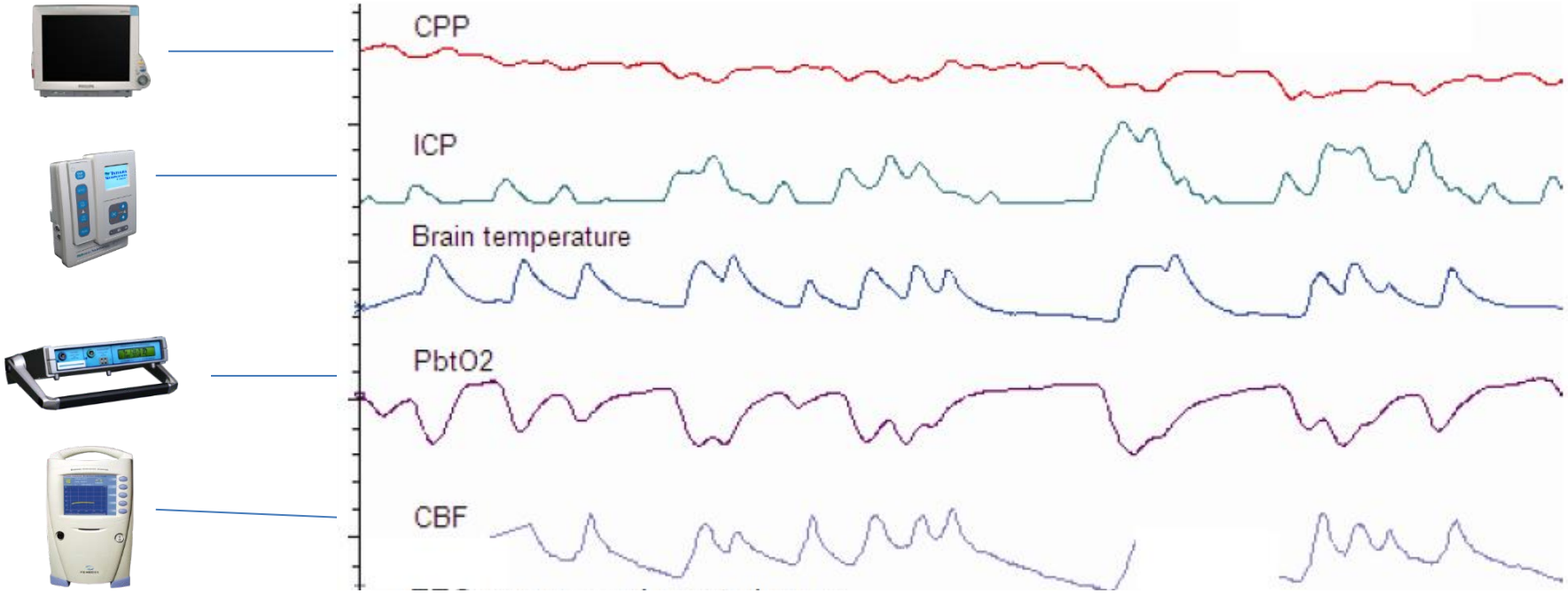
Dr. Michael Stiefel, Chair of Neurosurgery
Westchester Medical Center, Valhalla, NY

Brain System Interactions

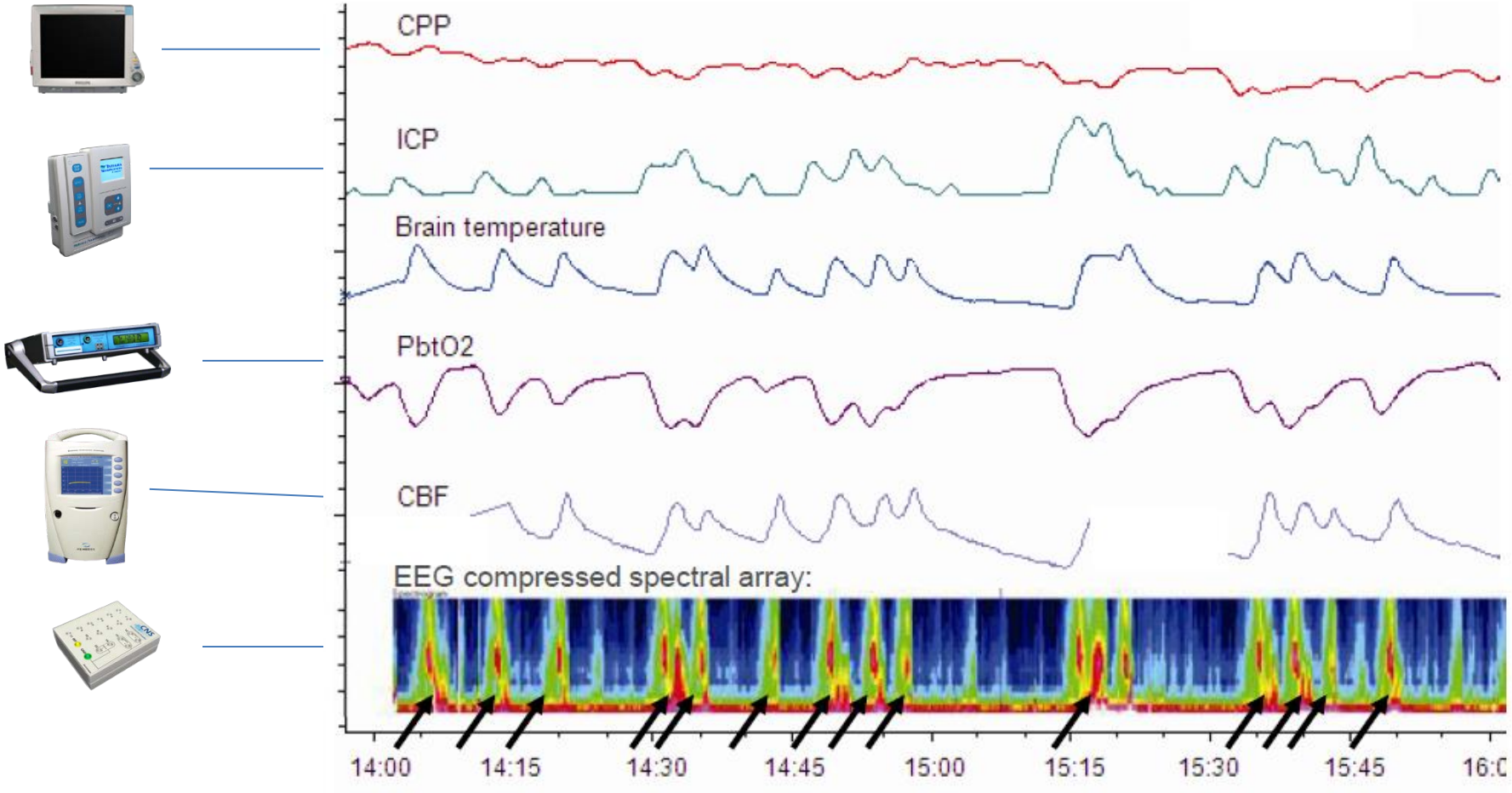


Courtesy: Howard Yonas, MD, Univ of New Mexico

Missing Data – Wrong Treatment

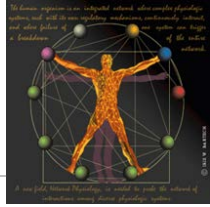


Missing Data – Wrong Treatment



Courtesy of Columbia University

Two Parallel Stories



1970s

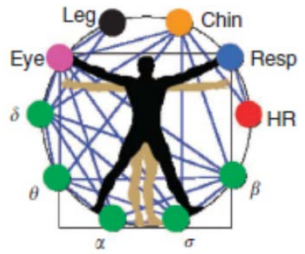
Secondary Injury in Spinal Cord	Secondary Injury In Brain but No Successful Trials

Traumatic Brain Injury

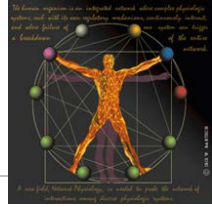
Brain Monitoring

Single Metrics - ICP - EEG - GCS	Multimodal Monitoring

Remaining Work

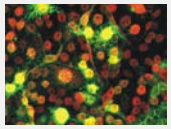


TRACK-TBI and CENTER TBI

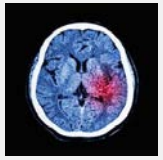


TRACK-TBI (large multi-center TBI trial) will produce advances in the **classification** of TBI patients as well as **outcome assessment**. It ignores the variability in patient management from site to site and from nursing shift to nursing shift.

Classification



Biomarkers



Advanced Imaging

Genomics

Management Assessment

The CNS Monitor guides the management of brain injured patients.

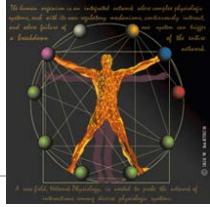
Outcome Assessment

Psychometric Testing

TED

Traumatic Endpoints Development

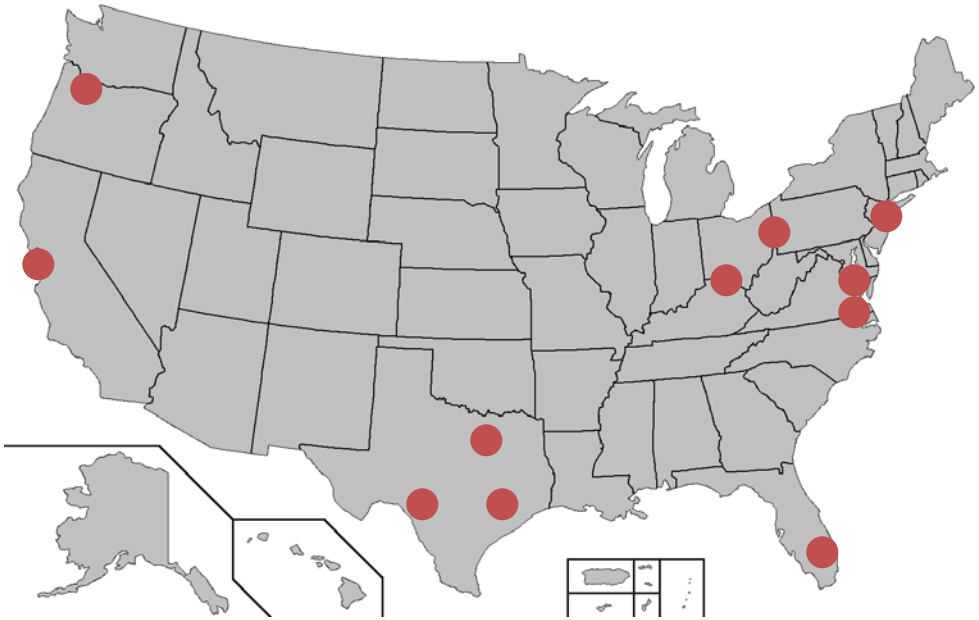
2014 TRACK-TBI and CENTER-TBI



Two large multi-center trials focused on characterizing TBI patients such that therapeutic measures can be targeted to the appropriate subgroup.

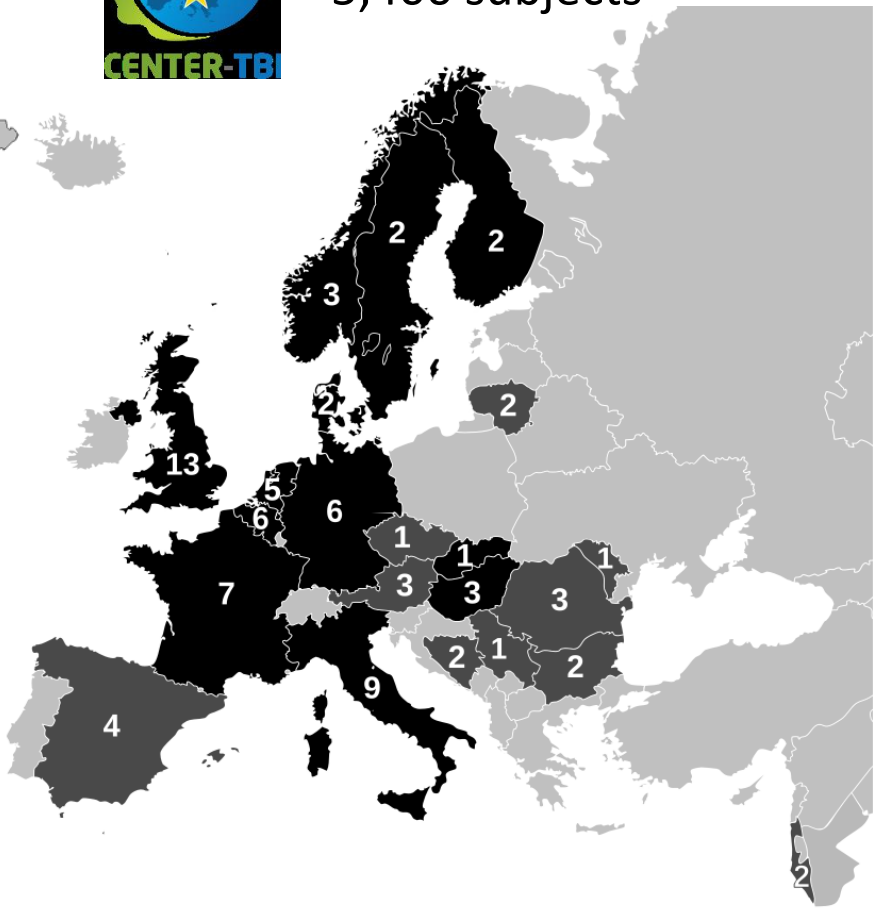
TRACK-TBI
Transforming Research and Clinical Knowledge in Traumatic Brain Injury
International Traumatic Brain Injury Research Initiative

11 sites
3,000 subjects

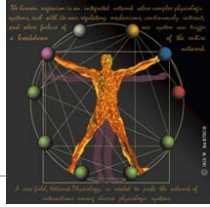


CENTER-TBI

80 sites, 21 countries
5,400 subjects



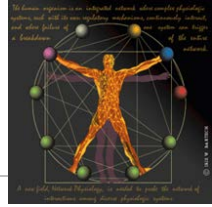
Big Data for a Complex Problem



- Lots of data being recorded
- Promise of progress with TBI
- Still a very complex problem to solve

- But how can we accelerate progress
  - How can we get innovative ideas to the clinics quickly

Two Parallel Stories



1970s

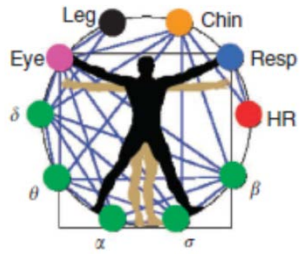
Secondary Injury in Spinal Cord	Secondary Injury In Brain but No Successful Trials	Secondary Injury In Brain - Progress

Traumatic Brain Injury

Brain Monitoring

Single Metrics - ICP - EEG - GCS	Multimodal Monitoring

Remaining Work



Electronic Medical Records

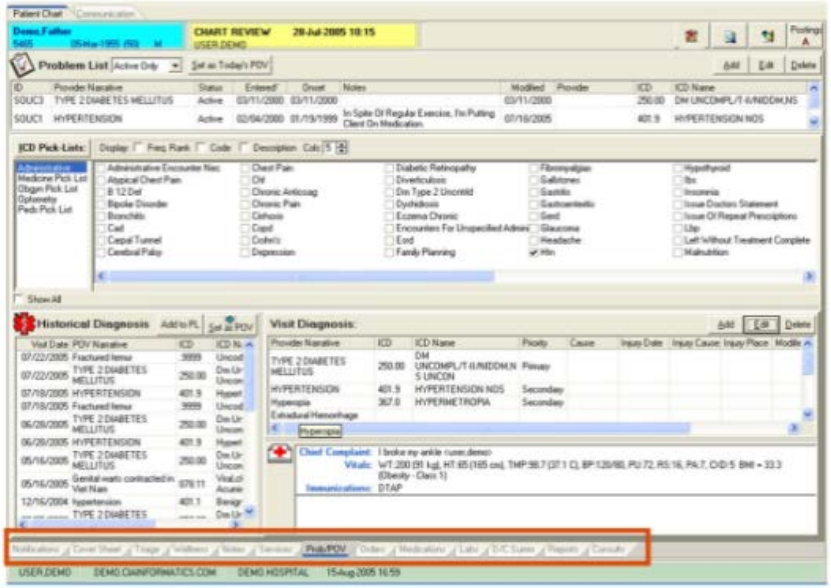
Larry Weed
(1923-2017)

Father of the Electronic Medical Record

Medical records that guide and teach
NEJM. **278** (11): 593–600.

Met in 1980. An “isolated dot”

Electronic Medical Records

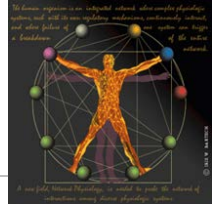


Very little information usable for managing head injury!

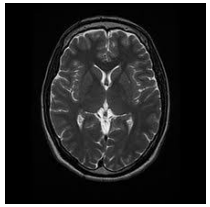
(In spite of spending 100's of millions of dollars on the software.)

How do you make progress in managing the injured brain without good records (data)?

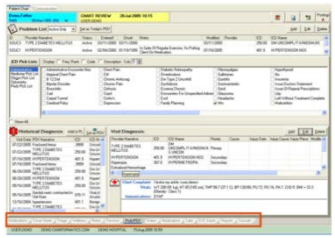
A New Medical Record for the Brain



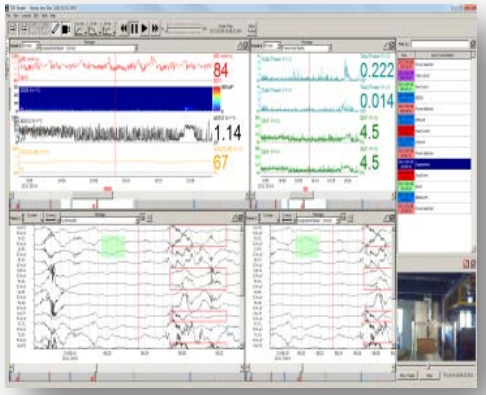
DOD Project



Current Medical Record



Brain Medical Record



Calculation of
Higher Order Metrics

External Analytics

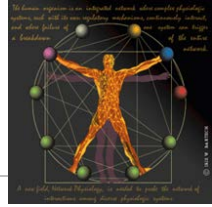
MOBERG

Open file format

- ***Moberg*** **CNS Reader** — EEG Reading & Analysis
- ***MathWorks*** **MatLab** — Time Series Analysis
- ***IBM*** **Streams** — Big Data Analysis
- ***Blackfynn*** **Cloud** — Cloud-based Analysis
- ***AIT*** **NeuroTrend** — EEG Reading, Annotation & Analysis
- ***Persyst*** **ICU Suite** — EEG Reading & Analysis
- ***Cambridge*** **ICM+** — Neuromonitoring Analytics

Others in development

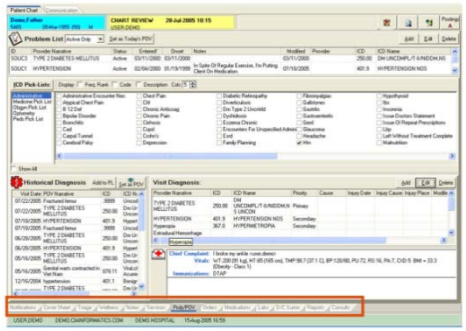
A New Medical Record for the Brain



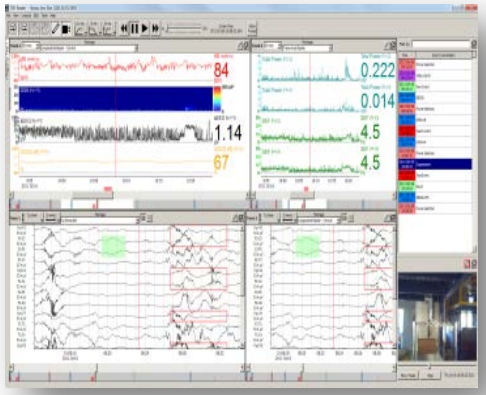
FDA Cleared
CE Mark

No FDA/CE

Current Medical Record



Brain Medical Record

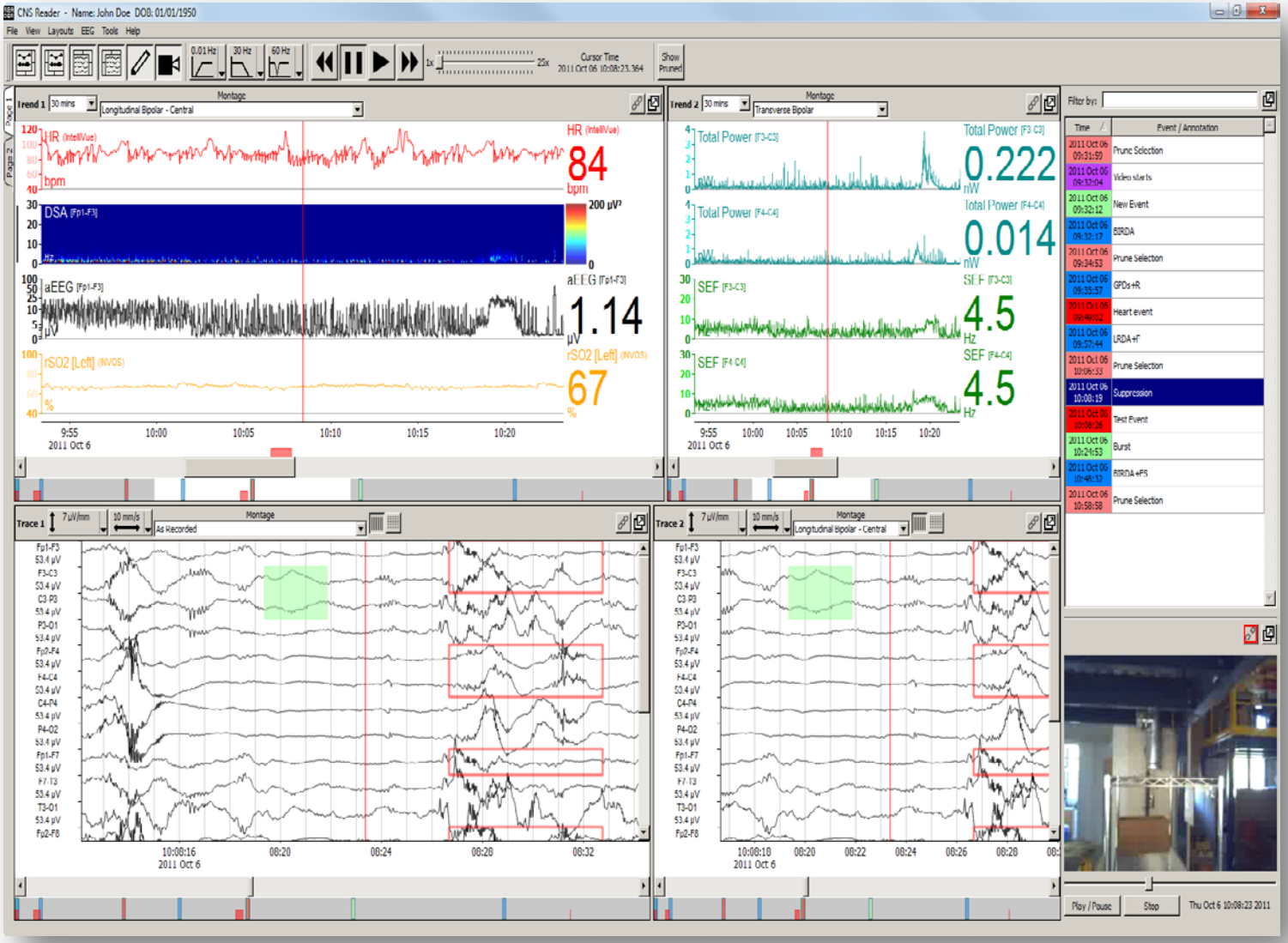


CNS Reader

MOBERG

Remote review of data

Data annotation tool

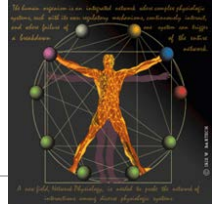


Switch Display: Monitor – Medical Record

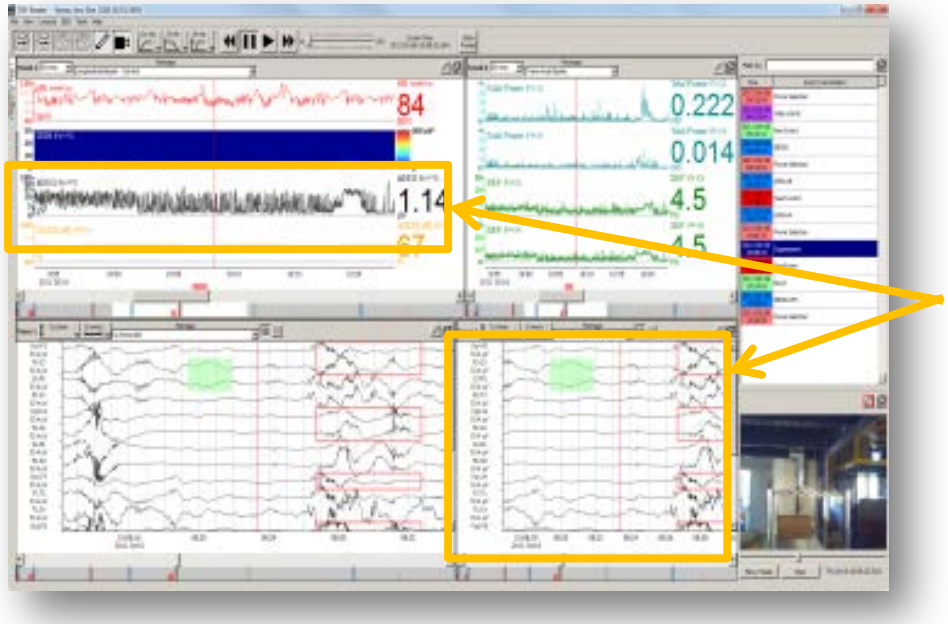
Brain Monitor

Brain Medical Record

Apps



Data



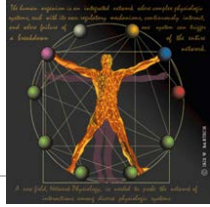
API

Apps

User defined apps

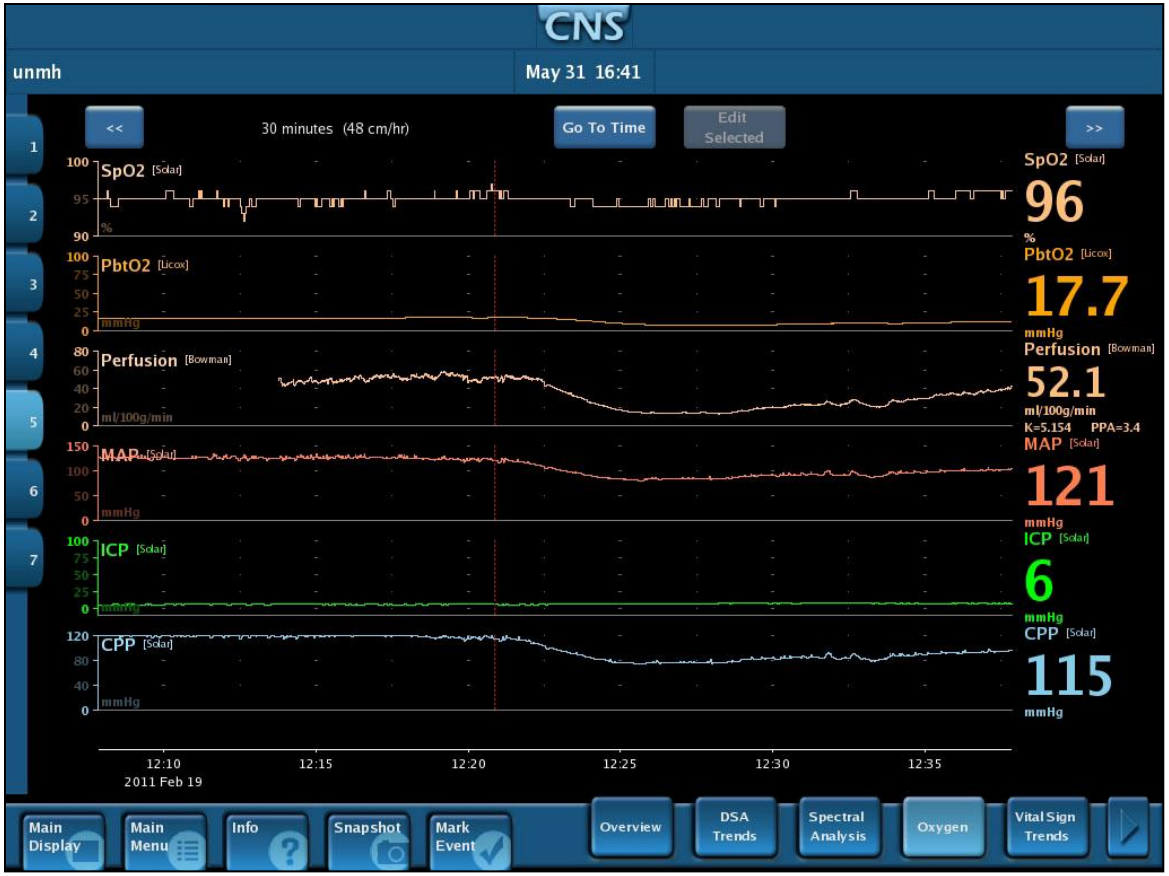
API can assign a region on
any display for the app results

App Examples



- PRx
- Blood Pressure Management
- IBM Patient Priorities
- Prediction of Events
- Spreading Depolarizations

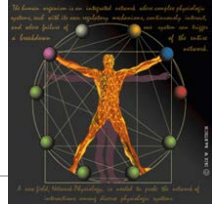
PRx – Loss of Autoregulation



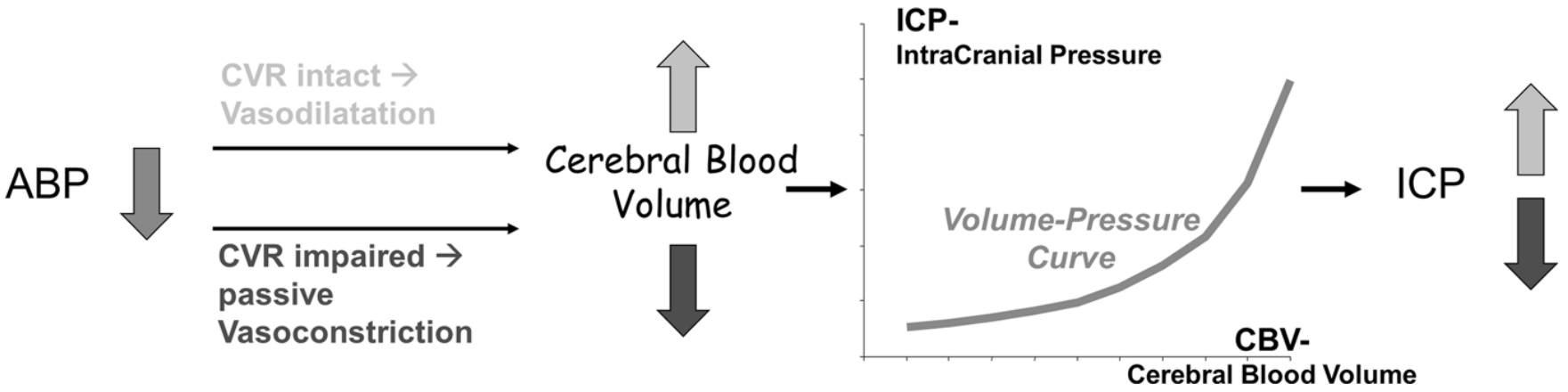
Correlation Coefficient

PRx

PRx – Loss of Autoregulation



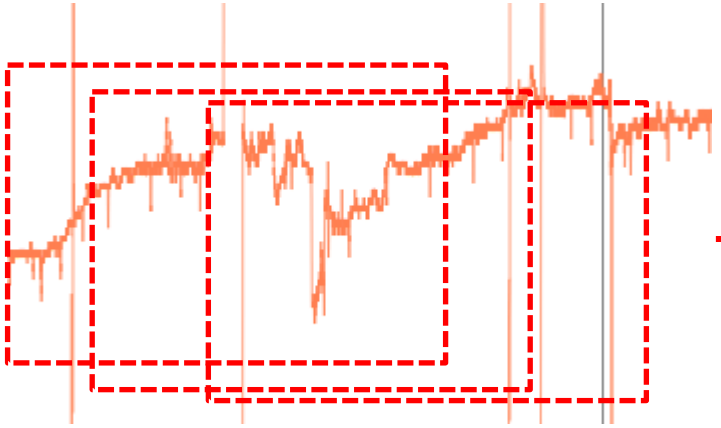
PRx **Correlation ABP-ICP assesses Cerebrovascular Reactivity (CVR)**



Calculation of PRx

An Index of Cerebral Autoregulation

MAP

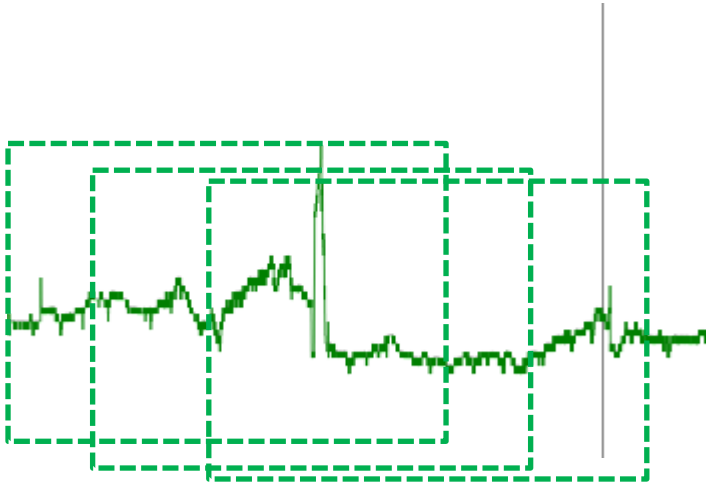


Average across 10 seconds of data to get one sample (non overlapping windows)

PRx

Compute Pearson's correlation coefficient across windows of 300 seconds, with an update rate of 60 seconds (80% overlap)

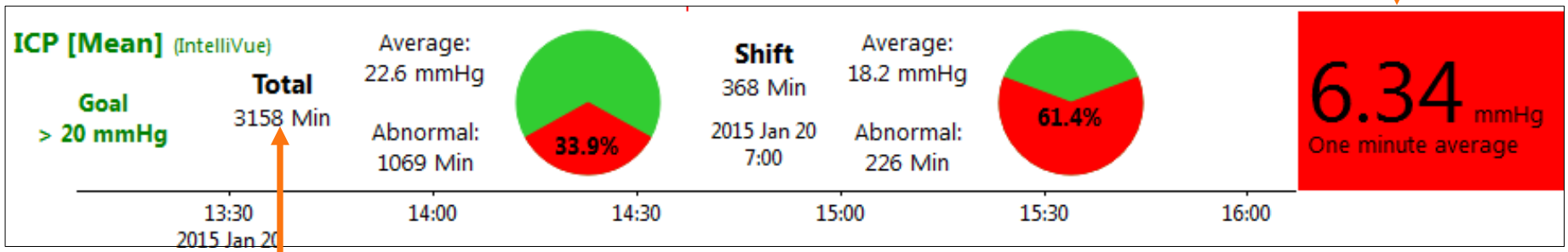
Mean ICP



Threshold Display Plug-In

MOBERG

One minute average at the cursor time.



Total number of minutes in the entire monitoring session.

Average value and number of minutes outside the desired goal, across the entire monitoring session.

The red area and % represent the relative amount of time spent outside the desired goal.

Metrics calculated within a shift.

Shifts are defined by going to ***Tools→Settings…***, in the *Threshold Display* tab.

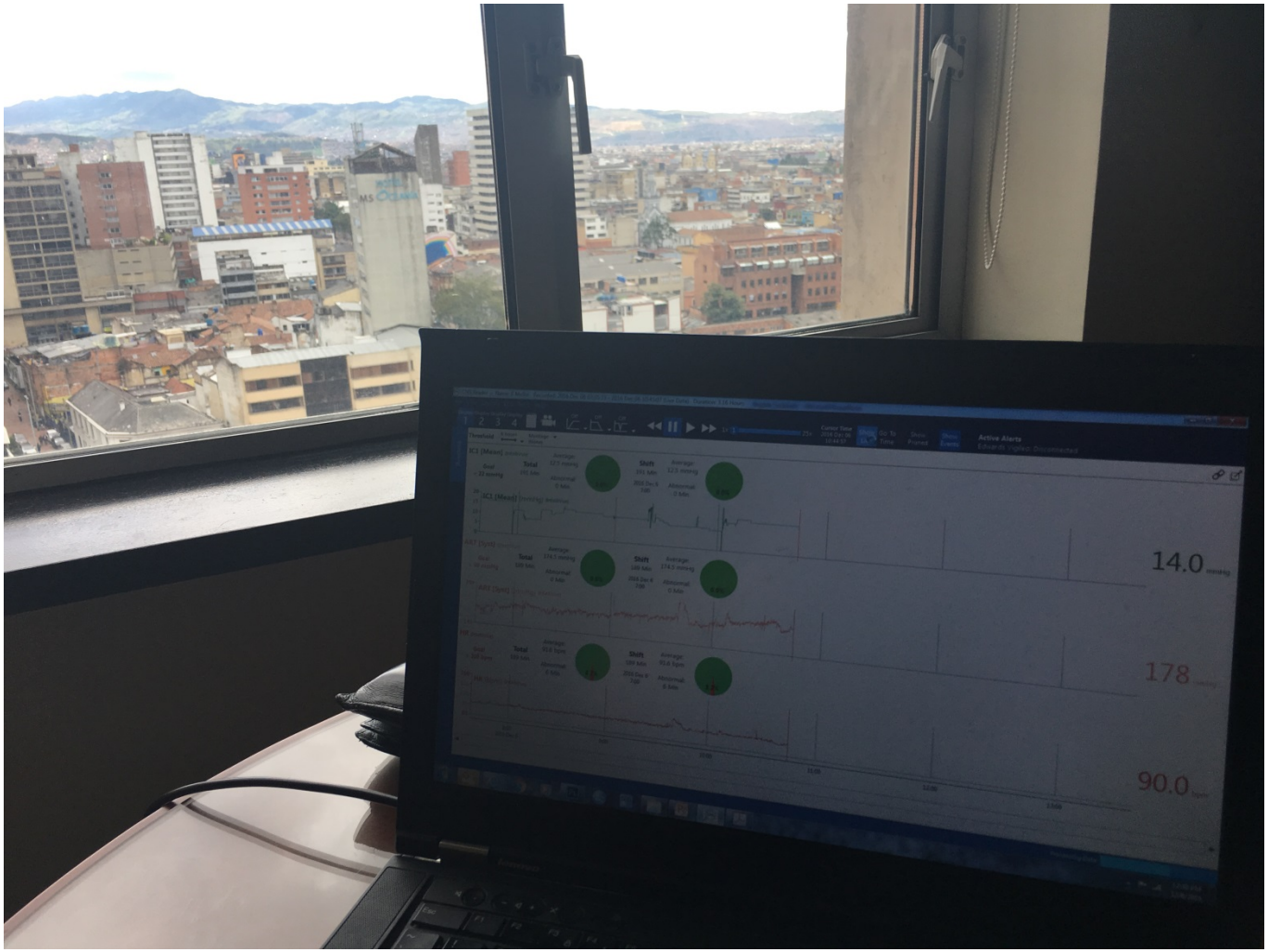
Alternatively, metrics can be calculated based on the display duration (by changing the ***Time Base*** in the measurement settings).

Dr. Greg Hawryluk – University of Utah

CNS Reader: Plug-in Architecture

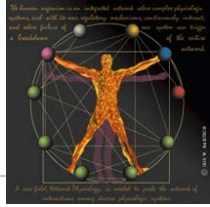
MOBERG

Remote Monitoring of Blood Pressure



Courtesy – Dr. Greg Hawryluk

IBM – Prioritizing Patients

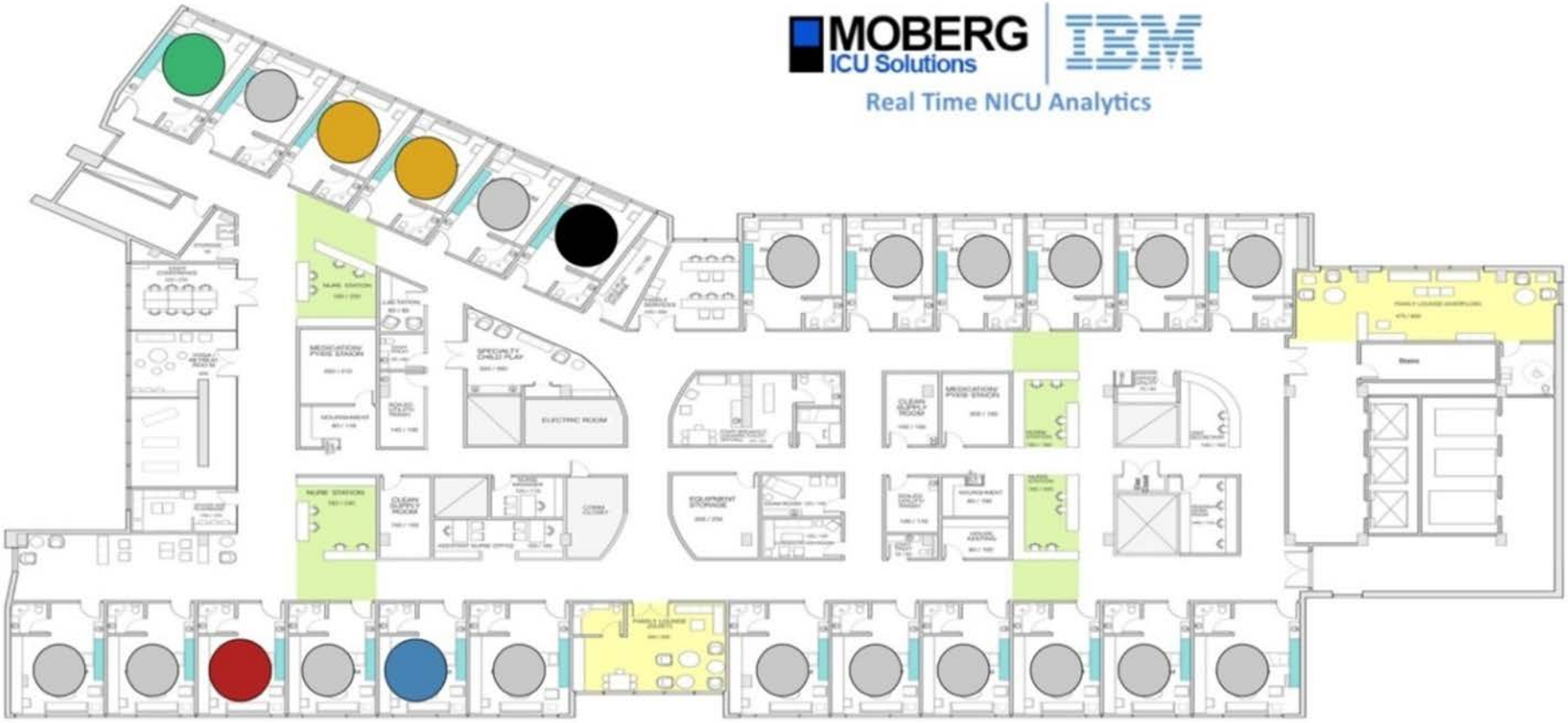


Safari File Edit View History Bookmarks Window Help 100% Tue Dec 8 9:27

172.16.5.138

MOBERG ICU Solutions | IBM

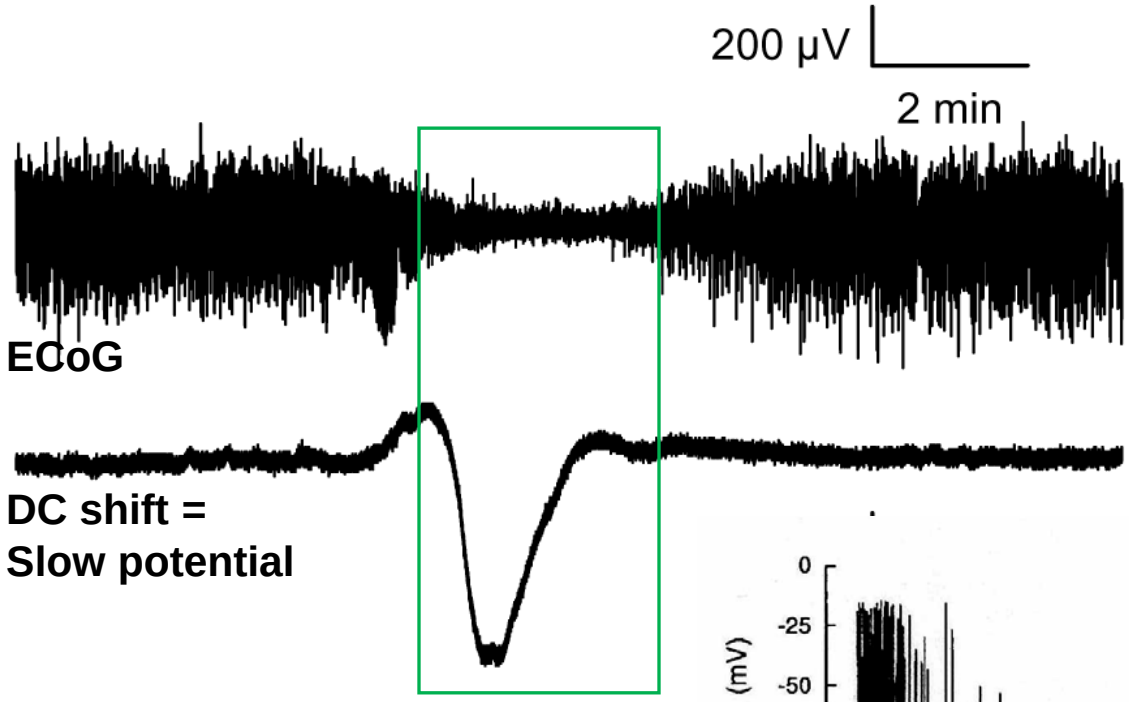
Real Time NICU Analytics



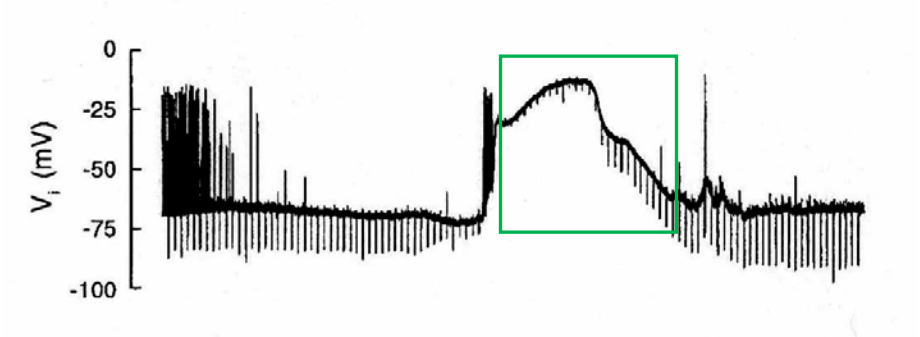
*** Connection Established ****

Spreading Depolarizations

Spreading depolarizations = class of pathologic waves characterized by near-complete sustained depolarization of neurons/astrocytes that propagate through gray matter at 1-5 mm/min



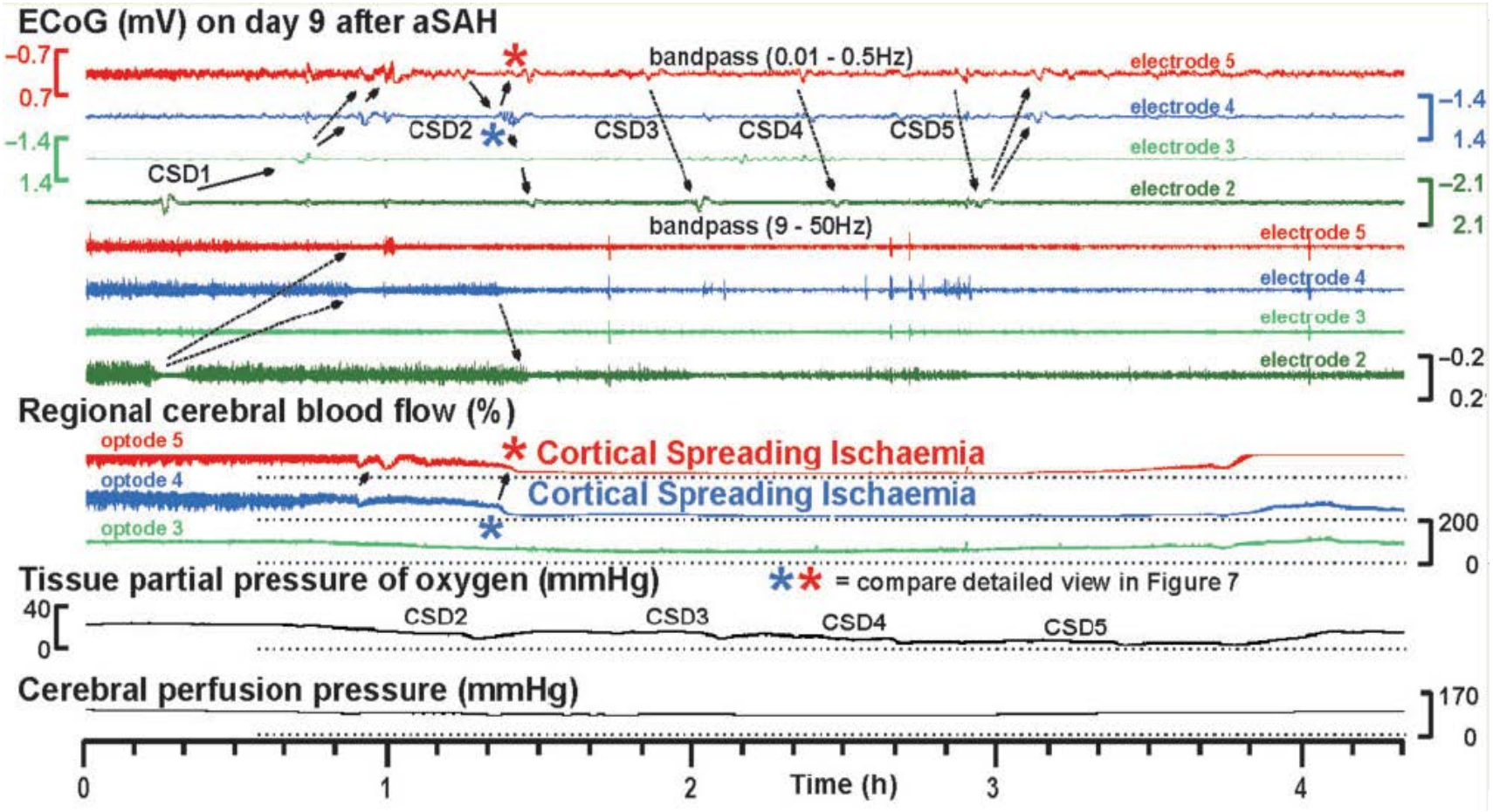
Physiological biomarker of brain injury.



https://www.charite-academy.de/

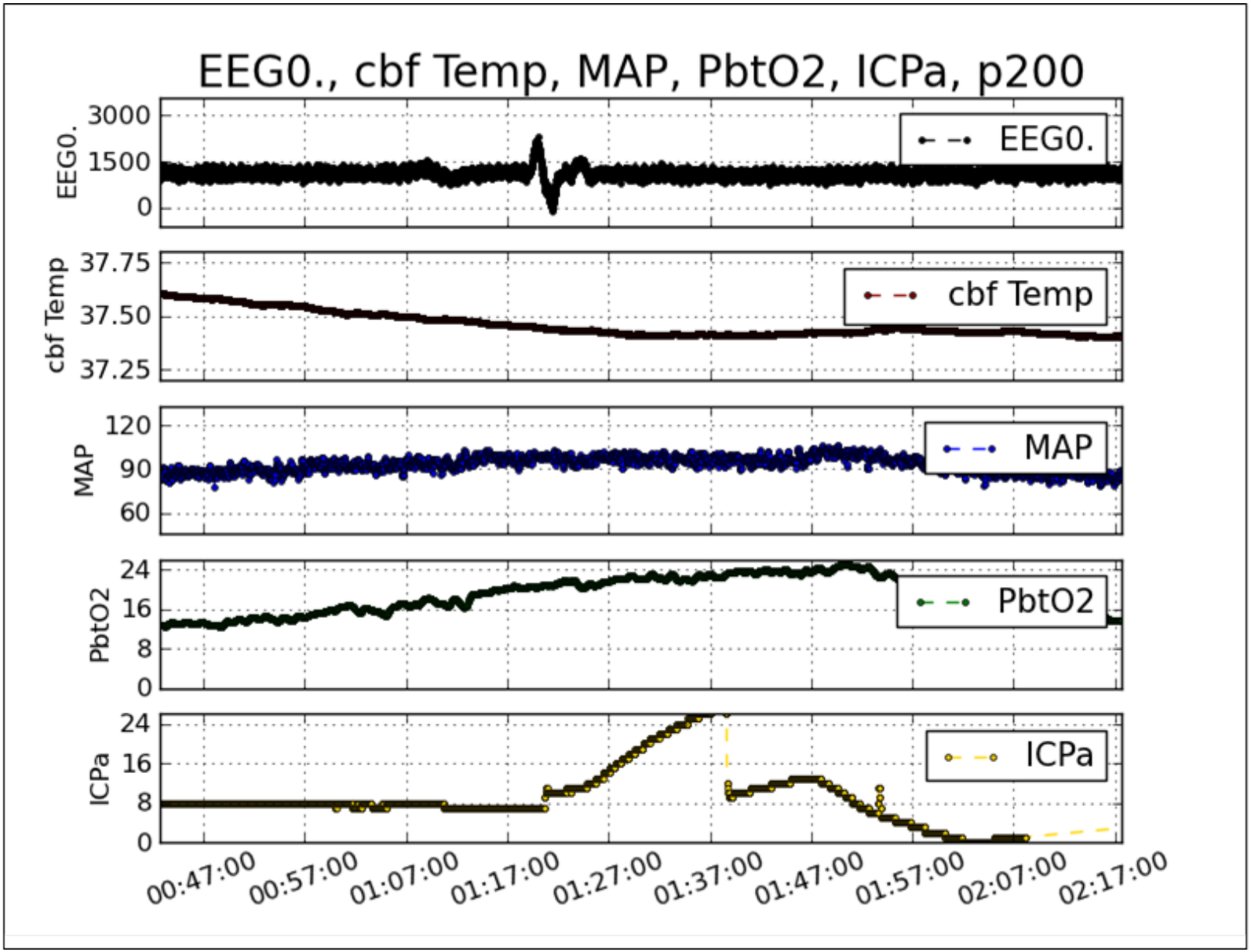
www.YouTube.com/MobergICUSolutions

SDs – Prolonged perfusion deficits

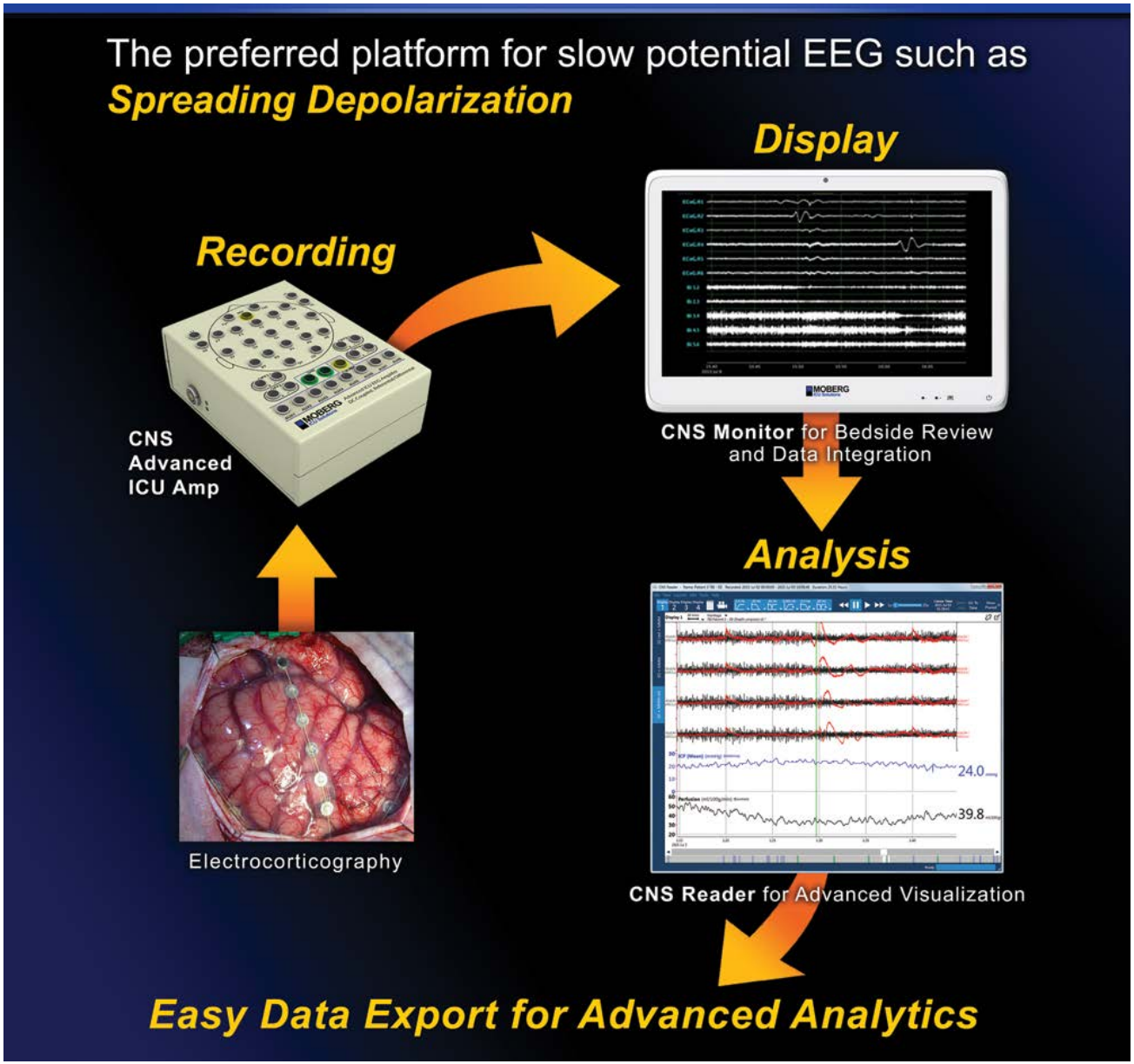


Dreier et al., Brain 132 (Pt7): 1866-81, 2009

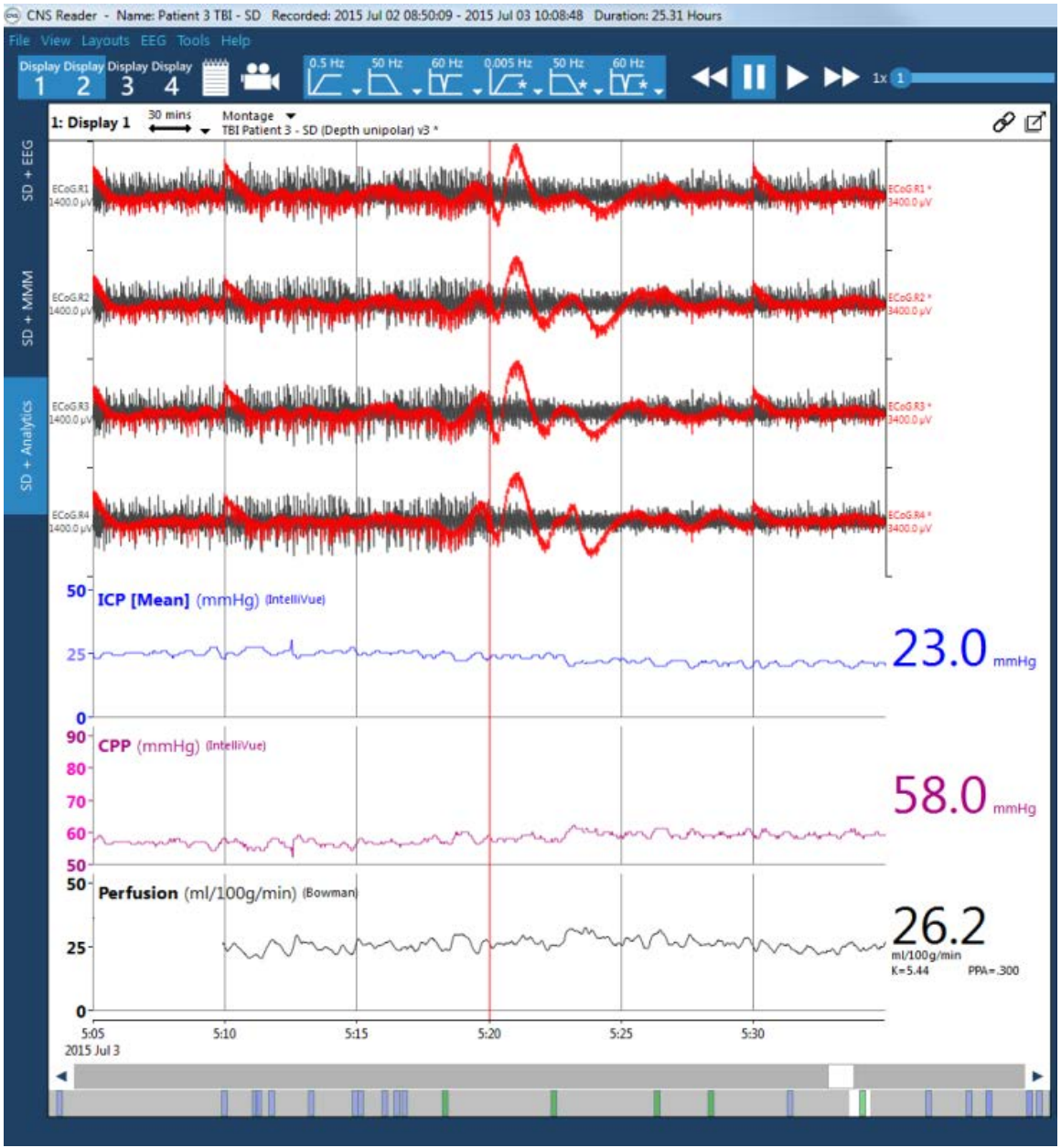
SDs - Correlates to other physiology



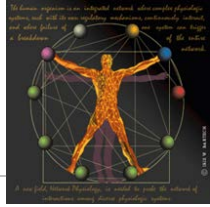
Preferred Platform



SD App Display



Two Parallel Stories



1970s

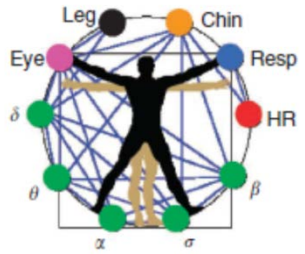
Secondary Injury in Spinal Cord	Secondary Injury In Brain but No Successful Trials	Secondary Injury In Brain - Progress

Traumatic Brain Injury

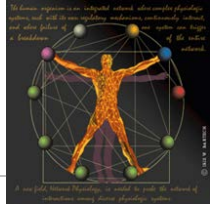
Brain Monitoring

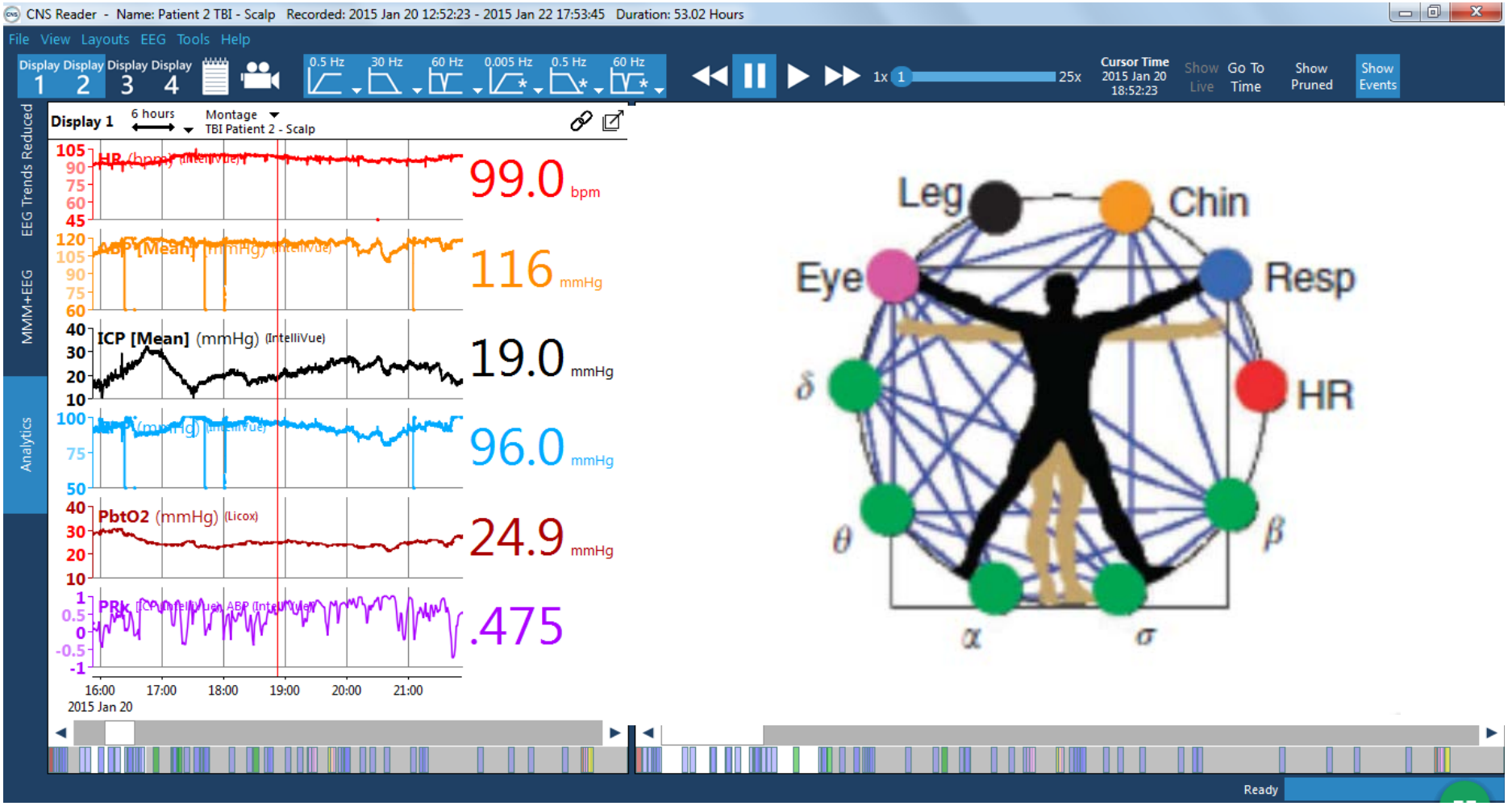
Single Metrics - ICP - EEG - GCS	Multimodal Monitoring	Brain Record Tools

Remaining Work



Brain Injury and Network Physiology



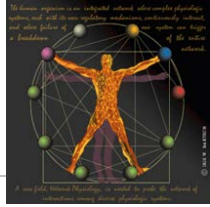


Brain Systems

What system interactions do we explore?

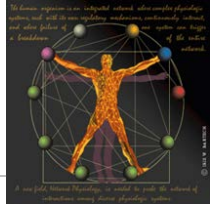
- Start simple
- Not all data on every patient
- Append to existing trial

Some ideas for Network Physiology



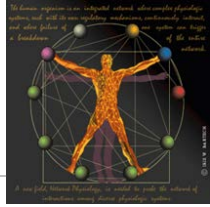
- NP can help quantify endpoint of TBI
  - Example is sleep after TBI
- Determination of Patient State
  - Detect a downward transition
- Origin of seizures
- Blood pressure management.
  - We lose the “network connection”…the neurovascular coupling in TBI.

Conclusions



- Neuro is about 30 years behind cardiology
  - Due to complexity of the brain and monitoring technology
  - Look at what's going on in cardiac…this is where neuro will be
- We are just starting to get data that can answer questions
  - This area is ripe for investigation
  - We don't even know the questions to ask in some areas
- Funding seems to be available

Advice



- Starting a company, being an entrepreneur
  - Extremely rewarding, extremely risky
  - Never had a boss
    - Always worked for myself
    - Never been married
- My Mentor was/is Making Mistakes
- I am amazed at how much “luck” played in the success of my company
- One of the most important characteristics that helped me was “persistence”
- Follow your passion, the money will follow