# HBOT:
# MECHANISMS OF ACTION

**HBOT's mechanisms of action are well known and well characterized both in scientific literature and in clinical practice.**

**Translational Medicine Methods are Necessary to make these treatments for these conditions ROUTINE!**

Typical Monoplace Hyperbaric Chamber

Typical Multiplace Hyperbaric Chamber

**Hyperbaric Medicine has been used for 75 years to treat brain insults!**

**HBOT is approved and on-label for 13 indications and treatment is reimbursed by all major third party payers including Medicare, Tricare and the Veterans Administration.**

**Hyperbaric oxygen therapy is the only non-hormonal treatment approved by the FDA for biologically repairing and regenerating human tissue.**

**It is FDA-approved and effective for the treatment of 3 kinds of non-healing wounds.**
**It is currently FDA-approved as the primary treatment for 3 different kinds brain injuries: carbon monoxide poisoning, arterial gas embolism, and cerebral decompression sickness.**

**Hyperbaric Oxygen Therapy is not Black-Labeled by the FDA, as are many drugs currently being prescribed off-label for post-traumatic stress disorder or traumatic brain injury.**

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# FDA Accepted HBOT Indications

HBOT as used by the team is currently in use for 13 FDA-accepted indications (which means the manufacturer or practitioner can advertize those indications) by hundreds of physicians at nearly 1,000 locations across the nation, delivering approximately 10,000 treatments per day. The thirteen accepted indications for HBOT treatment include:

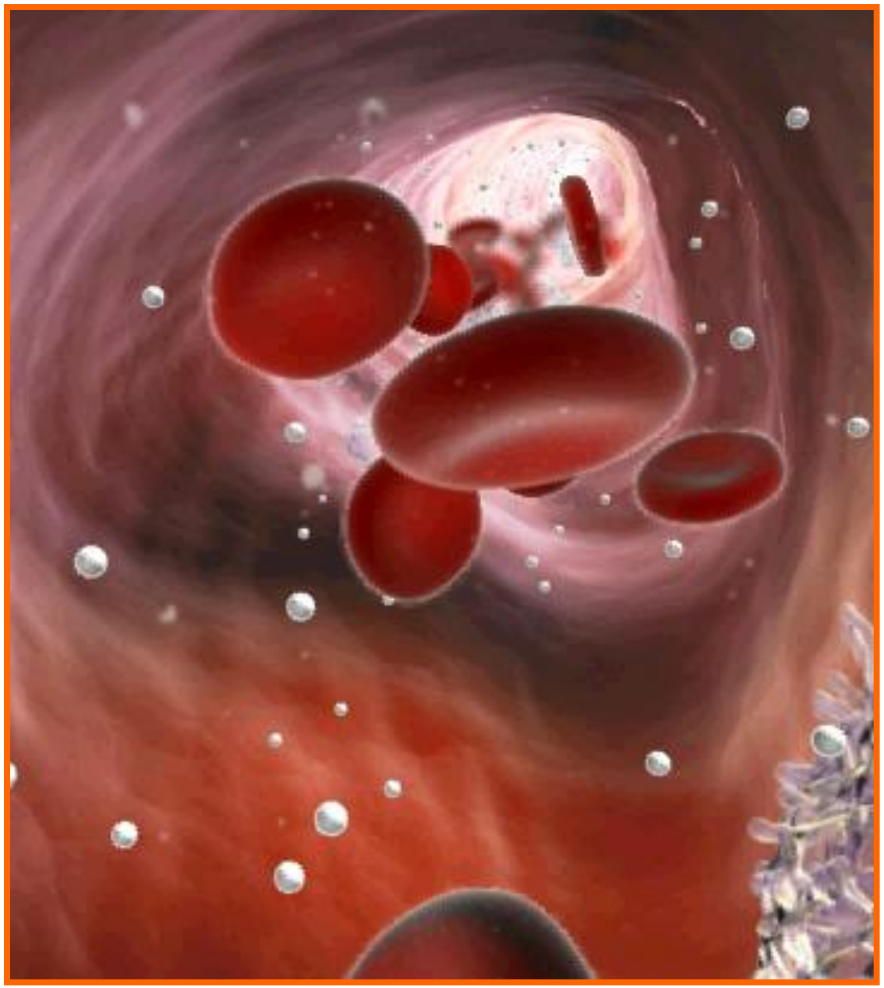
1. Air or gas embolism.
2. **CO poisoning, CO poisoning complicated by cyanide poisoning** ***(Neurological)***
3. Clostridial myositis and myonecrosis (gas gangrene)
4. Crush injury, compartment syndrome, and other acute traumatic ischemias
5. **Decompression sickness** ***(Neurological)***
6. **Arterial Insufficiency:** ***(Non-Healing Wound)***

   **Enhancement of healing in selected problem wounds** (includes uses like Diabetic Foot Wounds, Hypoxic Wounds, and other non-healing wounds, etc.)
7. Exceptional blood loss anemia
8. **Intracranial abscess** ***(Neurological)***
9. **Necrotizing soft tissue infections**
10. Osteomyelitis (refractory)
11. Radiation tissue damage (soft tissue and bony necrosis) ***(Non-Healing Wound)***
12. **Skin grafts and flaps (compromised)** ***(Non-Healing Wound)***
13. Thermal burns[1]

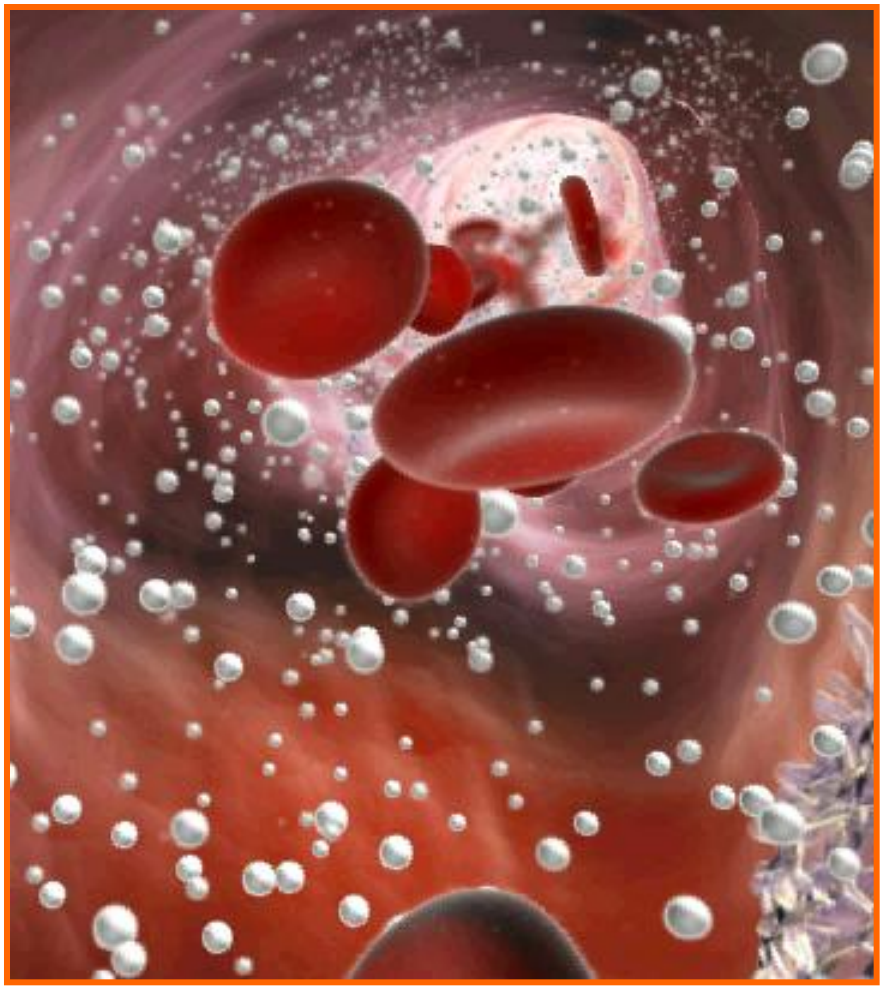
[1] Hyperbaric Oxygen Therapy: 1999 Committee Report. Editor, N.B. Hampson. Undersea and Hyperbaric Medical Society, Kensington, MD. See also: Harch PG. Application of HBOT to acute neurological conditions. Hyperbaric Medicine 1999, The 7th Annual Advanced Symposium. The Adams Mark Hotel, Columbia, South Carolina, April 9-10, 1999; and Mitton C, Hailey D. Health technology assessment and policy decisions on hyperbaric oxygen treatment. Int J of Tech Assess in Health Care, 1999;15(4):661-70.

# HBOT: It's About Oxygen Saturation

**The body's liquids are saturated with more oxygen, helping areas with compromised circulation.**



Before HBOT



After HBOT

Image Courtesy of Dr. Stoller

# Solution: It's Just Oxygen!

**HBOT: Oxygen is being used to repair an injury caused by a lack of oxygen!**

- **Simple: Lack of oxygen is bad**
- **O2 used in 5,769+ cellular processes**
- **HBOT activates 8,101 Genes!**
  - Down Regulates Inflammation Processes
  - Up Regulates Growth & Repair Processes
  - Normobaric O2 does not!
- **We know how HBOT works!**
  - Acutely stops swelling/reperfusion injury
  - Restarts stunned cellular metabolism
  - Restarts Stunned Mitochondria
    - Mitochondria then Request Oxygen (Blood Supply)
    - Body Re-grows Blood Vessels
  - Activates Stem Cells 8x Normal
    - to repair neural pathways
- **No wound can heal without oxygen**
  - Wounds that have not healed do
  - Wounds heal 50% faster with less scar tissue
  - Broken bones 30% faster & 30% stronger
- **Placebos have to have the potential of being inert.** Saturating injured tissue with any dose of oxygen has never been shown to have a placebo effect!

**Pressure causes oxygen to saturate tissues higher than normal breathing:**

**HBAT 1.3: 30%* more O2**

**HBOT 1.5: 700% or 7x**

**HBOT 2.4: 1200% or 12x**

HBAT is Compressed Air & HBAT 1.3 is the FDA Approved Treatment for Mountain Sickness

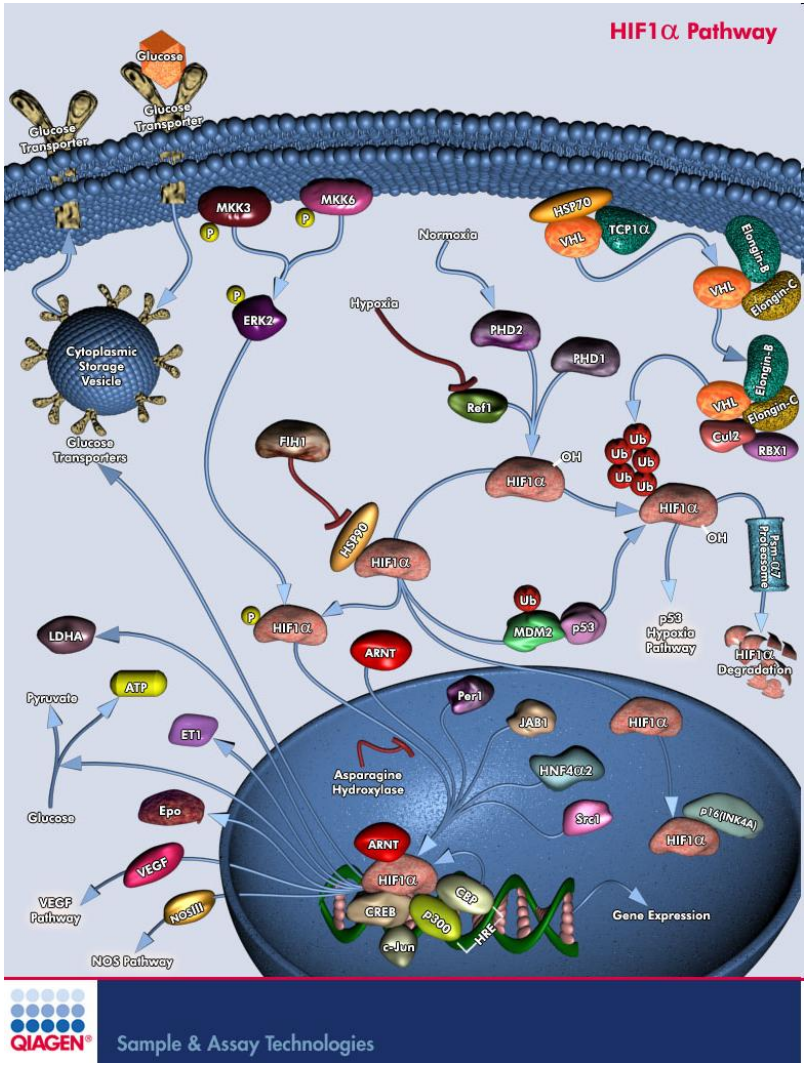
**HBOT is FDA-approved & available & On-Label for neurological conditions & non-healing wounds!**

*25% more O2 in tissues is so clinically significant that DoD medicine has spent millions in research trying to achieve it. It is already available on the battlefield with mountain sickness chambers using air!

# How Oxygen works - 5,769+* ways

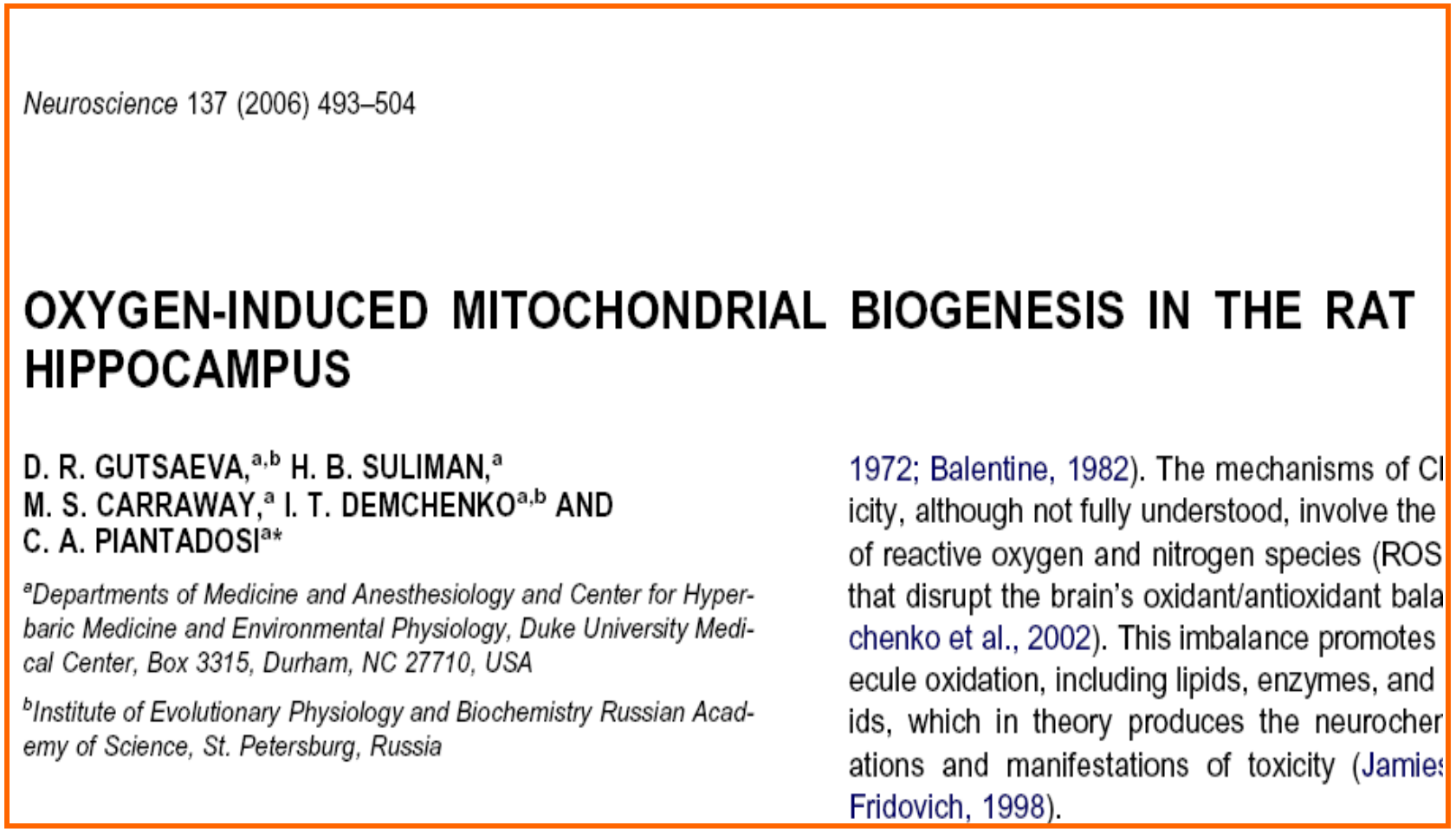
(~# of cellular processes studied)

- Upregulates growth factors
- Reduces edema/swelling
- Promotes neural pathway growth
- Activates senescent neurons [“sleeping”, not dead]
- Increases neuronal energy [ATP]
- Downregulates inflammation
- Reduces reperfusion injury [not enough O2]




*Rink C, Roy S, Khan M, Ananth P, Kuppusamy P, Sen CK, Khanna S. Oxygen-sensitive outcomes and gene expression in acute ischemic stroke. J Cereb Blood Flow Metab. 2010 Feb 10.

# HBOT: Its about the Mitochondria



*Neuroscience* 137 (2006) 493–504

## OXYGEN-INDUCED MITOCHONDRIAL BIOGENESIS IN THE RAT HIPPOCAMPUS

D. R. GUTSAEVA,[a,b] H. B. SULIMAN,[a]
M. S. CARRAWAY,[a] I. T. DEMCHENKO[a,b] AND
C. A. PIANTADOSI[a]*

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1972; Balentine, 1982). The mechanisms of Cl
icity, although not fully understood, involve the
of reactive oxygen and nitrogen species (ROS
that disrupt the brain's oxidant/antioxidant bala
chenko et al., 2002). This imbalance promotes
ecule oxidation, including lipids, enzymes, and
ids, which in theory produces the neurocher
ations and manifestations of toxicity (Jamies
Fridovich, 1998).

Image Courtesy of Dr. Stoller

# HBOT Acts on Mitochondria

## Restart Cellular Metabolism

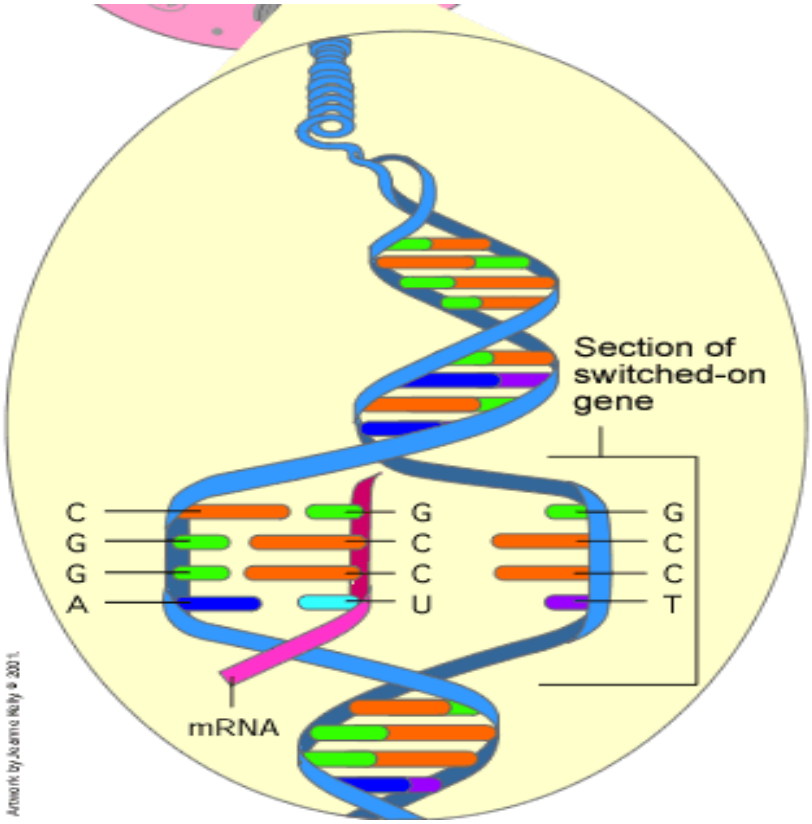
- Brain Death is diagnosed and declared when there is no blood in the brain. - Why?
- **The Brain is not asking for blood.** Why?
- The various cells in the brain are not asking for blood. Why?
- Mitochondria are not asking for Oxygen
- Idling Neuron-Lancet Letter
  - Neurons become Dormant before Death and can be reactivated by saturating body fluids with oxygen
- **Dormant Cells have now been found throughout the body, from hearts to lungs.**

## Request for Oxygen Supply

- **Dormant or stunned neuron mitochondria make 2 ATP**
- **HBOT Reactivated 36 ATP are made**
- **When Reactivated, mitochondria immediately begin requesting O2**
- **If O2 is not readily available because the blood supply has been compromised, DNA is signaled to start repair and grow a blood supply.**
- **HBOT-O2s Pulsed Dose in HBOT protocols keep the process going.**
  - **Academic Medical Research has been focused on trying to force the blood supply into damaged areas**
  - **The natural process repairs metabolism inside the cells, which then sends the repair signals out.**

**Source: Leo Germin, MD, Neurologist, Las Vegas, Nevada**

# HBOT works at the DNA level




- Decreases <u>hypoxia</u>-inducible factor-1$\alpha$ (hip-1$\alpha$) & multiple genes related to apoptosis
- Inhibition of apoptosis (programmed cell death) by HBOT translates into brain

Zhang, JH et al. Neuroscience and Critical Care  Yin, W Brain Res 926: 165-171

Badr et al 2001 brain Res 916: 85-90  Atochin, DN 2000 UHMS 27: 185-190

Image Courtesy of Dr. Stoller

# HBOT: It's About Your Own Stem Cells

**Stem cell mobilization by hyperbaric oxygen**

**Stephen R. Thom, Veena M. Bhopale, Omaida C. Velazquez, Lee J. Goldstein, Lynne H. Thom and Donald G. Buerk**

*Am J Physiol Heart Circ Physiol* 290:1378-1386, 2006. First published Nov 18, 2005;
doi:10.1152/ajpheart.00888.2005

In humans, HBOT at 2.0 atm and 100% oxygen for 2 hours per treatment for 20 treatments increased the number of circulating stem cells in the blood by 8-fold

Thom et al., 2006
Am J Physiol Heart Circ Physiol 290:1378-86

Image Courtesy of Dr. Stoller

# Non-Healing Wound of the Foot

**Diabetic Foot Ulcer: This Wagner Grade III was present for one year and unresponsive to conventional therapy.**

1 Day Prior to Scheduled Amputation

26 HBOT Treatments

50 HBOT Treatments

**Hyperbaric Oxygenation prevents 75% of amputations in diabetic patients. Therapy approved by CMS for Medicare upon application by IHMA to CMS for coverage, 2003.**

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Permission given by Dr. Stoller to the IHMA to publish on this CD (2004)

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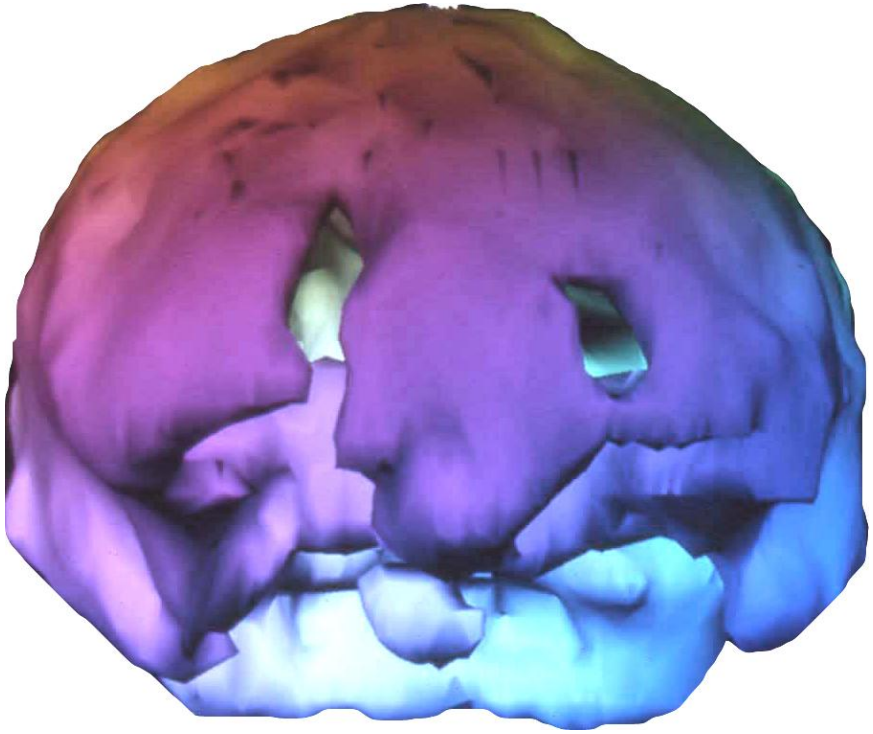
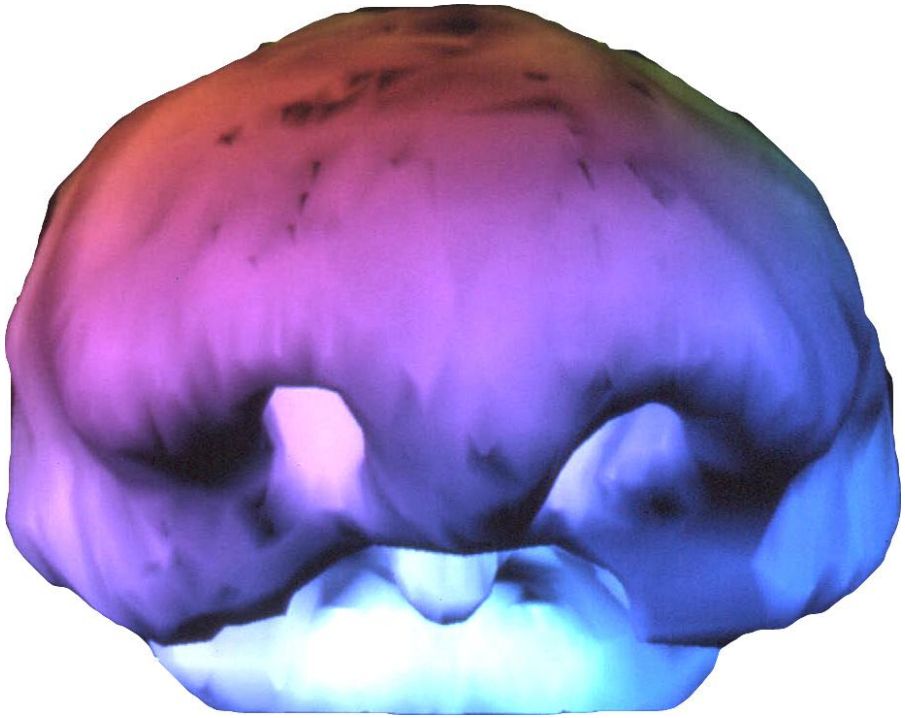
# Non-Healing Wound of the Brain

***Physical Abuse - 9 years after Injury - 21 y. female***



Pre-HBOT 1.5



Post-HBOT 1.5

**No wound will heal without oxygen!**

**What is the difference between the diabetic non-healing foot wound and the non-healing brain injury? Essentially nothing. FDA has already approved HBOT for 3 kinds of non-healing wounds and 3 neurological injuries!**

# Myth: “90% Recover from Brain Injury”

## “Recovery” does not mean “healed without residual effect” or restoration to prior mental capabilities.

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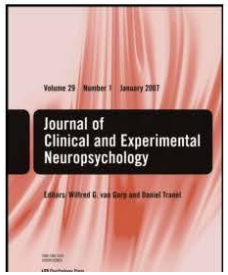


**Journal of Clinical and Experimental Neuropsychology**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713657736

**Persisting effects of minor head injury observable during hypoxic stress**

R. Ewing [a]; D. McCarthy [b]; D. Gronwall [c]; P. Wrightson [c]
[a] Royal New Zealand Air Force Base, Auckland [b] Auckland University, [c] Department of Neurosurgery, Auckland Hospital,

Online Publication Date: 01 October 1980



In conclusion, these results show that simulated altitude with mild hypoxia will cause a significant decrement in the performance of young subjects who have been concussed in the past, when compared with a control group. The decrement resembles that seen immediately after concussion and in old people. The hypothesis proposed in the introduction is, therefore, supported. The most likely explanation of this, and of the cumulative effects of concussion previously demonstrated (Gronwall & Wrightson, 1975), is that concussion produces some persisting deficits in intellectual function, although they may be subtle and only emerge under conditions of stress of further injury.

REFERENCE NOTE

# Acute Injury? Minutes Matter

Author's personal copy

Resuscitation (2008) 78, 200–214

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/resuscitation

EXPERIMENTAL PAPER

## Hyperbaric oxygen improves rate of return of spontaneous circulation after prolonged normothermic porcine cardiopulmonary arrest☆

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Received 13 August 2007; received in revised form 7 February 2008; accepted 20 February 2008

**KEYWORDS**
Hyperbaric oxygen;
Cardiac arrest;
Asystole;
Open chest cardiac compressions;
Advanced life support;
Bretylium;
Lidocaine;
Epinephrine (adrenaline)

**Summary**
*Aim:* This controlled, prospective, randomized porcine study tests the hypothesis that high-dose hyperbaric oxygen ($HDHBO_2$) compared with normobaric oxygen ($NBO_2$) or standard-dose hyperbaric oxygen ($SDHBO_2$), improves return of sustained spontaneous circulation (ROSC) after a normothermic, normobaric, 25-min, non-intervened-upon cardiopulmonary arrest. The study incorporated a direct mechanical ventricular assist device (DMVAD) for open chest continuous cardiac compressions (OCCC) to assist advanced cardiac life support (ACLS). The experiment demonstrates a dose response to oxygen concentration in the breathing mix used in resuscitative ventilation.
*Materials and methods:* Male pigs (average 30 kg weight) underwent a 25-min, normothermic, non-intervened-upon cardiopulmonary arrest. Following arrest all animals were ventilated with 100% oxygen and were subjected to OCCC, incorporating DMVAD-aided ACLS. The animals so treated were randomized to be in one of three groups, with six animals in each group. The $NBO_2$ group remained at 1.0 atmosphere absolute (ATA), while the $SDHBO_2$ and $HDHBO_2$ groups were initially placed at 1.9 and 4.0 ATA, respectively. Uniform, but not American Heart Association (AHA) protocol, ACLS was maintained as needed over the ensuing 2 h for all animals in all groups. At the end of 2 h, the animals were euthanized.

☆ A Spanish translated version of the summary of this article appears as Appendix in the final online version at doi:10.1016/j.resuscitation.2008.02.026.

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doi:10.1016/j.resuscitation.2008.02.026

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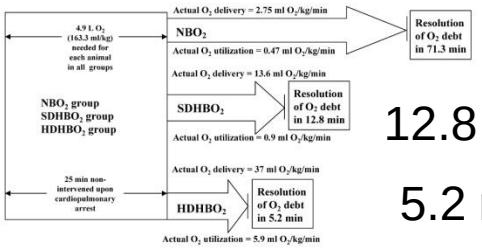



71.3 m

12.8 min

5.2 min

**Figure 9** Estimate of resolution of oxygen debt by dose response of oxygen in ALS after a 25 min, non-intervened upon cardiopulmonary arrest. Basal oxygen consumption for swine is reported as being 6.5 mL $O_2$/(kg min).[50] The basal oxygen requirement was estimated by the assumed oxygen requirement of 6.5 mL $O_2$/(kg min) over 25 min of cardiopulmonary arrest followed by 120 min of resuscitative effort with a variable measured oxygen uptake for each group (see calculations for same in appendix): 30 kg × 6.5 mL/min = 195 mL $O_2$/min. Based on calculations taken on actual measurements made on the animals over the 120-min resuscitation, it would take 71 min into the resuscitation to satisfy the hypometabolic accumulating oxygen debt for the $NBO_2$ group animals, 13 min for the $SDHBO_2$ animals, and just 5 min for the more normally metabolic oxygen consumption rate of the $HDHBO_2$ animals.

or for these animals whose weights averaged 30 kg (±2 kg) a consumption which average 6.5 × 30 kg = 195 mmHg oxygen per minute. Thirty-five minutes after the resuscitative effort began (or at 1 h after the cardiopulmonary arrest was imposed), the swine in the $HDHBO_2$ group had COs which averaged 3.01 L/min (or CI of 5.79 L/min). The ideal calculated average $DO_2$ for this group of animals would have been $DO_2 = CI \times CaO_2$ or $[(14\,Hgb/dL \times 1.36\,mL) + (0.003\,mL \times 2953\,mmHg)] \times 10 \times 5.79\,L/min = 1633\,L\ O_2/min$. The animals in the $NBO_2$ and $SDHBO_2$ group had essentially no oxygen delivery without the assistance of the DMVAD because they had no CO (CI) on their own. If the DMVAD were engaged, reduction of the oxygen debts would never be reduced over the resuscitative 2-h period in the $NBO_2$ group or the $SDHBO_2$ group during the 2-h resuscitative attempt. In the $HDHBO_2$ group (without the need of the DMVAD in five of the six animals), the oxygen debt would be reduced in 5 min given the oxygen ventilation profile administered (Figure 9). See appendix for the entire calculation of $VO_2$, $DO_2$ and oxygen debt reduction for each animal group from real measured values.

Ideally the $HDHBO_2$ swine at 4.0 ATA of pressure while being ventilated with 100% oxygen would potentially have the approximate $CaO_2$ of 28.2 vol.%, while the $SDHBO_2$ group and $NBO_2$ group would have at 1.9 and 1.0 ATA respectively of 23.6 and 21.32 vol.% $O_2$ (see Table 6).

Measured hemoglobin saturations in arterial and venous blood were essentially normal in all animals of all groups pre-arrest. The measured hemoglobin saturations in the 2-h period of resuscitative effort reflected dose response to administered oxygen, but were diminished in all groups (Tables 7 and 8). Perhaps the oxygen carrying capacity

**Table 6** Average of measured $CaO_2$ determinations by group for pre-arrest and 1 h, post-induction of ventricular fibrillation periods

| | Average baseline $CaO_2$ pre-arrest (vol.%) | Average $CaO_2$ 1 h post-induction of ventricular fibrillation |
|---|---|---|
| $NBO_2$ group | 19.86 | 11.32 |
| $SDHBO_2$ group | 19.65 | 14.79 |
| $HDHBO_2$ group | 20.03 | 19.57 |

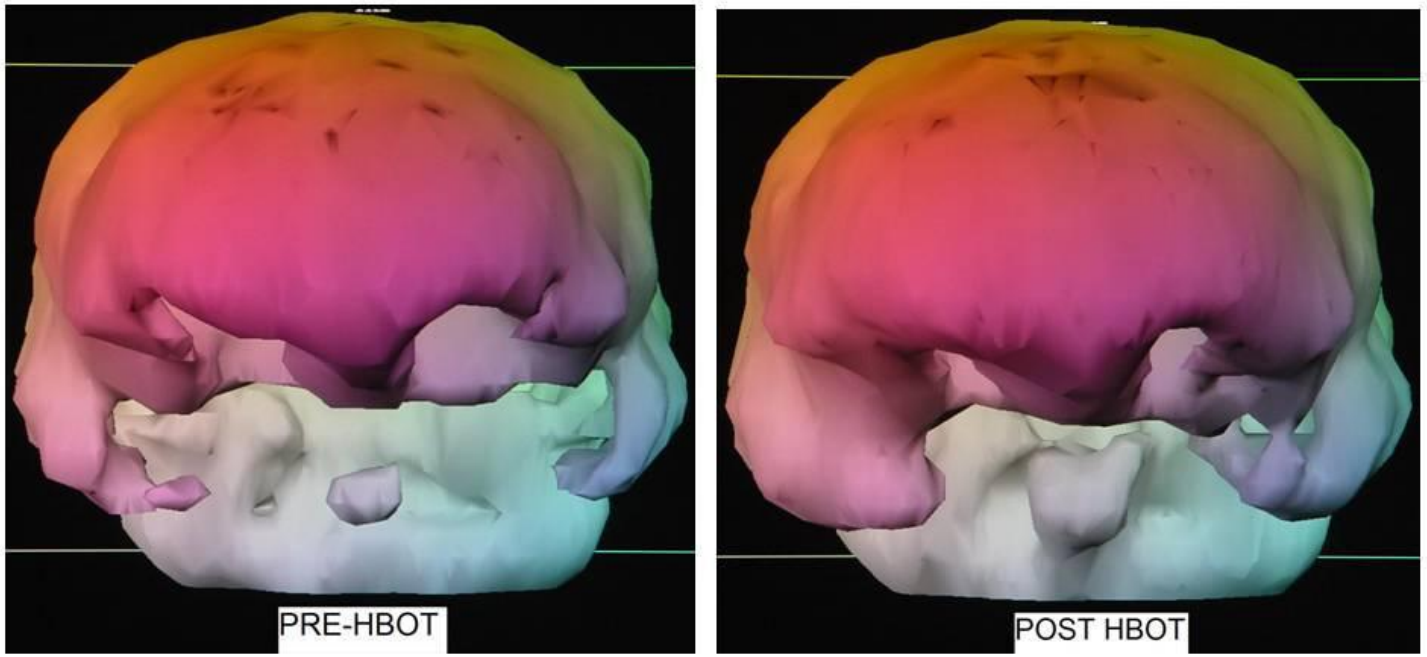
**Table 7** Average of $SvO_2$ determinations by group for pre-arrest and 1 h, post-induction of ventricular fibrillation periods

| | Average baseline $SvO_2$ pre-arrest (%) | Average baseline $SvO_2$ 1 h post-induction of ventricular fibrillation (%) |
|---|---|---|
| $NBO_2$ group | 66 | 46 |
| $SDHBO_2$ group | 58 | 65 |
| $HDHBO_2$ group | 81 | 74 |

# Solution to Brain Injury: Biologically Repair the Brain

## Non-Healing Wound in the Brain

**Case Report: Navy SG Meeting - Aug. 2008**
**25 year old Humvee Machine Gunner**
**40 HBOT 1.5 treatments (1/2 of the Protocol)**




©Retained 2008: Paul G. Harch, M.D., processed by Philip J. Tranchina.

Treated in 2008. PTSD disappeared. From living in a dark room since returning from Iraq, he became gainfully employed, turned down ½ of his VA disability, worked and made $39,000 per year, and has returned to college after 2nd 40 treatments.

*Case Published in: Cases Report June 2009 http://casesjournal.com/casesjournal/rt/suppFiles/6538/31370*

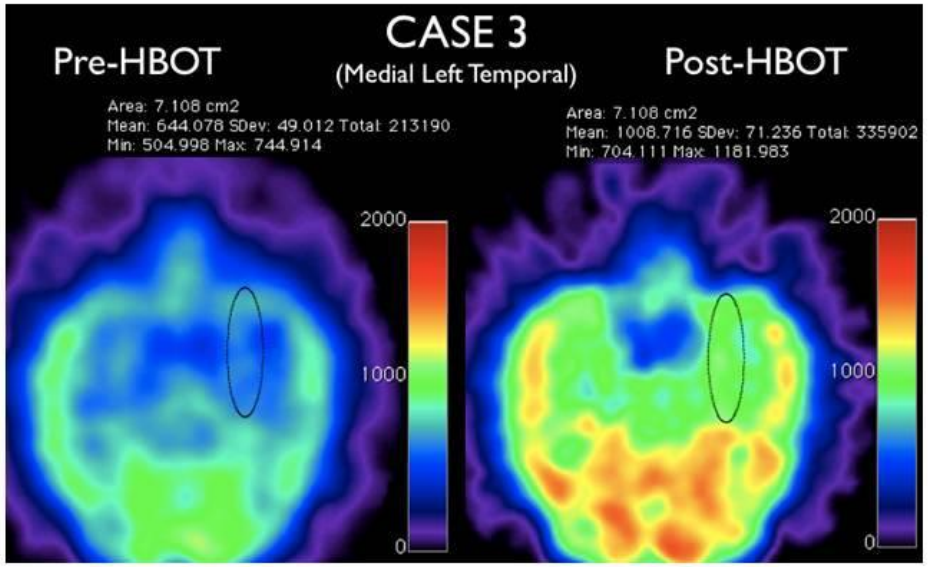
# Brain Insults often Result in a 50% Decrease In Brain Metabolism HBOT Restores Brain Metabolism

## HBOT 1.5 Restores Brain Blood Flow & Metabolism

Scale actually goes from 0 to 2000 so it ENDS at 2000. Those pixels that are hitting near 2000 are red and are the most active, the less metabolically active are "cooler" colors of yellow, green and blue. So if you draw a line across the middle of the scale you can see what pixels are registering at 1000 by the corresponding color.

Both pre and post HBOT sets of images are exactly on the same scale. Below is a a quantitative assessment that shows the actually percent increase in up take to an area of the brain quite vulnerable to TBI. Note the mean uptake in the area went from 644 to 1008. Similar changes are evident everywhere else.

**In ballpark numbers a change from green to red is a doubling of metabolism.**




Analysis of blast injured veteran in LSU IRB Study # 7051: Edward Fogarty, MD, Neuro-radiologist, Chair, University of North Dakota School of Medicine, (701) 751-9579 **40 Treatments: ½ of NBIRR Protocol**

*Case Published in: Cases Report June 2009 http://casesjournal.com/casesjournal/rt/suppFiles/6538/31370*

# The Specific Science for HBOT 1.5

- 1977 Study: Holbach & Wasserman PMID: 75249 : HBOT 1.5 puts the most oxygen into the brain because more triggers an autonomic response to keep extra O2 out! Chronic Stroke patients treated at numerous locations.
- 1990: Harch treats first demented diver for delayed decompression sickness. Numerous small studies published. (See Memorandum)
- 2002: US Army verifies HBOT 1.5 repairs white matter damage in children. ISSN1524-0436
- 2007: Rat HBOT 1.5 study for Chronic TBI published in Brain Research. Human protocol in Animals. First improvement of chronic brain injury in animals in the history of science. PMID: 17869230
- August 14, 2008: Briefing to Surgeon General of the Navy & Deputy Commandant, US Marine Corps: 5 blast injured veterans treated. All five made improvements, some dramatic. Four of five were able to return to duty or civilian employment! First Case was Published April 2009 PMID: 19829822 [PubMed]
- September 2008: US Air Force Hyperbaric Researcher & Special Forces Command Physician treats two airmen. Results verified by ANAM neuropsych test. Both are restored to duty saving the Federal government an estimated $2.6 million each in lifetime costs. They continue their careers. More active duty personnel are treated. Published in January, 2010 in Peer Reviewed Journal (PMID: 20112530) (See Research www.HyperbaricMedicalFoundation.org)
- **March 12, 2010: Report on 15 Blast Injured Veterans under LSU IRB-approved study. Report is clinically and statistically significant and sufficient proof because of dramatic improvement in patients. ½ of protocol given (WBIC0653)**
  - **15 point IQ jump in 30 days p<0.001, 40% improvement in Post-concussion symptoms p=0.002 (np), (10% is considered clinically significant enough to warrant approval and payment for HBOT according to DoD researchers in December 2008.)**
  - **30% reduction in PTSD symptoms p<0.001, 51% Reduction in Depression Indices p<0.001**
- **NBIRR-01 Begins Enrolling Patients March 2010. Preliminary Results from multi-site study support Harch's Findings.**
- **LSU Pilot Published in the Journal of Neurotrauma,** J Neurotrauma. 2011 Oct 25. **A Phase I Study of Low Pressure Hyperbaric Oxygen Therapy for Blast-Induced Post Concussion Syndrome and Post Traumatic Stress Disorder** PMID: 22026588
  - **Subjects as a group showed significant improvements on most measures of intelligence, function and quality of life**
  - **All subjects received 1/2 the clinically recommended protocol being used in NBIRR-01 (NCT01105962)**
  - **Nearly 15 point IQ Increase (average) (Difference between a high school dropout & a college graduate)(14.8 P<.001 )**
  - **Post-Concussion Syndrome (PCS): 39% Reduction in PCS symptoms (p=0.0002); 87% substantial headache reduction**
  - **30% Improvement in PTSD (20 points of a 85 point scale; 10% is considered clinically significant)**
  - **51% Reduction in Depression Indices with Large Reduction in Suicide Ideation(p=0.0002)**
  - **64% had a reduced need for psychoactive or narcotic prescription medications**
  - **100% showed sustained improvement on neuropsychological tests 6 months post treatment**
  - **Functional Improvements: Cognitive 39% (p=0.002); Physical 45% (p<0.001); Emotional 96% (p<0.001)**
    - **Significant Reduction in Anger Issues!**
  - **Placebo Effect Ruled Out! Results too great to be placebo effect and neurological imaging is inconsistent with a placebo effect**

# HBOT 1.5 Provided the Largest Published Reduction in PTSD

- LSU Pilot Study: 30% Reduction
- Cognitive Processing Therapy [TAU]: 14%↓ or 4.8%↓
  - -Chard, 2011 & Alvarez 2011
- Trauma Focused Group Treatment [TAU]: 2.2%↓
- Prolonged Exposure Therapy [PE]: 28%↓ -Wolf, 2012
- Transcendental Meditation [TM]: 21%↓ -Rosenthal, 2011
- Virtual Reality Exposure Therapy [VRET]: 23%↓
  - Rizzo, 2011

Note: All results are time adjusted for the length of treatment in the LSU study

# HBOT is Rapidly Deployable

- **Note the Level of Education needed for health care professional providing treatment in the previous slide.**
  - Subjects in other therapies had a Masters or Ph.D. or Physician level therapist.
- **HBOT can be delivered** by a health care provider with **EMT level 1 or better training**, with overall physician supervision.
- **Thus HBOT is more readily deployable, a lower strain on resources, and more effective than any other published therapy.**

# IHMF Is Solving the TBI/PTSD Problem

- The Challenge is Getting Paid for Treatment So We can Restore People's lives!
  - State Medicaid Rules Restrict Treatment Locations
  - Payment is NOT made even when patients recover! (HR396 will help)
- No Other Such Clinic Treatment Network Exists!
- Our Team Leaders have decades of experience with Hyperbaric Medicine
  - Our Team Leaders have over 20 years of experience treating Brain Injury & restoring lives with this protocol
  - The NBIRR-01 Study is IRB-approved and is Listed at www.ClinicalTrials.gov
    - Public Officials can send case work for treatment
    - Public officials & Judges can put individuals on a path to treatment
  - The National Call Center Number is: (800) 288-9328
- **TODAY IHMF is Helping to Solve the Real Problems of Brain Injured Persons with Biological Repair for their Injury**

# Airman B ANAM Percentile Scores

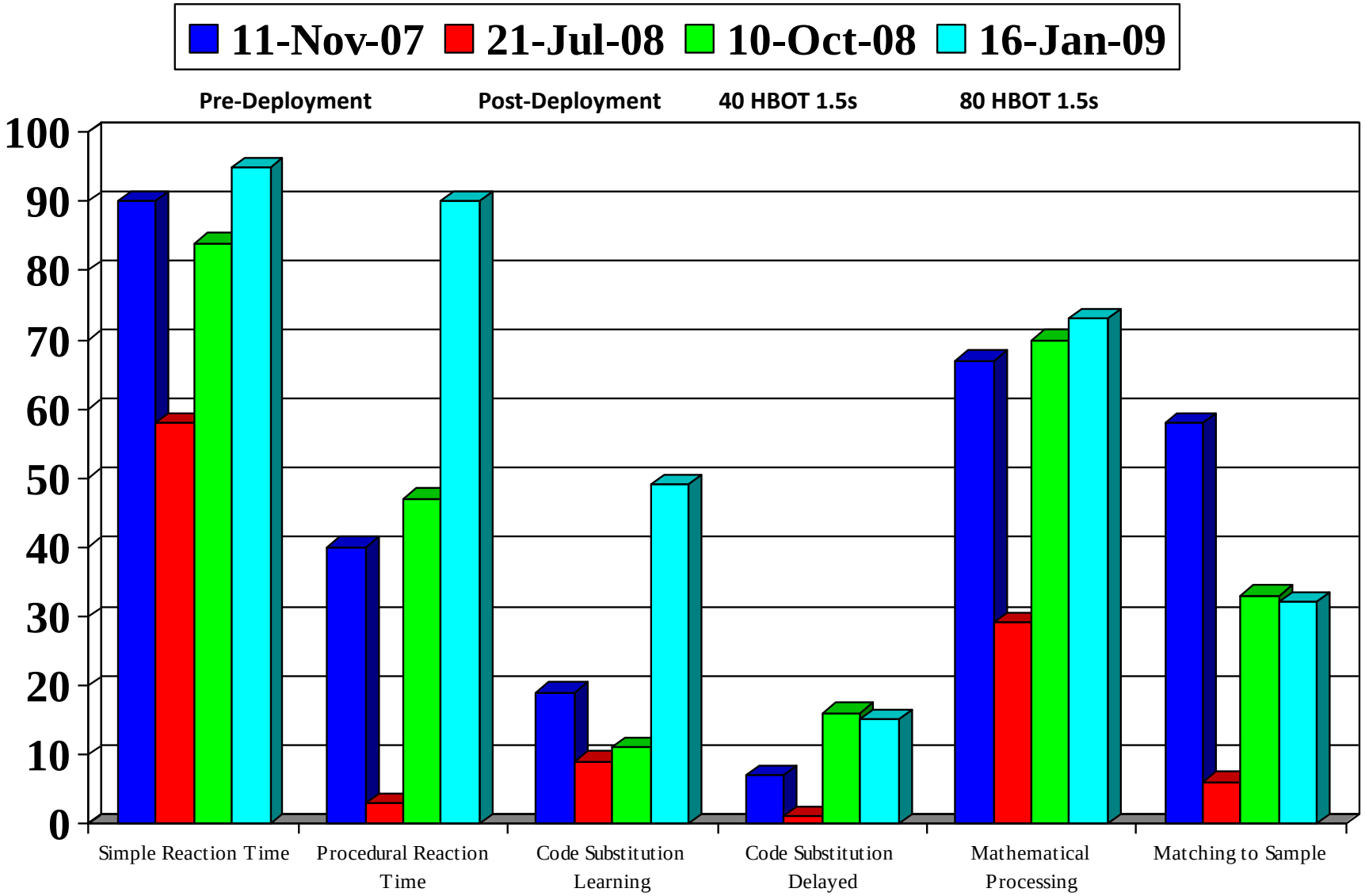


Figure 1:
The passenger side of the M915 truck showing the damage caused by the IED.

**Conclusion by article authors:**

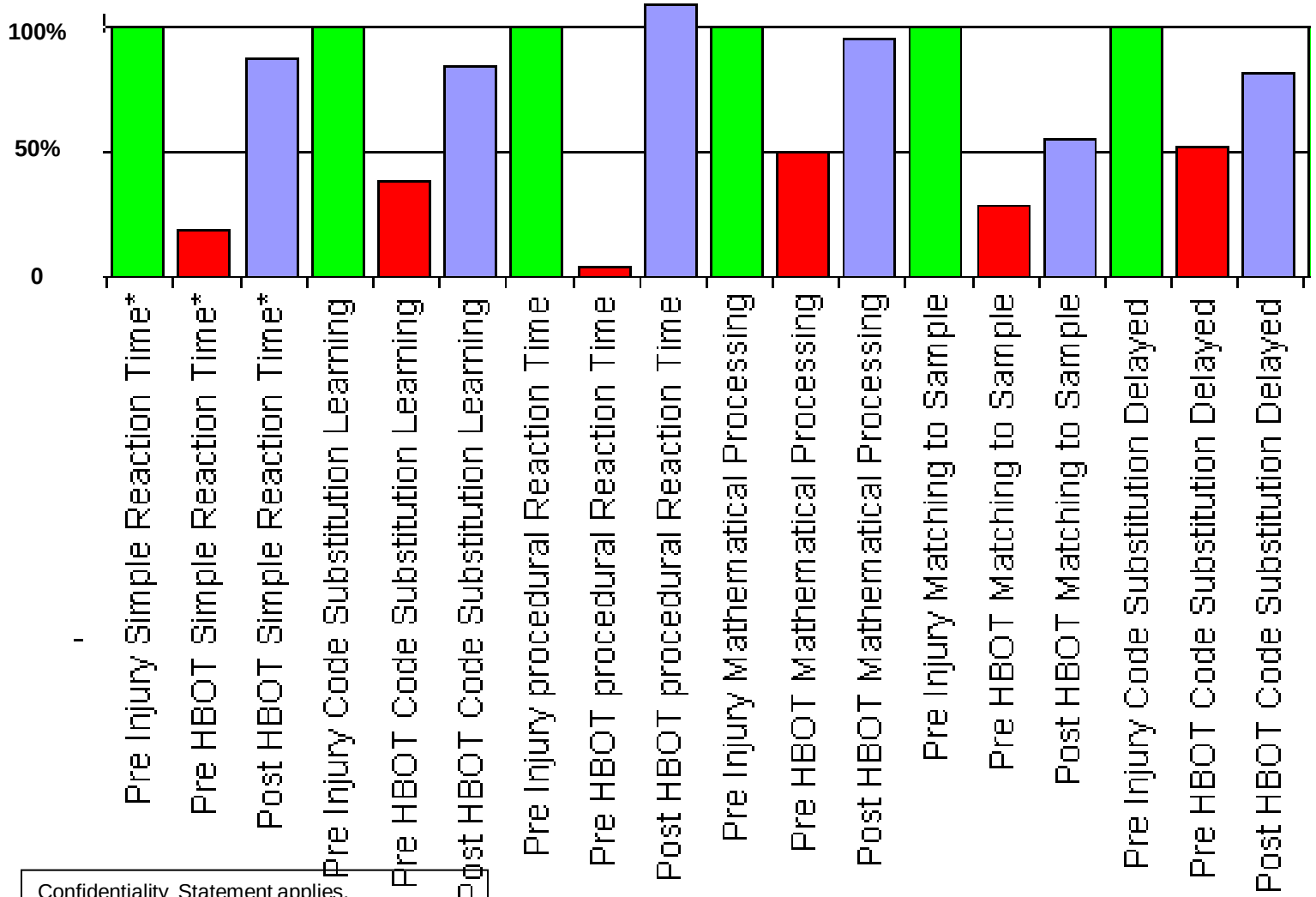
Several aspects of these two cases demonstrate the efficacy of HBO for the airmen treated. Although both airmen had stable symptoms of mTBI/post-concussive syndrome, which had not improved for seven months; **substantive improvement was achieved within ten days of HBO treatment. The headaches and sleep disturbances improved rapidly while the irritability, cognitive defects, and memory difficulties improved more slowly.**

Fortunately both airman had taken the ANAM and presented objective demonstration of their deficits from TBI and their improvements after HBO treatment. Both airmen, who were injured by the same blast sitting side by side, had similar symptom complexes of TBI and improved at similar rates after initiation of HBO treatment. Neither airman had any other form of treatment for TBI. **It seems unlikely to the authors that any explanation other than the HBO treatments can be offered for their improvements.**

*"Case report: Treatment of Mild Traumatic Brain Injury with Hyperbaric Oxygen: Colonel James K. Wright, USAF, MC, SFS; Eddie Zant, MD; Kevin Groom, PhD; Robert E. Schlegel, PhD, PE; Kirby Gilliland, PhD"*

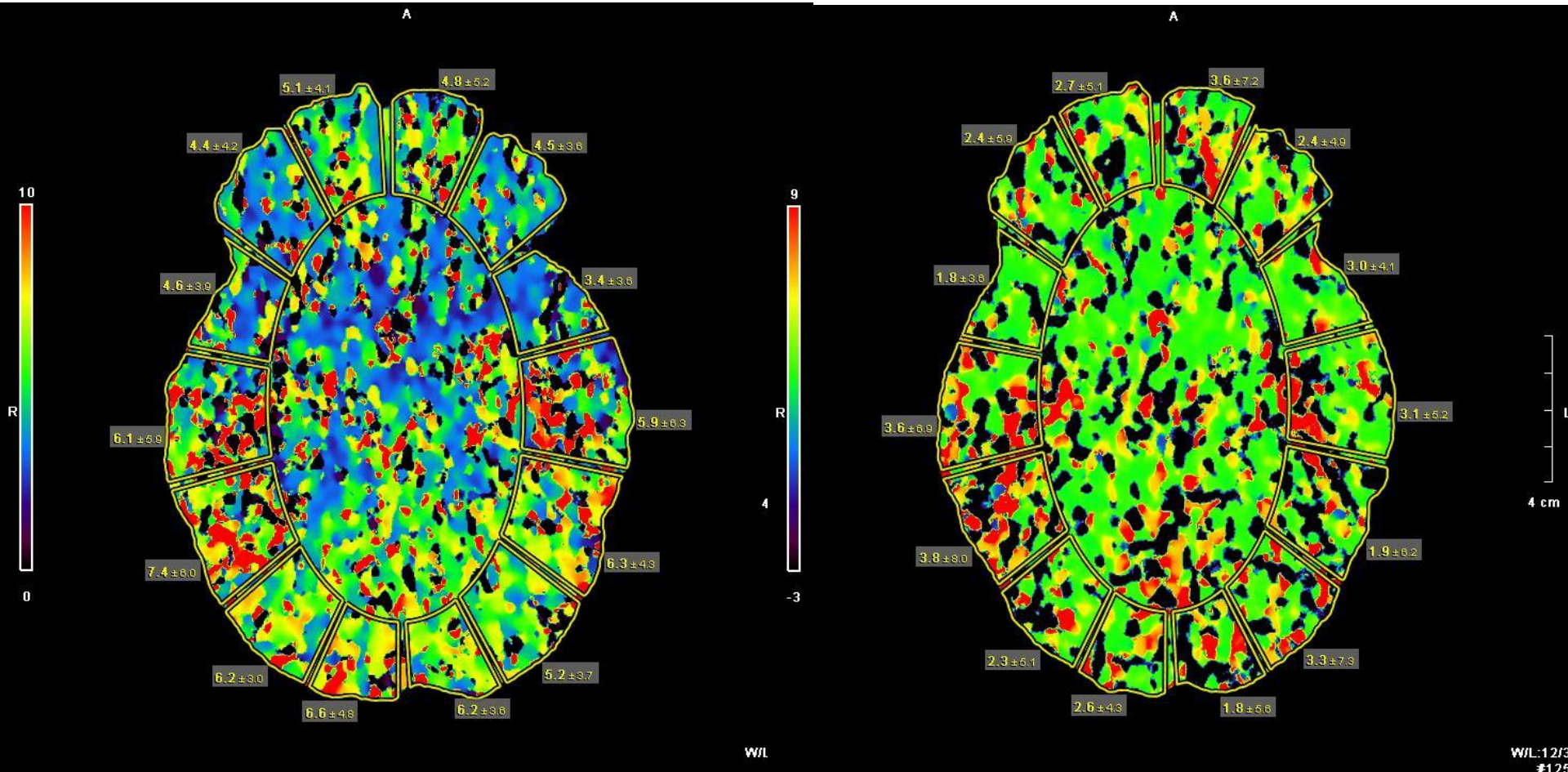
# ANAM Scores - pre-injury, post-injury, after HBOT

**Budget Savings from Restoring 4 Military Personnel to Duty: $11.2 million**
**Long Term Additional Savings: $8 million ($19.2 million) Cost? $96,000**




Confidentiality Statement applies.

# Severe TBI Patient: Whole Brain CT Perfusion Pre & Post HBOT




Pre HBOT – 10/16/09  Post HBOT – 10/28/09

Images Courtesy of Dr. Germin, Las Vegas

# Fractures

- **Dr. Wright's Air Force Research Demonstrated that Fractures heal 30% faster and 30% stronger when Hyperbaric Oxygen is used.**
  - Shorter back to work time
  - Stronger Fusion
- Cost Effective through reduced down time

*The effect of hyperbaric oxygen on fracture healing in rabbits, completed 2003. J Wright*

# Is Hyperbaric Medicine Safe?

Source: "HBOT for TBI" Consensus Conference, December 2008

- **Treatment involves simply breathing pure oxygen under pressure** (often while sleeping or watching TV).
- **Ten thousand plus similar treatments are given every day at 1,200+ locations nationwide for other indications.**

- The DoD White Paper stated: **"side effects are uncommon and severe or permanent complications are rare…"** *(White Paper for the HBOT in TBI Consensus Paper, 12/08)*
- The DoD After Action Report stated: **"safety of the treatment is not an issue."** *(After Action Report HBOT in TBI Consensus Conference, Defense Centers of Excellence, 16 Dec 2008)*

# Examples: HBOT is Synergistic with Other Treatments

- Drug Protocols
  - Patients in the LSU Study were on no medication or less medication
  - Medication was now more effective at controlling remaining symptoms
- Nutritional Programs
  - NBIRR Nutritional Program reduced Aberrant Violent Behavior in Felons in 30 RCT Studies by 39-41%
  - Harch did not use NBIRR supplement in his study
- Cognitive Rehabilitation
  - Treatment Cannot Begin until a Patient can Sleep Through the Night
  - HBOT Repairs Sleep Cycles and most Patients can begin sleeping at 10 HBOT Treatments
  - When Brain Tissue is Recovered, it is somewhat disorganized!
- Acupuncture
- Bio-Feedback
- Counseling & Coping Skills

# Micro Air Embolism Contribution to Blast-Induced Mild Traumatic Brain Injury

**Reimers, SD[1]; Harch, PG[2]; Wright, JK[3]; Slade, JB[4]; Sonnenrein, R[1]; Doering, ND[1]**

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## INTRODUCTION

Massive air embolism (AE) from lung disruption is the accepted principal etiology of mortality in blast injury (White et al., 1971; Sharpnack, Johnson & Phillips, 1990). For sub-lethal blast injury, air embolism has been ignored, considered innocuous or believed to have not occurred. The high incidence of post-concussion syndrome (PCS), neurocognitive deficits, and mental health issues resulting from sub-lethal blast injuries in U.S. Iraq and Afghanistan War veterans has vexed military authorities and medical specialists. We propose that micro air embolism is a heretofore unappreciated etiologic factor.

## MATERIALS AND METHODS

Materials and Methods: Using PubMed, PsychInfo, Google Scholar, Sci.gov, and PubCrawler, a systematic review of the literature was conducted identifying published papers in the following domains: biodynamics and physics of blast overpressure; primary blast injury; microbubbles in systemic circulation from diving and iatrogenic causes; neurological problems and microbubbles. When necessary, key documents were obtained from U.S. Government archives. Reference lists of articles were also scanned. Papers with both significant and null findings were included.

## RESULTS

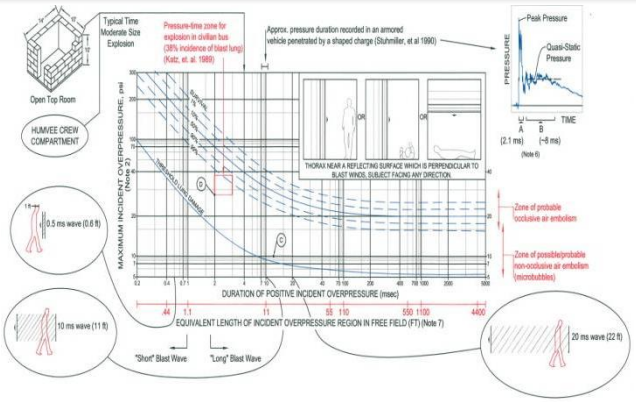
**Blast-induced AE**

- For mammals that die promptly from either air or underwater blast, air embolism has long been recognized as the primary cause of death (Desaga,1950; Shapnack, Johnson & Phillips, 1990; Richmond & Damon, 1991). Lung disruption is proportional to both magnitude and length of blast overpressurization (Buamoul, 2009) with disruption beginning to occur at modest overpressures easily within the range of pressures experienced by U.S. combat troops from improvised explosive devices (IED) (Fig 1 & 3).
- The disruption threshold is lowered by exposures near reflective surfaces, exposures inside structures that impede dispersion of the blast gases, and by longer exposure times. It is further lowered by repeat exposures in less than 24 hours (Stuhmiller, Phillips & Richmond, 1990).
- Benzinger (1950) concluded that because symptoms were only present when a blast hit the thorax, air embolism must originate in the thorax and becomes effective when it travels to the brain. Benzinger also found that small amounts of air in arterial circulation could readily reproduce neurologic symptoms seen in blast injury to dogs and humans. Only 1 cc of air injected into the pulmonary veins of a dog was sufficient to reproduce the electrocardiographic changes seen in blast-injured dogs (Phillips & Richmond, 1990).
- Maison (1971) outfitted a dog with a Doppler bubble detector on the carotid artery, exposed the dog to an LD50 air blast, and subsequently observed bursts of Doppler deflections going up the carotid correlating with respirations for approximately 30 minutes post-blast. The dog's carotid blood flow was observed to temporarily drop to near zero following each group of echoes, possibly indicating reduced blood velocity due to temporary distal occlusions (Fig. 2). The dog initially showed severe respiratory distress, but recovered. Postmortem exam showed evidence of residual lung hemorrhage, but no other damage. Maison concluded that the bubbles were "clinically silent".
- A conceptual model of how AE sequelae to blast exposure occurs, confirmed with rabbit model data, can be found in White (1971). Any fast-rising blast pressure wave long enough to produce significant chest compression is likely to produce some AE.
- Goh (2009) and Mayo & Kleger (2006) in separate articles regarding civilian blast casualty management advise that AE is a possible complication of exposure to air blast. However, neither author addresses the possibility of neurocognitive sequelae from AE.
- Protective vests reduced mortality & neural fiber degeneration in rats exposed to air blast (Long, et.al., 2009)

**Evidence that microbubbles are NOT harmless**

- Microbubbles were first recognized as a medical hazard in open-heart surgery decades ago (Barak & Katz 2005). Air emboli from various sources in the extracorporeal circulation (ECC) set and tubes can drift into the aorta and systemic circulation, carrying microbubbles to the brain. Clinical results of this unwanted event include major and minor neurologic injury, neurocognitive deterioration and an overall general decline in patient health (Barak, Nakhoul & Katz, 2008; Shaw et al., 1987). The degree of decline in cognitive performance has been correlated to the amount of air emboli delivered during the ECC (Deklunder et al., 1998[1,2]). Patients with neuropsychological deficits 5 to 7 days after coronary bypass graft surgery averaged nearly twice the number of emboli compared to those without deficits (Stump, et al., 1996).
- In mechanical heart valve carriers, bubbles are chronically delivered into the arterial system at variable rates, which can rise as high as 800 per hour in the cerebral circulation. Patients with these devices have been found to have impairment in episodic memory and deficits in working memory (Deklunder et al., 1998[1,2]).
- Multiple brain lesions in divers with no reported history of neurological DCS have been found to be strongly correlated with patent foramen ovale of high haemodynamic relevance. This finding lead the authors to a hypothesis that the brain lesions were the consequence of subclinical cerebral gas embolism (Knauth et al., 1997).
- A review of 140 cases of delayed DCS treatment (avg. delay 93.5 hrs) reported findings of neurocognitive symptoms including severely reduced executive function, apathy and antisocial behavior in 49% of the patients. 100% of the neurocognitive symptoms resolved with hyperbaric oxygen therapy (HBOT) (Cianci & Slade, 2006).

**Fig. 1: Blast Waves Are More Than Simple Shock Waves, Duration Makes a Difference**




**Notes to Fig. 1**

1.Figure is based on the survival curves for a 70 kg man where the thorax is near a surface against which a blast wave reflects at normal incidence (Bowen, Fletcher, & Richmond,1968). data shown is for a single reflection where the total overpressure is ~2x incident pressure. Total pressures can be up to 8x incident pressure if circumstances are right (Richmond & Damon,1991). In free field exposures (no reflections) the damage thresholds are approx. 2x those shown. When used, free field pressure data values are plotted at 50% of actual.

2. "Short" and "Long" refer to the ratio of the length of the overpressure region to thorax dimensions. Long blast waves produce much greater chest compression (White et al., 1971).

3. Repeat exposures in less than 24 hours, lower the lung damage threshold (Stuhmiller, Phillips & Richmond 1990).

4.The lung damage threshold curve is based on an estimated damage threshold of 20% of the 50% mortality level (White et al., 1971). Recent data (Yang et al., 1996) suggests the threshold pressures for lung damage may be lower (circa 50%) than those shown.

5.Blast waveform is also important. However, that is beyond what can be addressed in this paper.

6.A = shock wave period, B= period where expanding blast gases maintain compartment pressure

7. Based on a wave speed of Mach 1. Most blast waves are faster (up to Mach 2+) increasing the wave length for the same time..

**Fig. 2 Blood Velocity & Embolus Indications Following Canine Exposure to LD50 Air Blast**

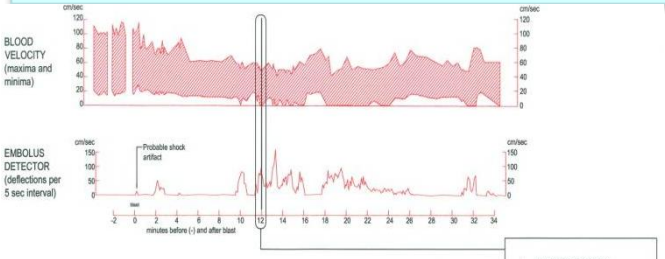
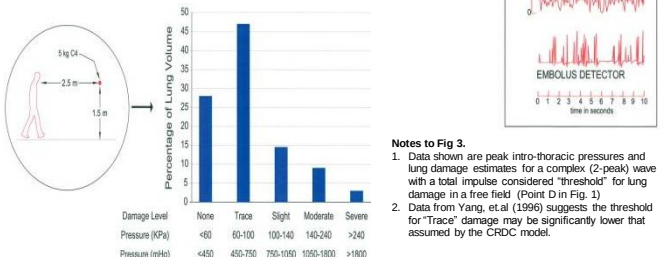



**Fig. 3 . Lung Injury Prediction from CRDC Model**




**Notes to Fig 3.**

1. Data shown are peak intro-thoracic pressures and lung damage estimates for a complex (2-peak) wave with a total impulse considered "threshold" for lung damage in a free field (Point D in Fig. 1)
2. Data from Yang, et.al (1996) suggests the threshold for "Trace" damage may be significantly lower that assumed by the CRDC model.

## RESULTS (CON'D)

- In hemodialysis, CNS abnormalities attributed to microbubbles have been correlated with the duration of dialysis treatment. Barak & Katz (2008) attributed the abnormalities to microbubbles and stated "a small quantity of microbubbles may be clinically silent, while recurrent exposure has a slow, smoldering, chronic effect" (p. 2921)

**Recent Combat Medical Literature**

- Bauman et al. (2009) provides a summary of the test conditions and initial results from the PREVENT (Preventing Violent Explosive Neurotrauma) research program being conducted by DARPA. In the tests reported (swine model), the thorax and upper abdomen were protected to minimize the possibility of brain injury by indirect pathways. Some neurological damage was observed, and its significance is still being determined. However, the test conditions are of interest as they are also ones where lung injury can readily occur. Point C on Fig. 1 represents a typical Friedlander wave reported for the blast tube. Test set-ups were built to simulate exposures in the crew compartment of a Humvee with a blast under its floor and an open gunner port and in semi-confined space (open top room with dimensions as shown in Fig 1). In both cases the overpressure durations from a moderate sized charge were reported to be about 4 ms. The overpressure data was reported in general form only without numerical values. However, at 4 ms duration, the pressures required to produce lung injury are not large. In situations where the Humvee or building were to be fully closed, both the magnitude and duration of blast overpressures can be expected to be greater.
- Buamoul (2009) reports results from a computer model developed by Defence R & D Canada (CRDC) for estimating the blast damage to the lungs of sheep and humans. He reports the intra-thoracic pressure range currently accepted as the "threshold" for lung damage is 70 kPa (695 cmH20) to 110 kPa (1,091 cmH20), which corresponds roughly to the intra-thoracic pressures predicted by the model at exposures near the lung damage threshold line on the Bowen charts. The intra-thoracic pressures produced by even moderate size blasts can be very substantial (Fig. 3). They also vary widely with both time and location in the lung, suggesting that opportunities for localized AE may be plentiful. The model also indicates that complex (multi-peak) blast waves can produce higher lung pressures, and therefore greater risk of lung damage than do single peak, classic Friedlander waves of the same impulse value.
- **Recent work by Yang et al.,1996 (sheep model) suggests the lung damage threshold pressure may be as much as 75% lower than the Bowen charts (Fig 1) indicate when the threshold pressure is taken as the lowest pressure at which lung tissue damage is observable by light and/or electron microscopy.**
- It is well established that AE is a possible/probable sequelae of exposure to air blast.
- It is also well established that microbubbles are harmful to brains, and that symptoms may not manifest immediately.
- Blast overpressure exposures typical of the current wars in Iraq and Afghanistan, particularly blast exposures in confined spaces, are sufficient to create risk of lung damage. Quickly repeated exposures increase the risk.
- It is reasonable to expect that the degree of blast-related AE is a continuum ranging from no bubbles, to a few microbubbles to massive amounts depending on the exposure.
- The blast-related intra-thoracic pressures can be very substantial (Fig 3). The range customarily accepted as the threshold for lung injury is 7 to 11 times higher than the 80 mmHg (10.7 kPa) differential known to produce disruption of aveolar-capilary boundary tissues in slowly varying pressure environments such as diving (Neuman, 1997).
- Work by Yang, et. al (1996) suggests that lung tissue damage, and the concurrent possibility of transient microbubble release, can occur at lung damage levels insufficient to produce clinical blast lung and at overpressures substantially lower than indicated by the widely-used Bowen charts.
- The CRDC model confirms suggestions from prior efforts that complex blast waves typical of confined space exposures are more likely to be damaging to lungs than are the simpler waveforms typical of free-field blasts.
- Blast related bubble production, when it does occur, has been shown to be transient, lasting only 15 minutes to 3 hours for significant AE (Mayo & Kluger, 1996). The duration of microbubble production can be expected to be shorter still making them hard to detect.
- All recent publications that we found, including a recent review article (Cernak & Noble, 2009), were silent on the possible role of microbubbles as a mechanism for blast-related brain injury.
- When all the factors that may favor microbubble production are considered, it is difficult to expect they do not occur.
- Undetected arterial microbubbles have the potential to significantly confound research into other mechanisms of blast-related brain injury. **In research studies where there is a possibility of microbubble production, monitoring for their occurrence is recommended.**

**The contribution of micro air embolism to blast-related brain injury may be significantly greater than has been previously believed.**

Available literature suggests that transient AE from primary blast exposure is possible, perhaps probable, at sub-lethal overpressures similar to the overpressures experienced by U.S. combat Veterans. Arterial microbubbles have been shown to be neurologically harmful and may contribute to the high incidence of post-concussion syndrome in blast injured veterans. Current research efforts are almost exclusively focused on the direct cerebral effects of blast waves. The AE pathway deserves prompt and thorough investigation.

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# Types of Hyperbaric Chambers

**Monoplace and Multi-Place Hyperbaric Chambers**

Sechrist

SOS Hyperlite

Perry

ETC Bara-med XD

Reimers Q-Ball