Hyperbaric Medicine & Acquired Brain Injury

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Faculty Disclosure For: Dr. A.W. Evans

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- Educational Support - ONF
- Consultation Service Provider in Hyperbaric Medicine .
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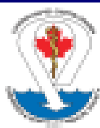

CANADIAN CHAPTER -CHAPITRE CANADIEN

Friday Oct. 21 (WorkSafeBC, Richmond, BC)

Clinical hyperbaric medicine

07:30 – 08:15	Registration
08:15 – 08:20	Introduction and welcome – Ken LeDez
08:20 – 08:25	Greetings from the Undersea and Hyperbaric Medical Society – Tom Workman
08:25 – 08:30	Welcome from the Medical Director, Vancouver Hyperbaric Unit – Dr. David Harrison
08:30 – 08:35	Welcome on behalf of WorkSafeBC
	Clinical hyperbaric medicine 1: Wounds / Complications / Safety
08:35 – 09:00	Wound assessment and care and the role of hyperbaric oxygen – Dr. Ron Linden
09:00 – 09:25	Integrated wound management – Dr. Richard Belley
09:25 – 09:55	Long lasting influence of HBOT on cardiovascular parameters among patients - Marie-Ludivine Chateau-Degat, PhD
09:55 – 10:30	Clinical hyperbaric safety issues – Kevin "Kip" Posey, International Atmo Inc.
10:30 – 10:50	**Coffee / exhibits / posters**
	Clinical hyperbaric medicine 2: Standards / accreditation
10:50 – 11:05	Quality assurance in hyperbaric medicine units – Dr. David Harrison
11:05 – 11:20	Standards of practice in Canadian hyperbaric medicine – Dr. Ken LeDez
11:20 – 11:40	UHMS accreditation program for clinical hyperbaric facilities – Tom Workman
11:40 – 11:55	Accreditation of Canadian hyperbaric treatment facilities – Dr. Ron Linden

	Clinical hyperbaric medicine 4: Complications / Training / Controversies
15:45 – 16:15	Immersion pulmonary edema – Dr Michael Koehle
16:15 – 16:45	HBOT for the treatment of post-concussive syndrome following mild traumatic brain injury: Initial results and lessons learned – Steven L. West, PhD
16:45 – 17:10	Traumatic brain injury and HBOT – summary of Toronto meeting – Dr. Wayne Evans
17:10 – 17:30	Discussion

	• Wound healing case – Dr. Ron Linden
15:00 – 15:20	Staff and patient fitness for hyperbaric exposure – Dr. Dominique Buteau
15:20 – 15:45	**Coffee / exhibits / posters**
	Clinical hyperbaric medicine 4: Complications / Training / Controversies
15:45 – 16:15	Immersion pulmonary edema – Dr Michael Koehle
16:15 – 16:45	HBOT for the treatment of post-concussive syndrome following mild traumatic brain injury: Initial results and lessons learned – Steven L. West, PhD
16:45 – 17:10	Traumatic brain injury and HBOT – summary of Toronto meeting – Dr. Wayne Evans
17:10 – 17:30	Discussion
19:00	**Reception / banquet (Guest of honour, Dr. Michael Lepawsky)**

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HBOT and TBI

Exploring the potential of hyperbaric oxygen therapy in the treatment of traumatic brain injury

Workshop Time and Location

SEPTEMBER 12, 2011 BY ABI RESEARCH LAB LEAVE A COMMENT

Hyperbaric Oxygen Therapy and Traumatic Brain Injury Workshop
September 16, 2011

Chestnut Conference Centre, St. Patrick Room

University of Toronto

89 Chestnut Street

Toronto ON M5G 1R1

Learning Objectives: By the end of the session participants will:

- be acquainted with literature which supports the physiologic effects of HBOT utilized for patient benefit in ABI.
- appreciate the nature of risk assessment issues to avoid hyperbaric environment hazards.
- Consider some research designs for developing next steps.

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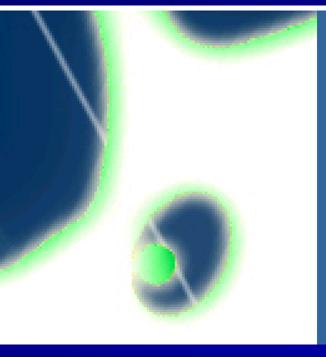

The Toronto Hyperbaric Medicine Symposium 2008

Neurological Aspects of Hyperbaric Medicine

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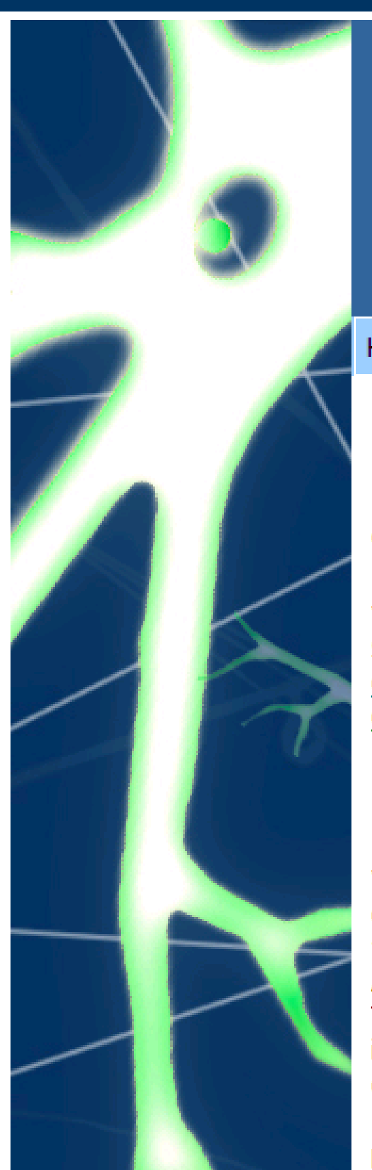
Return to HyperbaricMedicine.ca



The Toronto Hyperbaric Medicine Symposium 2008

Neurological Aspects of Hyperbaric Medicine

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NASA and the US Congress gives THMS a thumbs up.

We are now officially supported by the United States Congress and NASA.
Click Here for the US Congress Letter
Click Here for the NASA Letter

New Schedule and Speakers!

We're pleased to welcome **Dr. Nora Cullen** to our speakers list! Dr. Nora Cullen comes to us from the Toronto Rehab Institute and is an Associate Professor at the University of Toronto. She will be discussing the interdisciplinary approach to the management of traumatic brain injury.

Please note that the schedule has been

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Hyperbaric oxygen for neurologic indications

Action plan for multicenter trials in:
stroke, traumatic brain injury,
radiation encephalopathy & status
migrainosus

Helms A, Evans AW, Chu J, Sahgal A, Ostrowski R,

Sosiak T, Wolf G, Gillet J, Whelan H

Wayne Evans, M.D.

Hyperbaric oxygen for neurologic indications

Action plan for multicenter trials in: stroke, traumatic brain injury, radiation encephalopathy & status migrainosus

HELMS A[1], EVANS AW[2], CHU J[2], SAHGAL A[2], OSTROWSKI R[3], SOSIAK T[4], WOLF G[5], GILLETT J[6], WHELAN H[1]

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[2] University of Toronto, Toronto, Canada
[3] Loma Linda University School of Medicine, Loma Linda, California, USA
[4] Toronto General Hospital, Toronto, Canada
[5] Brooks Air Force Base, Brooks City Texas, USA
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ABSTRACT

The 2008 Toronto Hyperbaric Medicine Symposium was convened to discuss research into neurologic indications [illegible] oxygen therapy (HBO_2T). Four topics were particularly addressed:

Hyperbaric oxygen for neurologic indications

Action plan for multicenter trials in:
stroke, traumatic brain injury,
radiation encephalopathy & status
migrainosus

Helms A, Evans AW, Chu J, Sahgal A, Ostrowski R,

Sosiak T, Wolf G, Gillet J, Whelan H

Wayne Evans, M.D.

Purpose

To develop and publish for public comment plans for randomized trials of hyperbaric treatment in neurologic conditions.

Four conditions were specifically targeted for future projects and clinical trials:
1) stroke
2) traumatic brain injury
3) radiation-induced necrosis
4) status migrainosus.

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Stroke

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Specific Aim

To determine whether the use of HBOT in the treatment of acute ischemic stroke is effective at improving outcomes.

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Rationale

- At the center of an infarct, blood flow is completely absent, causing neurons to die within a matter of minutes. This area, therefore, may not be amenable to treatment after the start of symptoms.
- The region of the brain that draws the most interest is the penumbra, where evidence has shown that blood flow is diminished, but not absent.
- The cells in this region remain viable for a prolonged period, and can be saved if adequate perfusion is restored.

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Rationale

- Cells subjected to prolonged ischemia will inevitably undergo apoptosis, either after prolonged ischemia or due to reperfusion injury.
- Interest in using HBOT for the added benefit of its anti-inflammatory and anti-apoptotic properties
- On MRI, penumbra is represented by perfusion diffusion mismatch (in animal & human studies).
  - In the rat focal ischemic stroke (middle cerebral artery occlusion), MRI revealed perfusion-diffusion mismatch persist up to 6-12 hours after the occlusion.
  - In patients such mismatch is usually present during the first six hours after stroke.*

*Chen 2008

Rationale

- Damage from focal cerebral ischemia is ameliorated after treatment with HBOT
  - Therapeutic window of 6 - 12 hours suggested by previous animal studies.
- HBOT was effective against experimental stroke if administered when a penumbra is typically present in the brain.*
- 3 randomized controlled studies that have evaluated HBOT
  - utilized HBOT beyond therapeutic window or lower dose than suggested by previous animal studies.

*Zhang 2005

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Study Design

- Acute Intervention
- RCT
- Blinded
- Placebo = air at minimal pressure

- Outcomes
  - Primary - mRS & NIHSS Neurological Scales
  - Secondary –
    - Barthel Index & GOS
    - Length of hospital stay, rate of ICH, mort

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Criteria

Inclusion

- Must be 18 years old
- Score ≥ 4 on National Institute of Health Stroke Scale (NIHSS)
- Treatment must begin ≤ 6hr onset of Sx
- If tPA candidate; must complete their tPA treatment prior to undergoing HBOT.
- MRI scan will be performed with diffusion-weighted and perfusion-weighted sequence to assess for the presence of a penumbra.

Exclusion

- Premorbid mRS >1
- Intracerebral hemorrhage (ICH)
- Intracranial pathology-
- Need for surg intervention
- ABG drawn, and chest X-ray done assessing for pulmonary disease (can be contraindication for HBOT)

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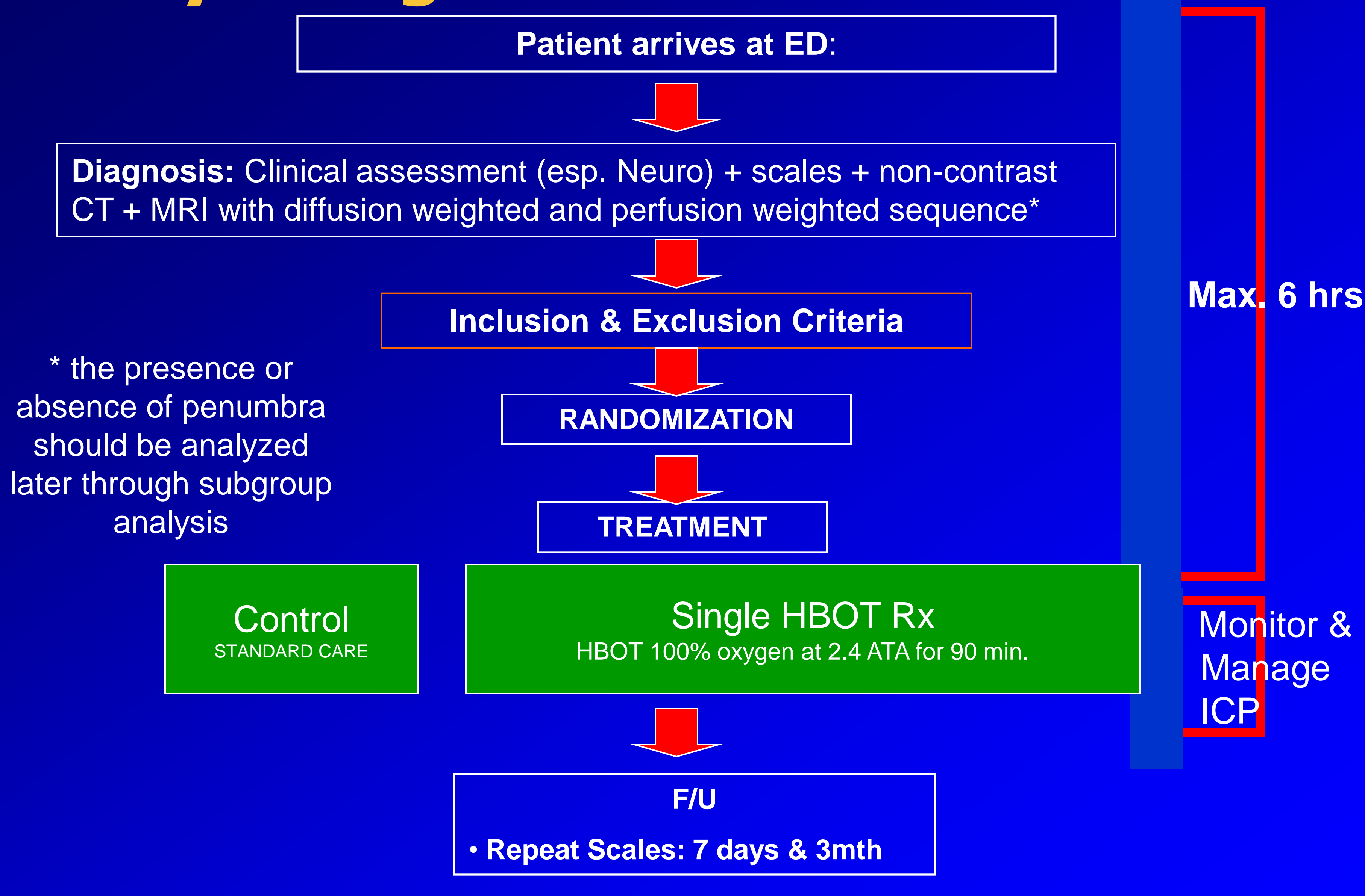
Study Design Stroke



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Traumatic Brain Injury

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Specific Aim

1) To determine whether use of HBOT in the acute state after traumatic brain injury is effective at improving functional and mortality outcomes.

2) To determine whether use of HBO_2T in the acute state after traumatic brain injury is effective at reducing elevated intracranial pressure (ICP).

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Rationale

- The primary injury to the brain sustained at the time of the trauma is usually not reversible.

HOWEVER

- The secondary injury occurring in the hours and days following the initial injury that provides more opportunities for treatment to preserve tissue and function.

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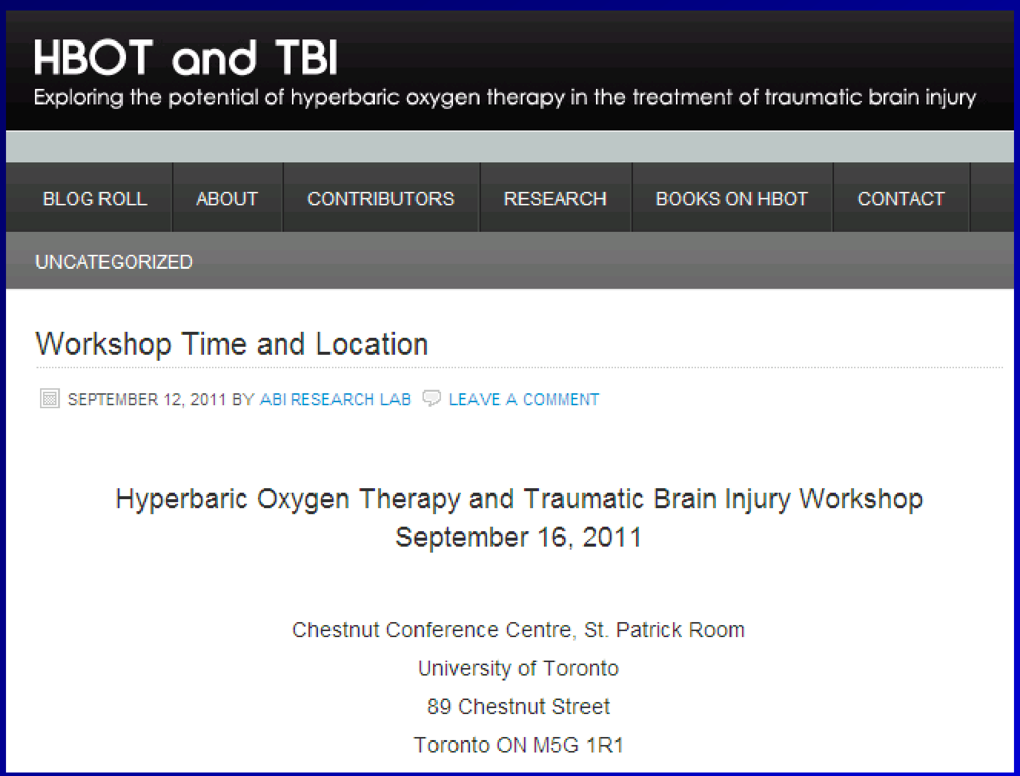
Contributing Factors

- hypoxia
- edema
- apoptosis



http://hbotandtbi.wordpress.com/

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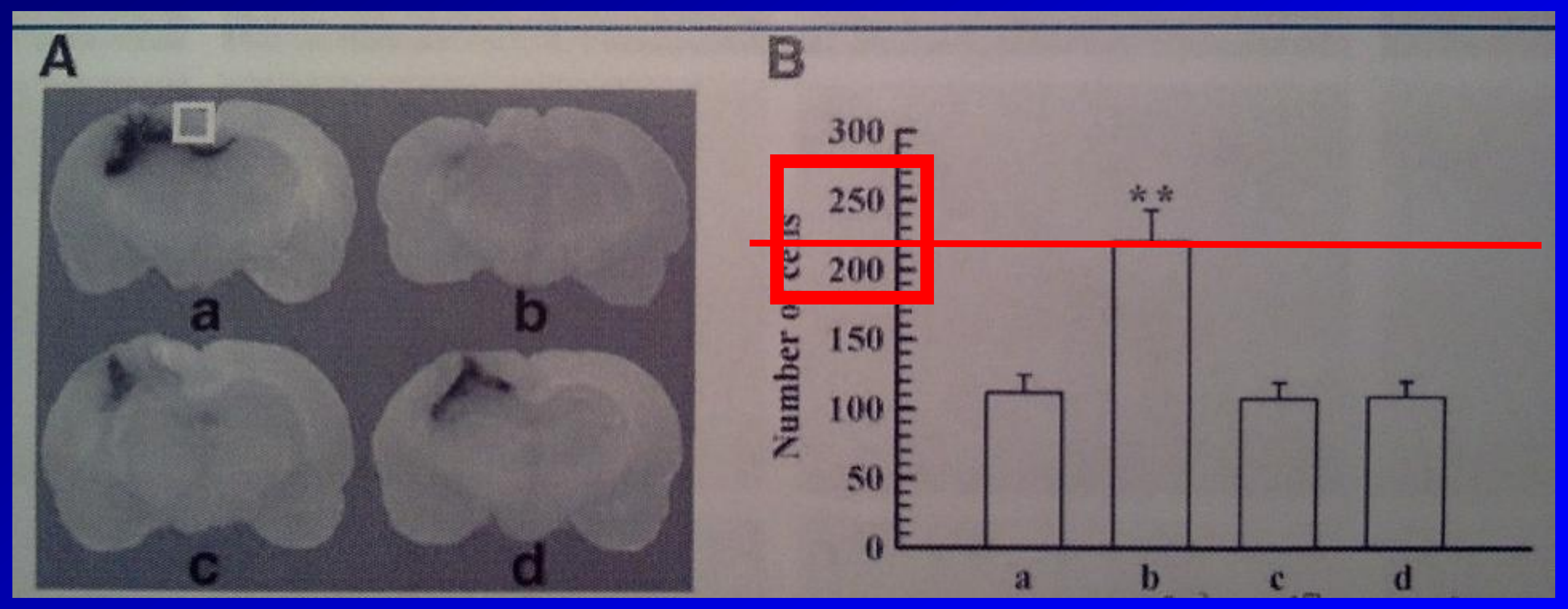
Wang 2010

- Pre-clinical - rat
- Injury – 20g drop
  a. Control
  b. HBO - 3ATA oxygen
  c. Normobaric oxygen
  d. HBA - 3ATA air
- Measurements
  a. Behavior , water content , cellularity

Wang 2010



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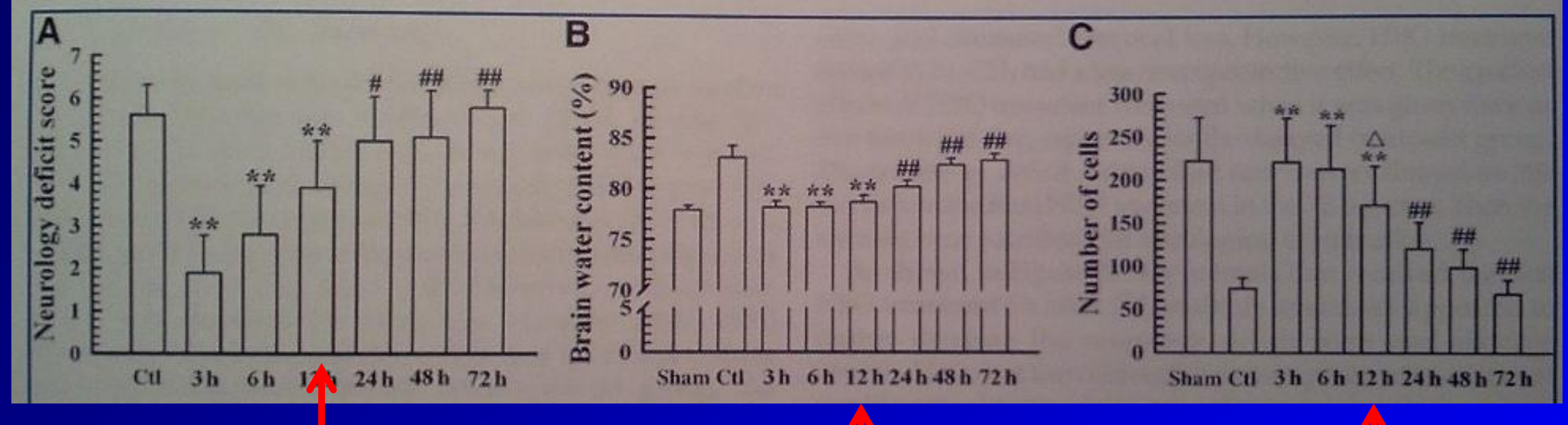

Wang 2010

- Time to treatment
  a. 3 hr 6 hr 12 hr linear loss of effect
  b. by 24 hr little effect ~ control
  c. by 48 hr ~ no effect
  d. by 72 hr no effect

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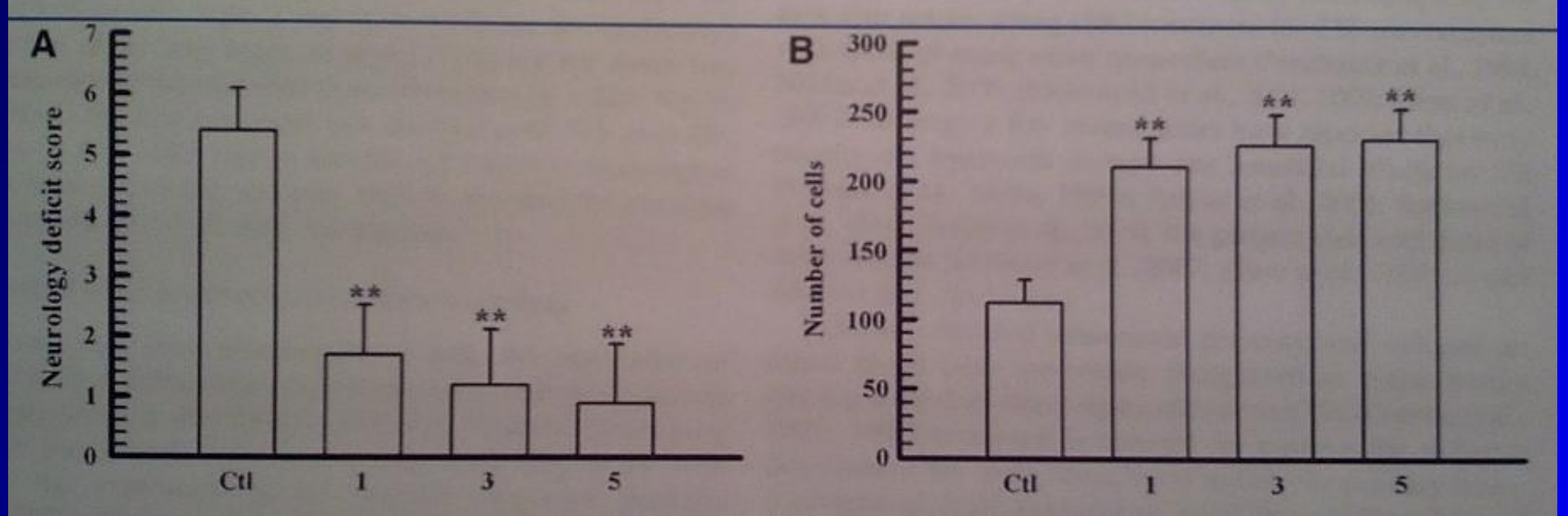

Wang 2010

- Multiple treatment 0 / 1 / 3 / 5

  1st treatment at 6 hr

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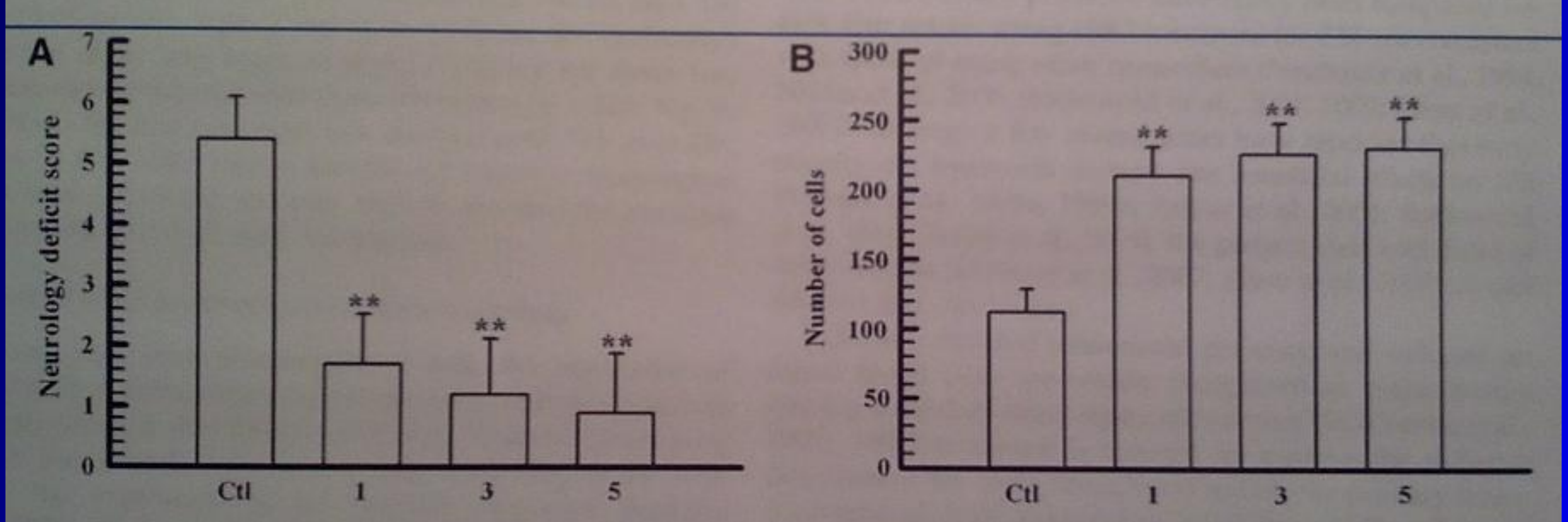

Wang 2010

- Multiple treatment

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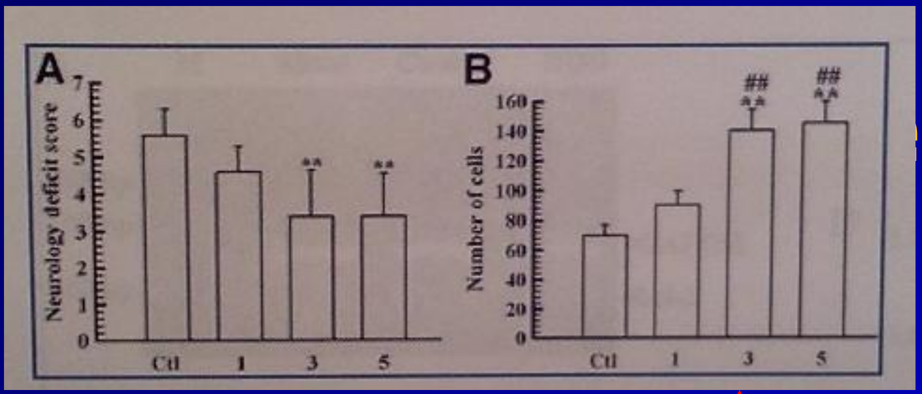

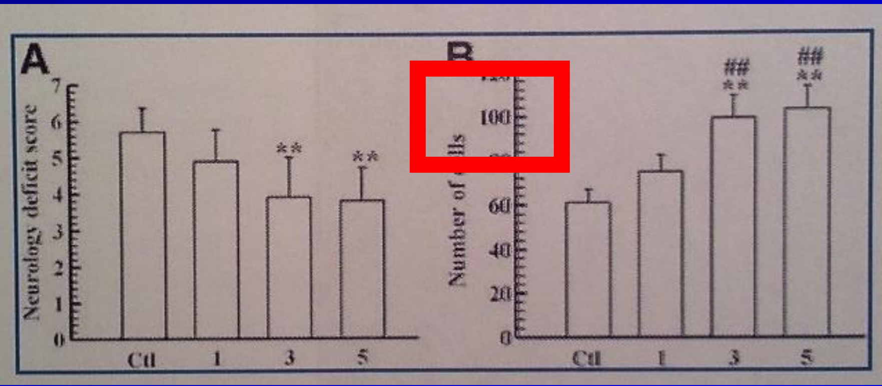

Wang 2010

- Multiple treatment

  1st treatment at 24 hr

  1st treatment at 48 hr

Rockswold 2010

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Rockswold 2010

- N=80
- RCT
- Severe
- Acute
- 1.5 ATA x 60 min
- Lowered ICP x 3 days

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Glasgow Coma Scale (GCS)

Eye Opening	Points
Eyes open spontaneously	4
Eyes open to verbal command	3
Eyes open only with painful stimuli	2
No eye opening	1
Verbal Response	
Oriented and converses	5
Disorented and converses	4
Inappropriate words	3
Incomprehensible sounds	2
No verbal response	1
Motor Response	
Obeys verbal commands	6
Response to painful stimuli (UE)	
Localizes pain	5
Withdraws from pain	4
Flexor posturing	3
Extensor posturing	2
No motor response	1

Total score = eye opening + verbal + motor

GCS<5: 80% die or remain vegitative

GCS>11: 90% complete recovery

Glasgow Coma Scale (GCS)

(Max is 15)

- Severe (GCS) ≤ 8
- Moderate (GCS) 9 - 12
- Mild (GCS) ≥ 13

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Effect of hyperbaric oxygen on patients with traumatic brain injury

J. W. Lin[1,2], J. T. Tsai[3,4], L. M. Lee[5,6], C. M. Lin[1,2], C. C. Hung[7], K. S. Hung[1], W. Y. Chen[1], L. Wei[1], C. P. Ko[1], Y. K. Su[1], W. T. Chiu[1,6]

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Lin 2008

Table 3. *GOS outcome for the patients 3 and 6 months after HBOT*

		GOS3a without improvement	GOS3a with improvement	GOS6a without improvement	GOS6a with improvement	Total
GOSb = 2	HBOT	8	3	7	4	11
	control	8	2	7	3	10
GOSb = 3	HBOT	2	2	2	2	4
	control	4	2	3	3	6
GOSb = 4	HBOT	3	4	1	6*	7
	control	3	3	3	3	6
Total		28	16	23	21	44

$p <$ *GOSb* The patient's GOS before the HBOT or the same timing for the control group.
GOS3a The patient's GOS at 3-month post injury or at the same timing for control group.
GOS6a The patient's GOS at 6-month post injury or at the same time for control group.
* $p < 0.05$ with significant difference.

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Glasgow Outcome Scale

5-level score:

1. Dead
2. Vegetative State (meaning the patient is unresponsive, but alive; a "vegetable" in lay language)
3. Severely Disabled (conscious but the patient requires others for daily support due to disability)
4. Moderately Disabled (the patient is independent but disabled)
5. Good Recovery (the patient has resumed most normal activities but may have minor residual problems)

Lin 2008

Table 3. *GOS outcome for the patients 3 and 6 months after HBOT*

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GOSb = 2	HBOT	8	3	7	4
	control	8	2	7	3
GOSb = 3	HBOT	2	2	2	2
	control	4	2	3	3
GOSb = 4	HBOT	3	4	1	6*
	control	3	3	3	3

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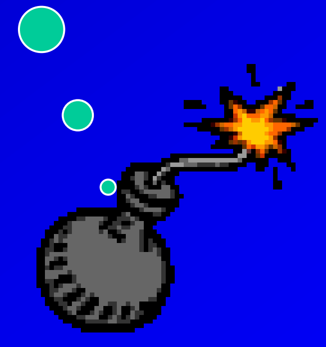
Lin 2008

- N=44
- CT – semi randomized
- Moderate to Severe
- Subacute (ave 28 days post insult)
- 2.0 ATA 90 min
- Improved GOS = 4 group at 6 mth

Proposed Study Design-TBI

- Acute Intervention
- RCT
- Non blinded
- No Placebo
- Severely traumatized
- Outcomes Neurological Scales
  - Primary - mRS
  - Secondary - Barthel Index & GOS



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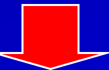
Study Protocol TBI

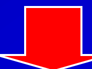
Patient arrives at ED:

Diagnosis:

- Neuro assessment
- Scales
- MRI with diffusion -weighted imaging



Inclusion & Exclusion Criteria



RANDOMIZATION

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Diagnosis

- Clinical Assessment
  - diagnosis of severe TBI = Glasgow Coma Score (GCS) ≤ 8 at time of presentation

Diagnosis

- Clinical Assessment
  - diagnosis of severe TBI = Glasgow Coma Score (GCS) $\leq$ 8 at time of presentation
  - estimate HBOT risks
    - Absolute contraindications
    - Relative contraindications

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HBOT SAFETY - Occupant Selection

- Physical Condition
  - Absolute Exclusions
    - Risk of gas trapping in Lungs

HBOT SAFETY - Occupant Selection

- Physical Condition
  - Absolute Exclusions
    - Risk of gas trapping in Lungs
  - Relative Contraindications
    - Ears / Sinuses
    - Confinement issues / CNS O2 Toxicity
    - Medically Compromised
      - Heart - LV Function
      - Glucose - DM

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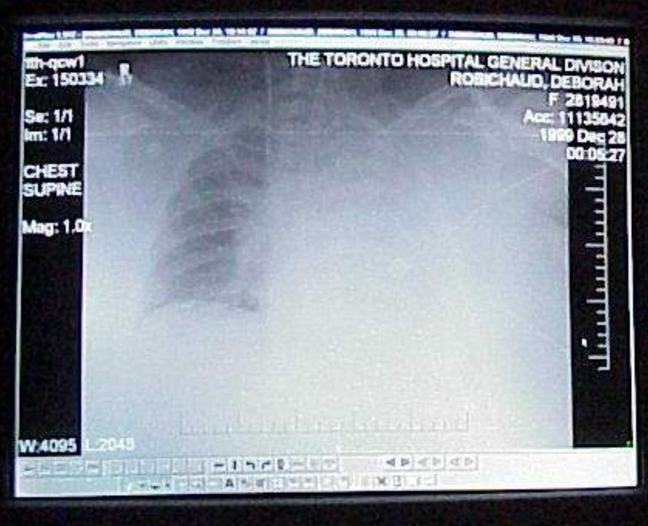
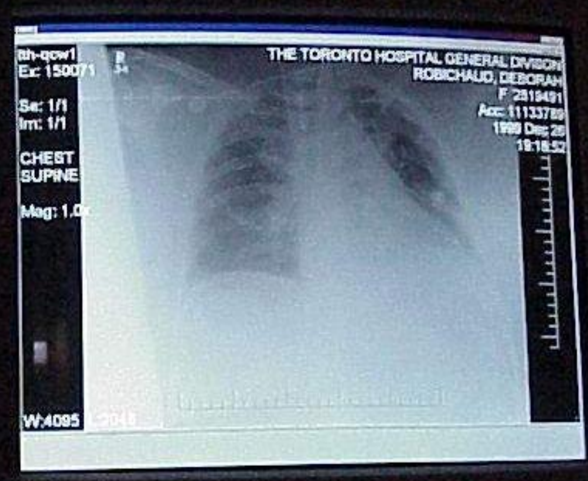
Fluid overload / CHF





Diagnosis

- Clinical Assessment
  - diagnosis of severe TBI
  - estimate HBOT risks
- Imaging – diffusion weighted MRI
  - confirm type and extent of injury
  - assess for intracranial pathology
  - baseline for comparison

Diffusion Weighted Imaging (DWI)

- In (DWI), each image voxel (three dimensional pixel) has an image intensity that reflects a single best measurement of the rate of water diffusion at that location.
- This measurement is more sensitive to early changes after a stroke than more traditional MRI measurements such as T1 or T2 relaxation rates.

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Diagnosis

- Clinical Assessment
  - diagnosis of severe TBI
  - estimate HBOT risks

- Imaging – diffusion weighted MRI
  - confirm type and extent of injury
  - assess for intracranial pathology
  - baseline for comparison

- Neurological Performance Scales
  - mRS = Modified Rankin Scale
  - Barthel Index
  - GOS = Glasgow Outcomes Scale

Modified Rankin Scale (mRS)

0 - No symptoms.
1 - No significant disability. Able to carry out all usual activities, despite some symptoms.
2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3 - Moderate disability. Requires some help, but able to walk unassisted.
4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6 - Dead

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- There are ten variables addressed in the Barthel scale.
- It is a scale used to measure performance in basic Activities of Daily Living.

THE BARTHEL INDEX

Patient Name: ____________________
Rater Name: ____________________
Date: ____________________

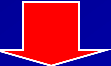
Activity	Score
FEEDING 0 = unable 5 = needs help cutting, spreading butter, etc., or requires modified diet 10 = independent	____
BATHING 0 = dependent 5 = independent (or in shower)	____
GROOMING 0 = needs to help with personal care 5 = independent face/hair/teeth/shaving (implements provided)	____
DRESSING 0 = dependent 5 = needs help but can do about half unaided 10 = independent (including buttons, zips, laces, etc.)	____
BOWELS 0 = incontinent (or needs to be given enemas) 5 = occasional accident 10 = continent	____
BLADDER 0 = incontinent, or catheterized and unable to manage alone 5 = occasional accident 10 = continent	____
TOILET USE 0 = dependent 5 = needs some help, but can do something alone 10 = independent (on and off, dressing, wiping)	____
TRANSFERS (BED TO CHAIR AND BACK) 0 = unable, no sitting balance 5 = major help (one or two people, physical), can sit 10 = minor help (verbal or physical) 15 = independent	____
MOBILITY (ON LEVEL SURFACES) 0 = immobile or < 50 yards 5 = wheelchair independent, including corners, > 50 yards 10 = walks with help of one person (verbal or physical) > 50 yards 15 = independent (but may use any aid; for example, stick) > 50 yards	____
STAIRS 0 = unable 5 = needs help (verbal, physical, carrying aid) 10 = independent	____

TOTAL (0–100): ____

.D.

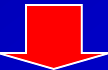
Study Design TBI

Patient arrives at ED:

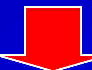


Diagnosis:

- Neuro assessment & full clinical
- Scales
- MRI with diffusion -weighted imaging



Inclusion & Exclusion Criteria



RANDOMIZATION

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Inclusion

- Must be 18 years old
- Have Glasgow Coma Score (GCS) ≤ 8 at time of presentation

Exclusion

- Premorbid mRS >1
- Intracranial pathology-
- Need for surg intervention
- ABG drawn, and chest X-ray done assessing for pulmonary disease (can be contraindication for HBO2T)

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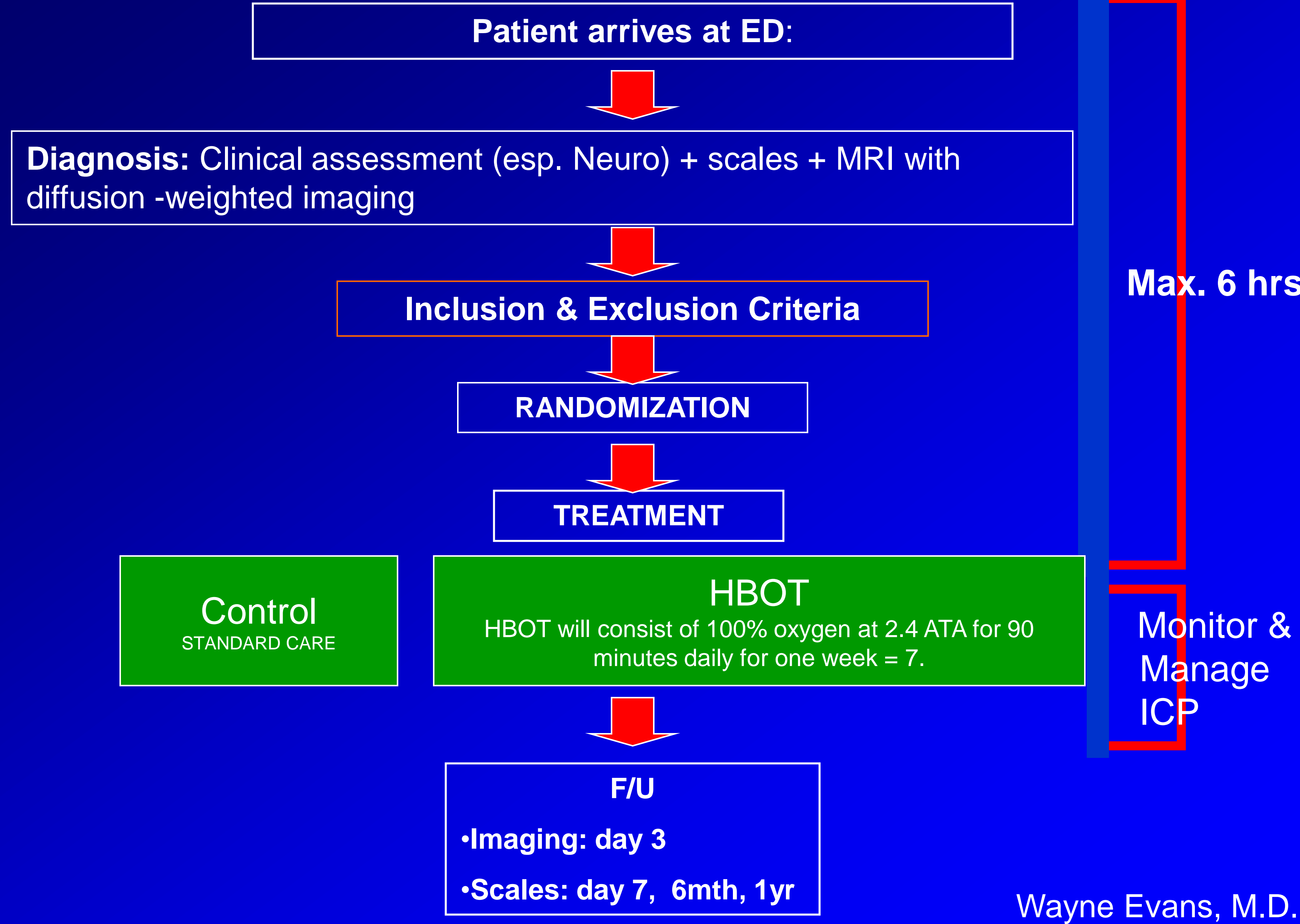
Study Design TBI



Protocol Rationale

- <6hr = Early intervention – avoid irreversible hypoxia and secondary insults
- 2.4 ATA intensity – ensure avoid missed efficacy due to under-dosing.
- Daily treatments x 7 -
  - Multiple-dose therapy because of the time course of secondary injury associated with TBI

Follow-Up

- repeat MRI @ 72 hours.
  - May pick up reduction in edema.
- mRS, Barthel Index and GOS
  - 7 days
  - repeat again at six and 12 months.

Radiation-Induced Cerebral Necrosis

Wayne Evans, M.D.

Specific Aim

To determine whether HBOT treatment of radiation-induced cerebral necrosis (RICN) of brain results in improvement of neurological function and reduction of necrosis.

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Proposed Study Design

- RCT
- Non blinded
- No Placebo
- Outcome - Primary
  - progression, stabilization or resolution of
    - Clinical symptoms
    - MRI imaging - RECIST criteria
- Outcome – Secondary – HVLT; steroid use

Hopkins Verbal Learning Test

Response Evaluation Criteria in Solid Tumors

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Criteria

Inclusion

- Must be 18 years old
- Bx negative
- MRI of the brain with gadolinium and evidence of a lesion in the radiation field that is consistent with RICN

Exclusion

- Recurrent tumor
- Currently receiving chemotherapy or radiotherapy.
- Other sites of disease progression (full staging investigations needed for patients with non-primary brain cancers)

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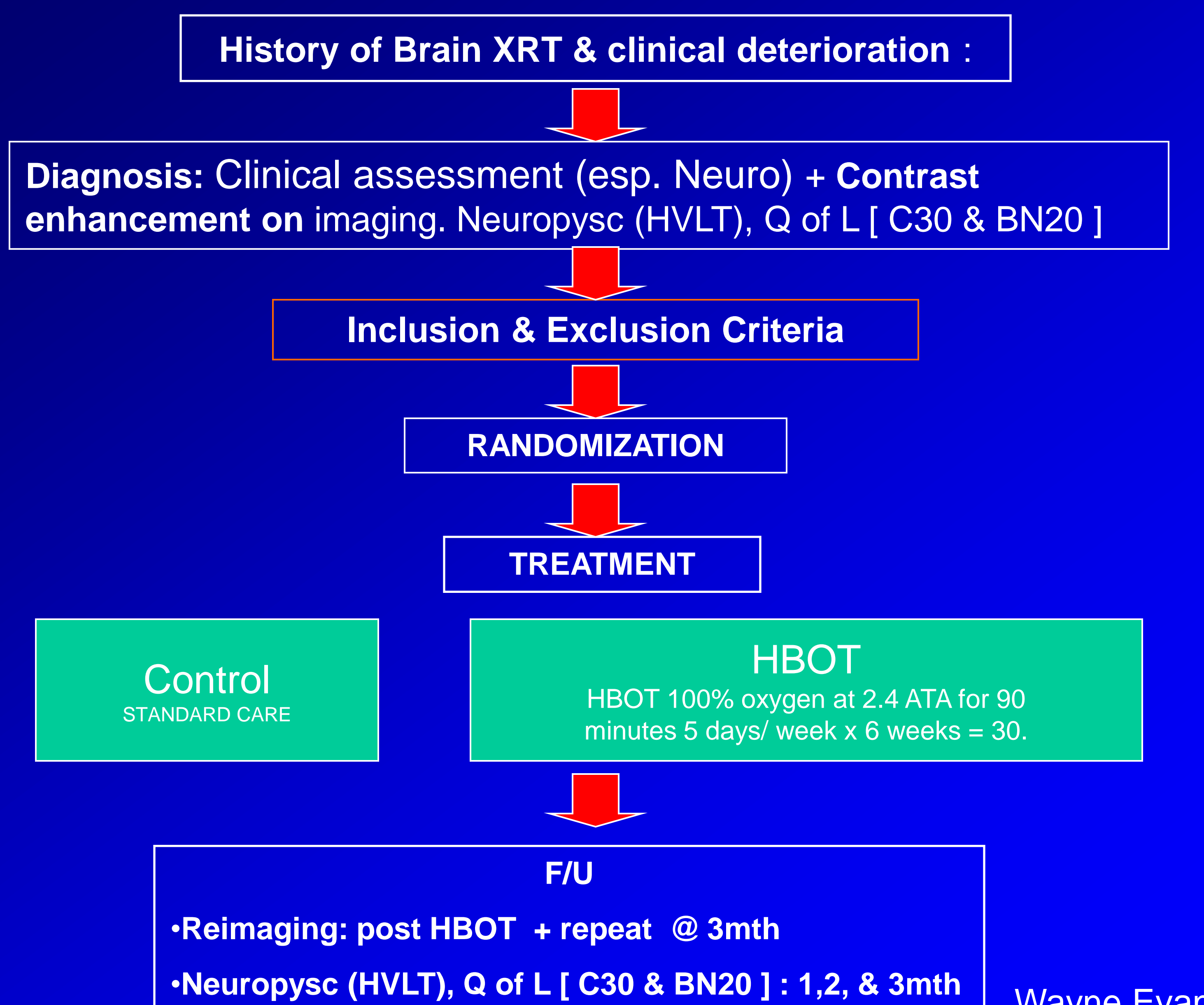
Study Design RICN (Radiation-Induced Cerebral Necrosis)



Underlying HBOT Mechanisms

- *Familiar*
  - **Oxygen delivery to ischemic tissue**
- *Less Familiar*
  - **Anti-apoptosis properties**
  - **Anti-inflammatory properties**
  - **Vasoactive properties**

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Current - Clinical Studies.gov

Lead	n	TBI Severity	Acuity	Extent [#Rx]	Intensity ATA x min.	controlled	placebo control parameters ATA x FiO2	Notes
Wright & Harch	1000	M/Mo	C	40-80	1.5x60bid	no		10 US sites
Wolf & Michealson	50	M/Mo	C	30	2.4 x 90	RCT	1.3 x 0.21	Measure pre&post 6/52
Churchill & Miller	96	M; PTSD	C	40	1.5 x 60	RCT	1.2 x 0.25	Must choose 1for Ph3 trial
Cifu & Hart & West	60	M	C	40	2.0 x 60 or 1.5x0.75	RCT	2.0 x0.105	1-Sx; 2 - Neuro/Function Measure pre/post 1-3/7;post 3/12

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Migraine

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Specific Aim

To determine whether use of HBOT will relieve headache pain in status migrainosus.

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Spinal Cord Injury

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