WELCOME

UHMS DELEGATES

TO SALT LAKE CITY

CONTINUING EDUCATION

The Undersea and Hyperbaric Medical Society (UHMS) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The UHMS designates the ASM educational activity for a maximum of 26 AMA PRA Category 1 Credits™ ; Physicians should only claim credit commensurate with the extent of their participation in the activity.

Nursing CEU will be provided by Diversified Clinical Services 4500 Salisbury Road, Suite 300, Jacksonville, FL 32216. Florida Board of Registered Nursing Provider # 56-531. ASM Credit hours 26.

NBDHMT: The ASM program has been reviewed and is acceptable for up to 26 Category A credit hours by the National Board of Diving and Hyperbaric Medical Technology.

Disclosure: All faculty members and planners participating in continuing medical education activities sponsored by UHMS are expected to disclose to the participants any financial relationships with commercial interests. Full disclosure of faculty and planner financial relationship will be made at the activity.

Continuing Education Credit: separate fee required for credits – EVALUATIONS must be turned in to receive credits.

Expected Results (Goals or Objective)

To provide a forum for professional scientific growth and development of the participants.

The meeting is designed to meet the following additional goals:

To provide an opportunity for participants to:

- meet and interact with other scientists and medical practitioners. Specifically, participants should have the opportunity to renew old acquaintances and establish new contacts with basic and applied scientists and medical practitioners in hyperbaric and diving medicine as well as in the fields ancillary to hyperbaric medicine, i.e. nursing, allied health sciences, engineering, and health care administration;
- attend oral or poster presentations in which ideas and data are presented pertaining to currently accepted uses of hyperbaric oxygen therapy and diving medicine;
- attend oral presentations of a special mini-course pertaining to the physiology and pathophysiology of decompression phenomena;
- attend oral or poster presentations pertaining to the physiologic, pharmacologic, pathologic, and biochemical effects of respirable gases with special emphasis on oxygen, nitrogen, carbon dioxide, and the inert gases, in the hyperbaric environment;
- be introduced to new diagnostic, research, or therapeutic techniques and equipment pertaining to hyperbaric medicine;
- participate in forums or discussions pertaining to technical factors and engineering pertaining to the development and use of equipment for hyperbaric environments;
- learn of the varied activities of the Society and the past and future directions of the Society; and
- become active in Societal affairs so that they could help influence the Society's future.

As a result of having attended the meeting, the participants should have had the opportunity to:

- meet and interact with other scientists and medical practitioners: specifically, participants should have had the opportunity to renew old acquaintances and establish new contacts with basic and applied scientists and medical practitioners in hyperbaric and diving medicine as well as in the fields ancillary to hyperbaric medicine, i.e. nursing, allied health sciences, engineering, and health care administration;
- attend oral or poster presentations in which ideas and data are presented pertaining to currently accepted uses of hyperbaric oxygen and diving medicine and, where applicable, incorporate these ideas into their practice;
- gain a more in-depth knowledge and appreciation of scientific issues involved in critiquing decompression schedules and/or in developing safer decompression schedules;
- gain a more in-depth knowledge of current issues pertaining to the physiology and pathophysiology of compression and decompression phenomena and, where applicable, be able to apply this information in their practice;
- gain a more in-depth knowledge of the physiologic, pharmacologic, pathologic, and biochemical effects of oxygen, nitrogen, carbon dioxide, the noble gases, especially in the hyperbaric environment, on different levels of biological organization and, where applicable, be able to incorporate this information into their practice;
- gain new knowledge about the future scientific and medical directions of hyperbaric medicine and, where applicable, be able to incorporate the appropriate information into their practice;
- present material pertaining to their experiences within the diverse field of high pressure biology and to receive critical reviews of their work;
- be introduced to new diagnostic, research, or therapeutic techniques and equipment pertaining to hyperbaric medicine and be able to incorporate the relevant knowledge and procedures into their practice;
- learn of the varied activities of the Society and the past and future directions of the Society;

AND become active in Societal affairs so that they could influence the Society's future.

UHMS Annual Scientific Meeting
Salt Lake City, UT
June 26-28, 2008

Disclosures

Planners:
The following planners had no financial relationships with commercial interests to disclose.
- **Lindell Weaver, MD; James Holm, MD; Dick Sample; Mary Hirsch; Kayla Deru; Susan Churchill; Paul Sheffield, PhD, CME Rep; Lisa Tidd**

Faculty:
The following faculty had no financial relationships with commercial interests to disclose.
- **Bret Stolp, MD; Lindell Weaver, MD; Claude Piantadosi, MD; Alessandro Marroni, MD; Dick Sample, CHT; William Orrison, MD; Richard Vann, PhD; Paul Sparks; David Cobb, MD; Robert Sheffield; Jaysen Yogaratnam**

The following faculty has disclosed a financial relationship.
- **Micahel Holick, MD- Merck, P&G, Lilly, Amgen, Novaitis, Quest Diagnostics, Consultant/Speaker; Neil B Hampson, MD - Masimo, Consultant/Speaker; Richard Clarke, CHT – National Baromedical Services owner**

Presenters:
The following presenters had no financial relationships with commercial interests to disclose.
- **A. Larsson; James Bell, CHT; R Brock Frost; Ahmet Korkmaz; James Holm, MD; Ramona O Hopkins, PhD; Aleksey S Sobakin; Jane Yen-Chen Chen; Rebecca Padilla Burgos; Alice Song; Jawad Kassem; Richard D. Vann, Ph.D; Amber-Louise E. Simpson; Jay B. Dean, PhD; Richard Dunford; Amir Mor; Jeffrey A. Niezgoda, MD, FACEP; Richard Mahon; Andrew D. Ray; Jessica Wall; Robert S. Michaelson, Col, USAF, MC, SFS; Anne Cherry; Joel Dovenbarger; Secil Aydinoz; Benjamin Bollinger; John Harrah, Jr.; Serdar Kaya; Bettina Magliato RN, MS, CIC, CWCN, CHRNC; John J Freiberger; Shao-Yuan Chen; Brett B Hart; Joseph L. Byrne MD; Shawn G. Rhind; Bruce A. Cameron; Kadir Dundar; Shepeleva Jaroslava; CDR Matthew J. Hickey, MC, USN; Kathleen Marie Rouse Jones, MD; Shinomiya Nariyoshi; Christian R. Gutvik; Keith Gault; Stacy Handley, RN, BSN, ACHRN, CWCN; Christine Schlaerth (Schaub); Kelly Johnson-Arbor; Stephen R. Thom; Dan E. Warkander; Kirill Larin; Suh, Hyejin; David R. Pendergast; Kiyotaka Kohshi; Sukru Oter; Dennis E. Weiland, MD; Laurens E. Howle, PhD; Svein Erik Gaustad; Dominic D'Agostino; Lavoute Cécile; Takkin Lo; Don W. Worthington; Lawrence E. Hightower; Tracy Wester; Donna M. Uguccioni, M.S; Lindell Weaver, MD; Tzong-Bor Sun, M.D., Ph.D; Edmond Kay, MD, FAAFP; Mahito Kawashima; Watanabe Satoru; Eynan Mirit; Marie A. Hawkins, B.S. R.N; Yehuda Arieli, PhD; G P Anderson. MD; Marshall Nuckols; Yu Suzuki; Gao Guangkai; Marvin Heyboer III, MD, FACEP; Ivo Torres Filho; Gary W. Latson, MD; Massimo Ferrigno; J. Travis Parsons, PhD; Gaylan L. Rockswold, M.D., Ph.D.; Michael P. Matott; Jakob Knudsen; Gerardo Bosco; Michael Strauss; Osamu Inoue, M.D. P.H.D.; Gerry Johnson; Mikael Gennser; Ozgur Yesilyurthakan Simsek; Mikulas Chavko; Petar J Denoble; Harry T. Whelan, M.D.; Nancy J Denke; Nina Subbotina M.D.; Igor Aksenov; Barbara Shykoff; Folke Lind ; Seth McEwan; Bradley B. Bailey, MD; George A. Perdrizet; Neal W. Pollock; Cameron R. Smith; Gunalp Uzun; Paul J. Sheffield; CE Wreford-Brown; LCDR Robert W. Perkins, MD, MPH; Roger B. Schechter, MD; Dr. David Fothergill; Matthew A. Schweyer, CHT; Vincenzo Zanon, MD.**

The following presenters have disclosed a financial relationship
- **Bryan Lopez – Intellicure, Employee; Caroline E. Fife - Intellicure, Owner; Harriet W. Hopf, MD - Oxyband Technologies & OxyHeal Health Groups Donated the dressings for this study, provided previous grant support (HWH); provided Chamber for study; Ivan Demchenko -; Kazu Suzuki, P.P.M. C.W.S. - KCI Wound VAC, Sechrist, Vasamed Speaker's bureau, Consultant; Kevin Klocek - Boehringer Wound Systems LLC, Employee; Pia Lawson-Smith; Ralph Potkin, MD - Dive Safety, Products/owner; Sergio Angelini - UWATEC AG, Employee.**

Commercial Support:
The following have provided commercial support to this activity
Hyperbaric Physicians of Georgia, Cubist Pharmaceuticals, OxyHeal Health Group, Seachrist Industries

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Morning Schedule

- 7:30-8:00 President's Address
- 8:00-9:00 Surviving the Abyss (A Marroni)

- 9:00-12:00 Associates/BNA Program
- 9:00-12:00 Session A: Diving/Decompression Illness: Theory & Mechanisms
  - 9:00-10:30 Abstracts A1, A2, A3, A4, A5, A6
  - 10:30-11:00 BREAK/EXHIBITS
  - 11:00-11:30 Posters
  - 11:30-12:00 Abstracts A7, A32

The President's Address

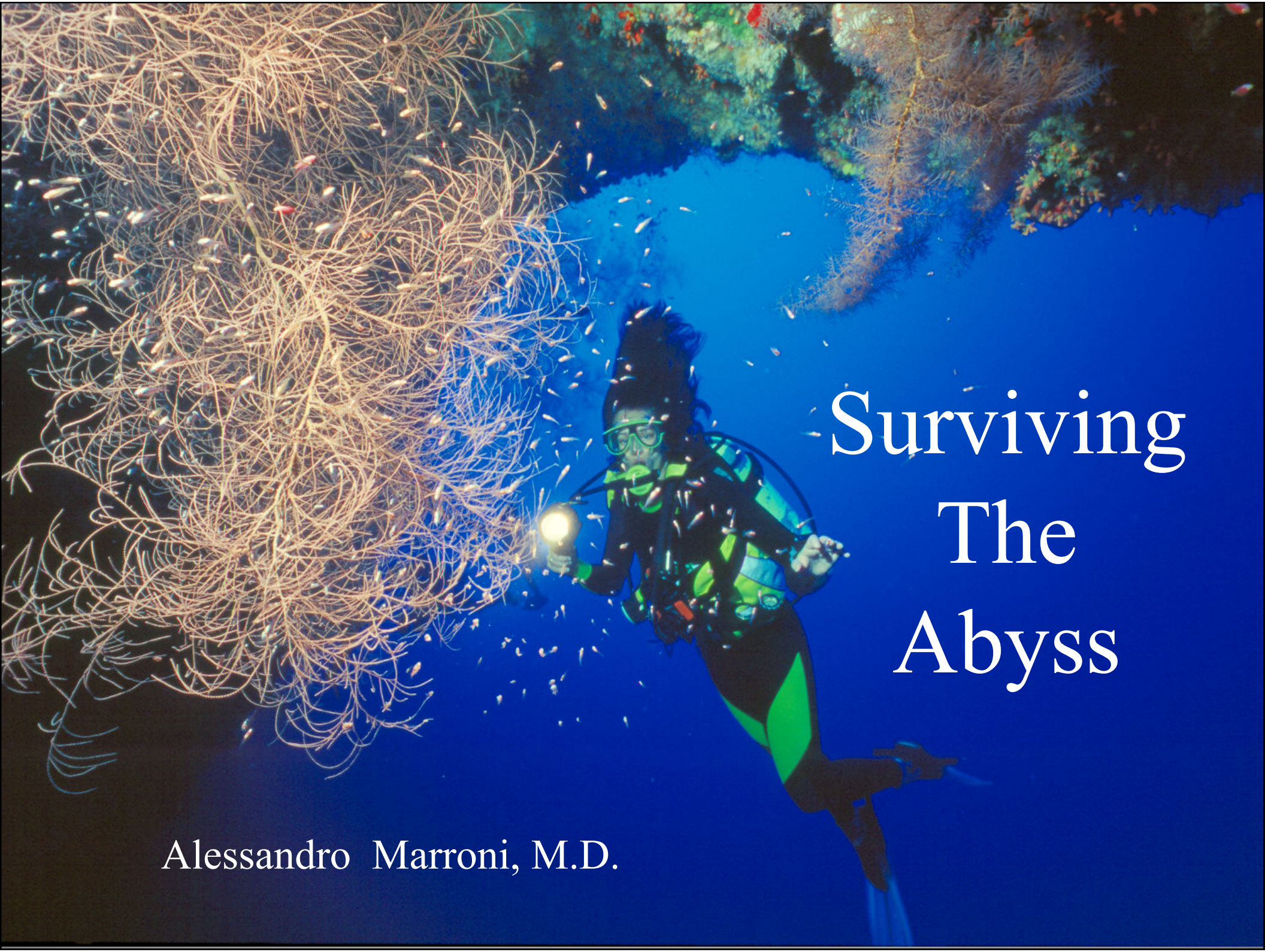
Bret Stolp, MD, PhD

Plenary Session

Surviving The Abyss

One hundred years of decompression sickness prevention: observation of natural events, mathematical models, biological research

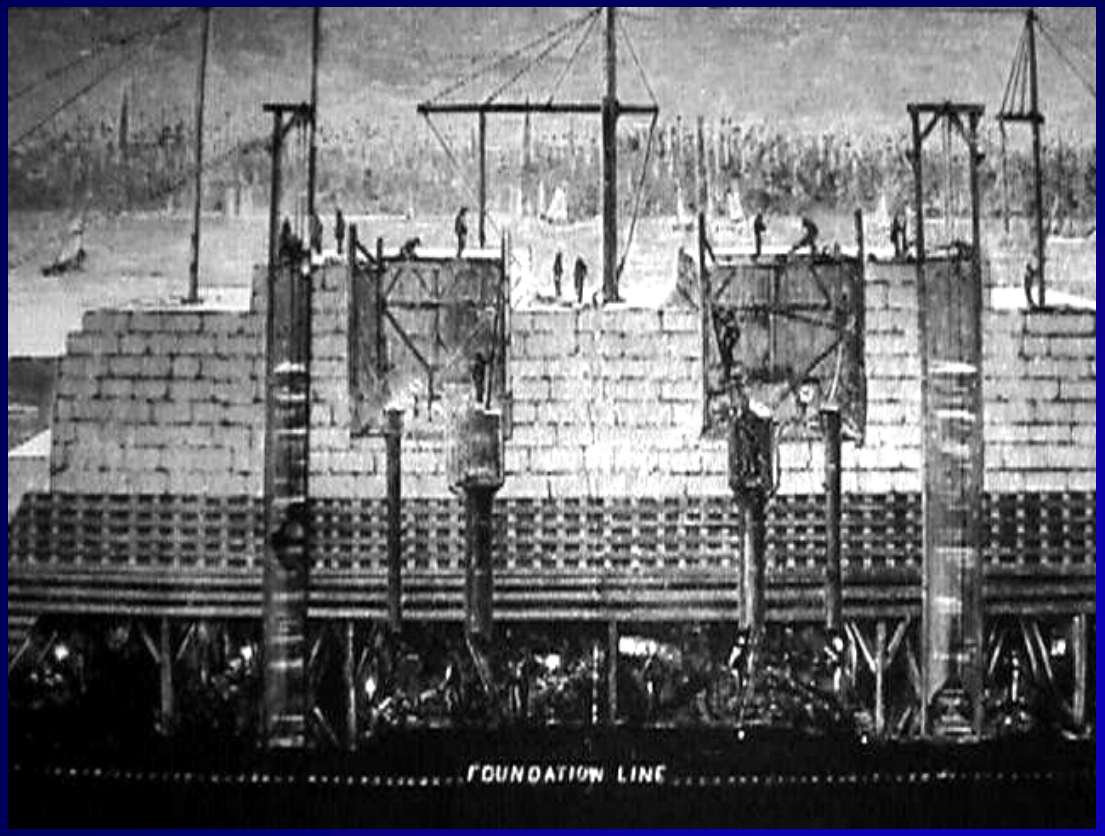
Alessandro Marroni, MD

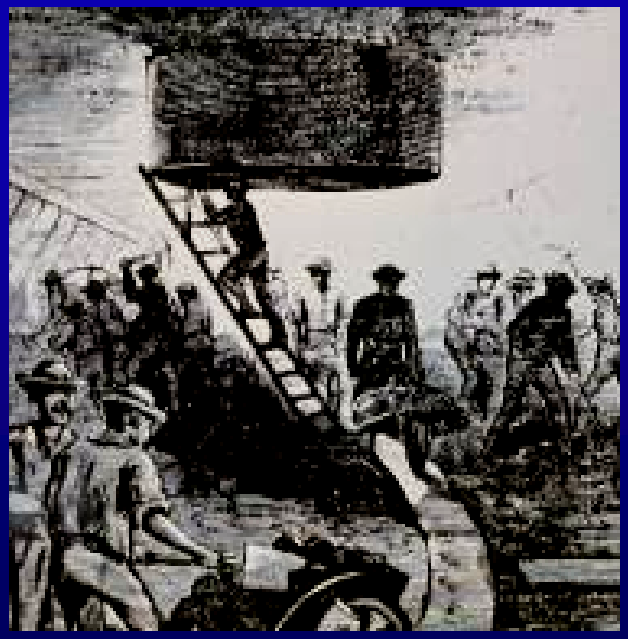


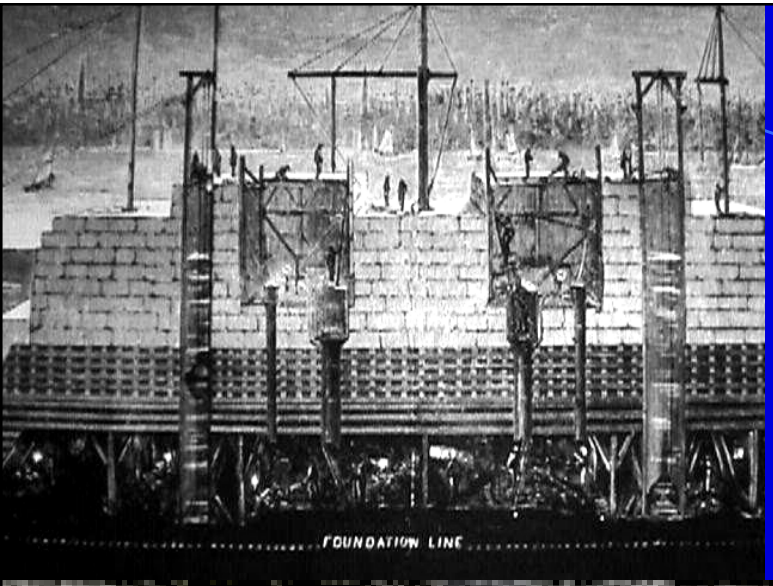
Surviving The Abyss

Alessandro Marroni, M.D.

The Bends





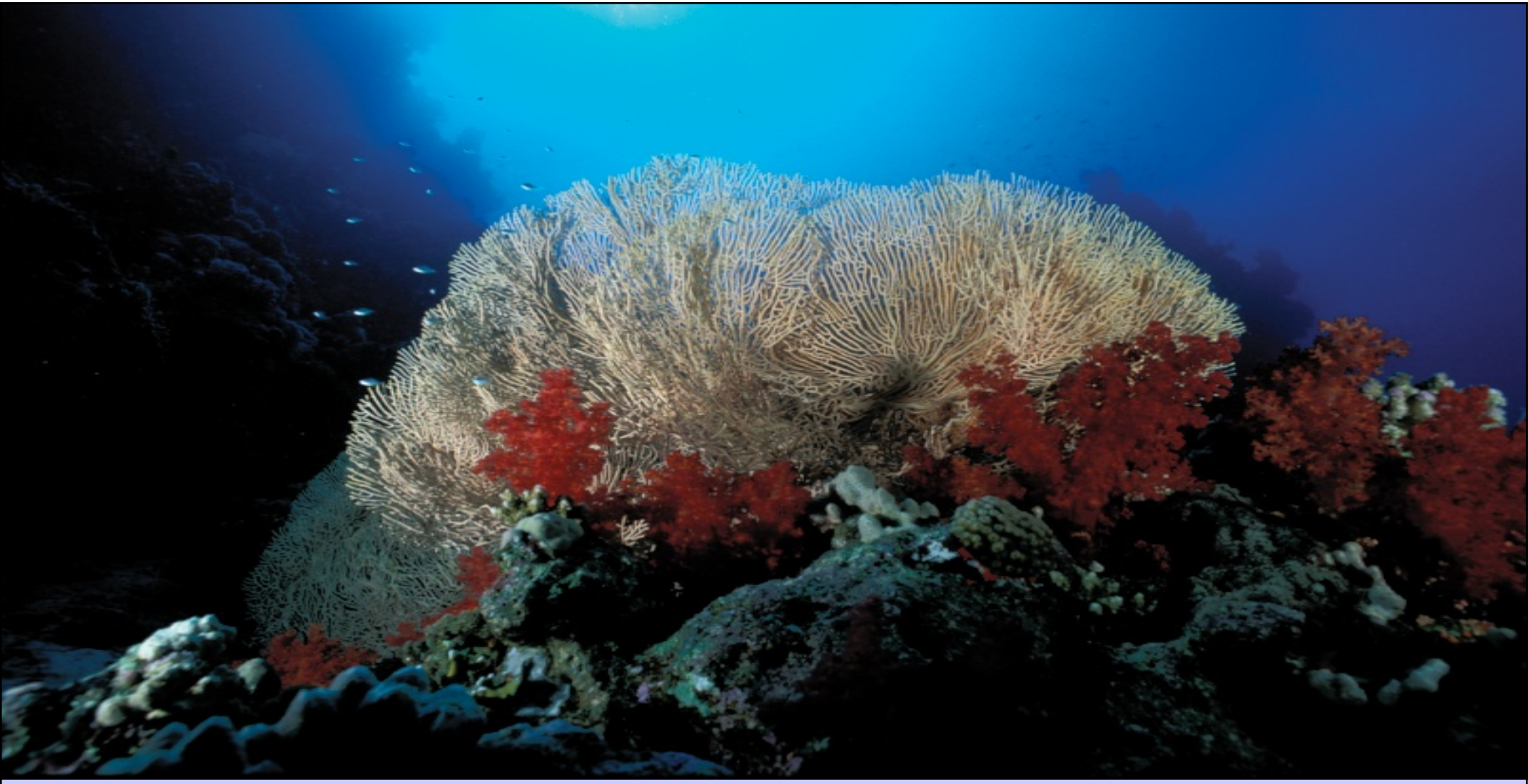


- 1896. Ernest Moir. Hudson River Tunnel
- Systematic use of recompression to treat Bends
- Recompression to 1/2 or 2/3 of working depth.
- Decompression at 1 psi / minute.

The Early Days

Petty Officer Andrew Catto should have died. Or at least been writhing in agony. It is 1907, and Catto has survived an "impossible" dive.

The Royal Navy considers diving below 110 feet estremely dangerous. Catto went to 180. No one before has spent more that 10 minutes that deep without getting bent. Catto stayed 29.



Catto's miraculous dive was based on Haldane's new decompression model and dive tables: Haldane's notions, assumptions and guesses – vague notions, broad assumptions and bold guesses – that today remain "virtually unchanged" in recreational diving tables and dive computers.

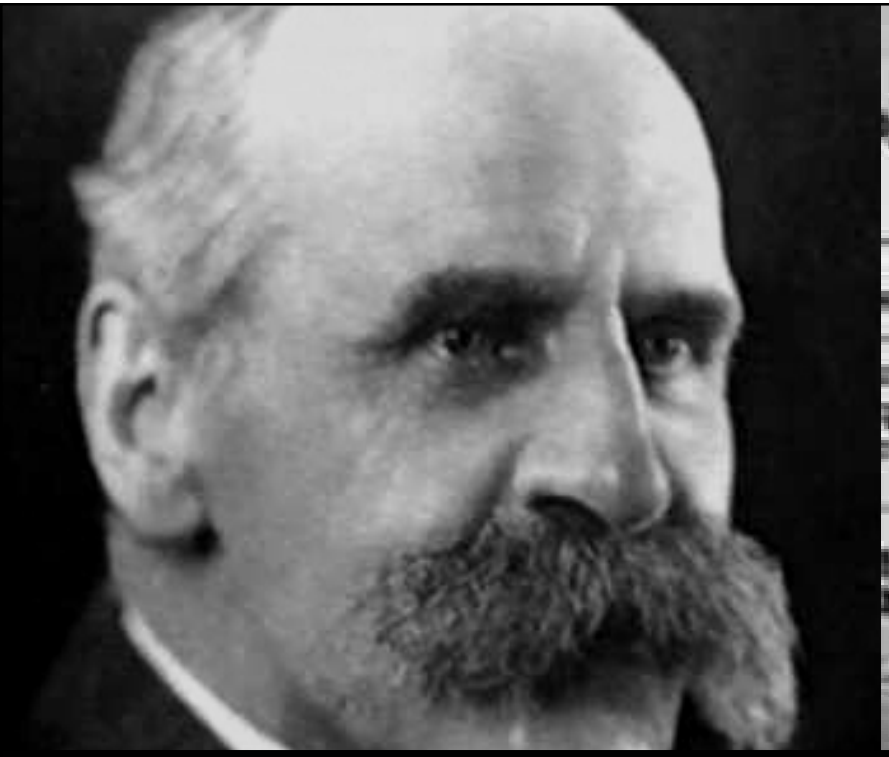
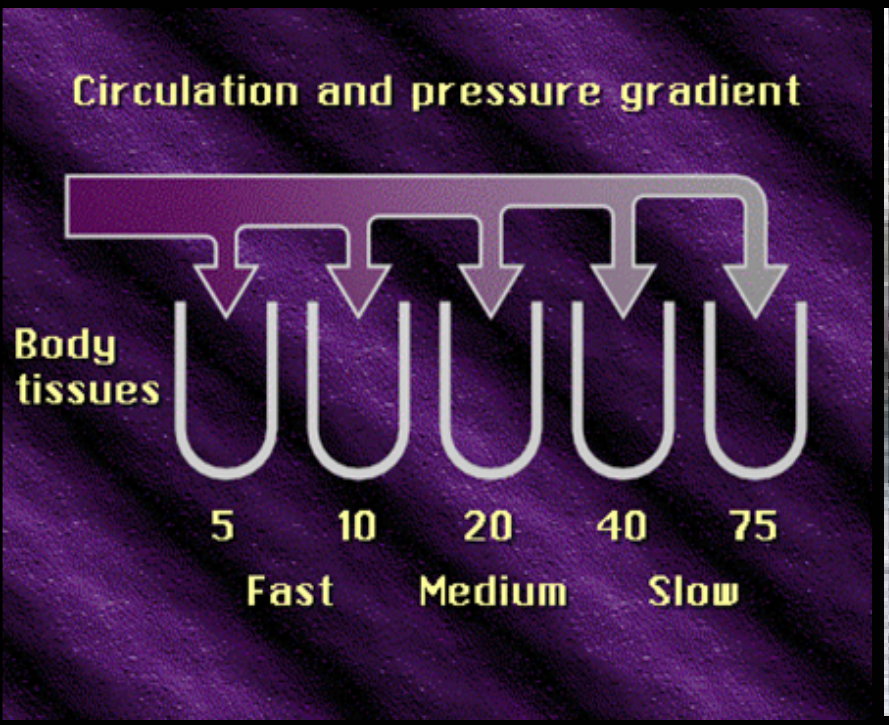
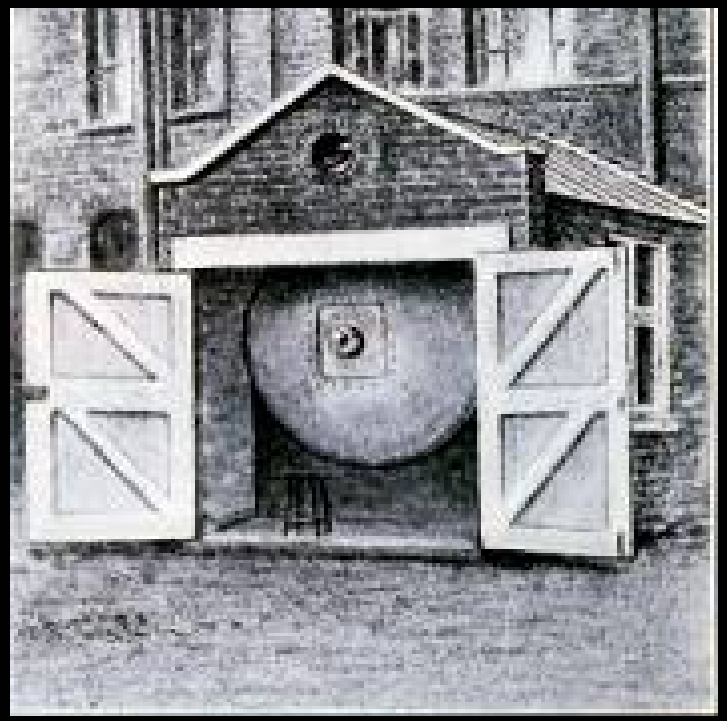


TABLE I.

the Ascent of a Diver after ordinary
from Surface.

	Time from Surface to beginning of Ascent.	Approximate Time to First Stop.	Stoppages in Minutes at			
			60 Ft.	50 Ft.	40 Ft.	30 F
	No limit	—	—	—	—	—
	Over 3 hours	1	—	—	—	—
	Up to 1 hour	—	—	—	—	—
	1-3 hours	1½	—	—	—	—
	Over 3 hours	1½	—	—	—	—



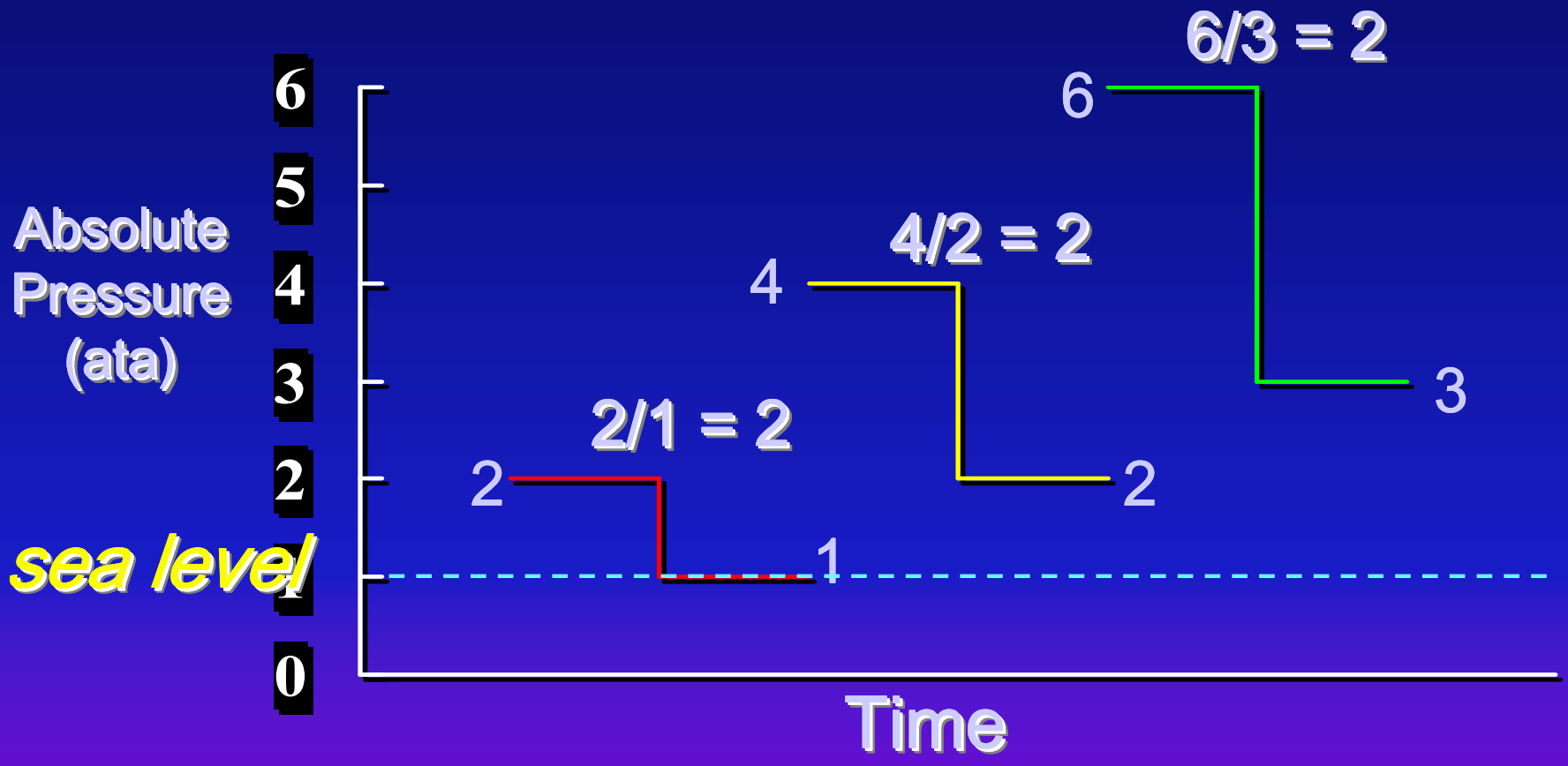


Boycott AE, Damant GCC and Haldane JS. *J Hyg* 8: 342-443, 1908.

DHMSTC

J.S. HALDANE

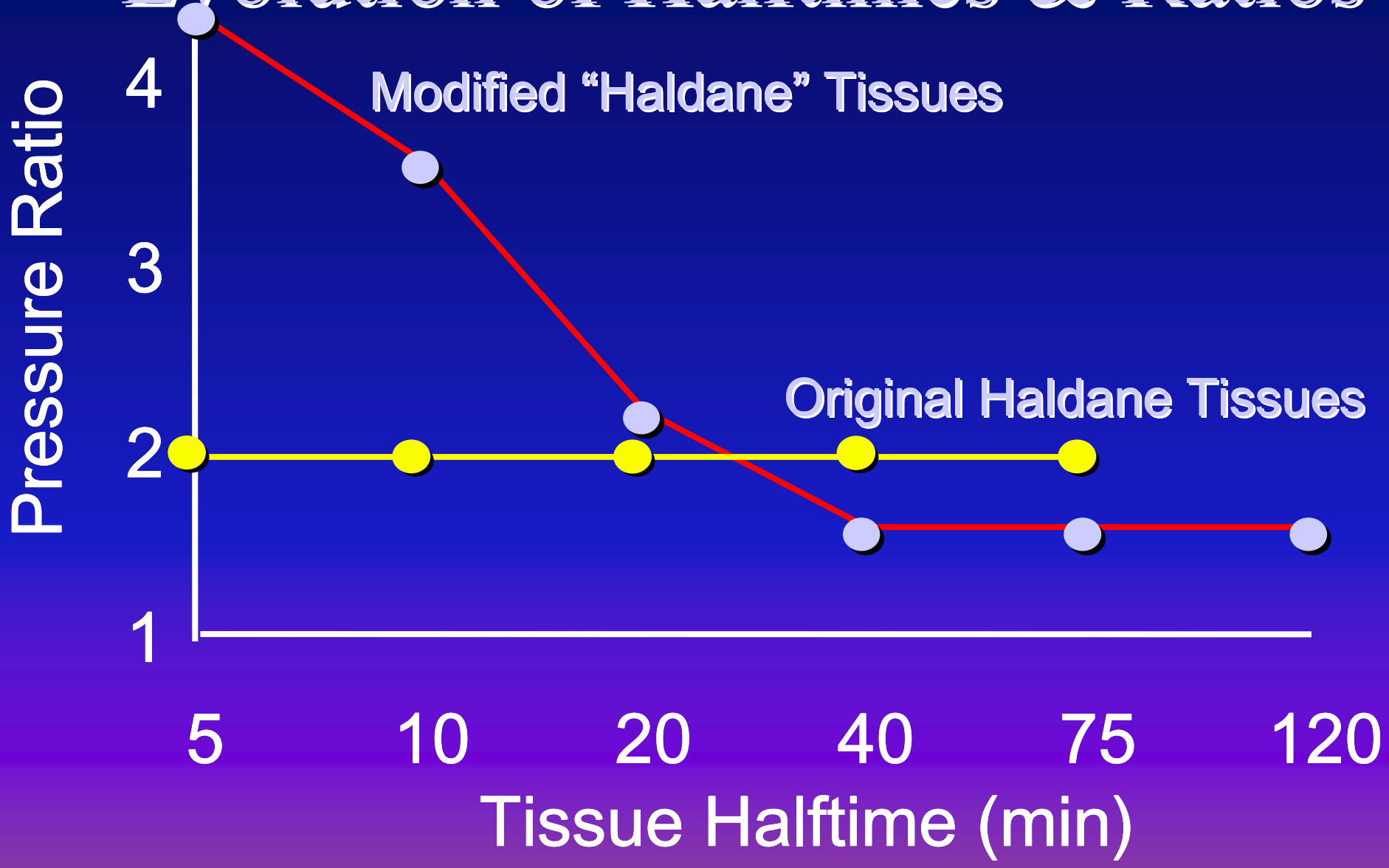
2:1 Rule

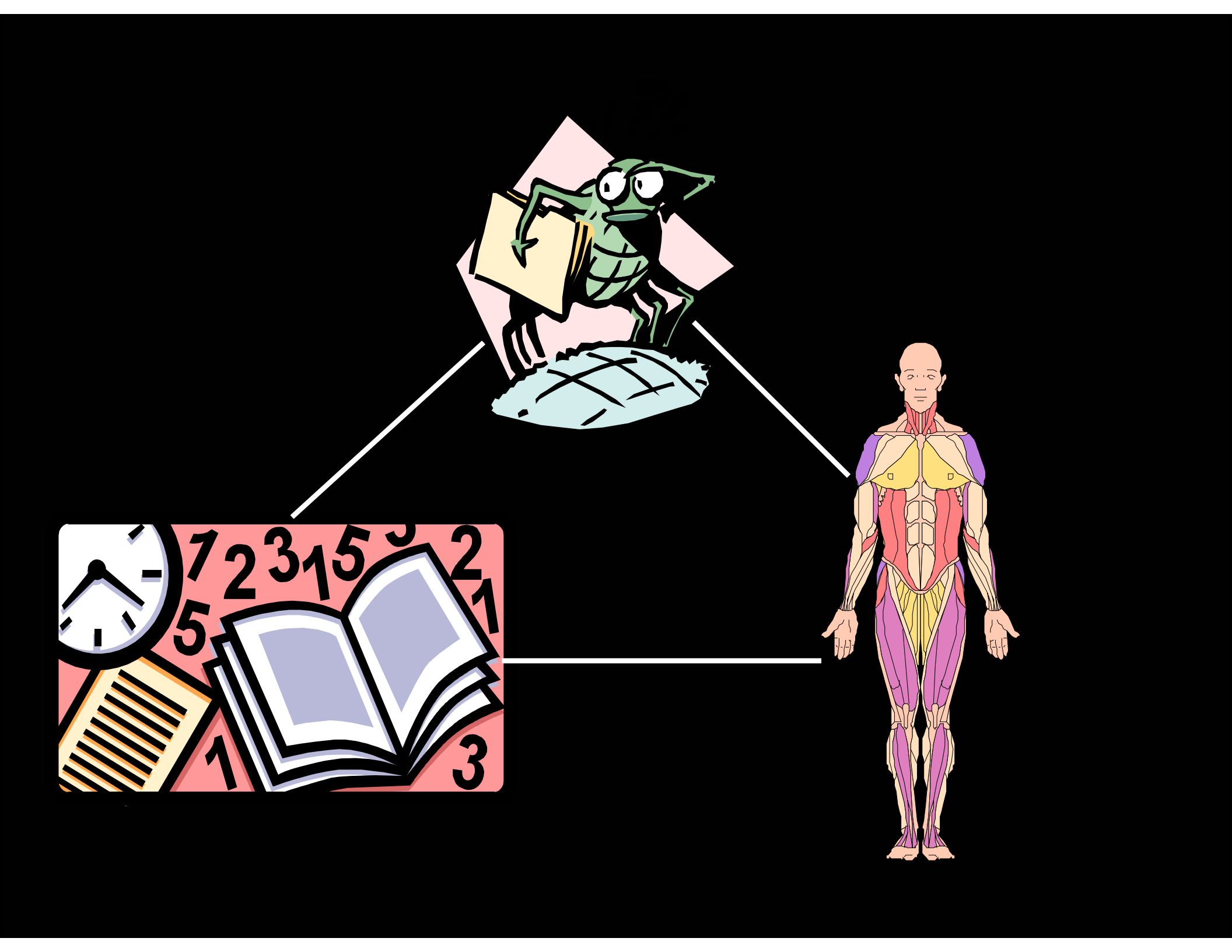


DHMSTC

Critical ratios for half-time tissues

Evolution of Halftimes & Ratios

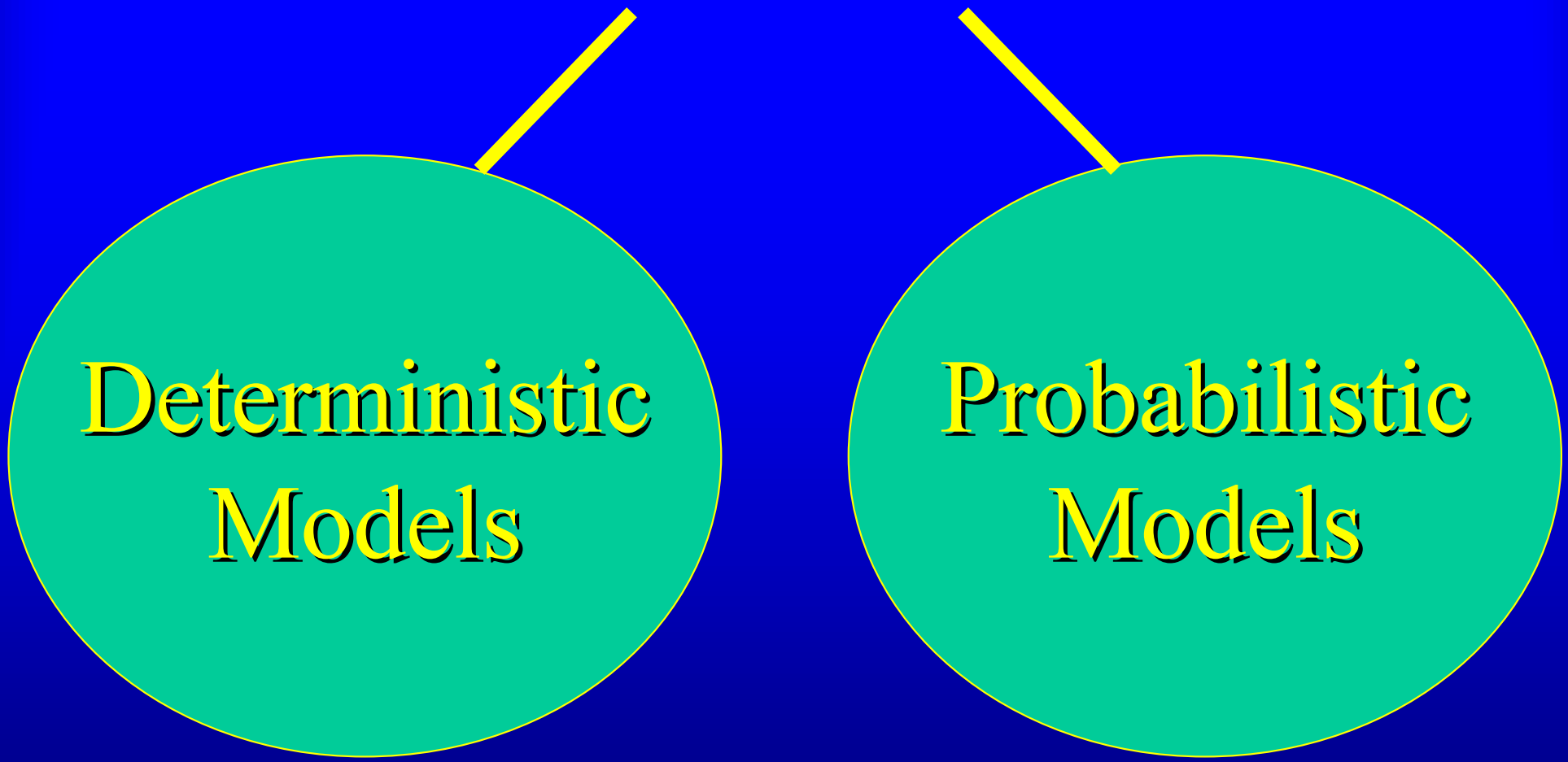




What is a Decompression Algorithm?

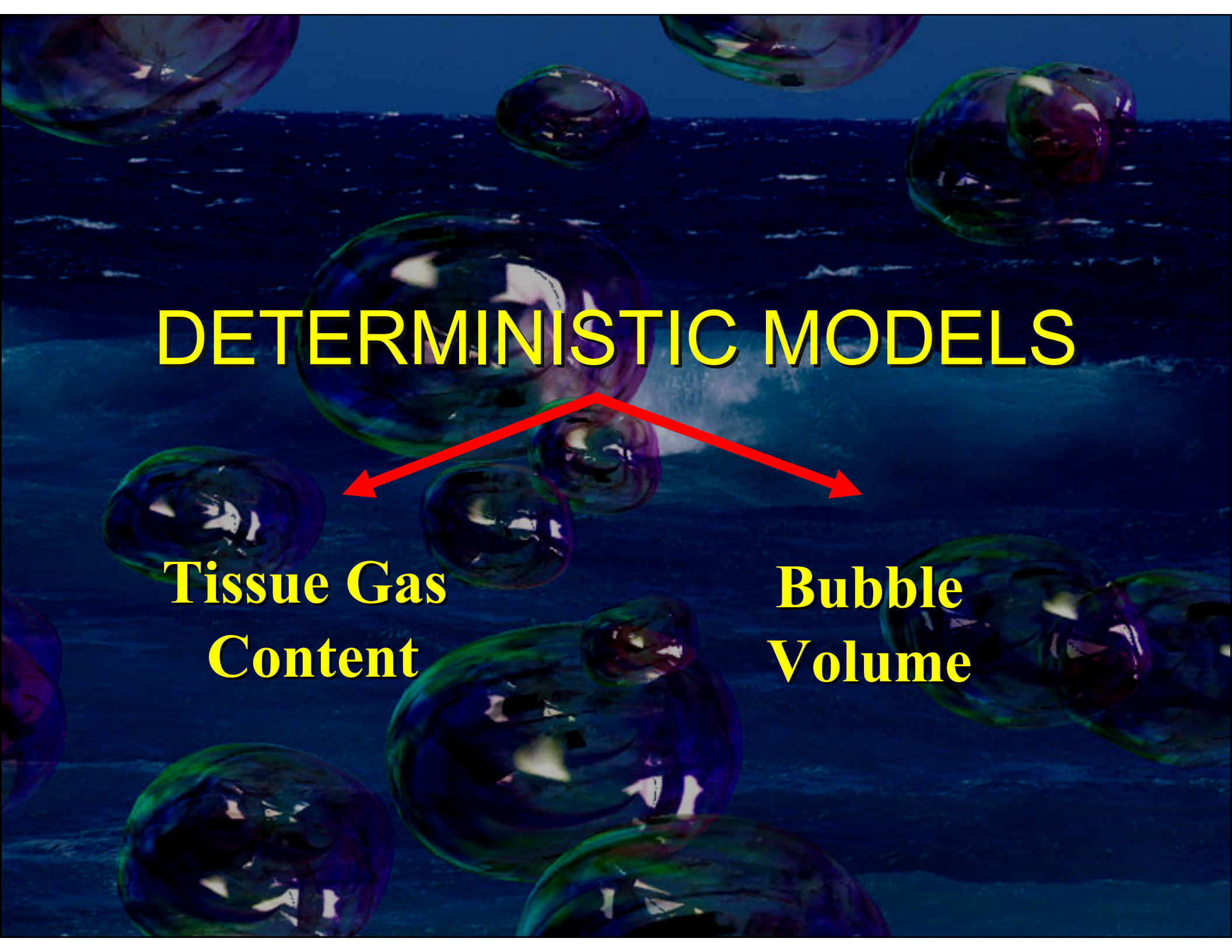
- A mathematical model or scheme for predicting inert gas flux within the body within certain parameters and in the absence of real time measurement and verification.
- Biological complexity is rendered to a workable ‘formula’.

Decompression Algorithms

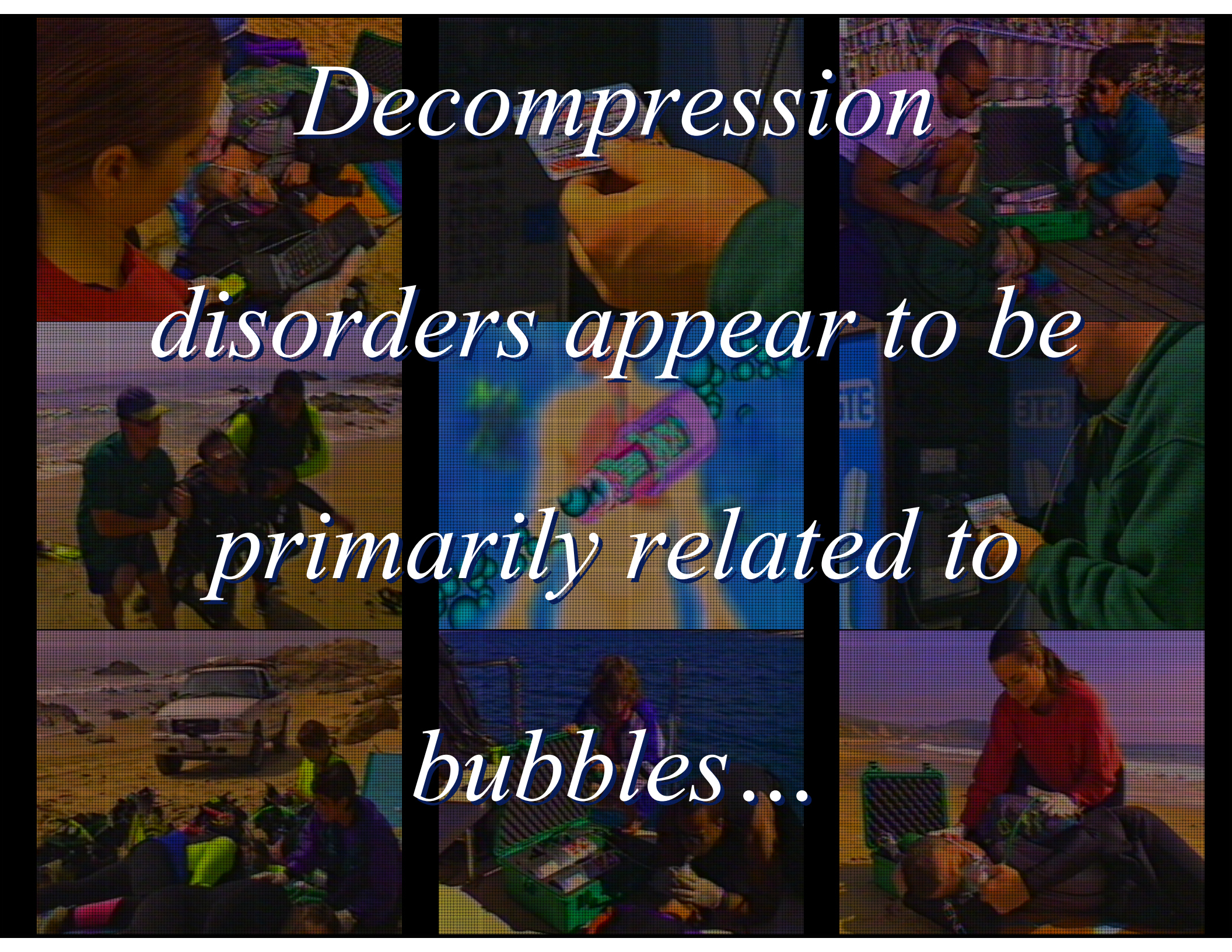


Exposure?

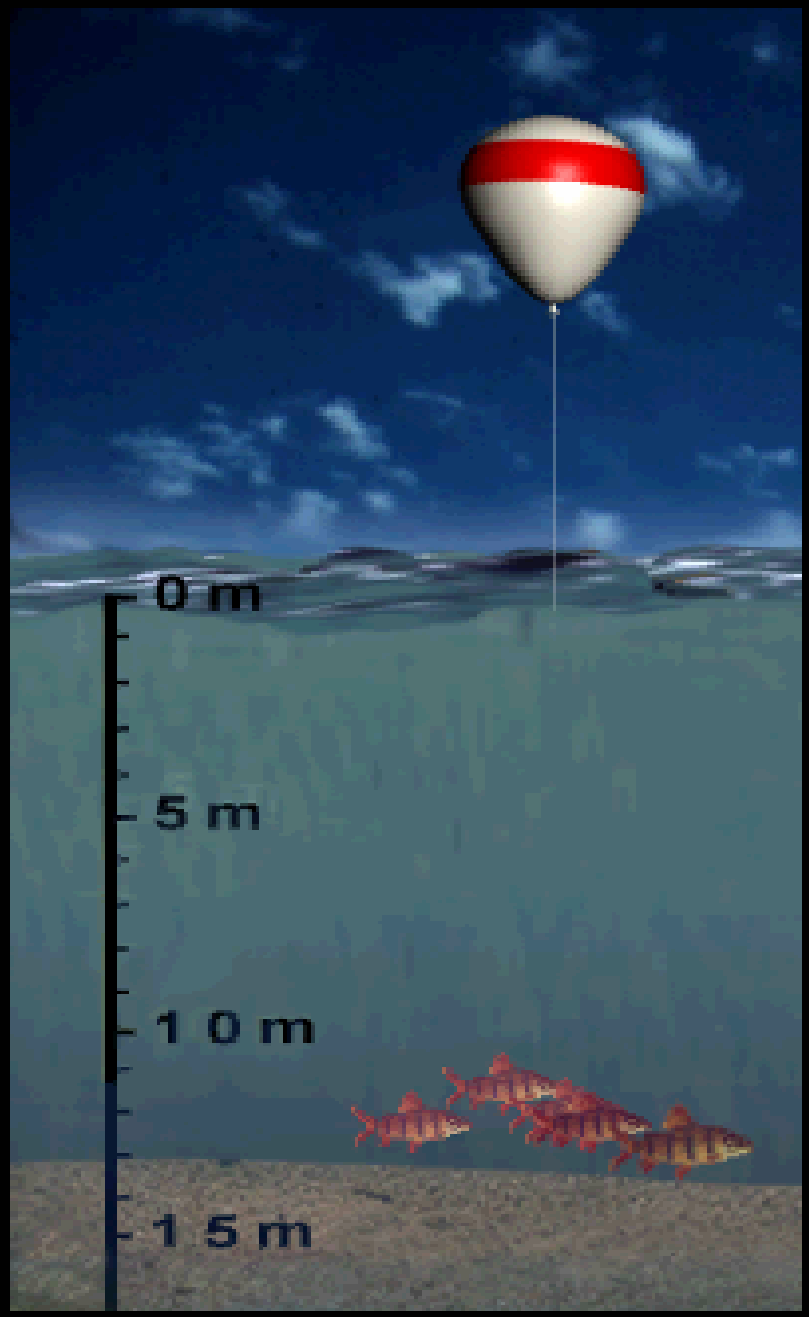
Risk?


DETERMINISTIC MODELS
Tissue Gas Content
Bubble Volume

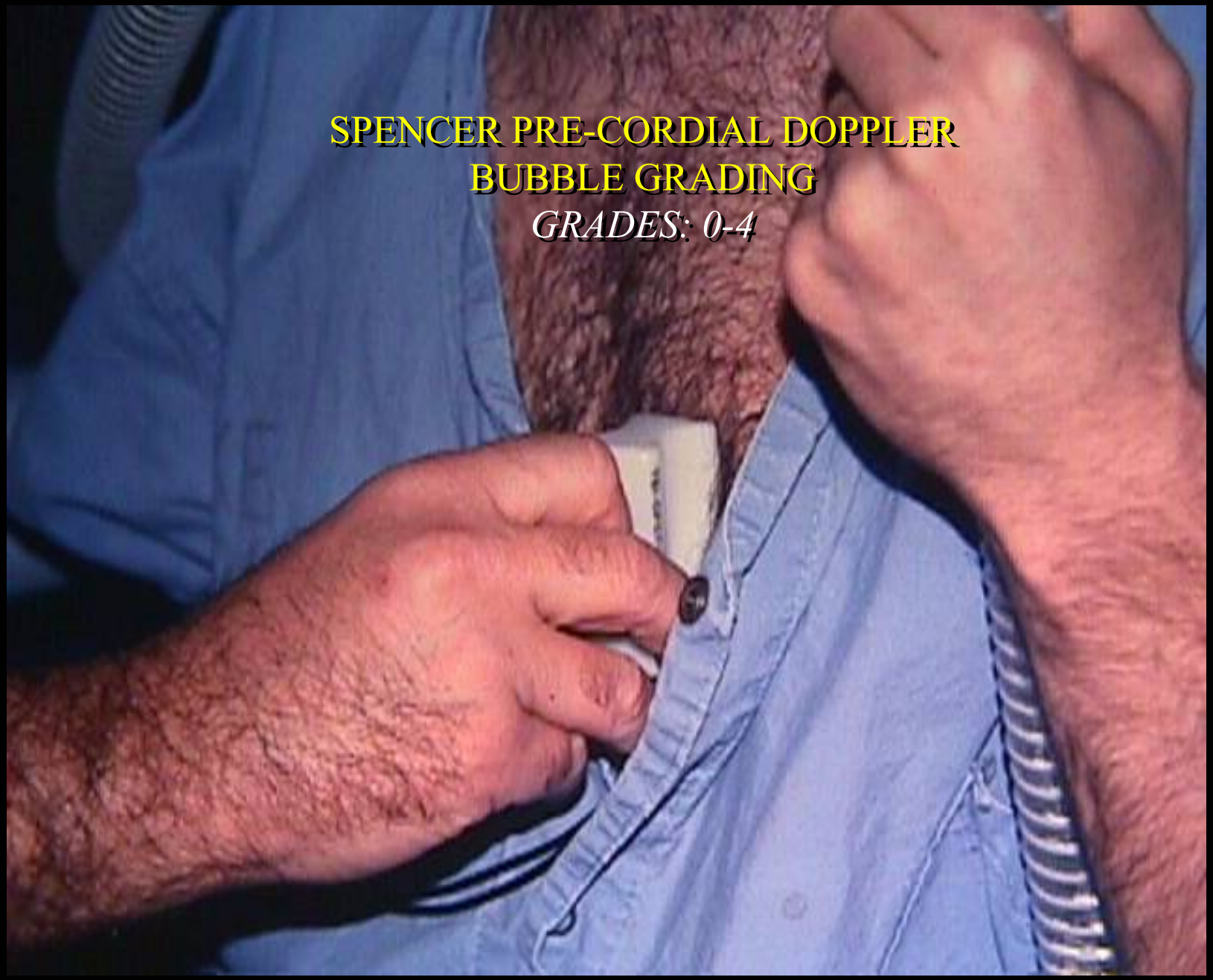

After 100 years of research
we can confidently say …


Decompression
disorders appear to be
primarily related to
bubbles…

Gas & Gas Expansion

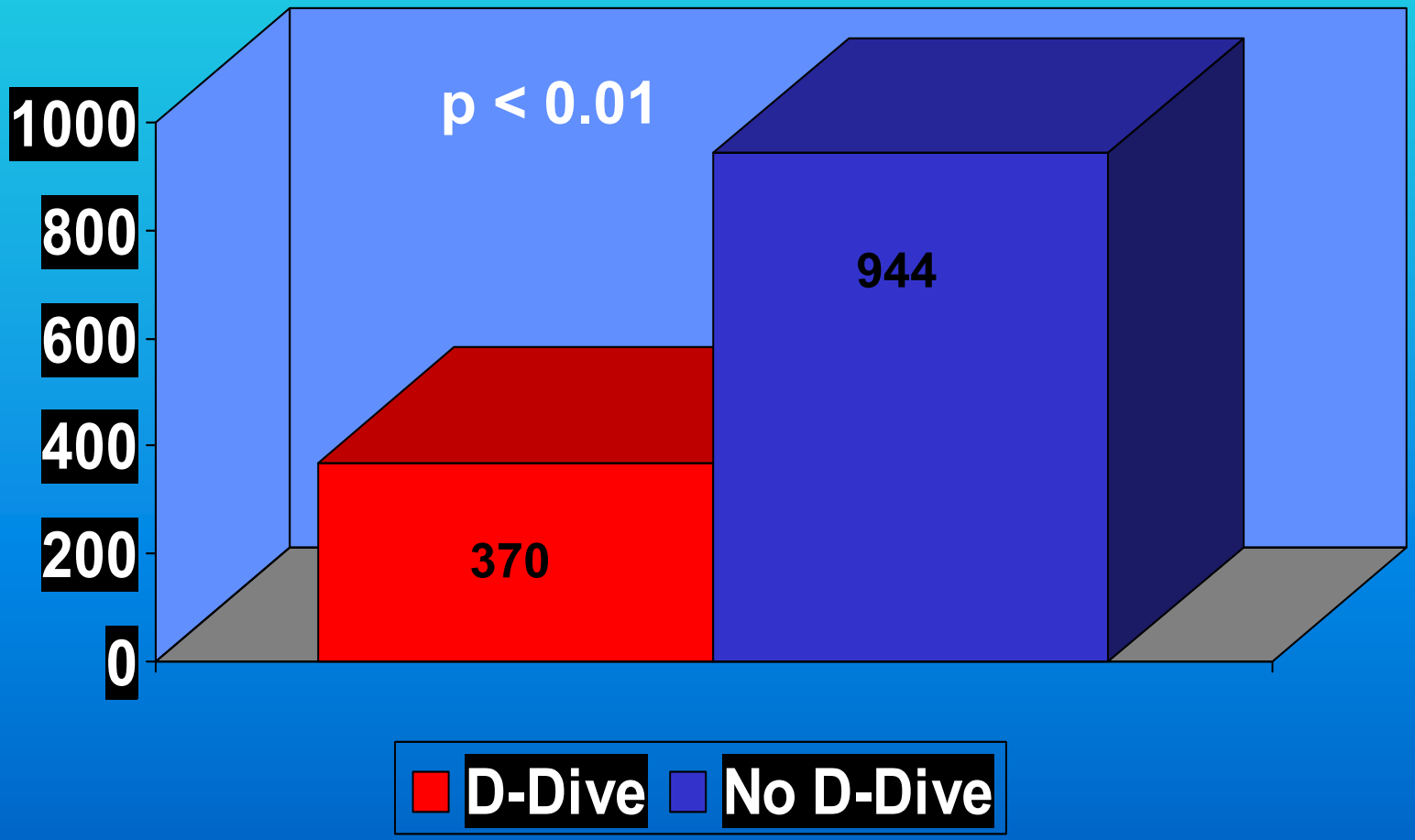


Intravascular Bubbles:



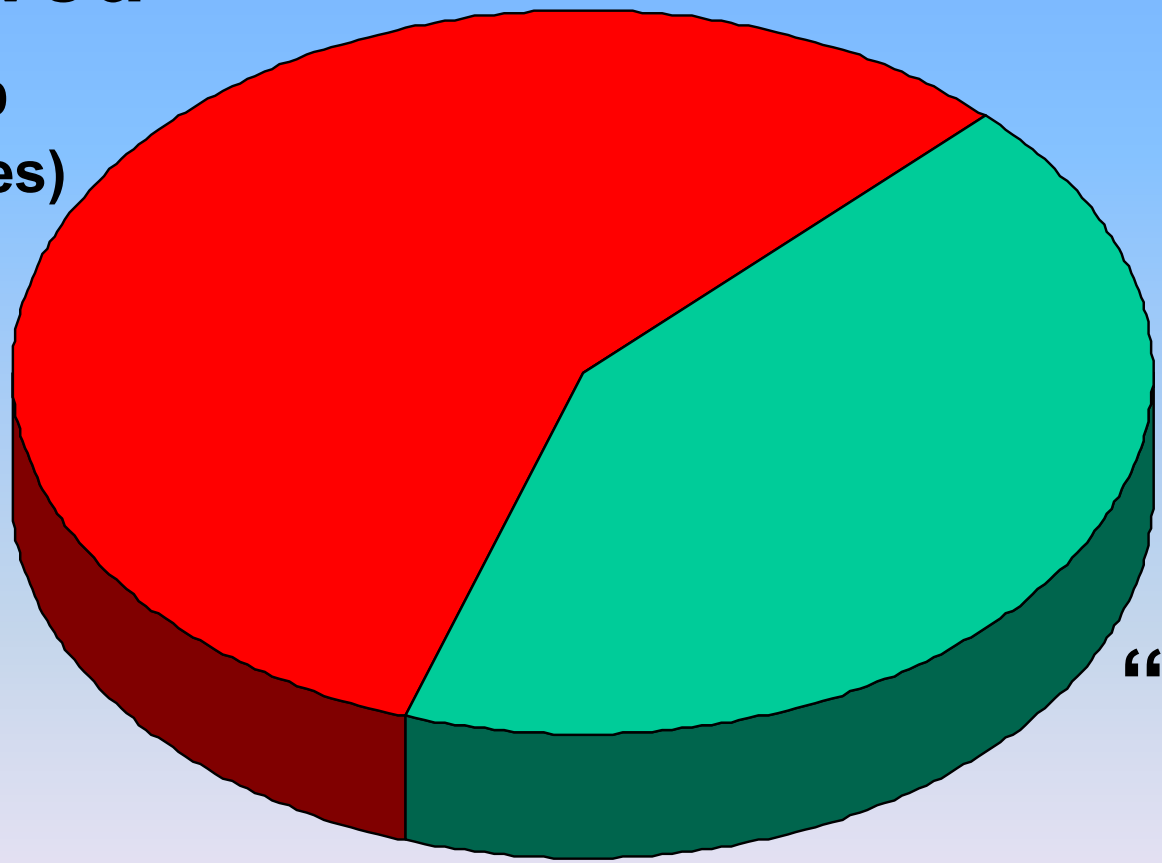
DAN Europe Database
D-Diving vs No D-Diving and DCI

1314 DCI cases



DAN Europe Database
"Undeserved DCI"

"Undeserved"
57,6%
(no mistakes)

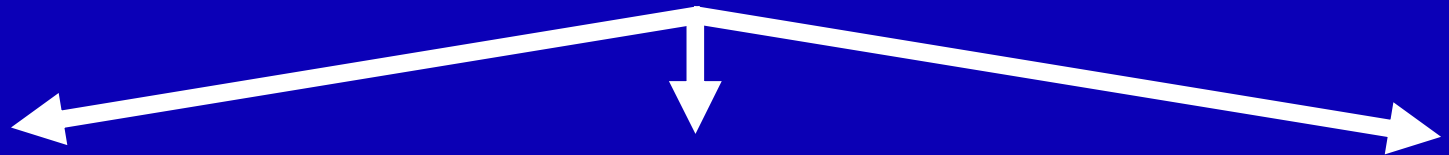


"Deserved"
42,4%
(mistakes)


FUMÉ

RETURNING TO AN OBSERVATION-BASED DEVELOPMENT OF DECOMPRESSION THEORY??

Bubbles



Economy of Decompression

Formation & Migration of Bubbles

Reactions to Bubbles

ECONOMY OF DECOMPRESSION

- **Combining pressure & gas gradients during decompression so as to:**
  - reach the surface quickly and safely
  - eliminate inert gas efficiently while:
    - avoiding excessive VGE
    - avoiding harmful tissue supersaturation

DAN Europe

Research

1995 – 2005:

over 30.000

monitored dives,

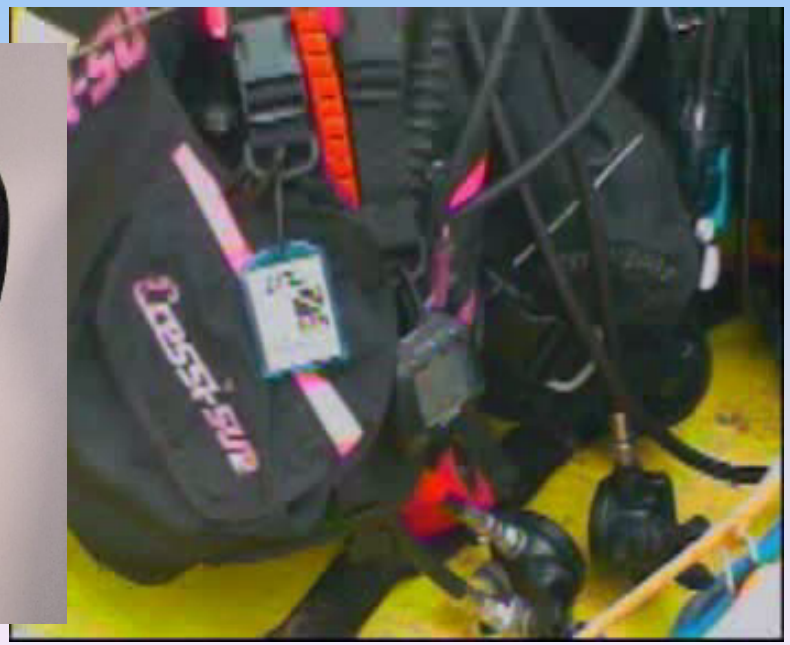
with dive profiles

questionnaires

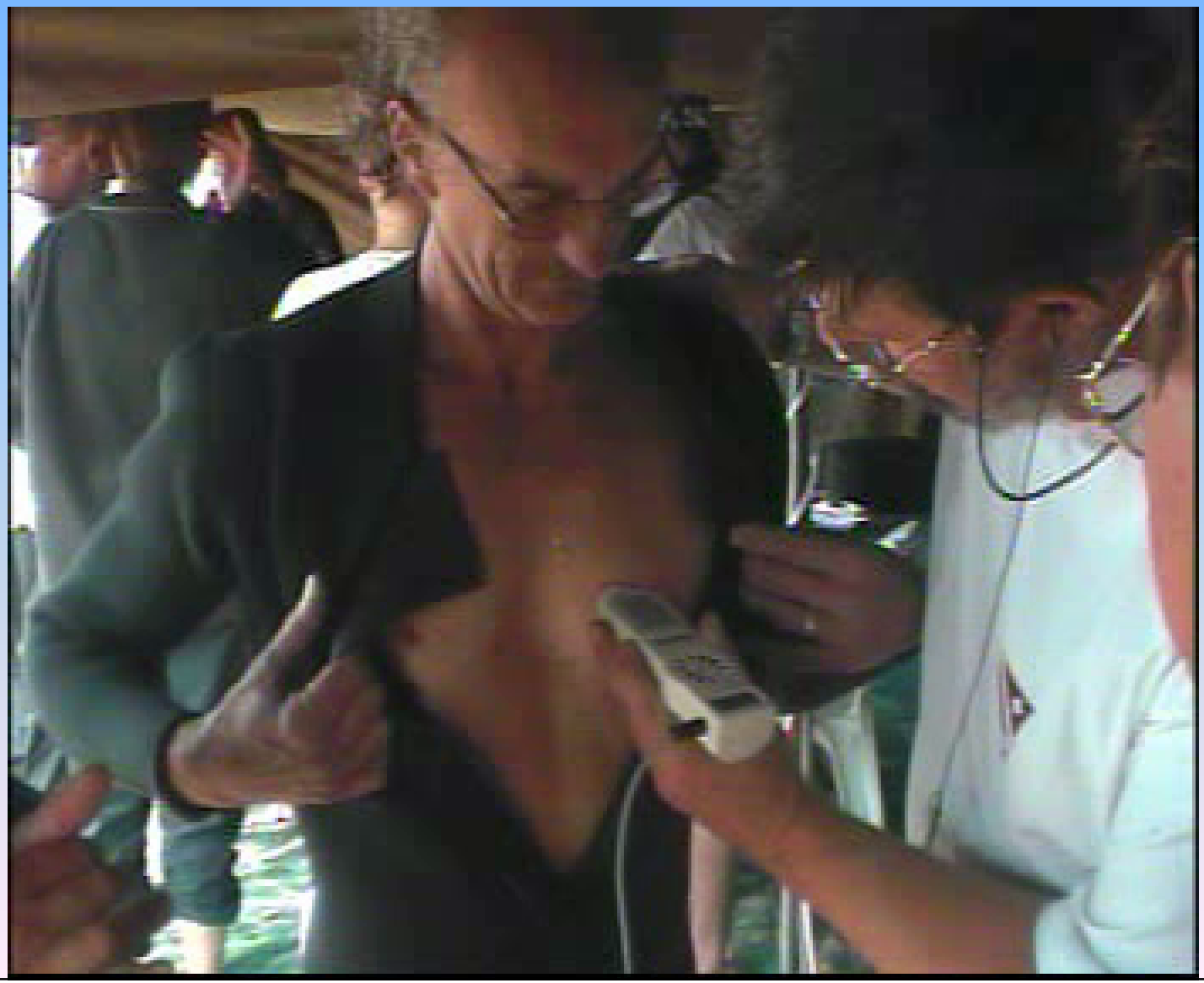
and Doppler

Recordings.

All dives are recorded for time/depth profile by “DAN Europe Black Boxes” – modified dive computers - which are worn by the divers to assure objective dive profile recording and the availability of data ready for mathematical analysis of the computed tissue saturation.



Doppler Recordings are performed by specially trained volunteer divers, with an Oxford Instruments 3,5 MHz probe and MP3 digital recorder, according to the methods developed by our group and qualified as “Research Technicians” .



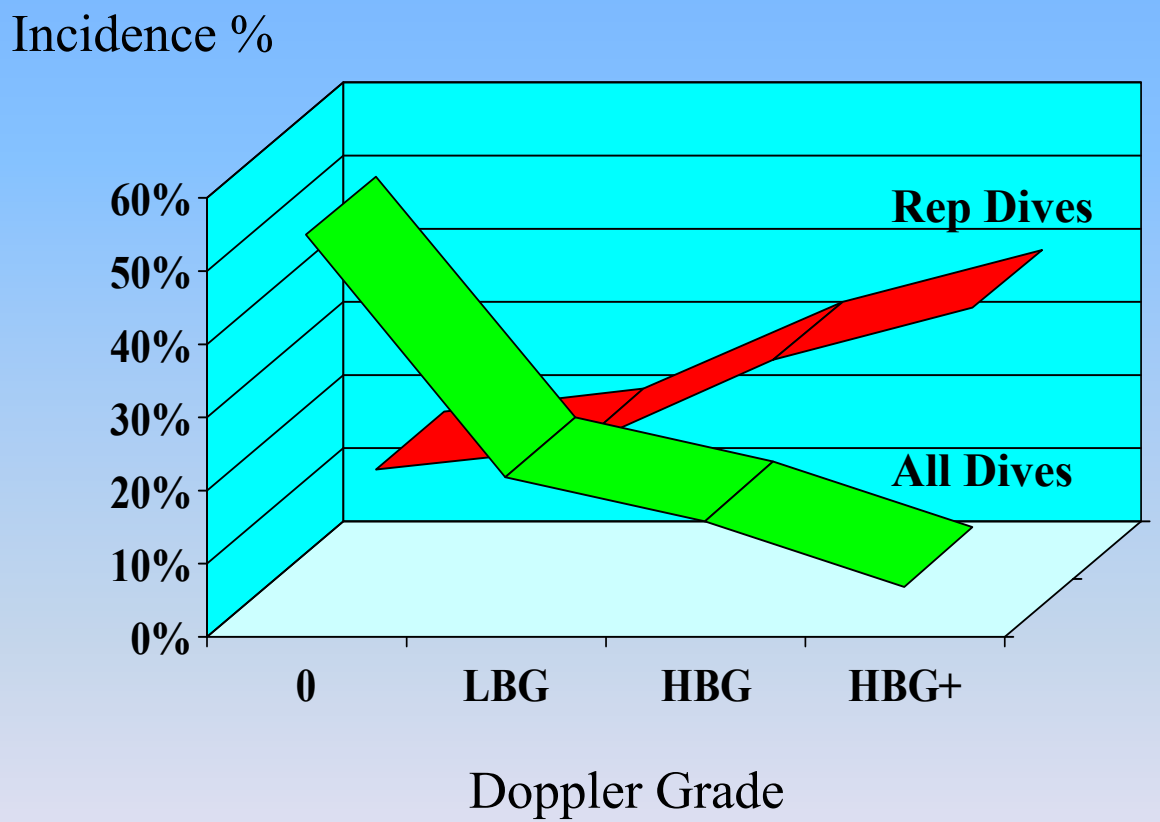
The recordings are made over 1 minute and every 15 minutes up to 90 minutes after the dives, and subsequently evaluated in undisturbed laboratory conditions by a blinded evaluator.

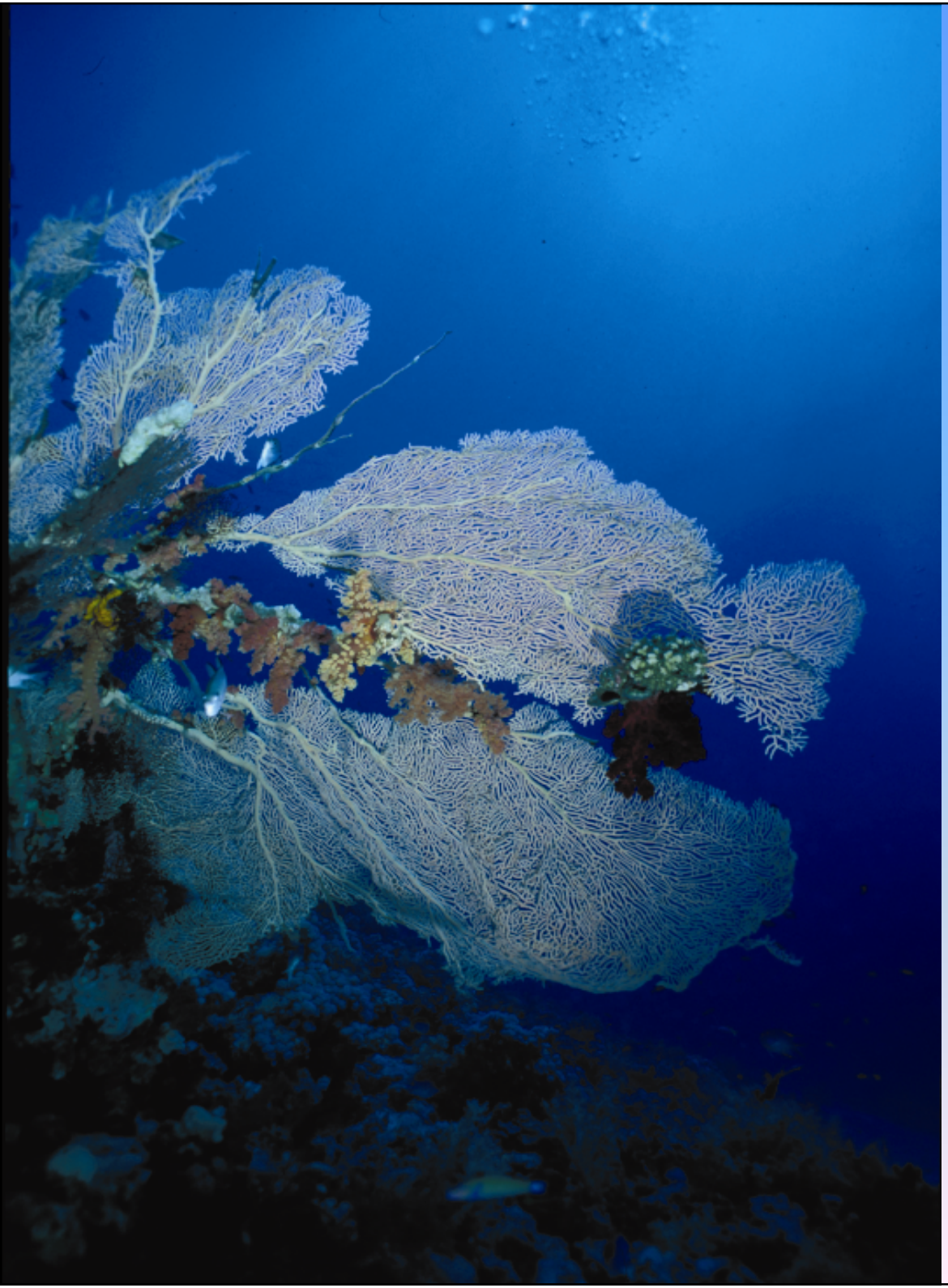
The Doppler Bubble Signals were scored according to the Spencer Method but with a simplified Doppler Bubble Grading System, as follows:

- LBG – Low Bubble Grade: occasional bubble signals, Doppler Bubble Grades (DBG) up to 2 in the Spencer Scale
- HBG – High Bubble Grade: Frequent to continuous bubble signals, > DBG 2 in the Spencer scale.

Incidence of Doppler Bubble Signals after Unrestricted Recreational Dives.

Repetitive Dives considered separately

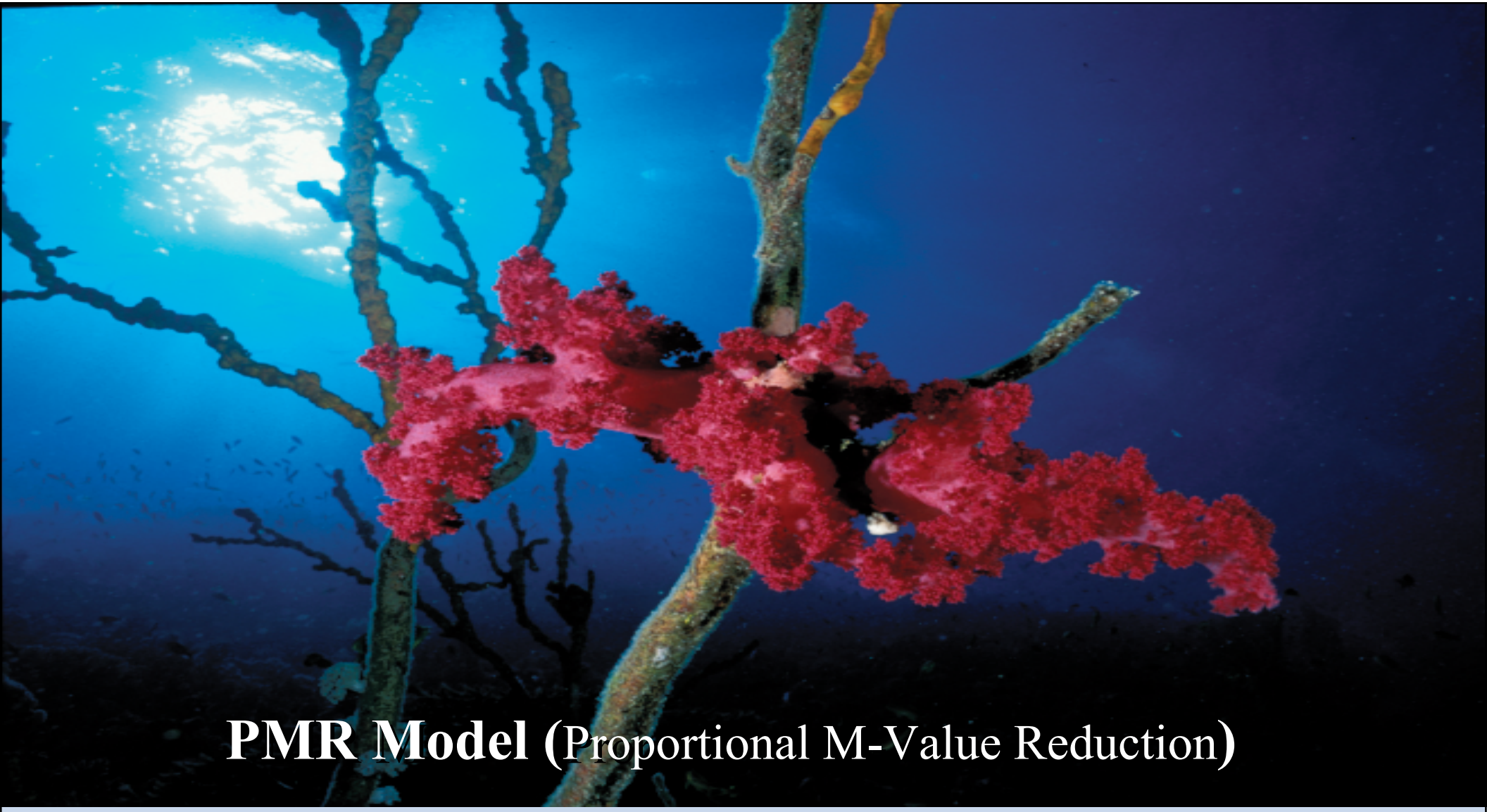




"High Doppler Bubble Grades" appeared to be

related to

- "Fast Tissues"
- $PltN_2$ > 80% of M Value

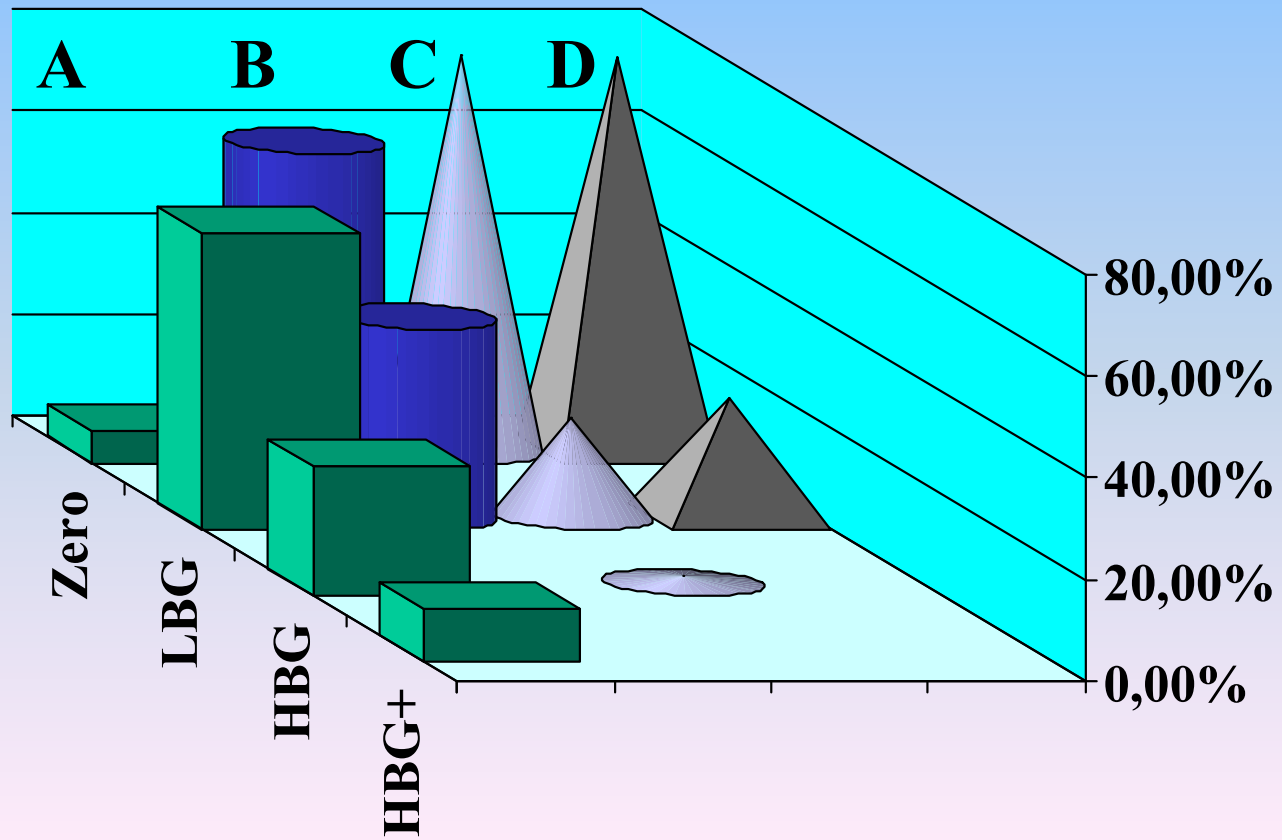


PMR Model (Proportional M-Value Reduction**)**

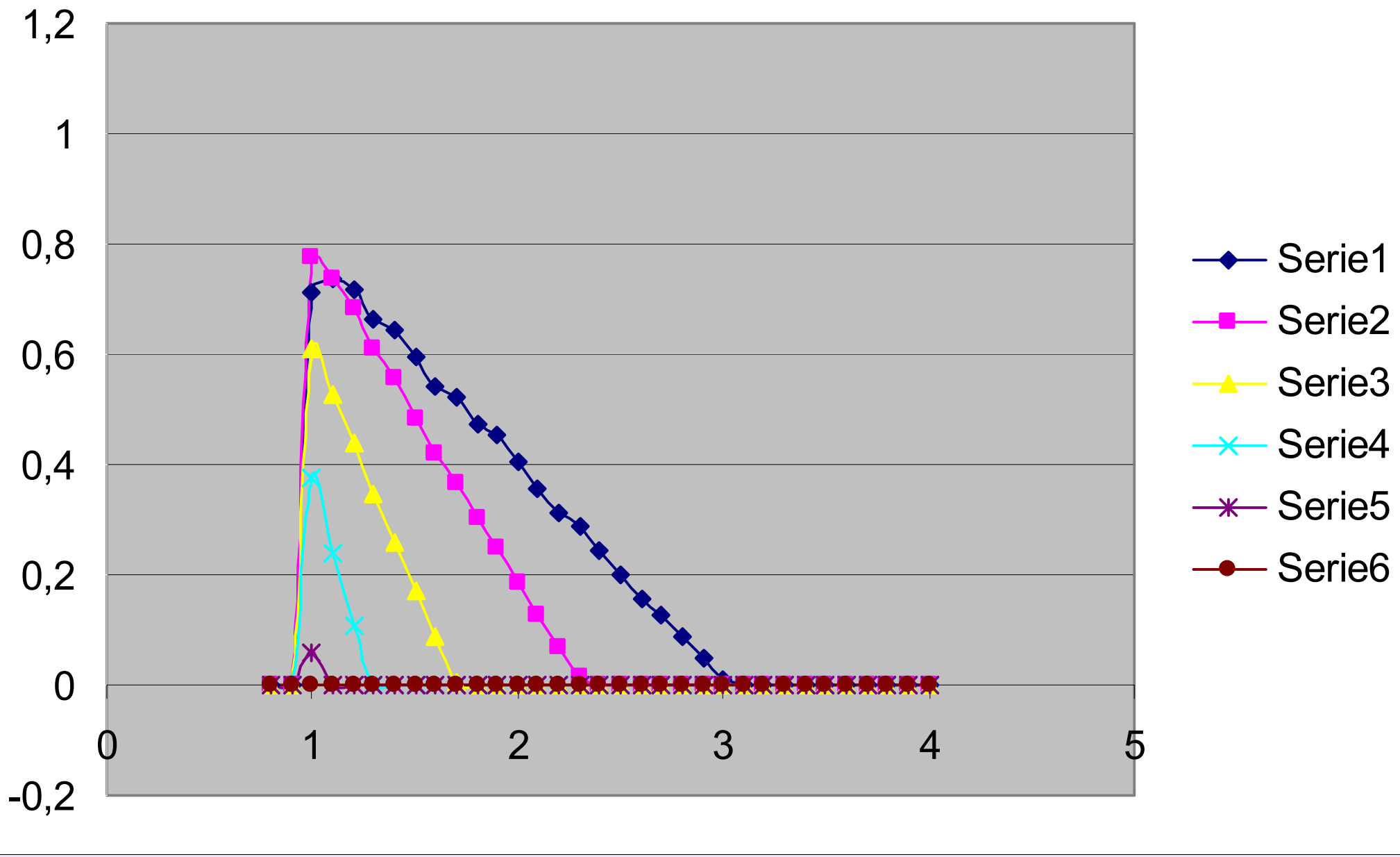
- Proportional Reduction of Leading Tissue M Value
- Introduction of extra deep stops during ascent
- Virtual elimination of Doppler-detectableVGE.

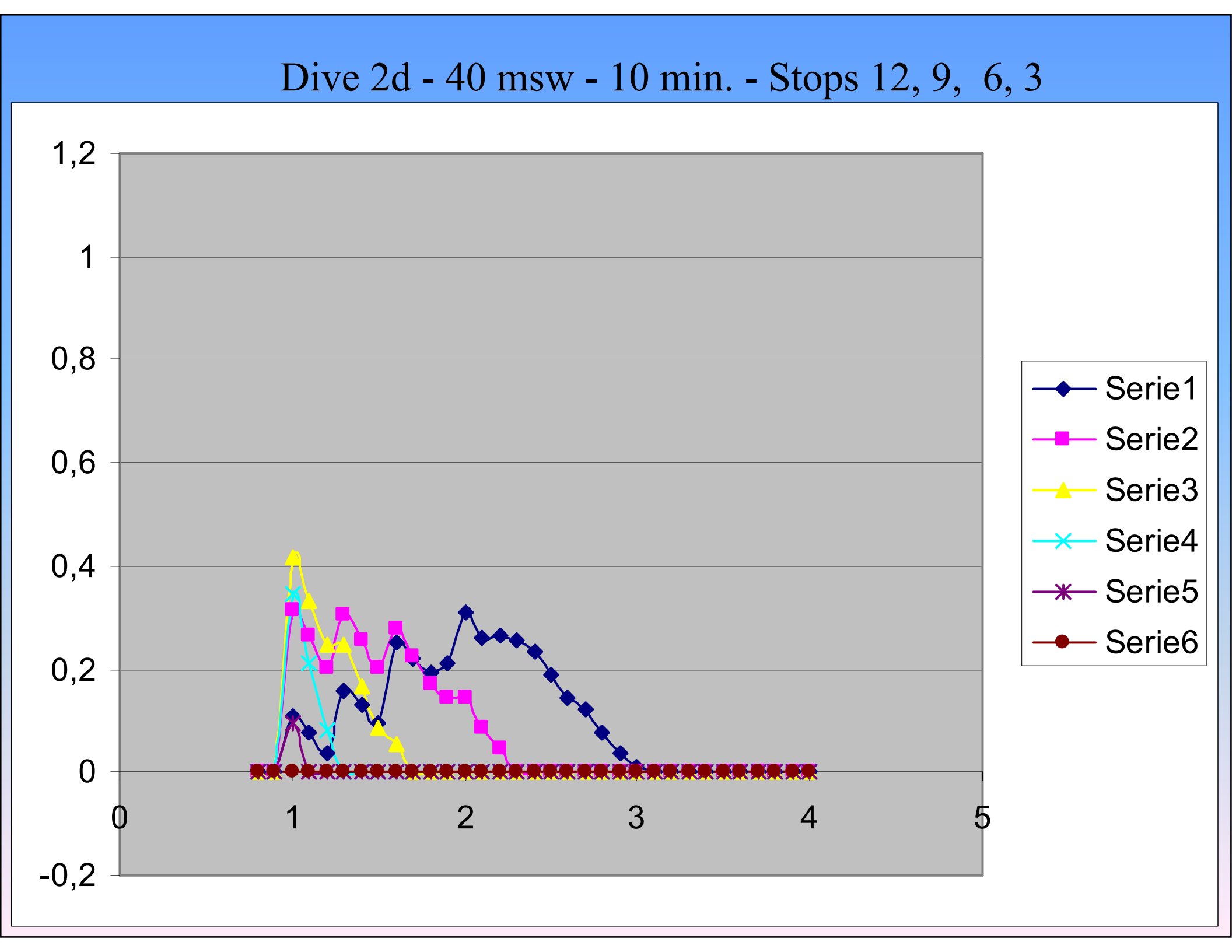
DSL Project 1-2001 - **PMR**
210 Man-dives - 388 Doppler Recordings

DBG	Zero	LBG	HBG	HBG+
Dives A	6,3%	58,2%	25,3%	10,2%
Dives B	60,8%	39,2%	---	---
Dives C	77,3%	19,4%	0,97%	---
Dives D	76,8%	23,2%	---	---



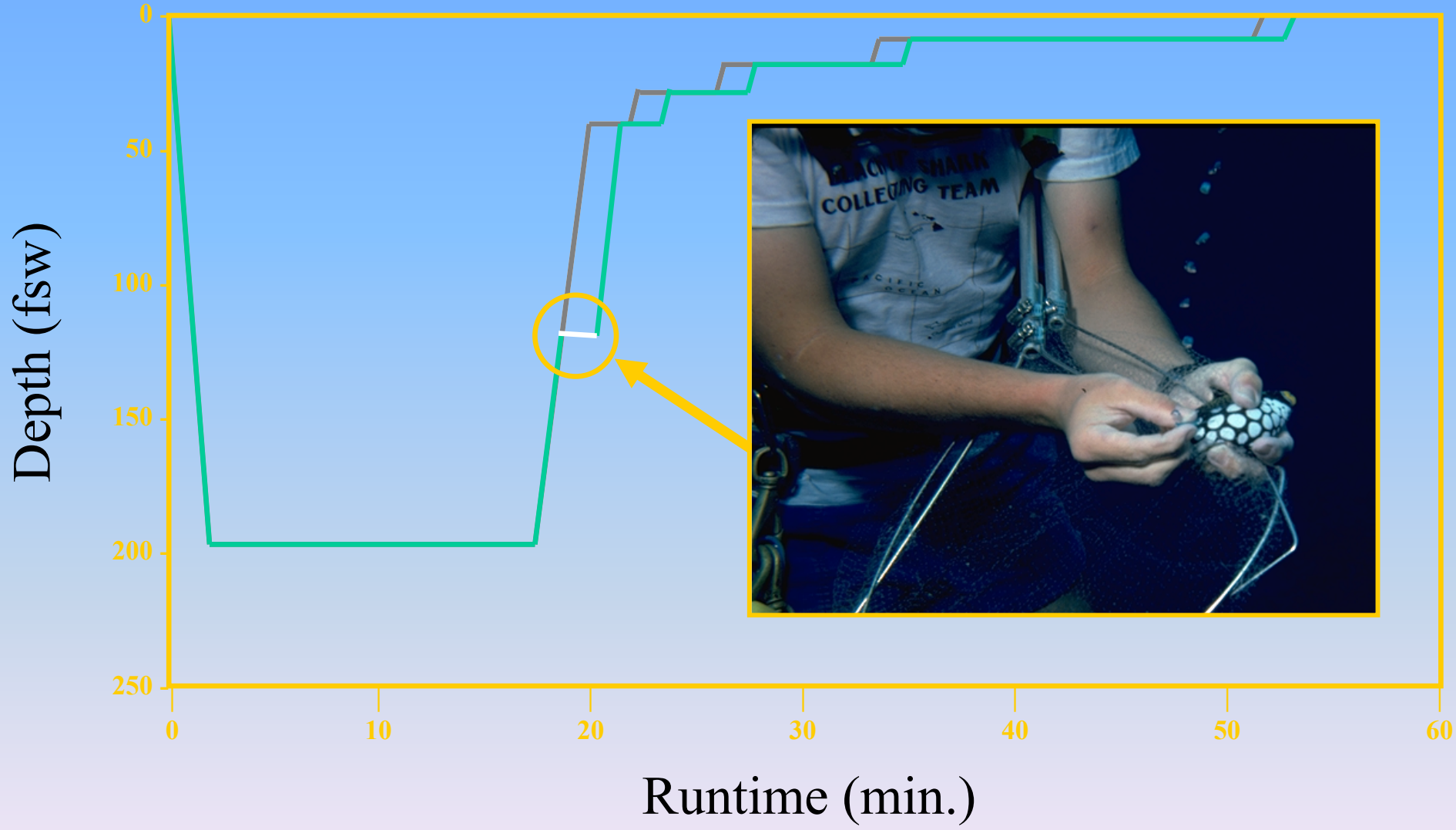
Dive 2a - 40 msw - 10 min. No Stop




Dive 2d - 40 msw - 10 min. - Stops 12, 9, 6, 3
1,2
1
0,8
0,6
0,4
0,2
0
-0,2
0
1
2
3
4
5
Serie1
Serie2
Serie3
Serie4
Serie5
Serie6

Our Data suggest that the Delta-P imposed on the pilot tissues, more than speed of ascent per se, is the critical factor for the formations of circulating gas bubbles.

Deep Stops

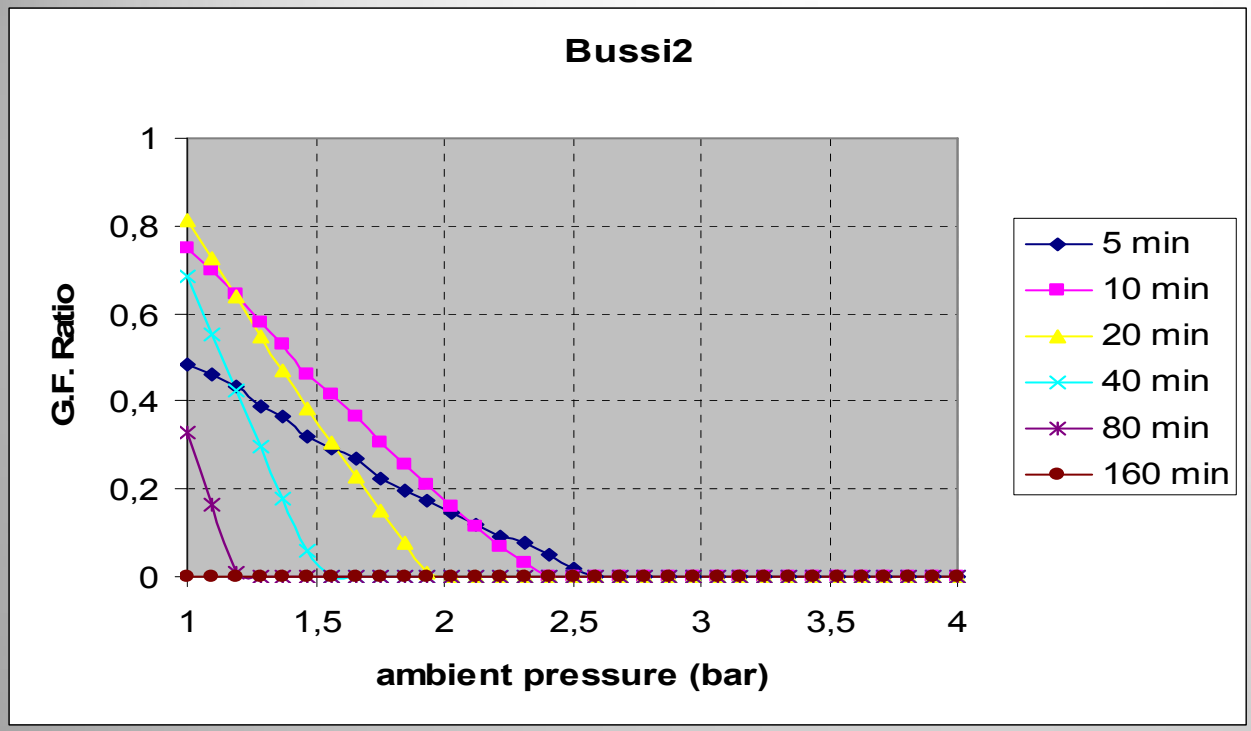


Richard L. Pyle. Ichthyology, Bishop Museum, Honolulu, Hawaii

Matrix of the experimental Dive Profiles

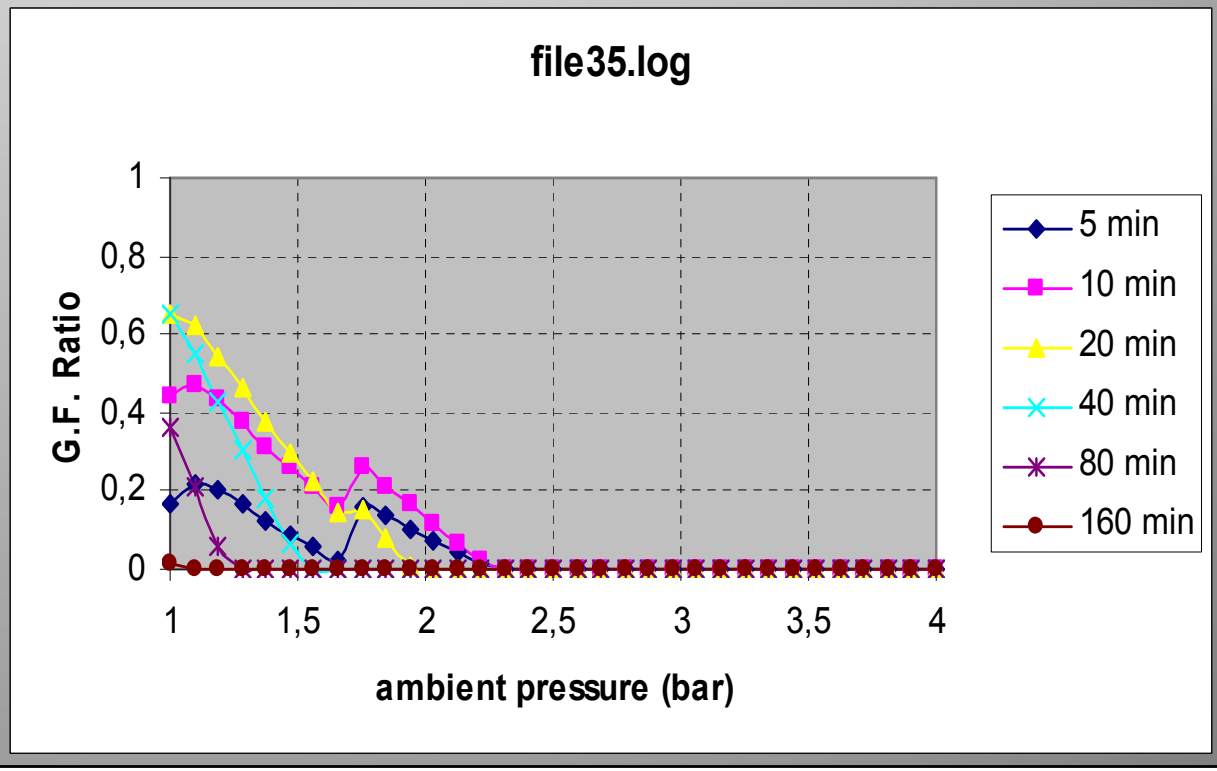
Profile	Depth	Time	Speed	15 m	6 m	Ascent Time
1	25	25	10	=	=	2,5
1R	25	20	10	=	=	2,5
2	25	25	3	=	=	8
2R	25	20	3	=	=	8
3	25	25	18	=	5	6,5
3R	25	20	18	=	5	6,5
4	25	25	10	=	5	7,5
4R	25	20	10	=	5	7,5
5	25	25	3	=	5	13
5R	25	20	3	=	5	13
6	25	25	10	5	5	12,5
6R	25	20	10	5	5	12,5
7	25	25	18	5	5	11,5
7R	25	20	18	5	5	11,5
8	25	25	3	5	5	18
8R	25	20	3	5	5	18

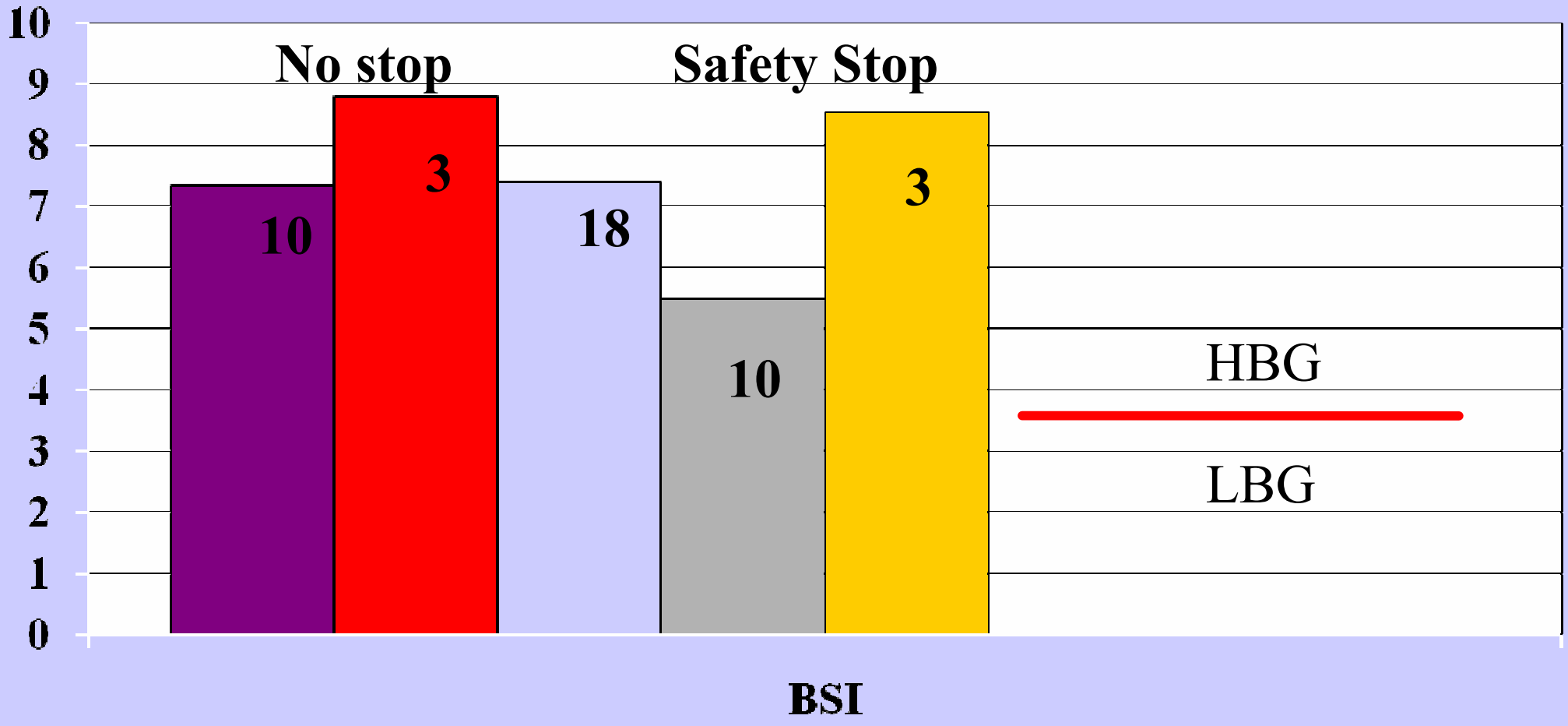
The volunteer divers dived all the profiles of the matrix and were precordially Doppler monitored every 15 minutes and up to 90 minutes after surfacing.



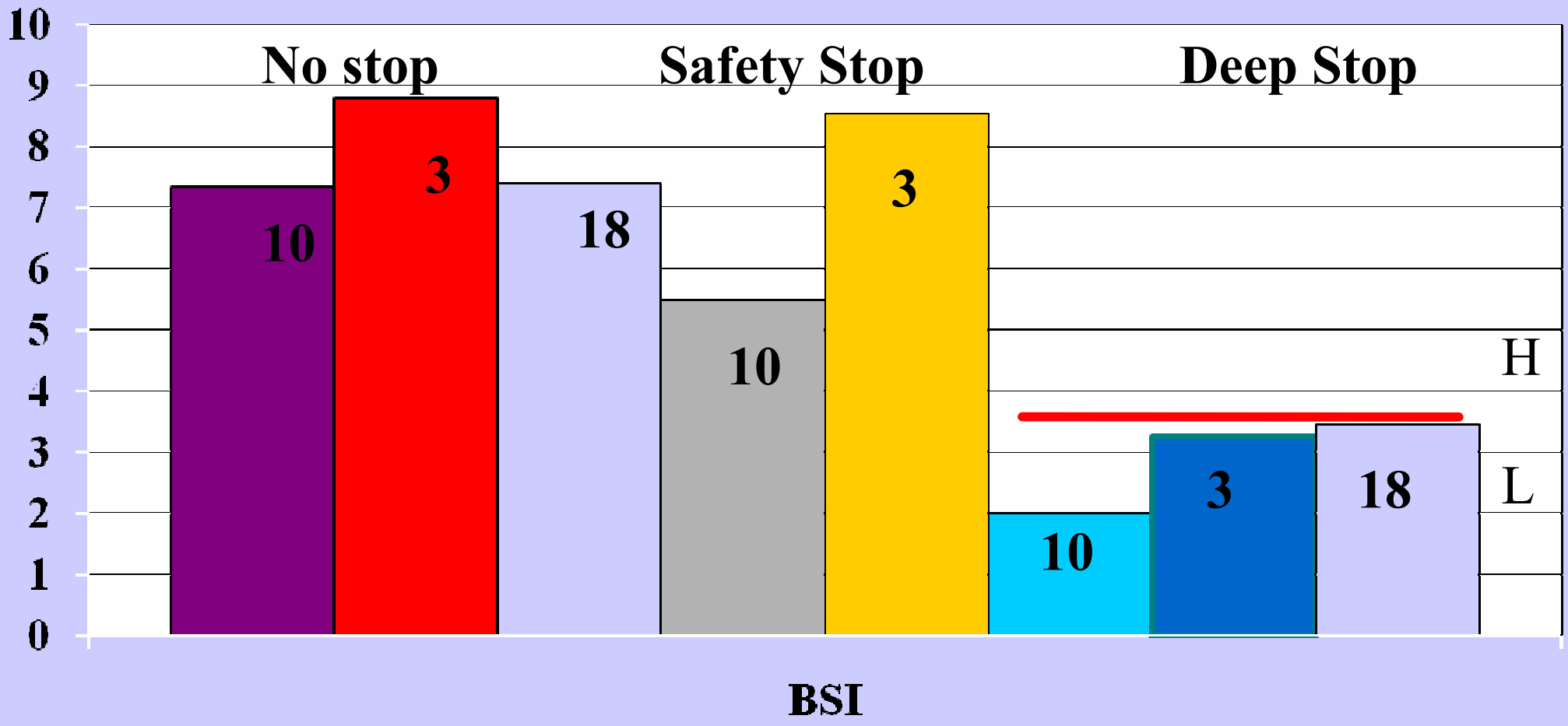
25 msw - 25min.
3m/min.No Stop

25 m – 25 min.
3m/min. DS + SS





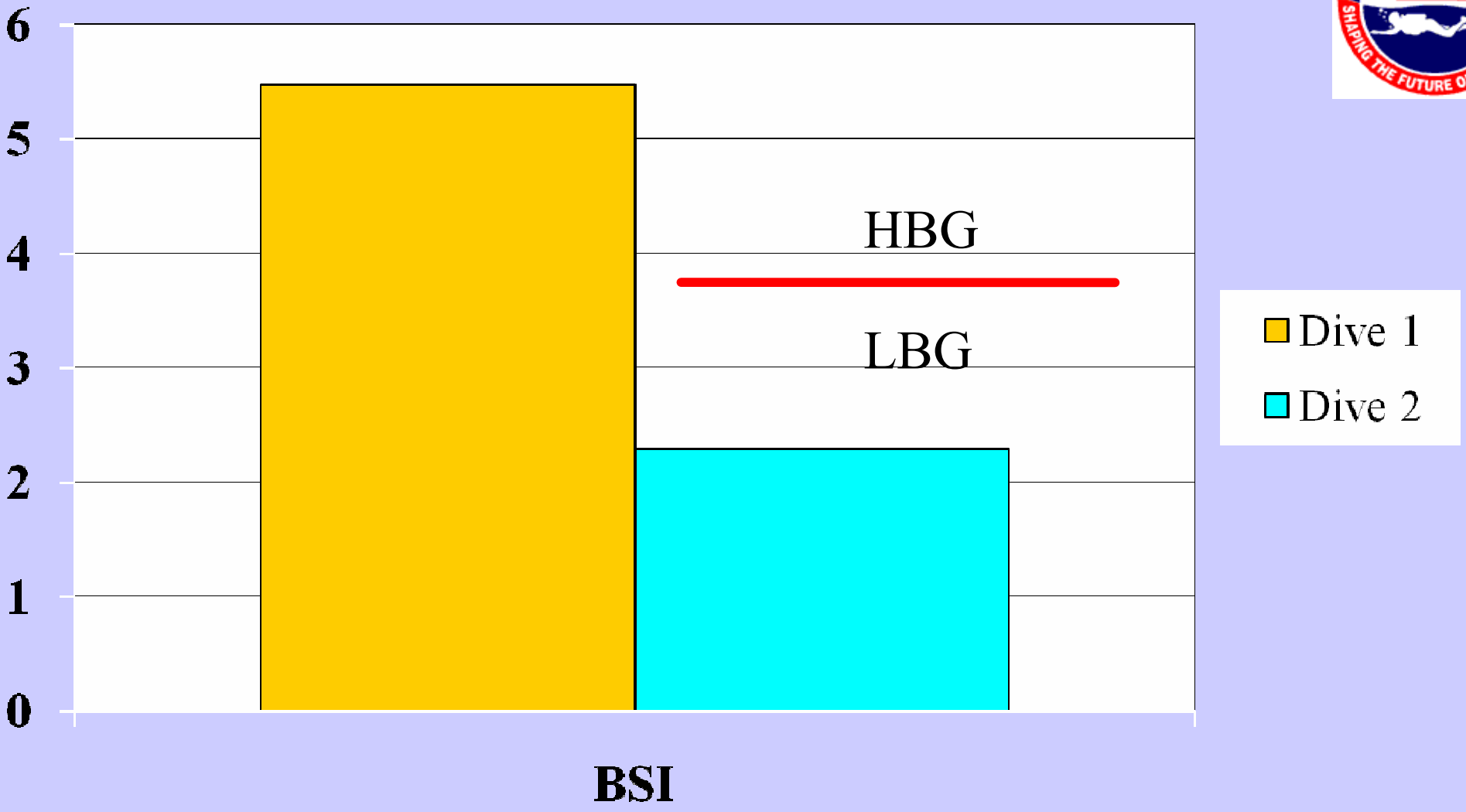
The highest Doppler scores were observed after the dives with a linear no-stop ascent or with the shallow “safety stop” only.



The highest Doppler scores were observed after the dives with a linear no-stop ascent or with the shallow "safety stop" only.

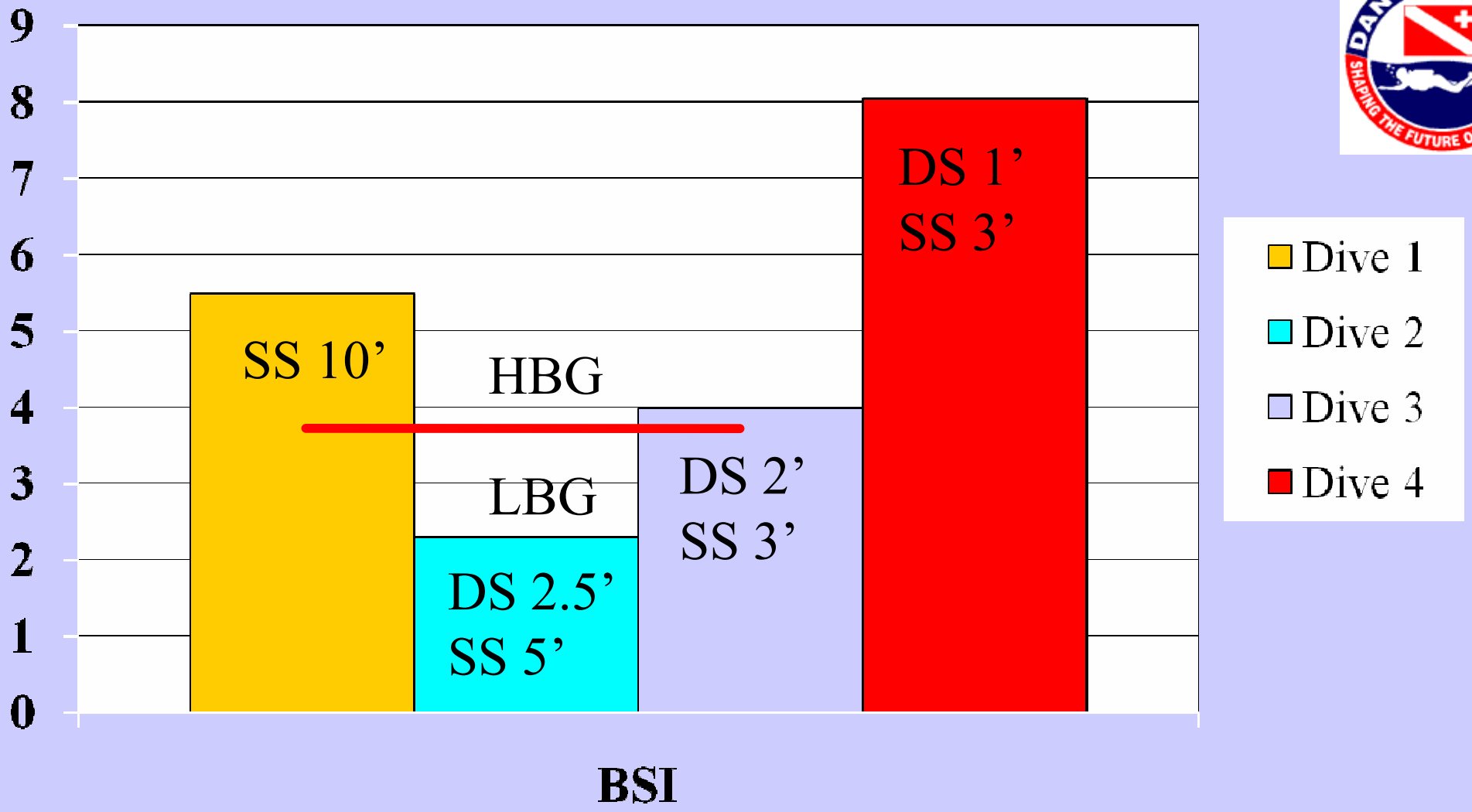
With the introduction of a 15 meter deep stop the bubble production becomes virtually absent, particularly with a 10 meters/minute speed of ascent.

We also studied other ascent profiles, to identify optimal ascent times representing the observed “biological” result.



Higher Doppler grades (BSI = 5.48) after prolonged shallow stops , notwithstanding longer decompression (12.5 vs 10 min

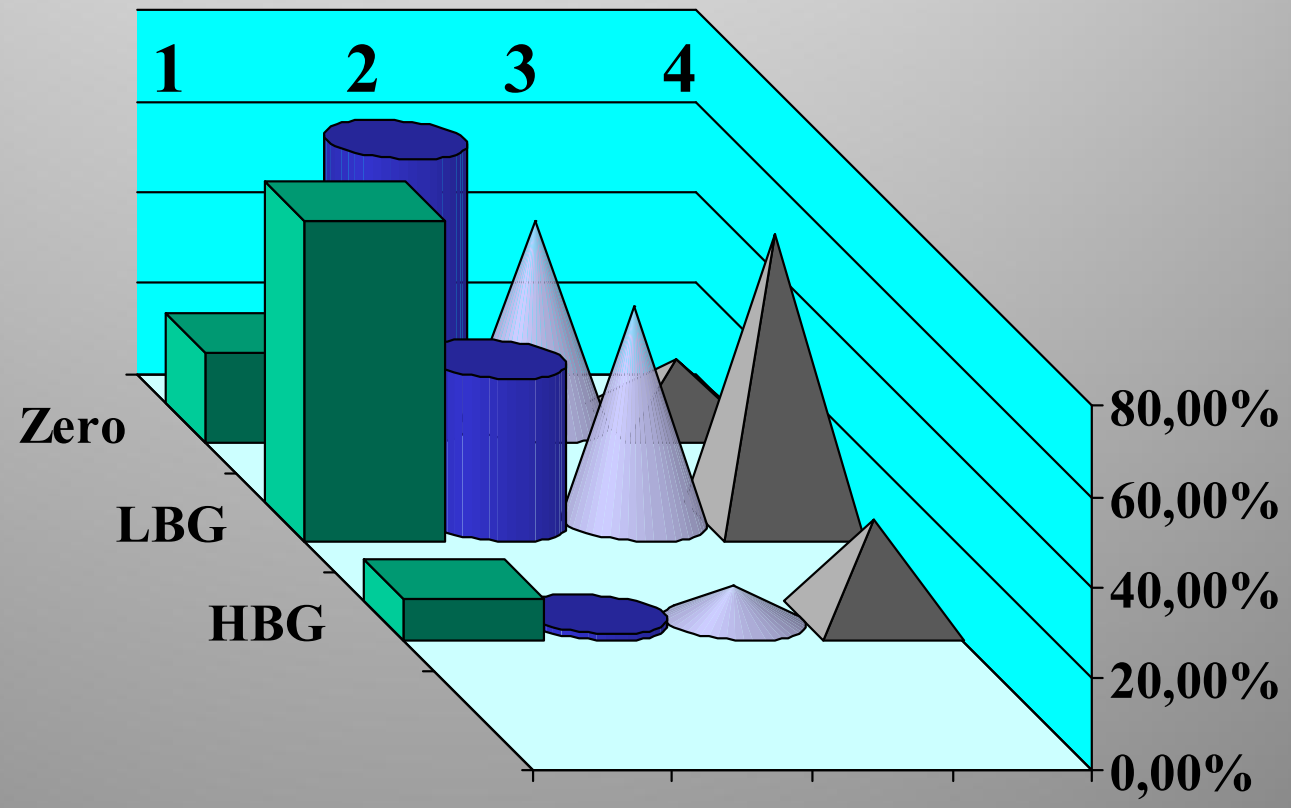
With deep stops BSI drops to 2.43 (highly significant difference - $R^2 = 0,98$).

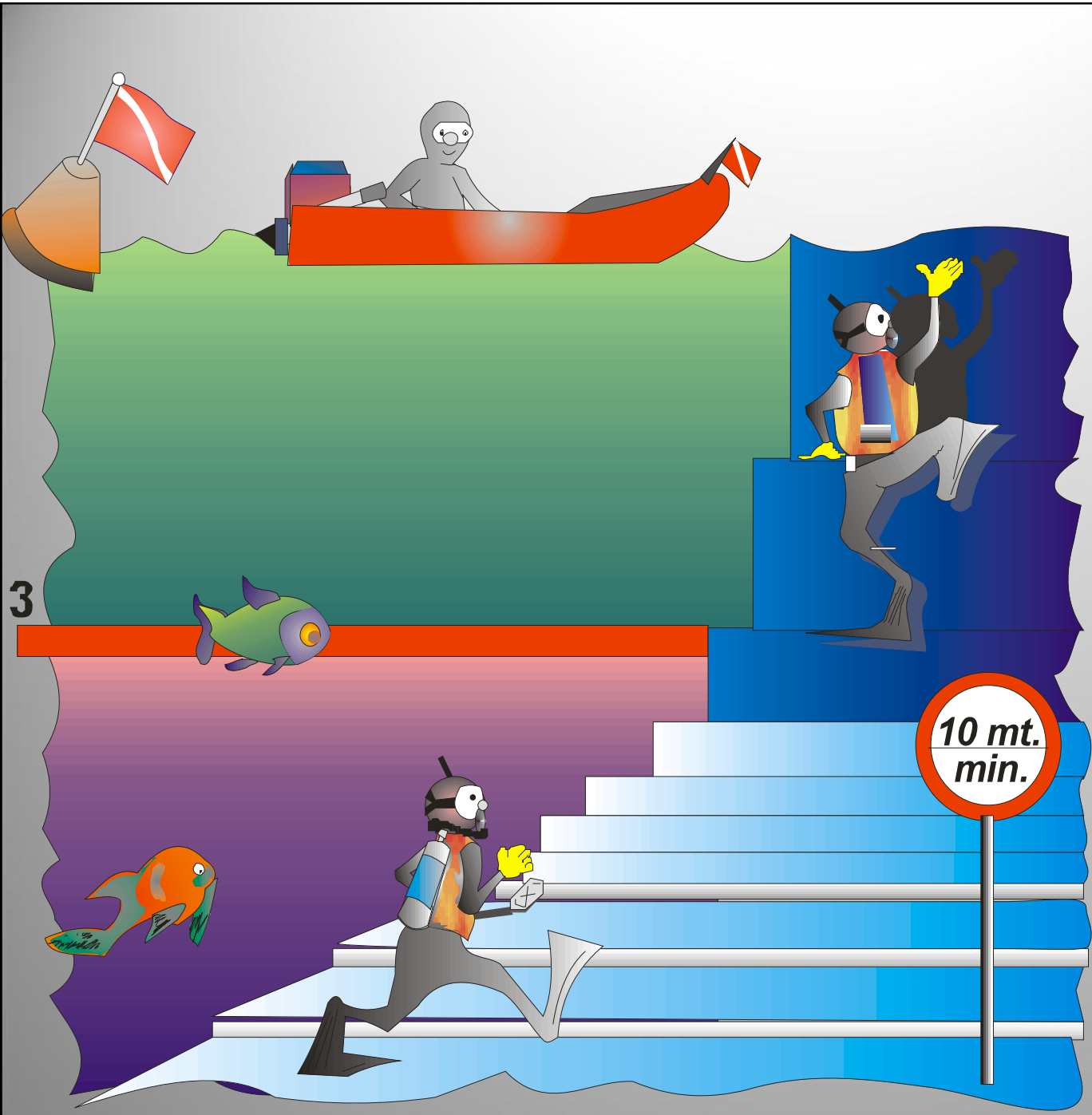


Reducing the Deep Stop reduces the positive effect on VGE and if the DS is reduced to 1 min only, VGE values increase significantly, with High Bubble Grades present in about 30 % of the recordings.

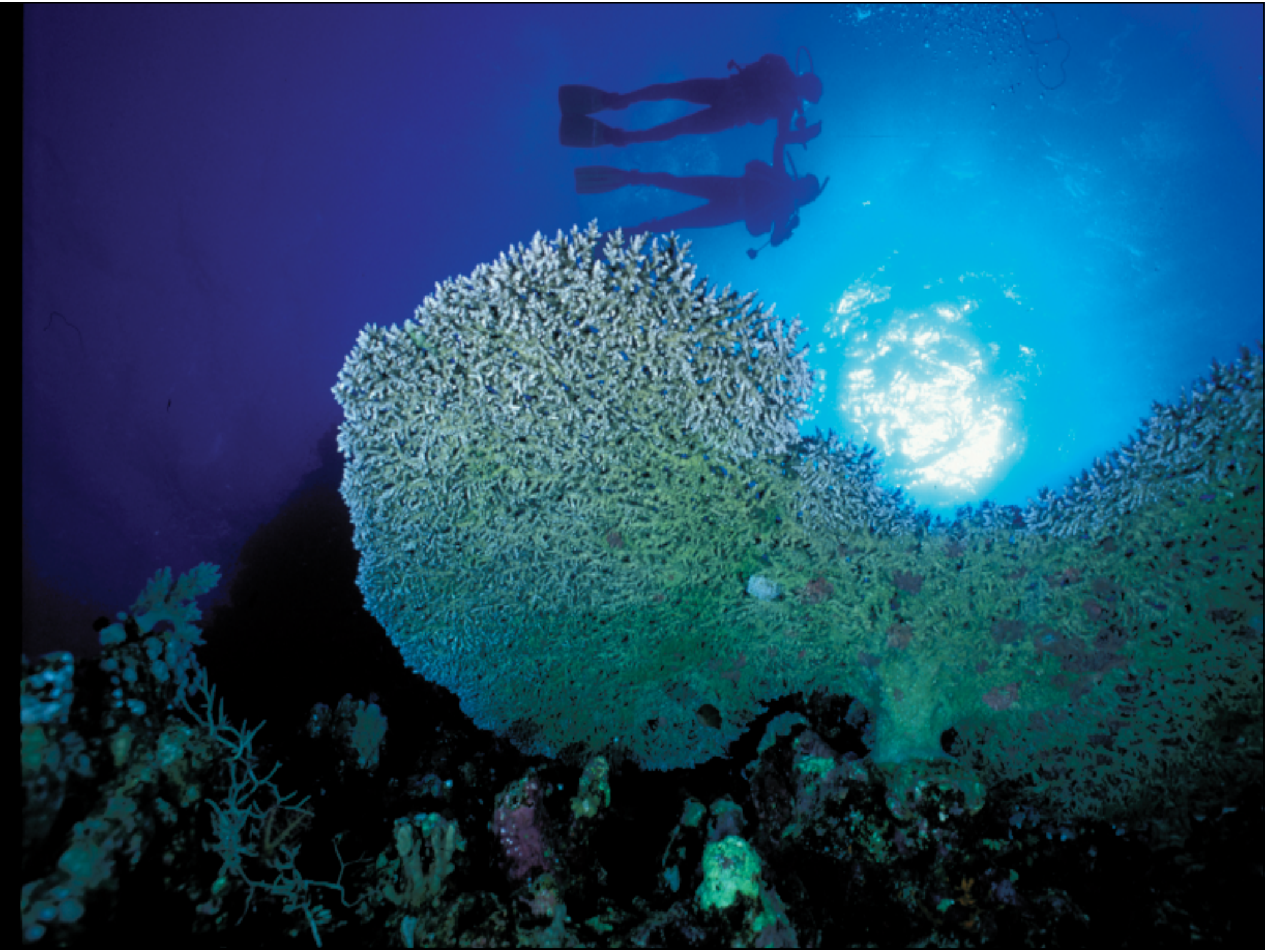
DSL Project Marben II
79 Man-dives - 553 Doppler Recordings

DBG	Zero	LBG	HBG	HBG+
Profile 1	19,7%	70,7%	9,5%	---
Profile 2	62,5%	35,7%	1,7%	---
Profile 3	44,4%	47,6%	7,9%	---
Profile 4	14,3%	63,4%	22,4%	---





The introduction of a deep stop, may significantly reduce the amount of circulating gas bubbles after recreational dives.



Bubbles,

apart directly causing symptoms,

are also a trigger

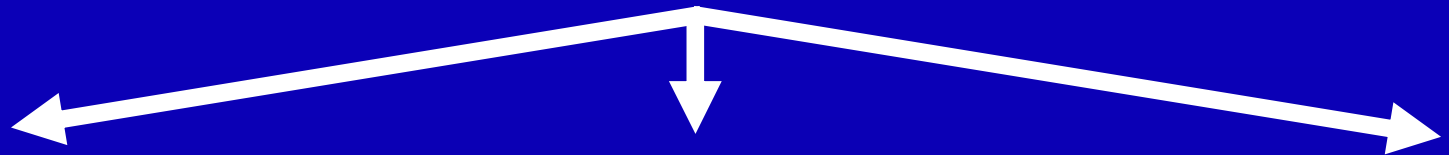
of complex pathophysiological reactions

accompanying and worsening

the cascade of biological events started

by circulating gas emboli.

Bubbles



Economy of Decompression

Formation & Migration of Bubbles

Reactions to Bubbles

REACTION TO BUBBLES

- **Understanding factors that determine or increase the biological reaction to bubbles**
  - Recognize and manage increased risk
  - Manipulate the risk by physical & chemical means
- **Understanding the direct and indirect effects of bubbles on biological systems**
  - physical damage
  - substances released due to / in response to damage
  - inflammatory and repair mechanisms

Bubbles & the body

Serotonin & vasoactive substances

Clark 1969

Coagulation Changes

Schimpf 1971

Platelets Studies

Philp 1974, Frattali 1974, Broussolle 1975, Philp 1979, Thorsen 1986, Bakke 1991

Fluorocarbons Studies

Lundgren 2005, Mahon 2006, Dainer 2007, Zhu 2007

Complement Studies

Many studies from the 80’ to date

Conditioning Body Reactions to Bubbles
New Trends

Dark Chocolate

Vit B6

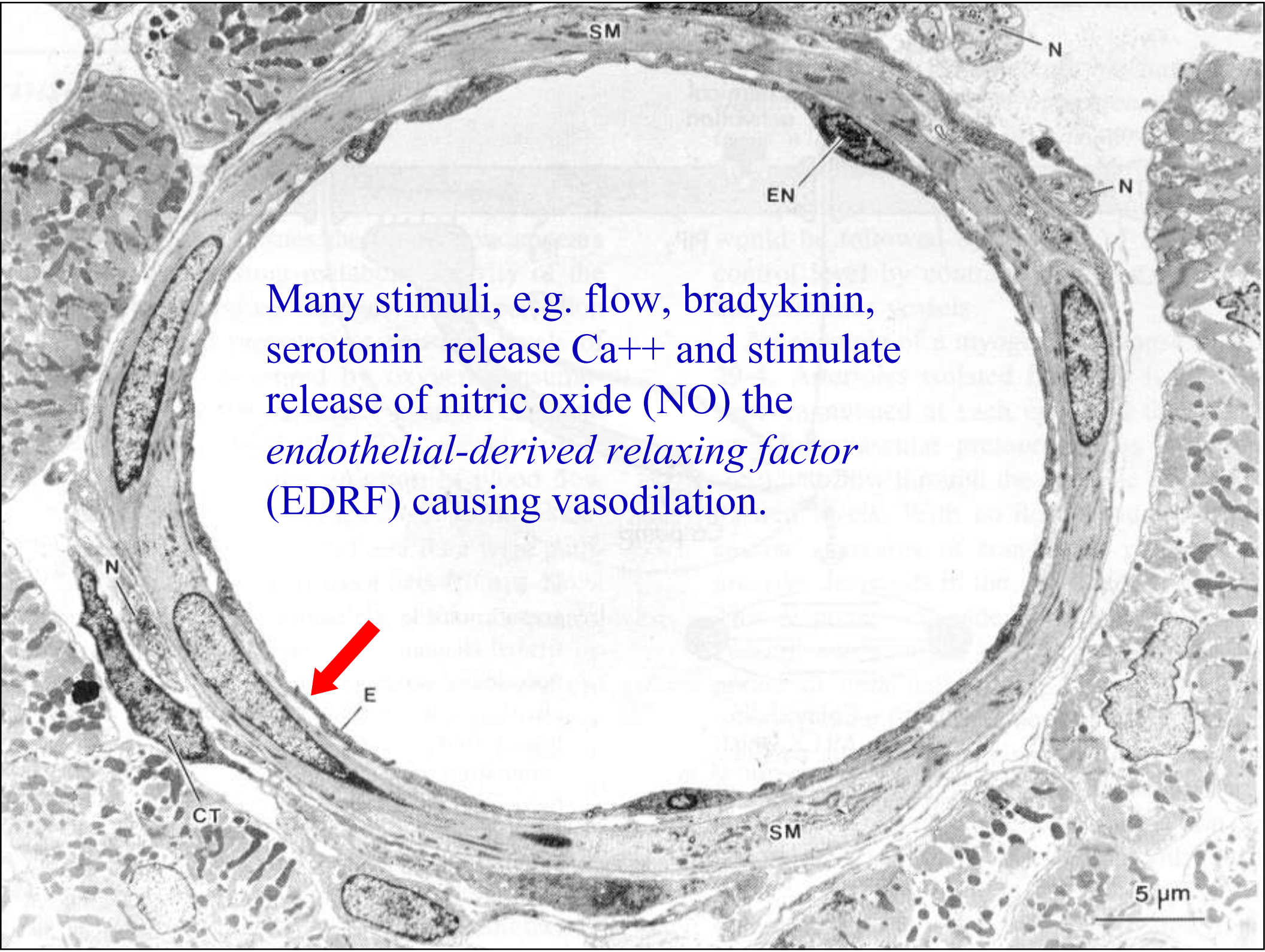
Antioxidants

Pre-oxygenation

Chemical Decompression

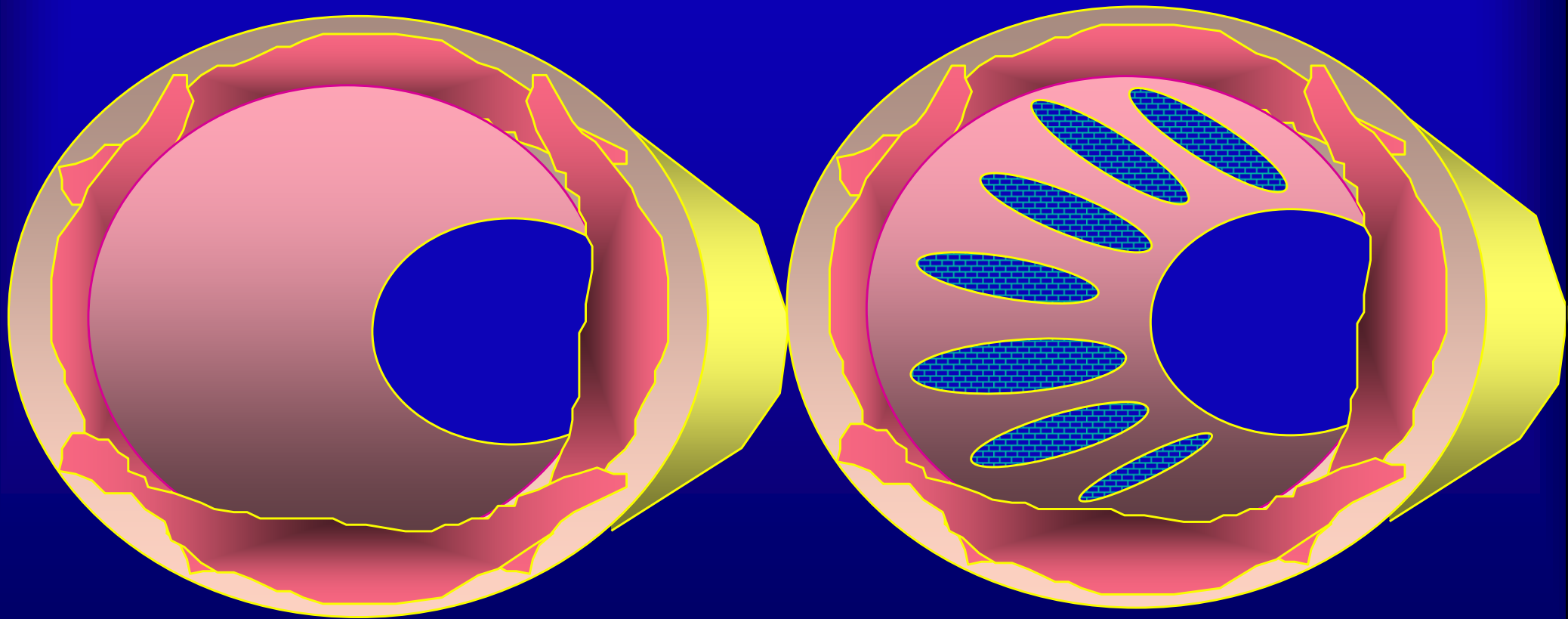
NO Stimulators

NITRIC OXIDE AND DCI

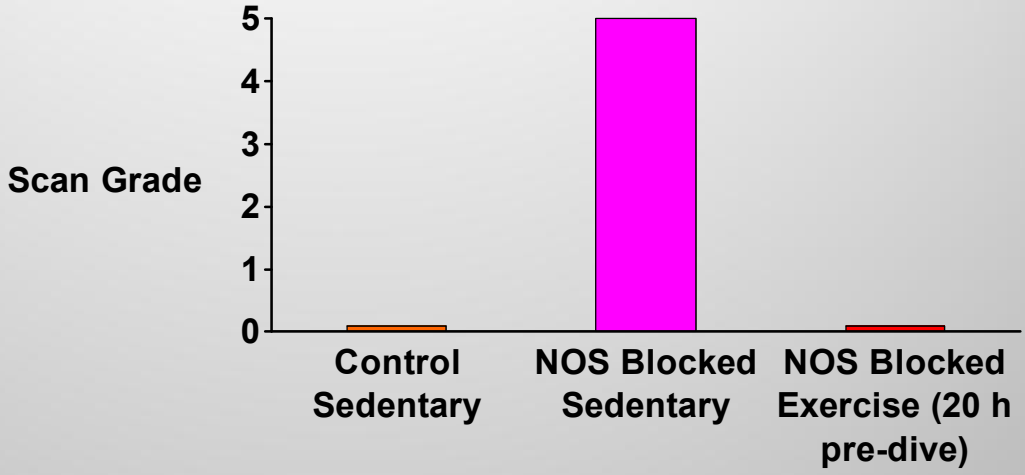


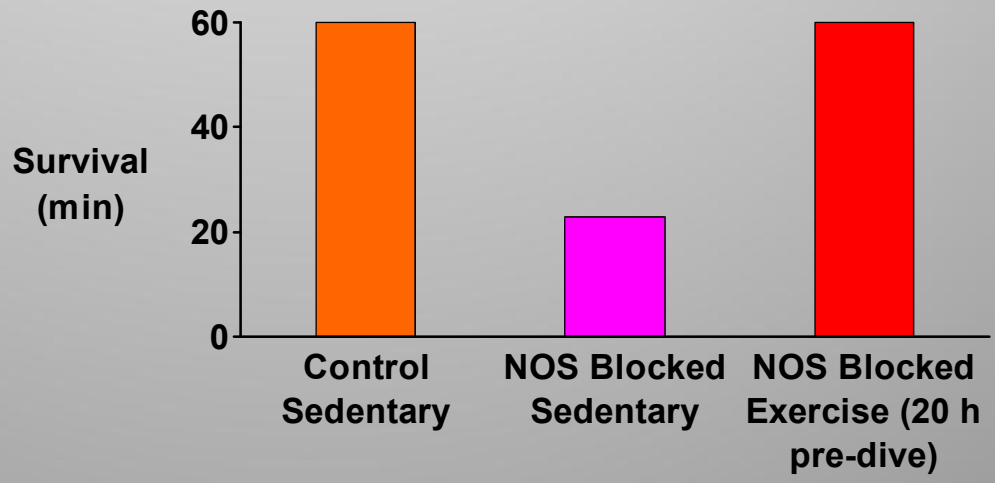
Many stimuli, e.g. flow, bradykinin, serotonin release Ca++ and stimulate release of nitric oxide (NO) the *endothelial-derived relaxing factor* (EDRF) causing vasodilation.

NO Actions on vessels and endothelial morphology



NOS Inhibition and DCI in Rats



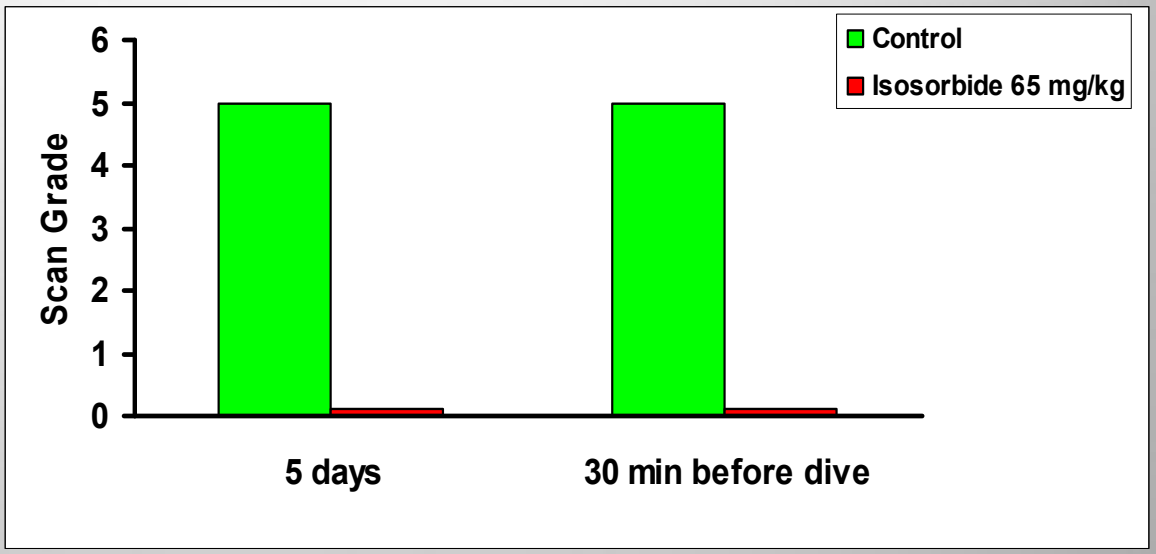


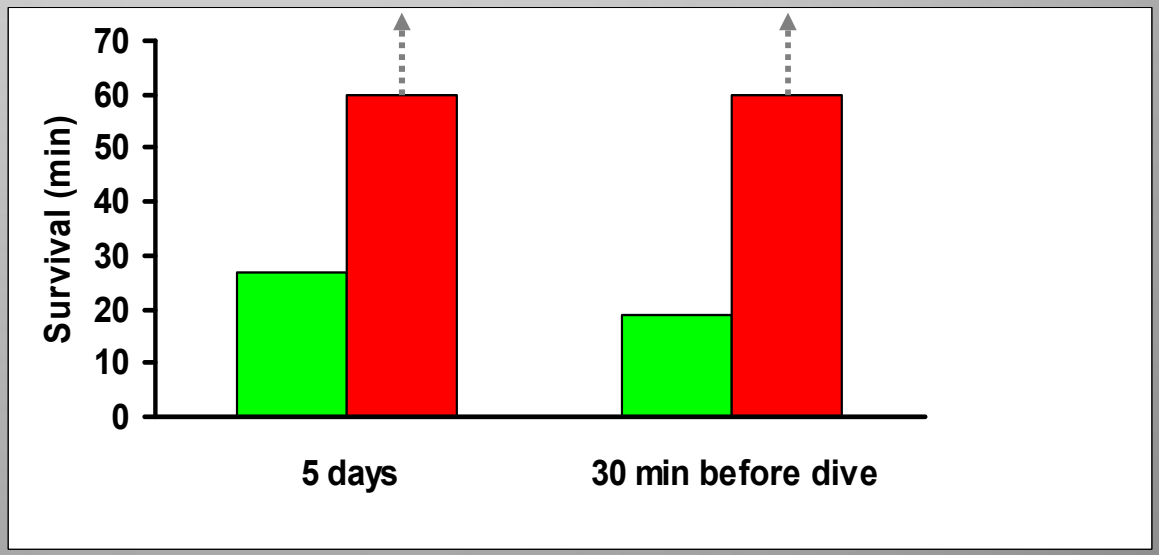
Wisløff, et al J Physiol 546:577, 2003

Courtesy R Moon

*Isosorbide 65 mg/kg Pre-Dive**

*** 60 m/45 min air**

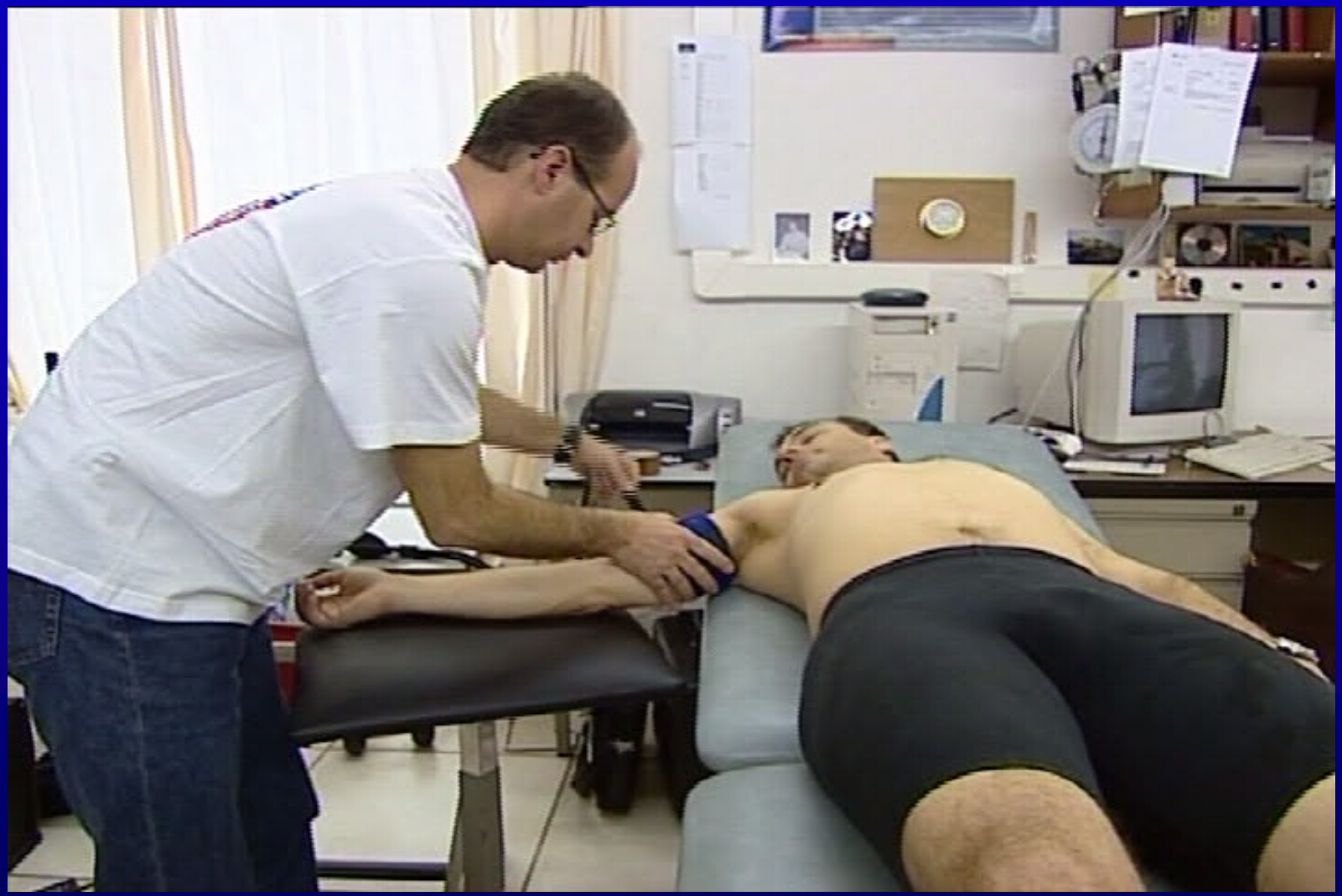




Courtesy R Moon

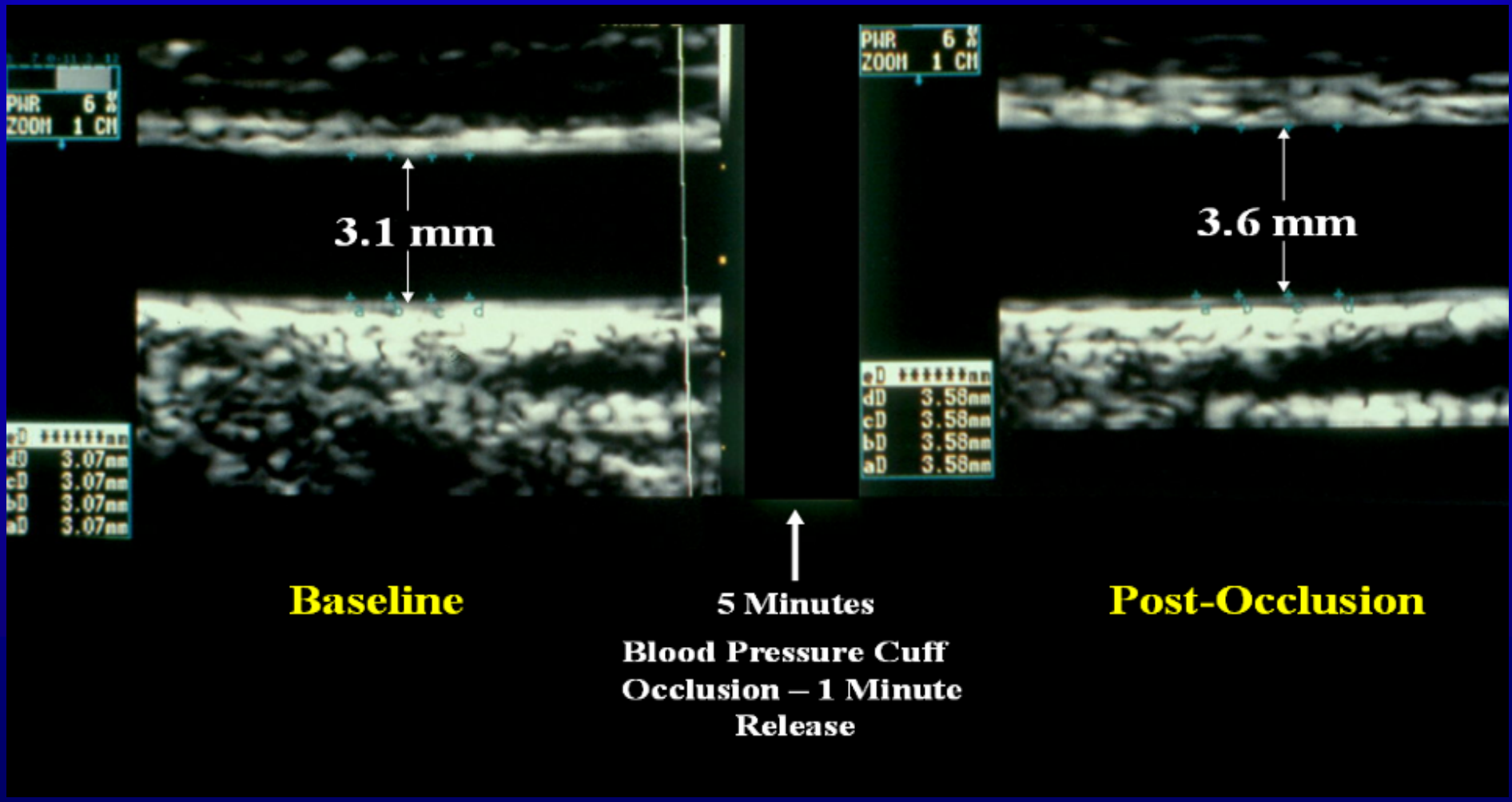
Wisløff, et al J Physiol 555:825, 2004

Flow Mediated dilation



Echography in parallel with plethysmography

Brachial artery Flow-Mediated Dilation




TIS0.4 TIB1.0 TICD.4 MI0.4
ID:_
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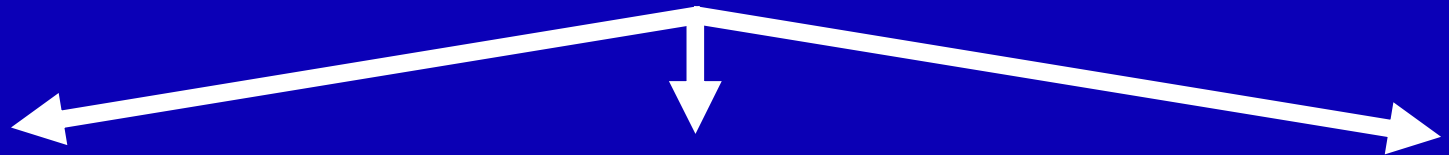
/20.0
15/13
6/6
85/1
5/ 90
4.0cm
11.0k
S.P. D.Z.SFT MODE SEL

Bubbles



Economy of Decompression

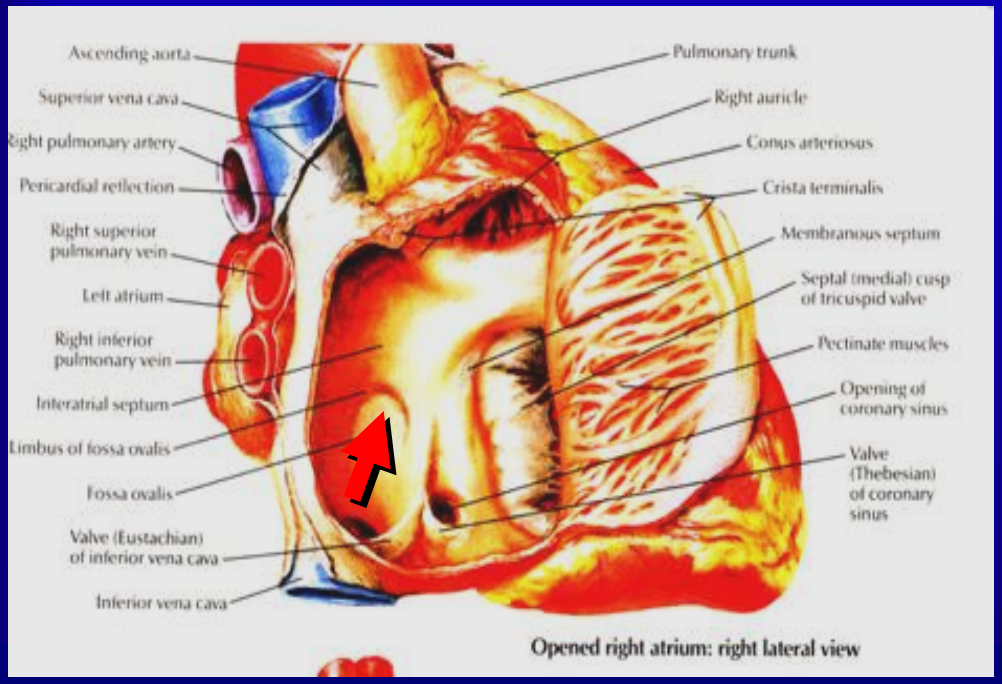
Formation & Migration of Bubbles

Reactions to Bubbles

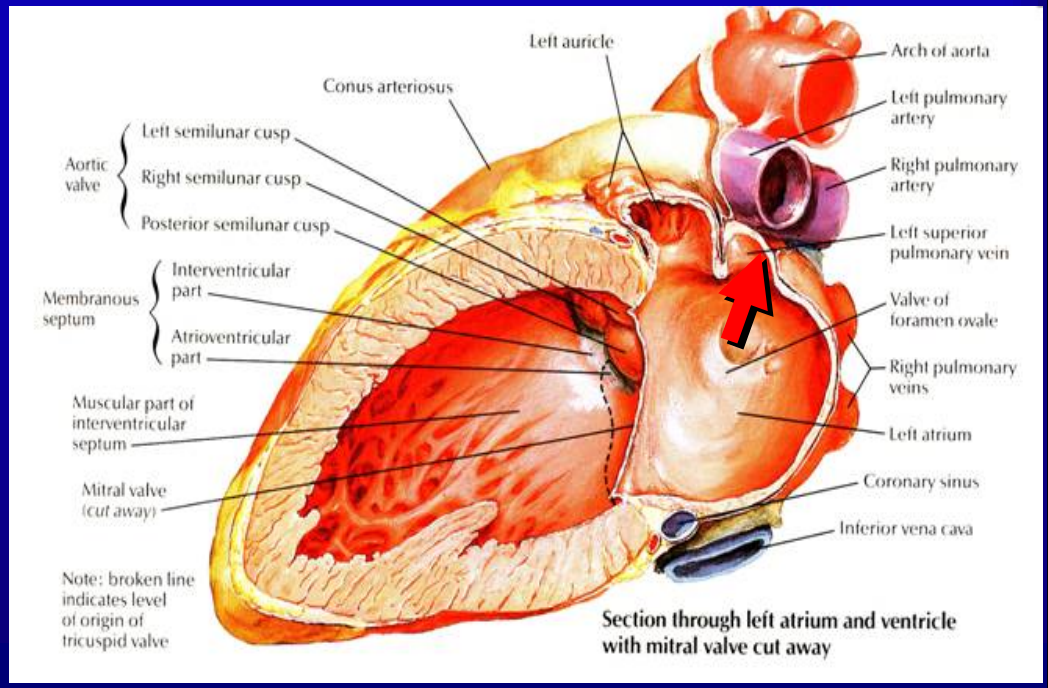
FORMATION & MIGRATION OF BUBBLES

- **Understanding factors that increase bubble formation so as to:**
  - Recognize and manage increased risk
  - Manipulate the risk by physical & chemical means
- **Understanding factors leading to the transfer of inert gas bubbles from harmless to harmful locations**
  - Shunting (Heart & Lungs)
  - Pulmonary filter effectiveness
    - bubble loads
    - bubble size (inert gases; repetitive diving)
    - vasodilatation (medication; effects of bubbles)

Fossa Ovalis – Patent Foramen Ovale



Right atrial view

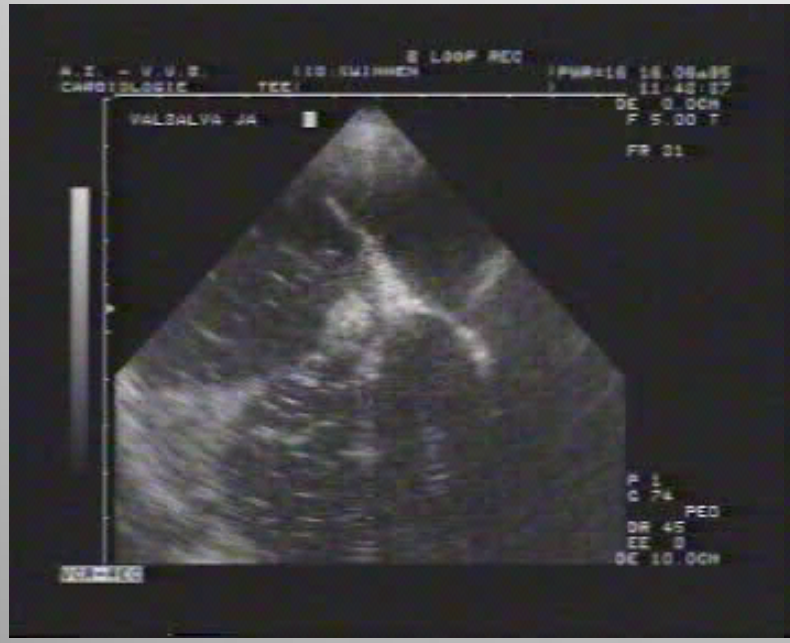


Left atrial view

Netter F. Human Anatom

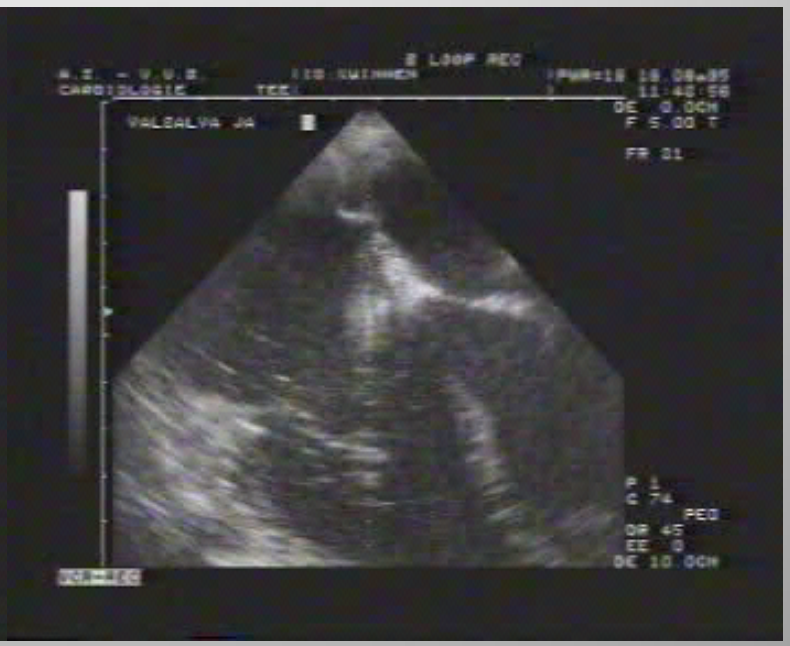
C-TEE Images with Valsalva

Insufficient Valsalva strain



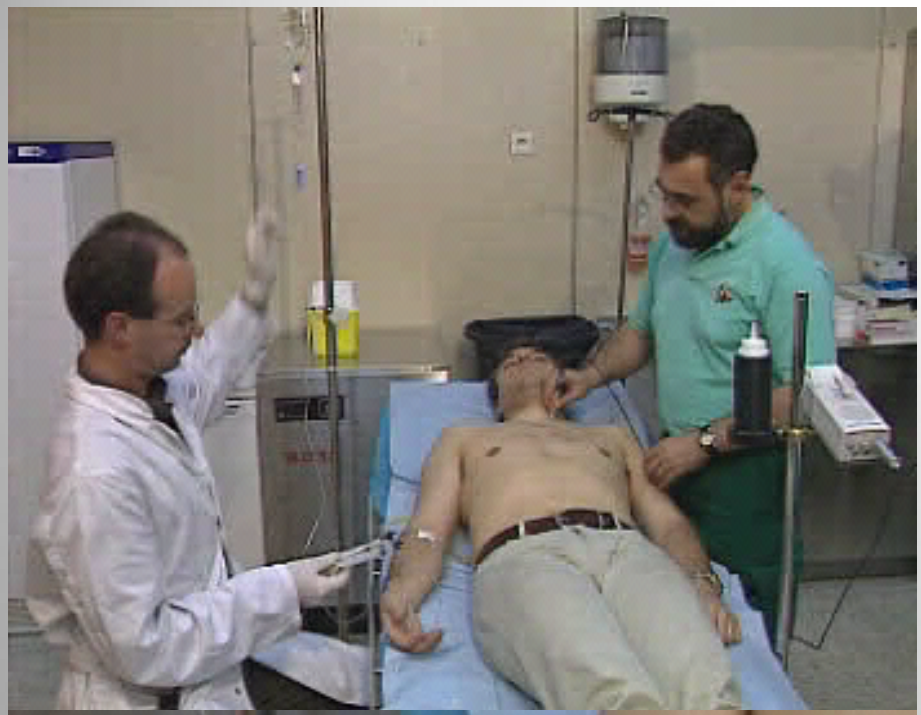
Low opacification next to septum, low contrast passage

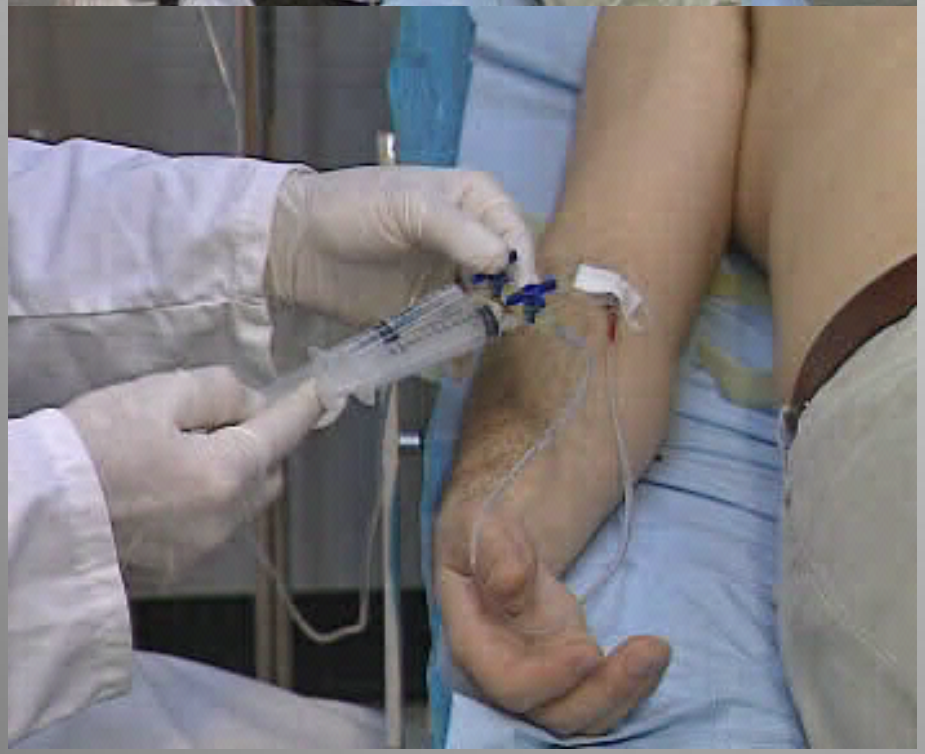
Good Valsalva strain



Good opacification, massive contrast passage (same patient)

Caveat: keep TEE probe immobile during Valsalva





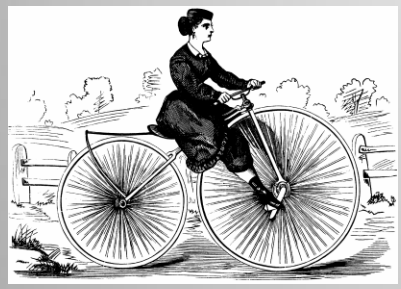
PFO Detection

Negative test

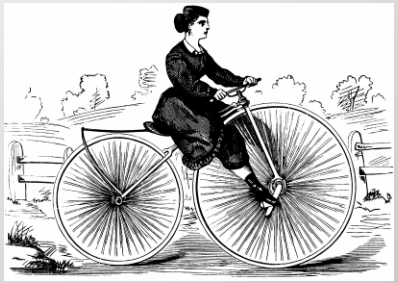
Positive test

DETERMINING THE EFFECT OF EXERCISE ON DCI

Effect of Exercise on DCS Risk

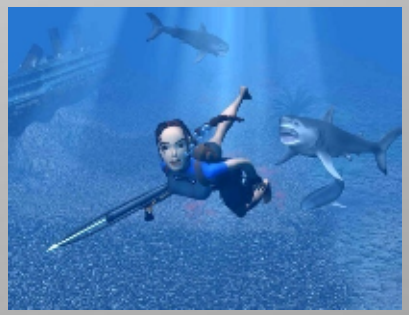


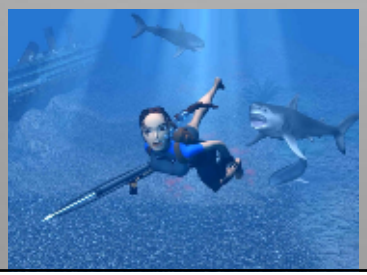
? Micronuclei depletion
? Micronuclei generation



? Micronuclei generation

↑ Inert gas washout



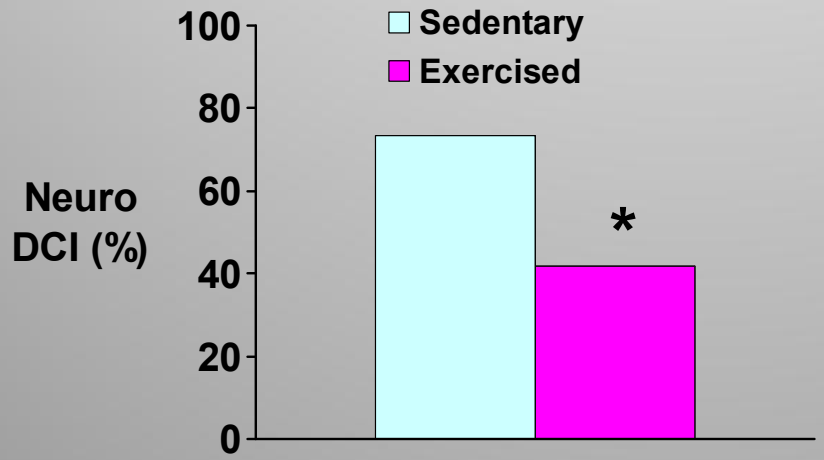


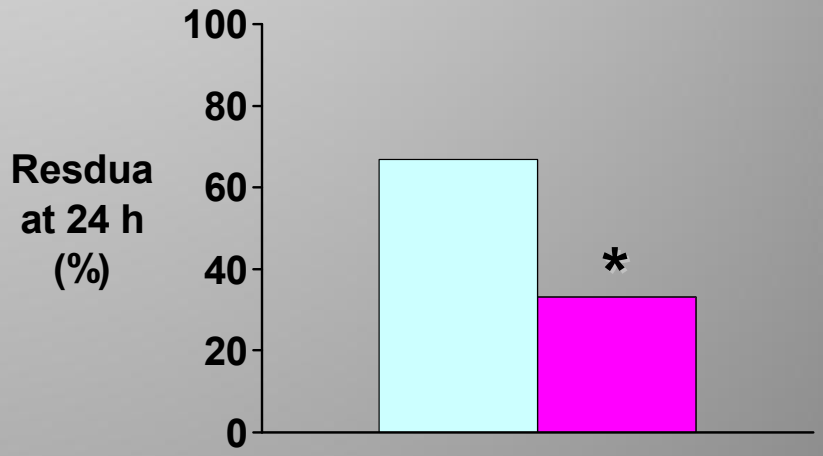
↑ Inert gas uptake

Courtesy R Moon

Exercise Conditioning to Prevent DCS in Swine

- **Pigs 18-22 kg**
  - **Sedentary**
  - **Exercised: daily treadmill**
- **Chamber dive: 60.6 m/24 min; ascent 18 m/min**



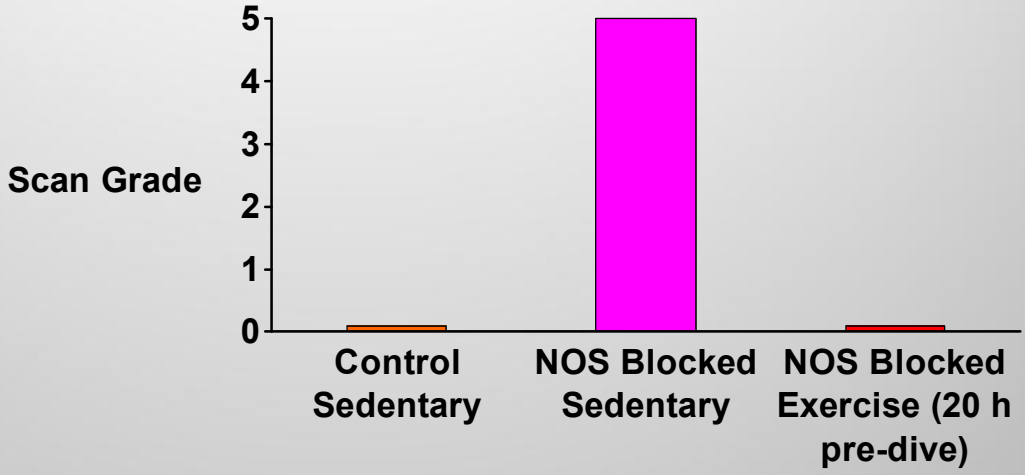


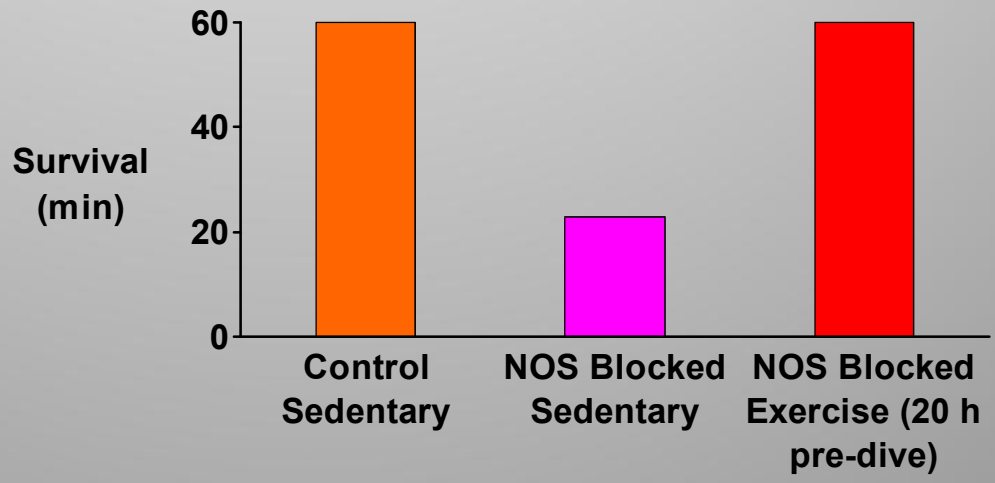
*P < .02

Courtesy R Moon

Broome JR. Undersea Hyperb Med 22:73, 1995

NOS Inhibition and DCI in Rats



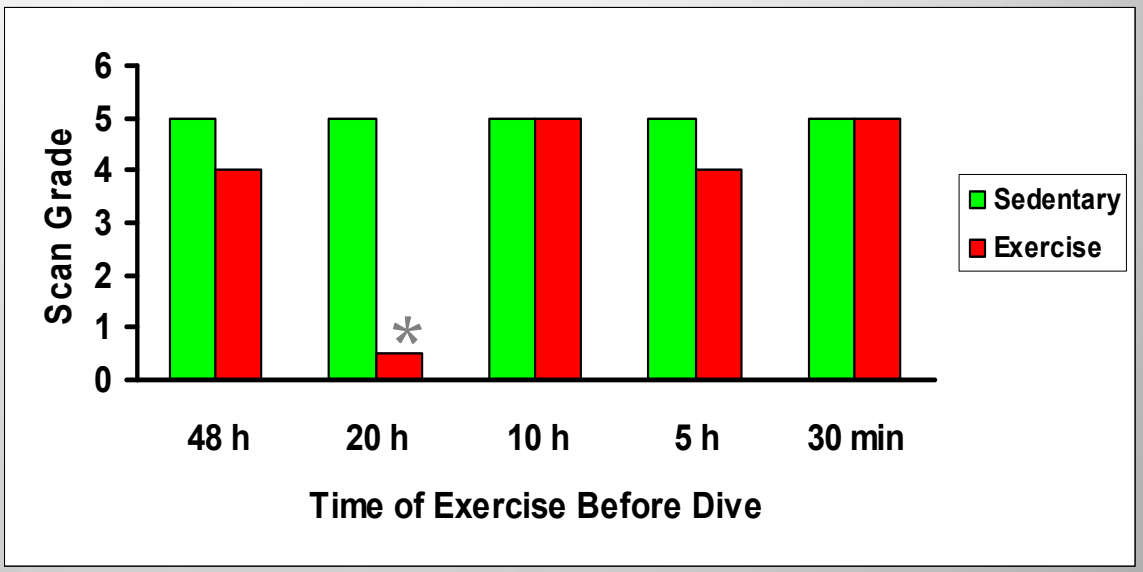


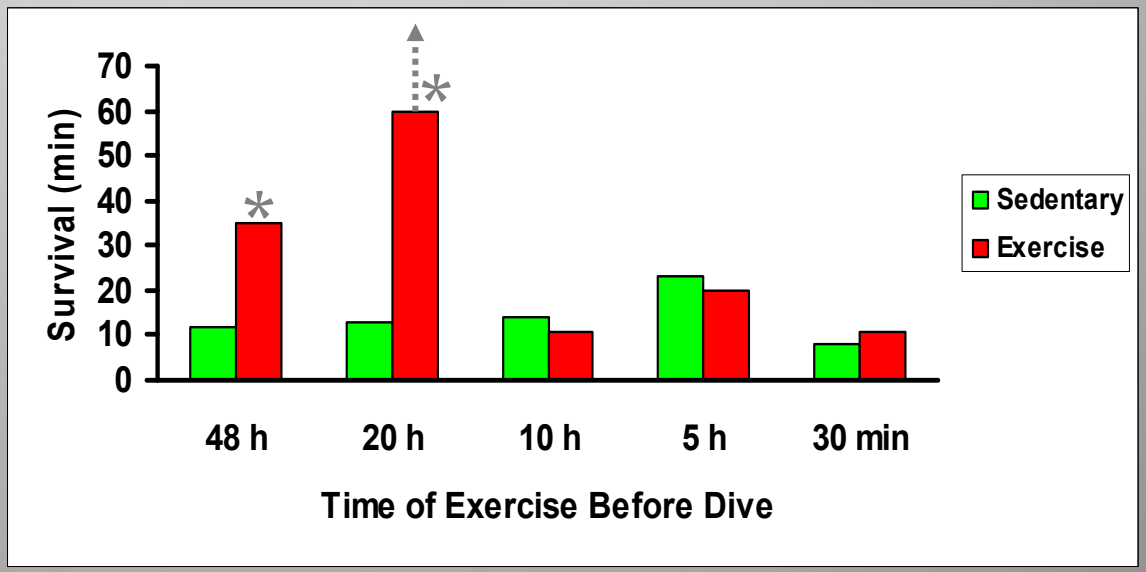
Wisløff, et al J Physiol 546:577, 2003

Courtesy R Moon

Exercise Before Diving in Rats*

*** 60 m/45 min air**

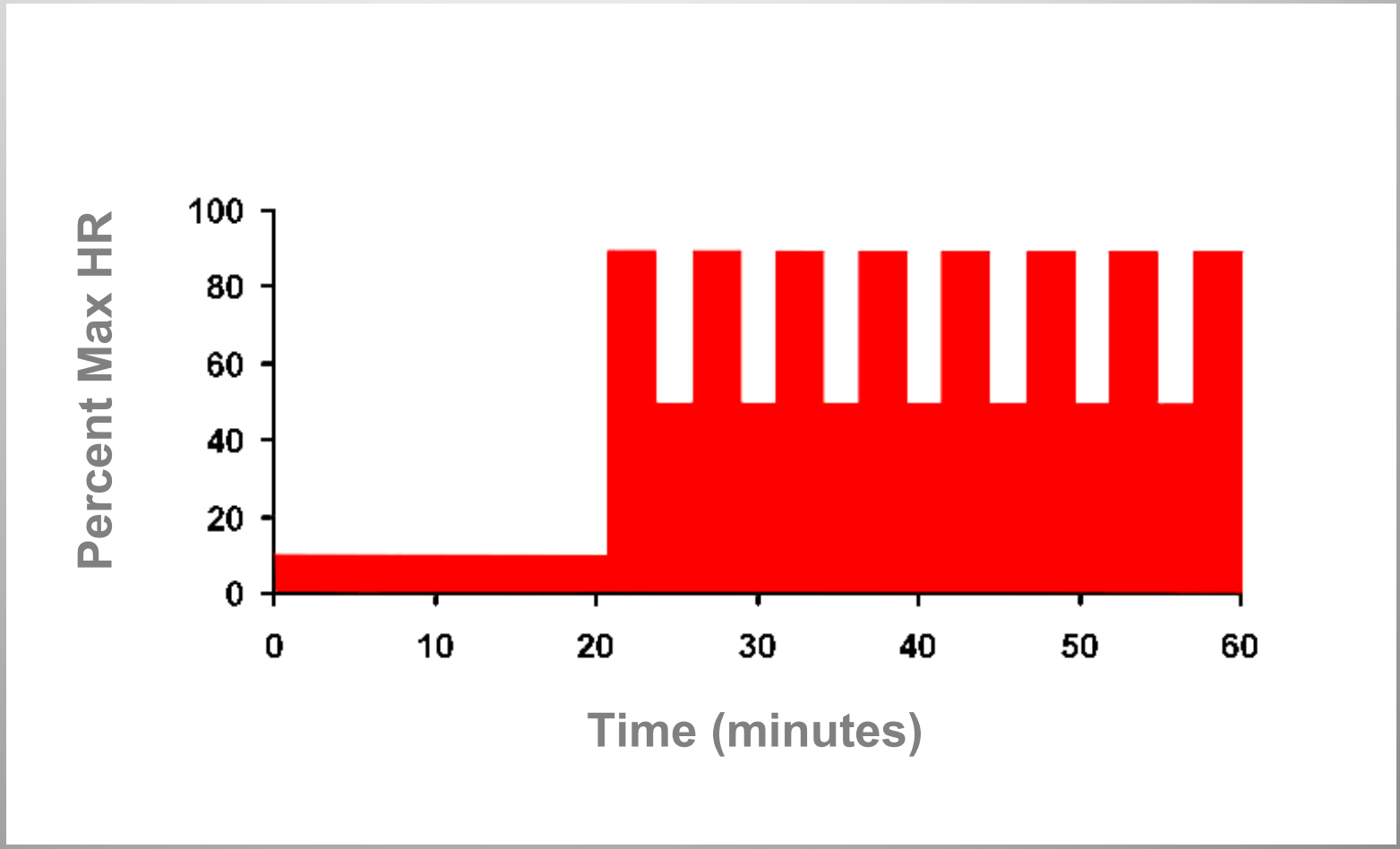




Courtesy R Moon

Wisløff, et al J Physiol 555:825, 2004

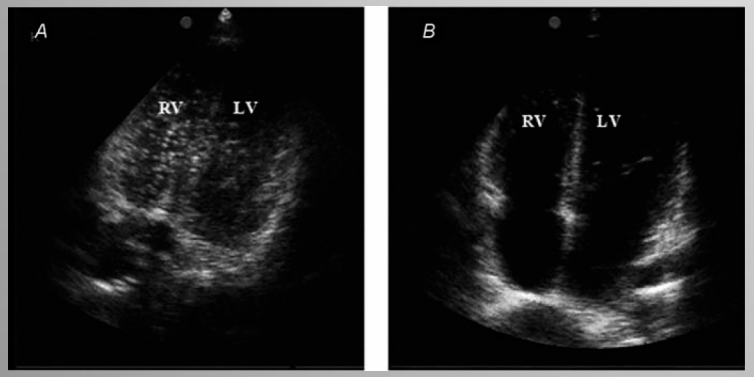
Exercise and VGE: 24 h Before Dive to 18 m/80 min



Courtesy R Moon

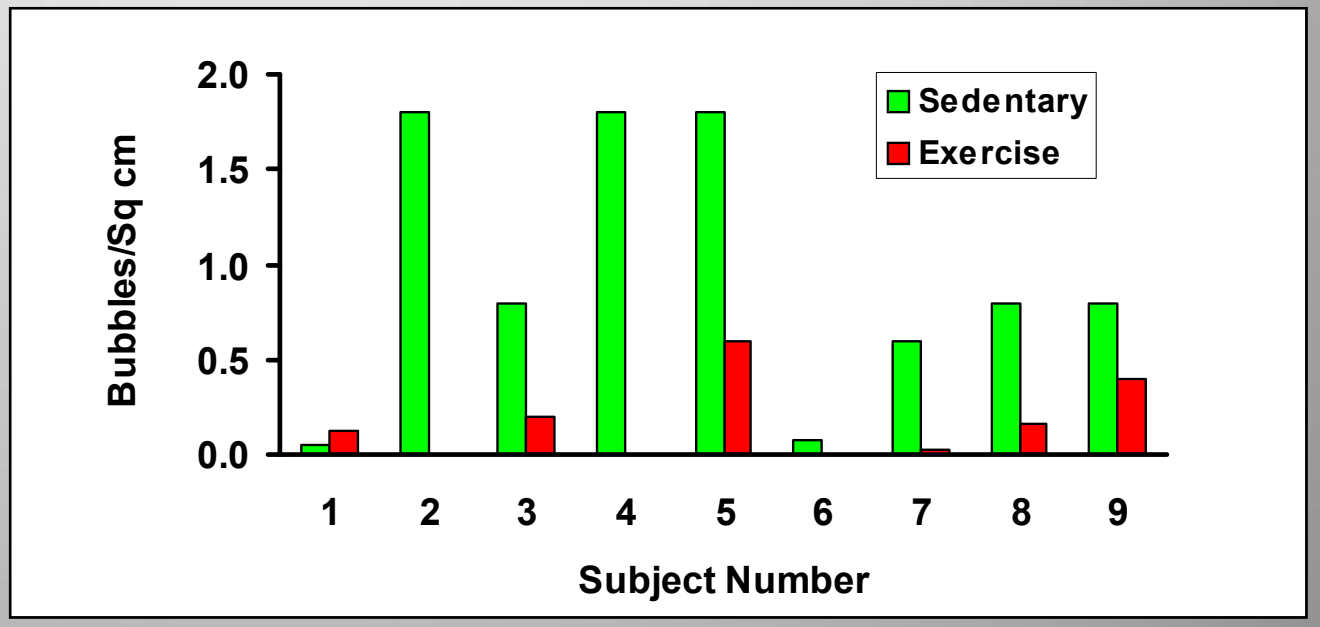
Dujić, et al J Physiol 555:637, 2004

Exercise Before Diving and VGE after 18 m/80 min Chamber Dive



No pre-dive exercise

Exhausting exercise 24 h pre-dive



Courtesy R Moon

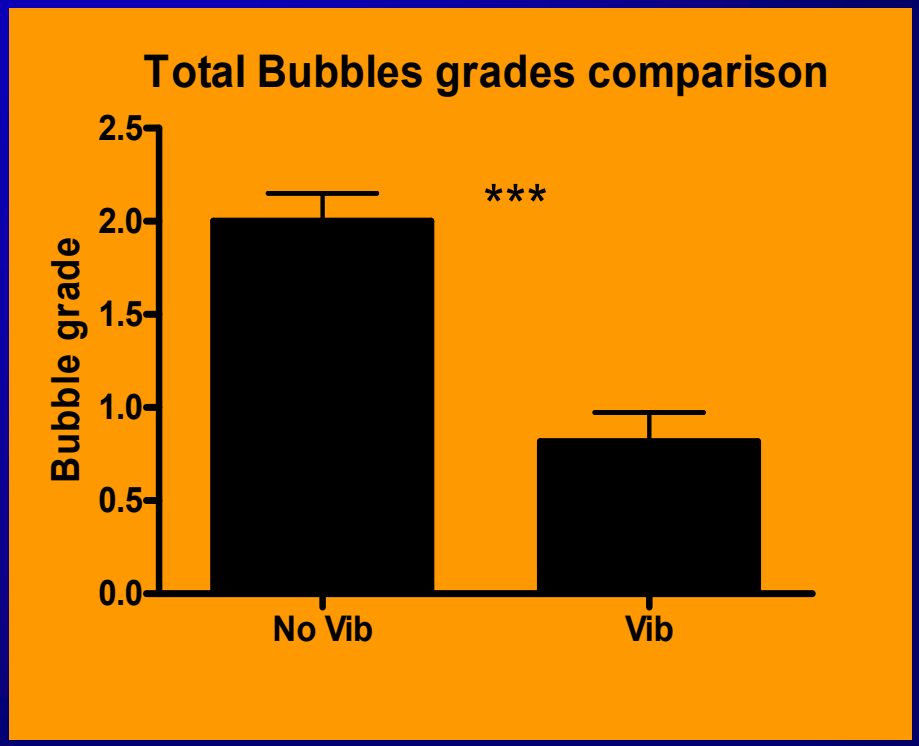
Dujić, et al J Physiol 555:637, 2004

What is this?

Vibration .....
Friend or Foe?

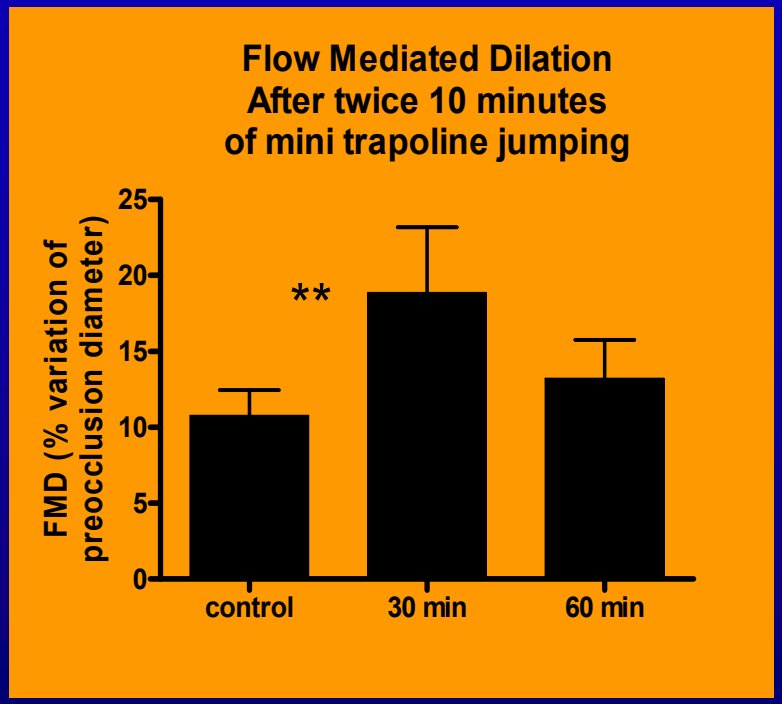
Vibration and Divers

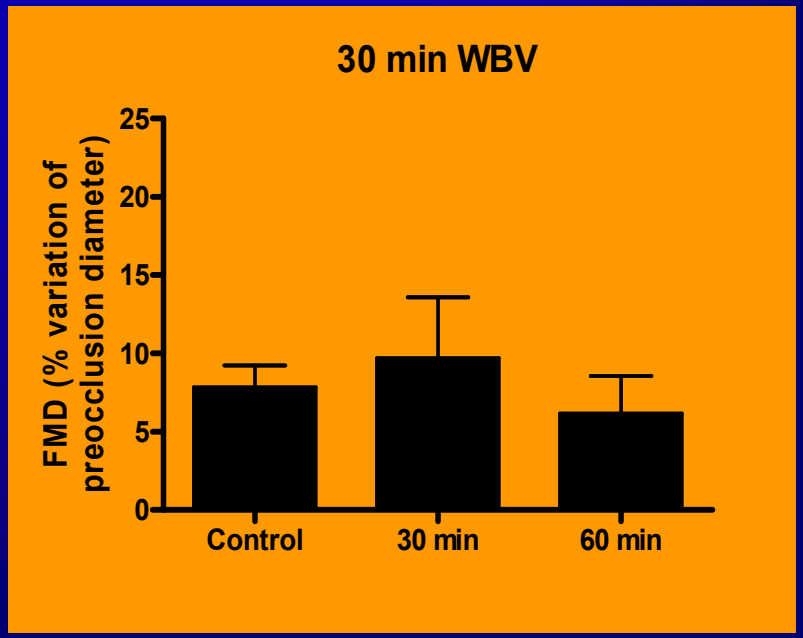
Pre Dive Vibration



Vibration and Divers

Why is this Happening ?





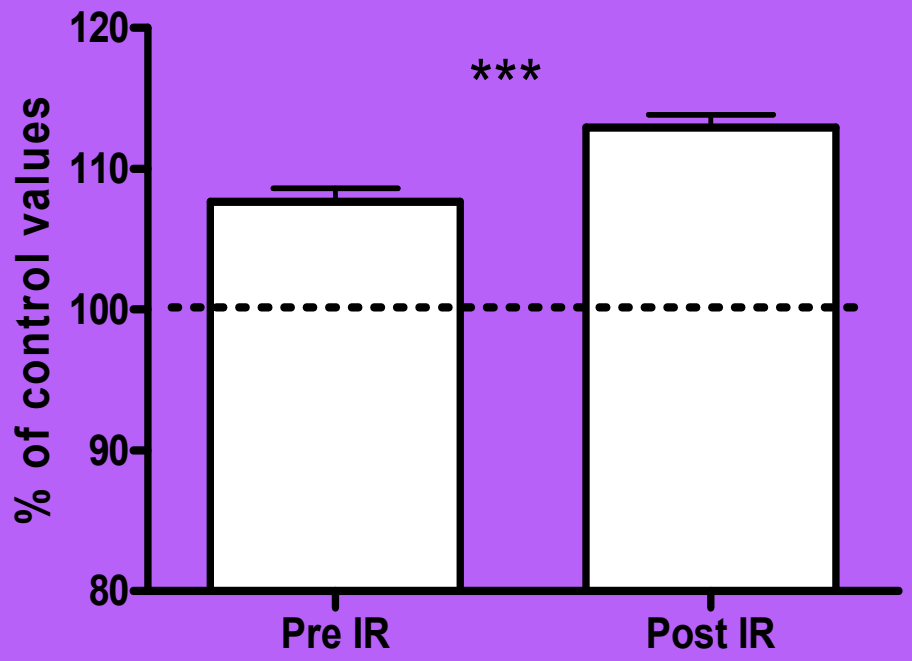
HSP

- Cali Corleo et Al. 1998
- Cali Corleo, Marroni et Al. 1998

HSP
« Prewarming? »

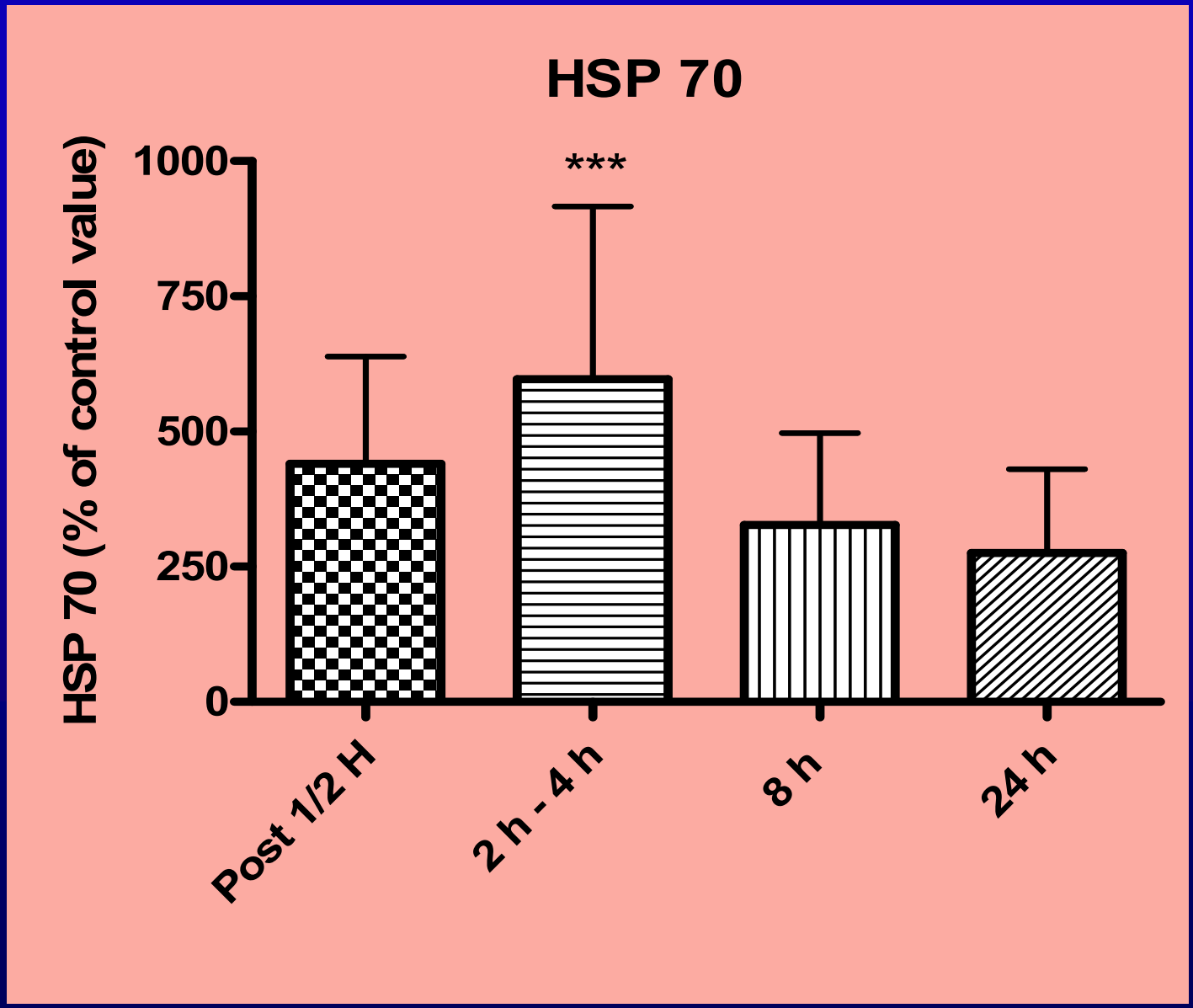
- 10 People (Students)
- 30 min Prewarming FIR Cabin
- Serum HSP70
- 24 h Sampling

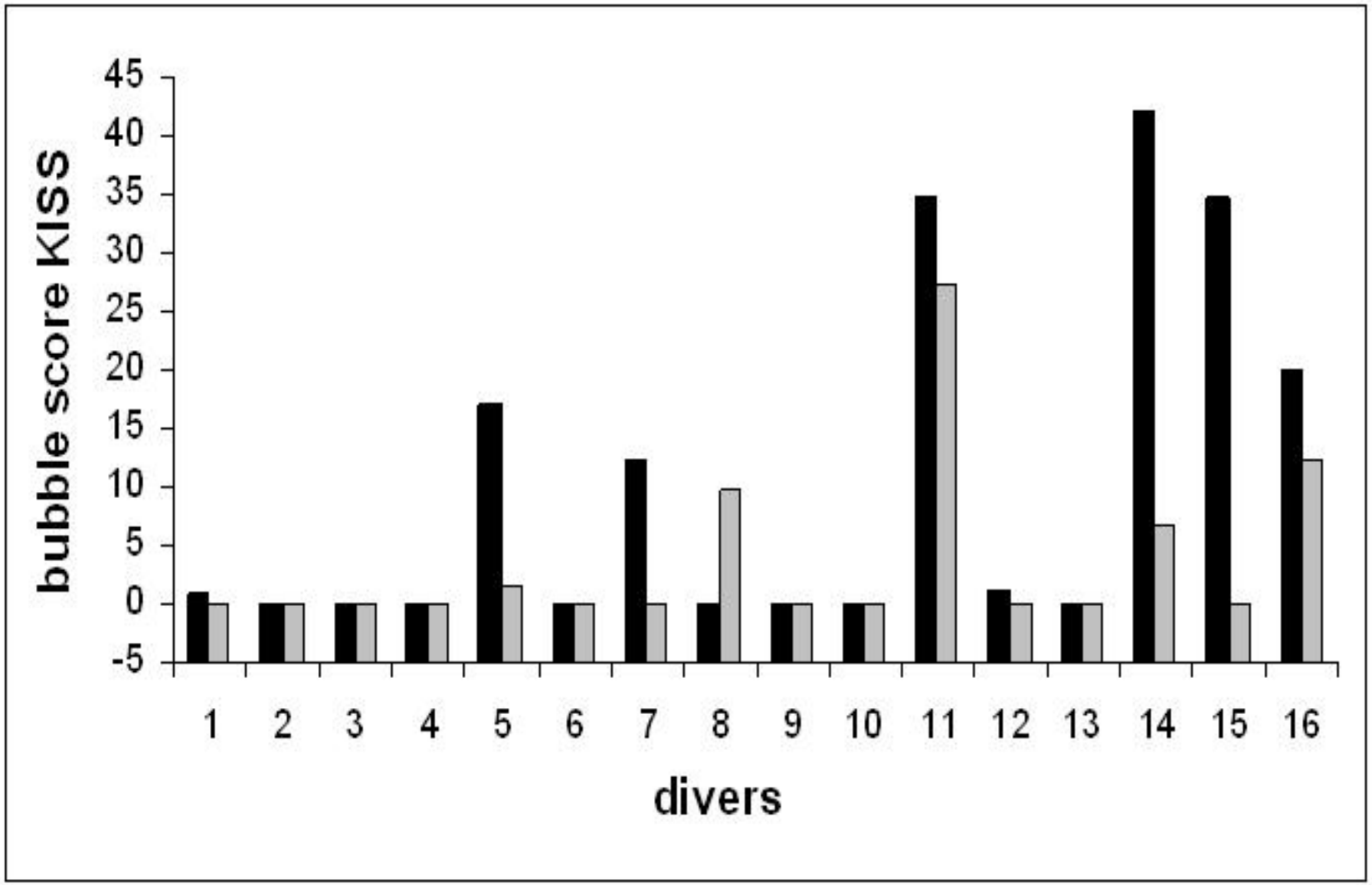
Flow Mediated Dilation after FIR Cabin treatement (30 min.)



Post IR FMD measurements are performed around 1h after sauna

30 min. exposure at 65°C




bubble score KISS
45
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35
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13
14
15
16
divers

Diving and Fluids

Dehydration

- A lot of clinical reports show dehydrated divers that are treated for decompressionpathologies.
- The well known « P phenomenon » can of course explain this situation.
- The scientific literature is clear about the dehydration of divers that enter the hyperbaric chamber, what about the others?

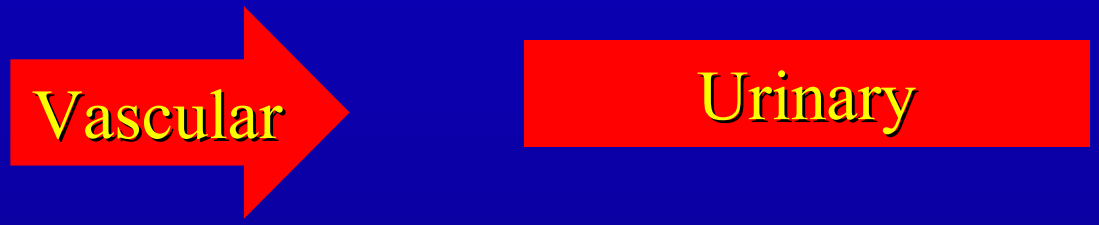
FluidCompartments

- Intracellular
- Extracellular
- Vascular

Fluid Balance during diving

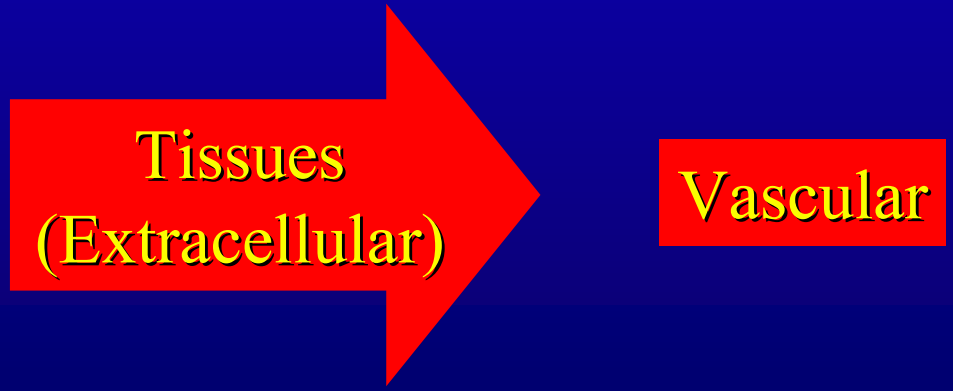
Step One

Icreased
Venous return

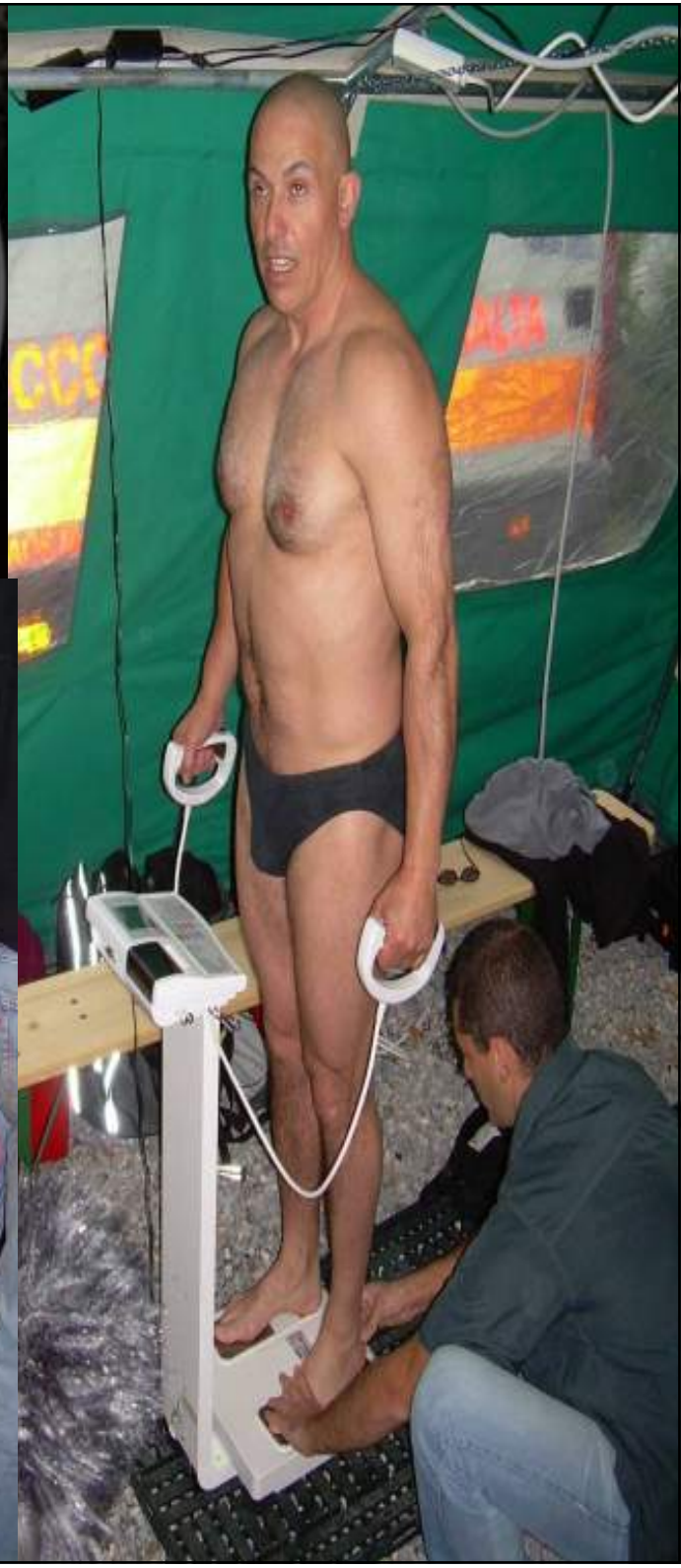


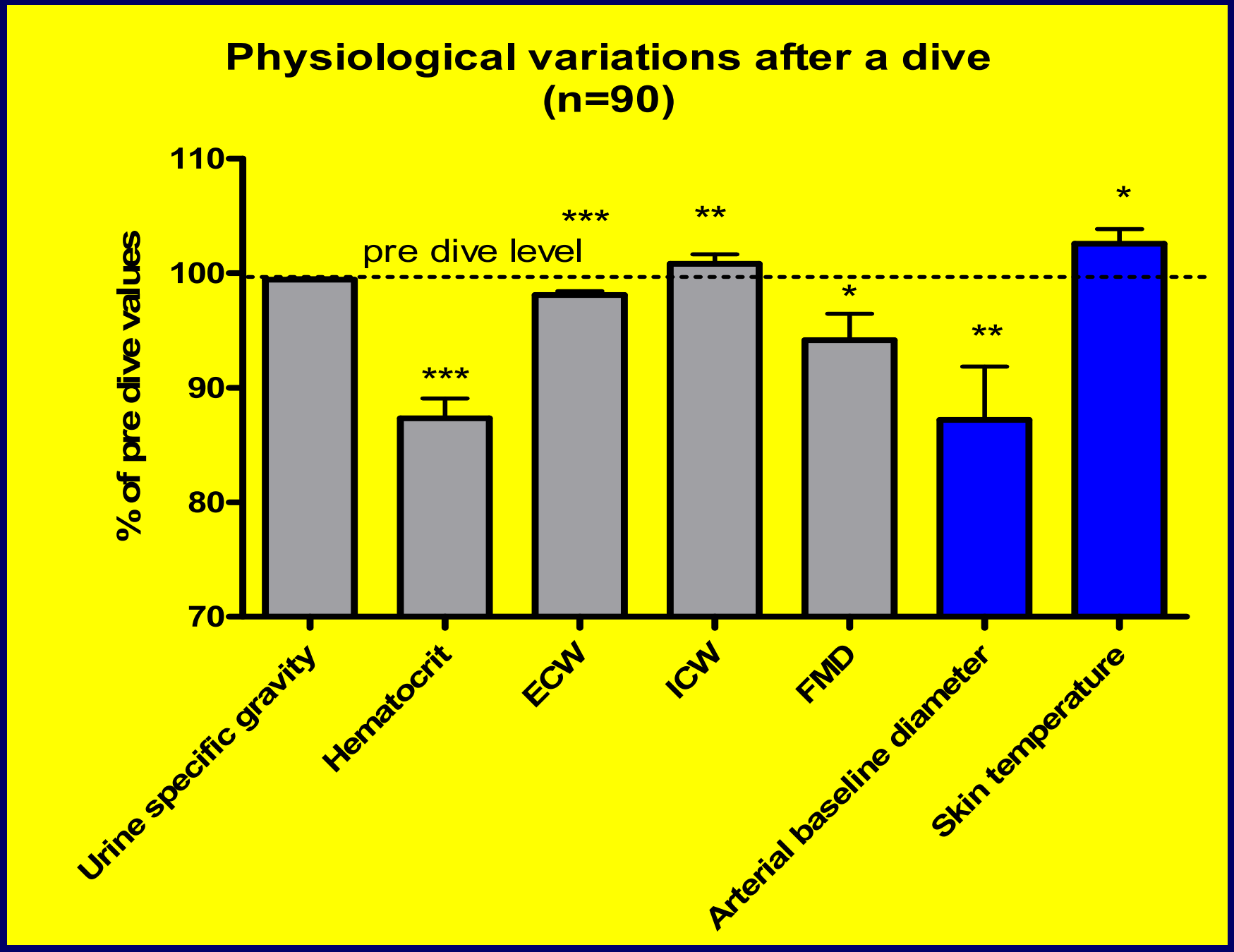
Step Two

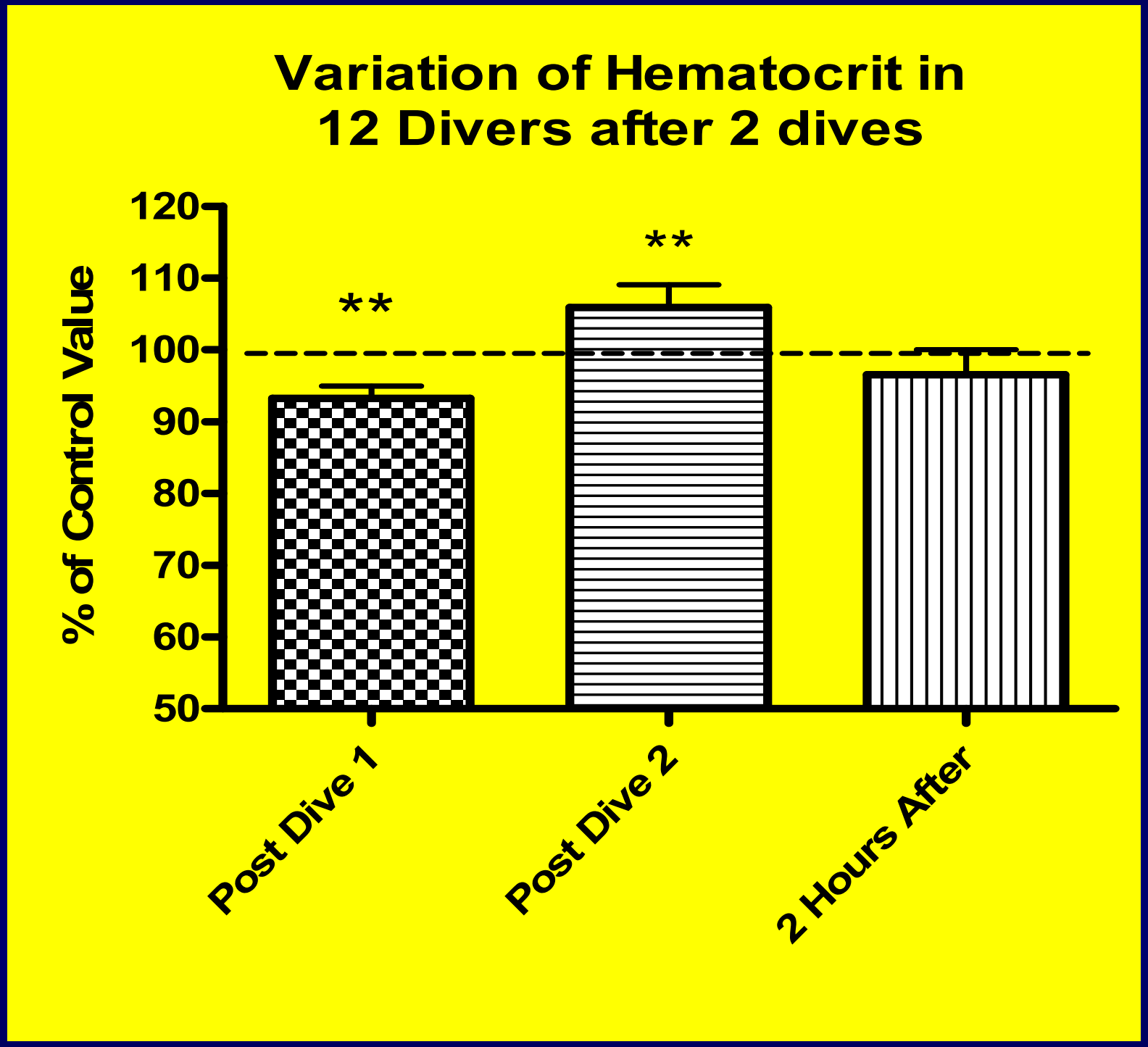
Compensated
Hemoconcentration

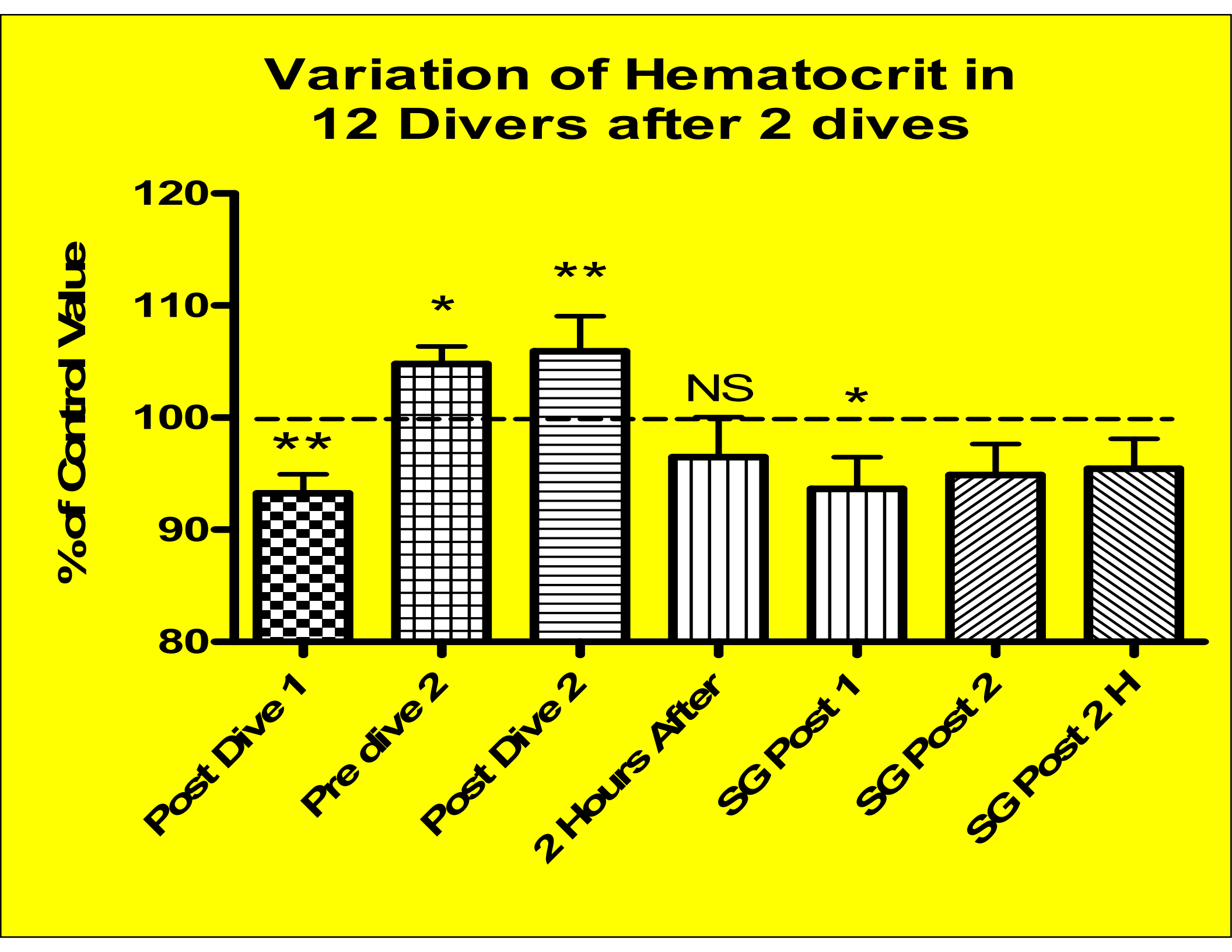




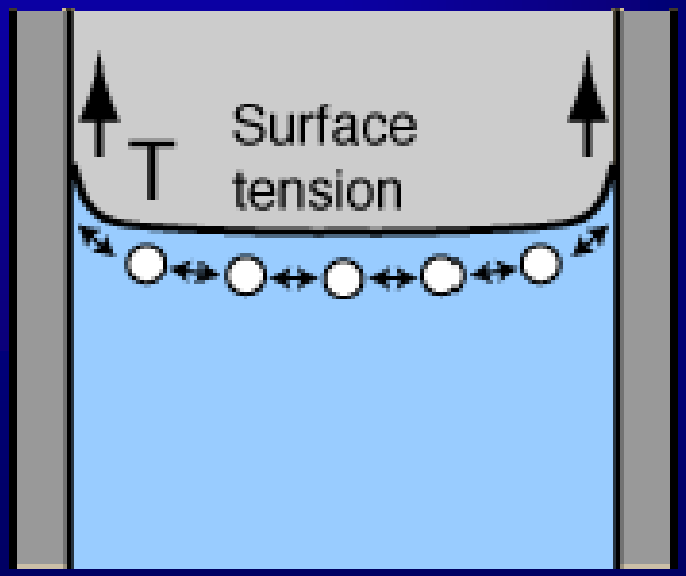



Physiological variations after a dive
(n=90)
% of pre dive values
110
100
90
80
70
pre dive level
***
***
**
*
**
*
Urine specific gravity
Hematocrit
ECW
ICW
FMD
Arterial baseline diameter
Skin temperature

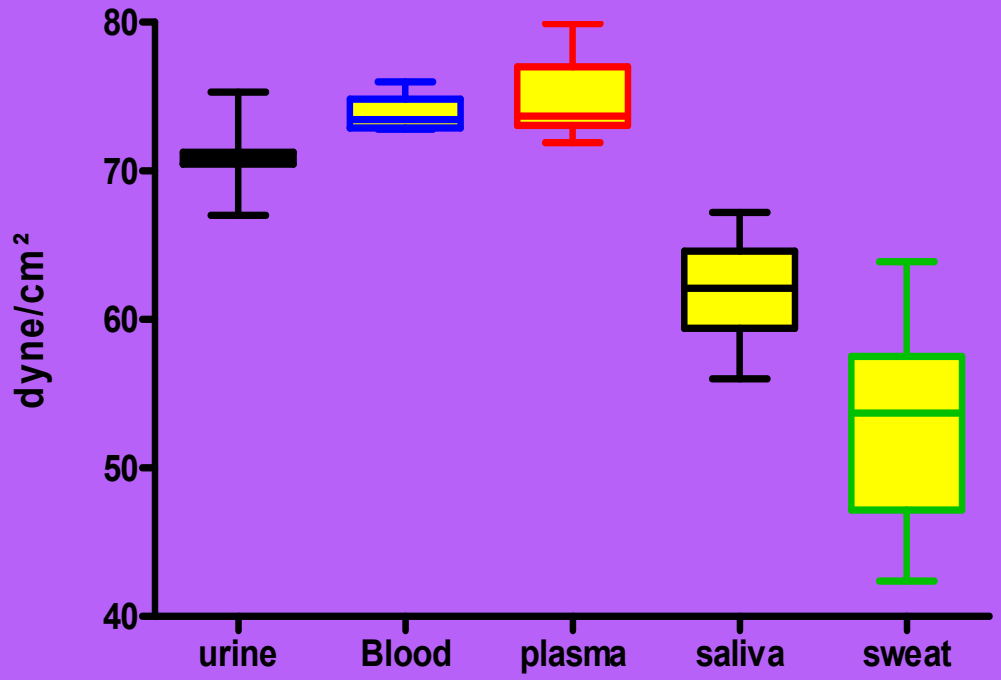

Variation of Hematocrit in
12 Divers after 2 dives
% of Control Value
120
110
100
90
80
70
60
50
**
**
Post Dive 1
Post Dive 2
2 Hours After


Variation of Hematocrit in
12 Divers after 2 dives
%of Control Value
120
110
100
90
80
**
*
**
NS
*
Post Dive 1
Pre dive 2
Post Dive 2
2 Hours After
SG Post 1
SG Post 2
SG Post 2 H

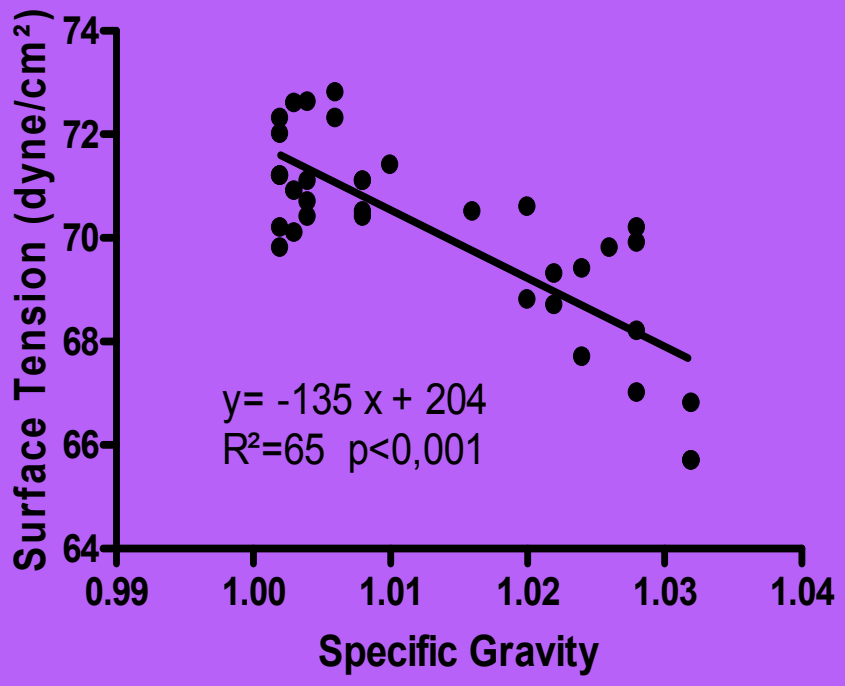
Surface Tension

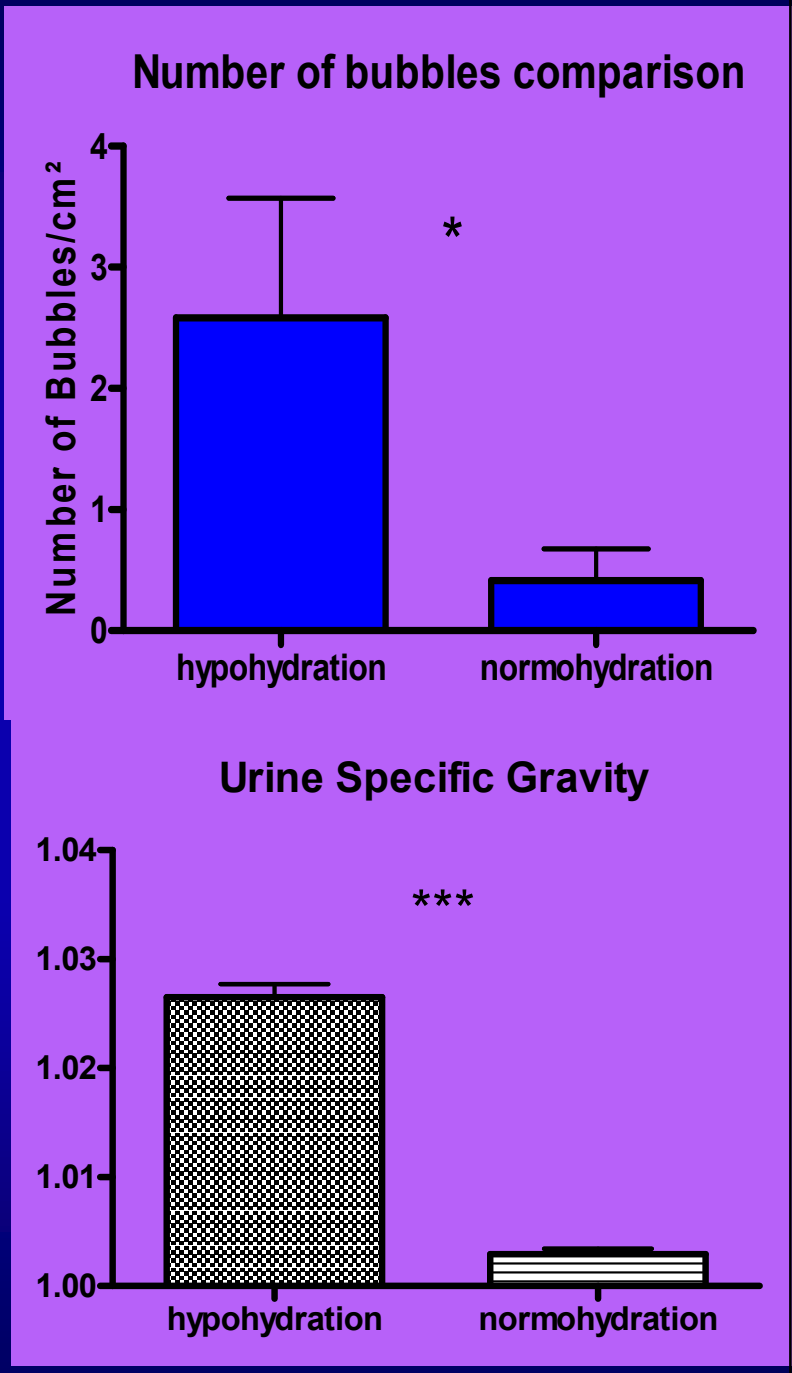


Surface tension of body fluids

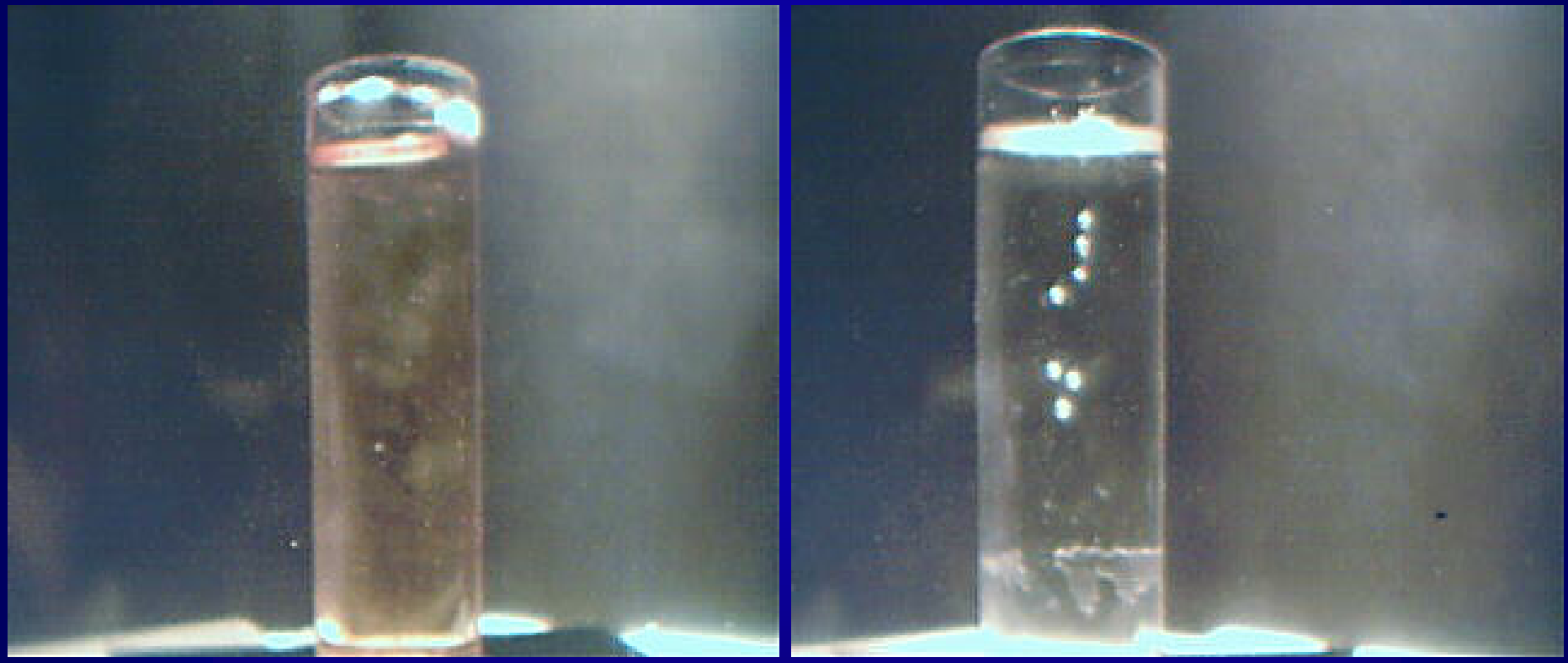


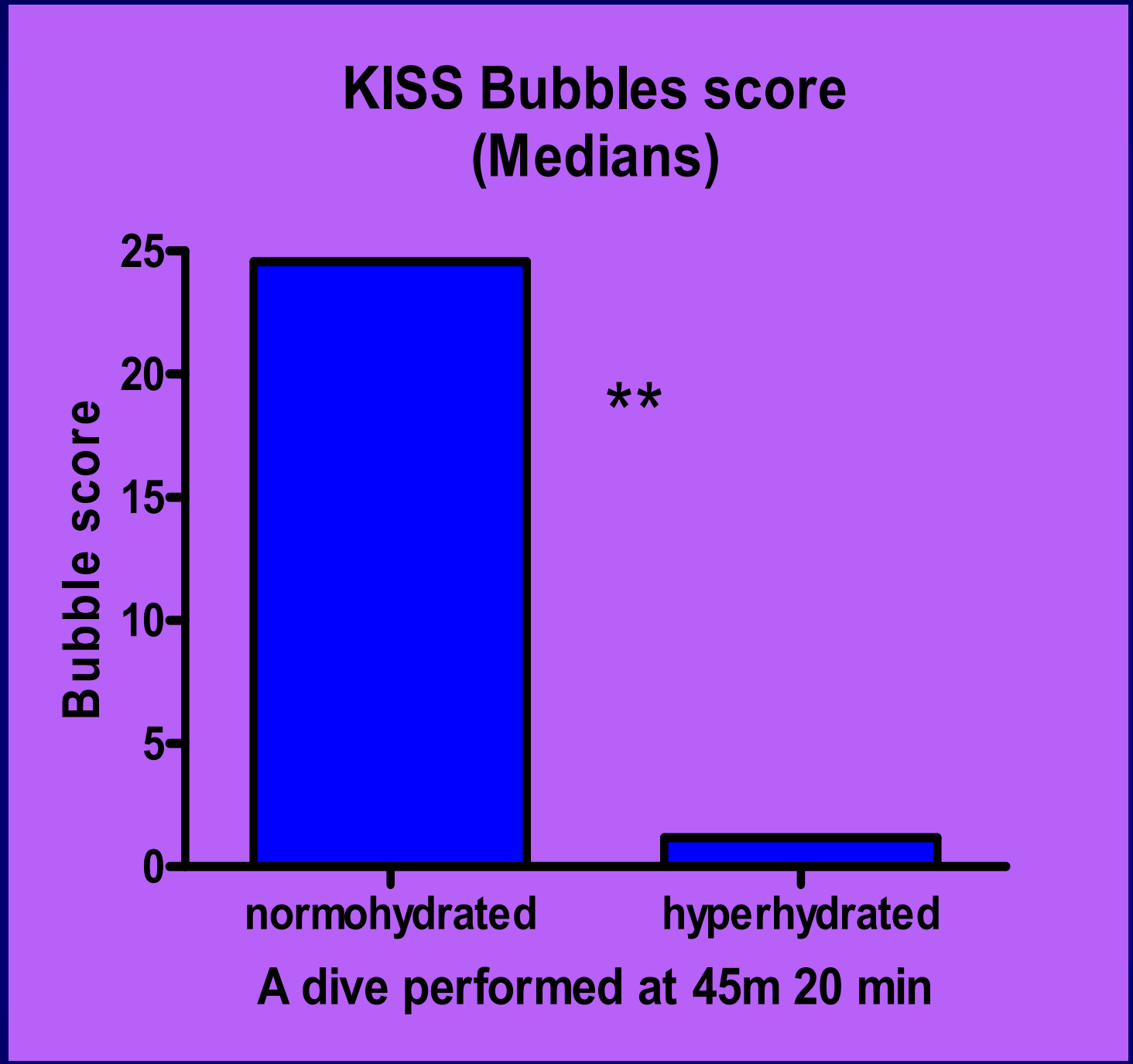
Urinary Surface tension as a function of specific gravity





Increased Surface Tension helps Reducing Post Dive bubbles




KISS Bubbles score
(Medians)
Bubble score
25
20
15
10
5
0
**
normohydrated
hyperhydrated
A dive performed at 45m 20 min

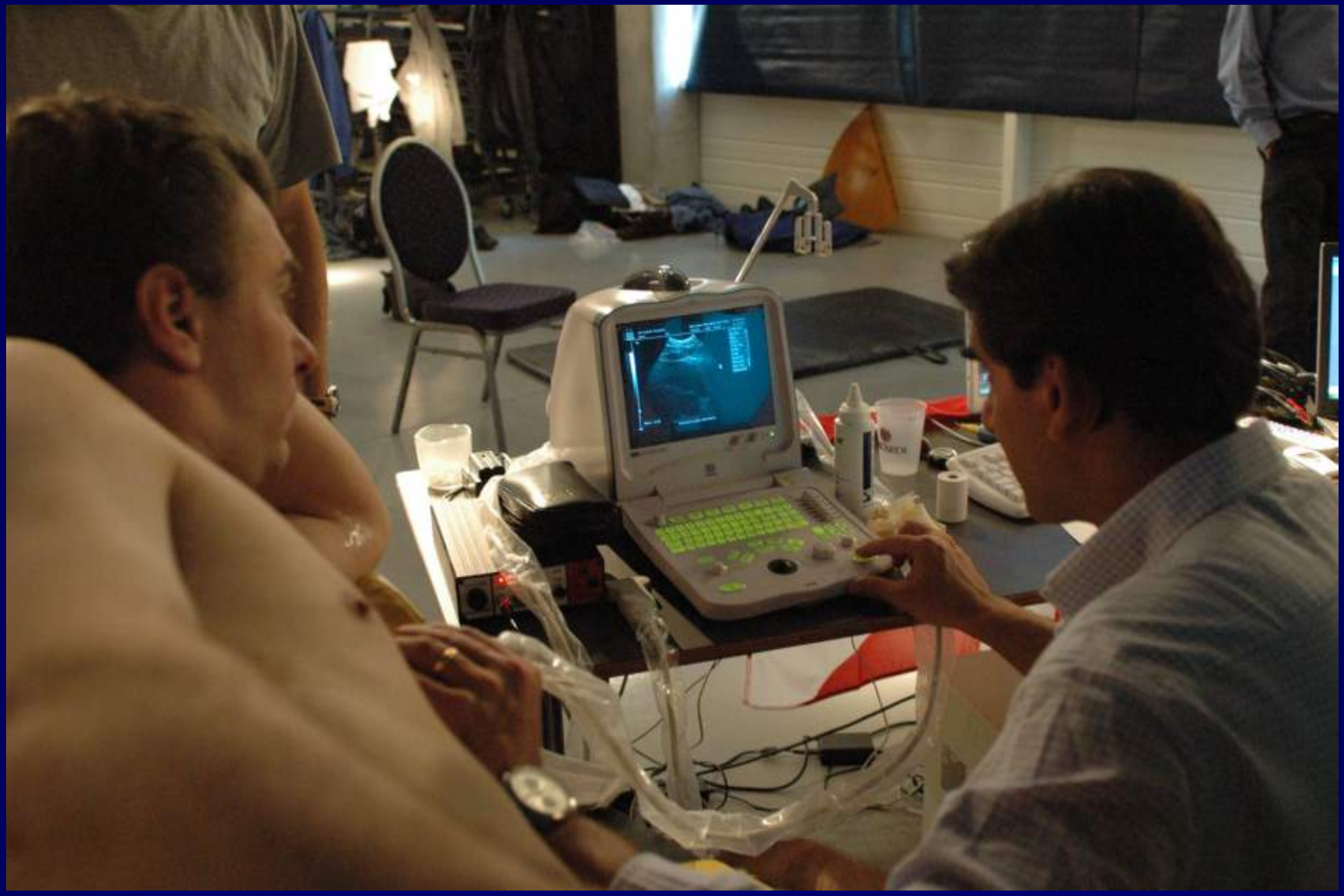
Pre-dive “Wellness” as the future approach to safe diving and Diving Tourism Operations?

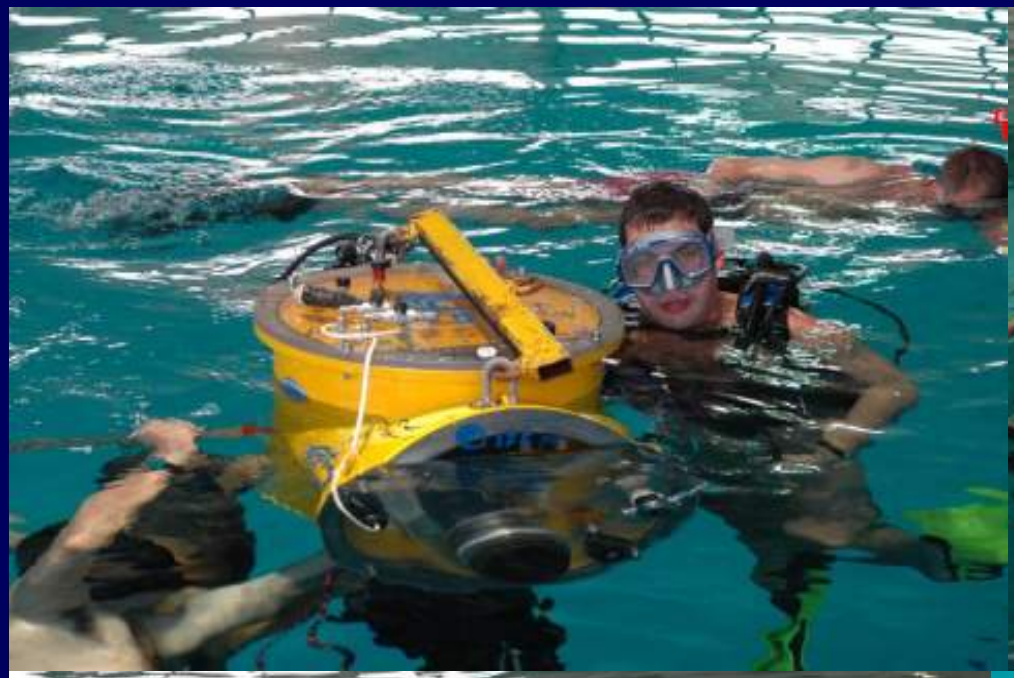
DAN Europe
Field
Diving
Medicine
Research

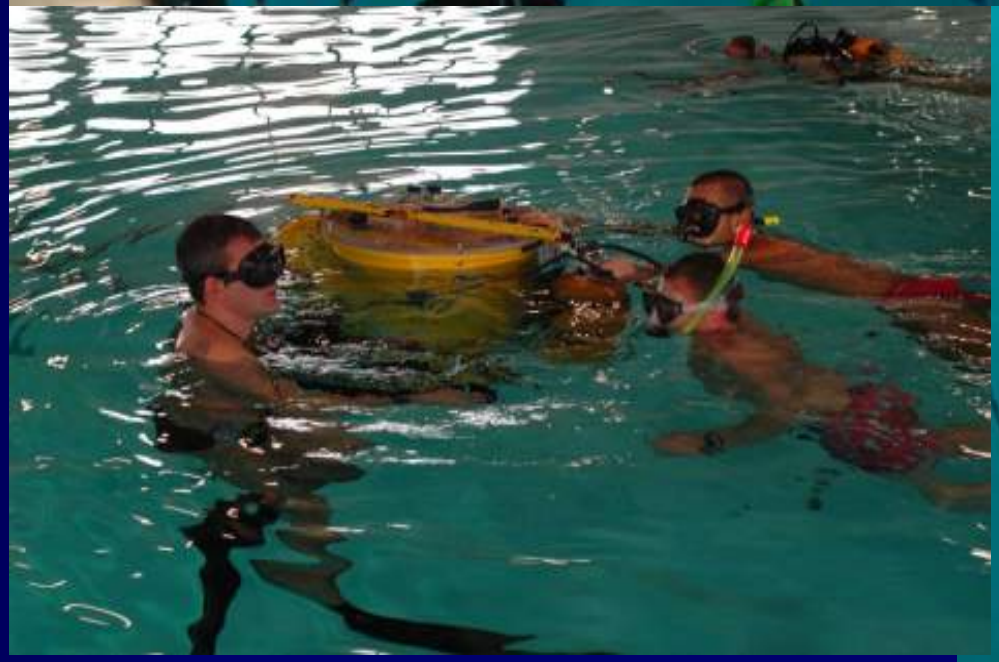
DAN Europe's Wet Lab

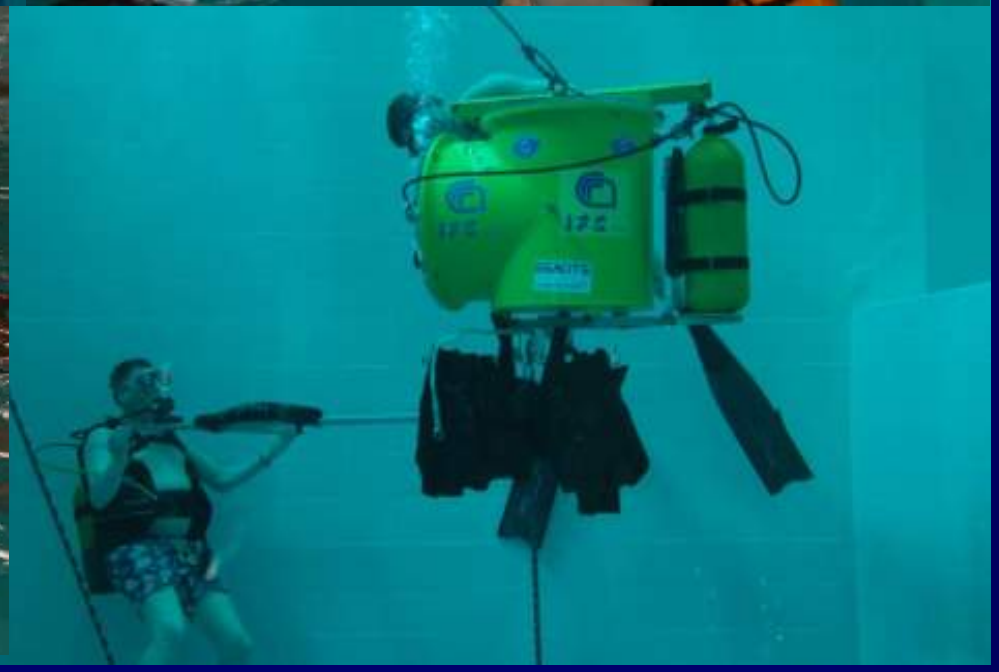

depth
ALADIN
dive time
25.1
19:
27.7
NO STOP
6:
max. depth
deco info
UWATEC


POLAR
OnTime
1:34:23
64
START

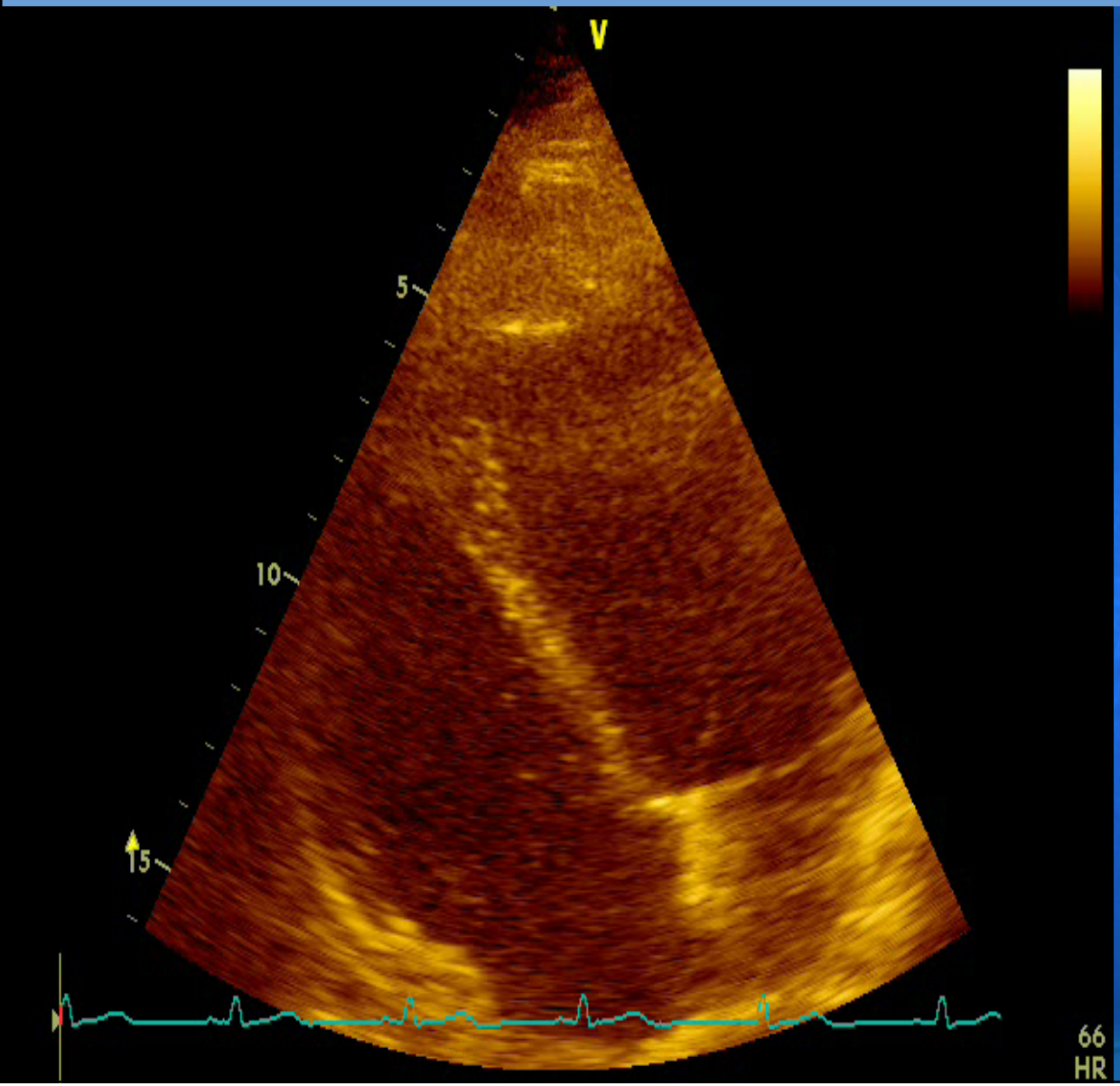






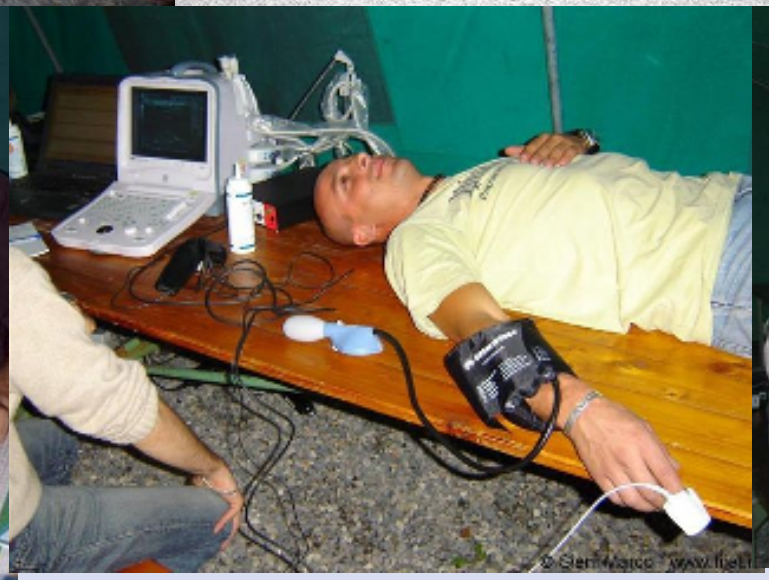


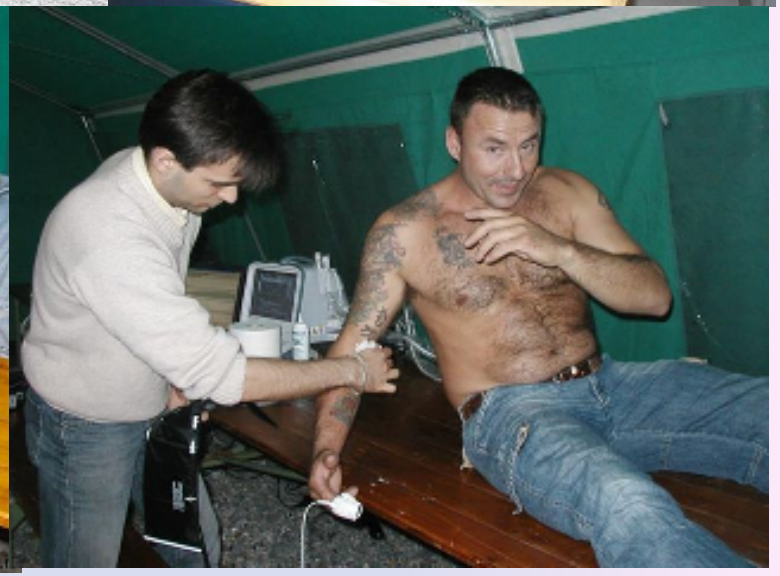
Cardiac echography after a 25m/25min. Dive



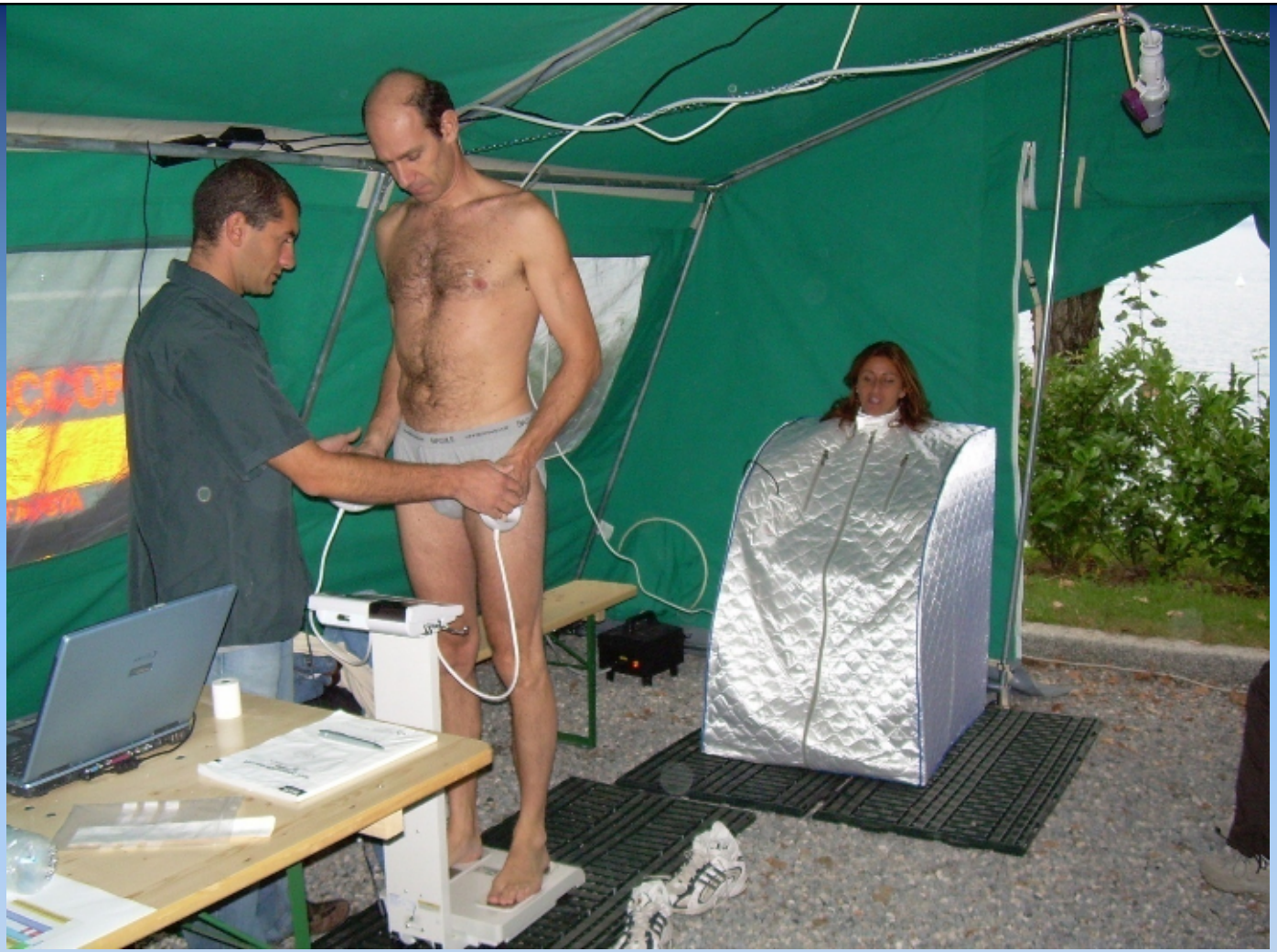
Lake Maggiore Field Research.
September 2006 108 Divers – May 2008 97 Divers
30 to 130 meters Air, Nitrox and Trimix

Lake Maggiore, Italy, September 2006

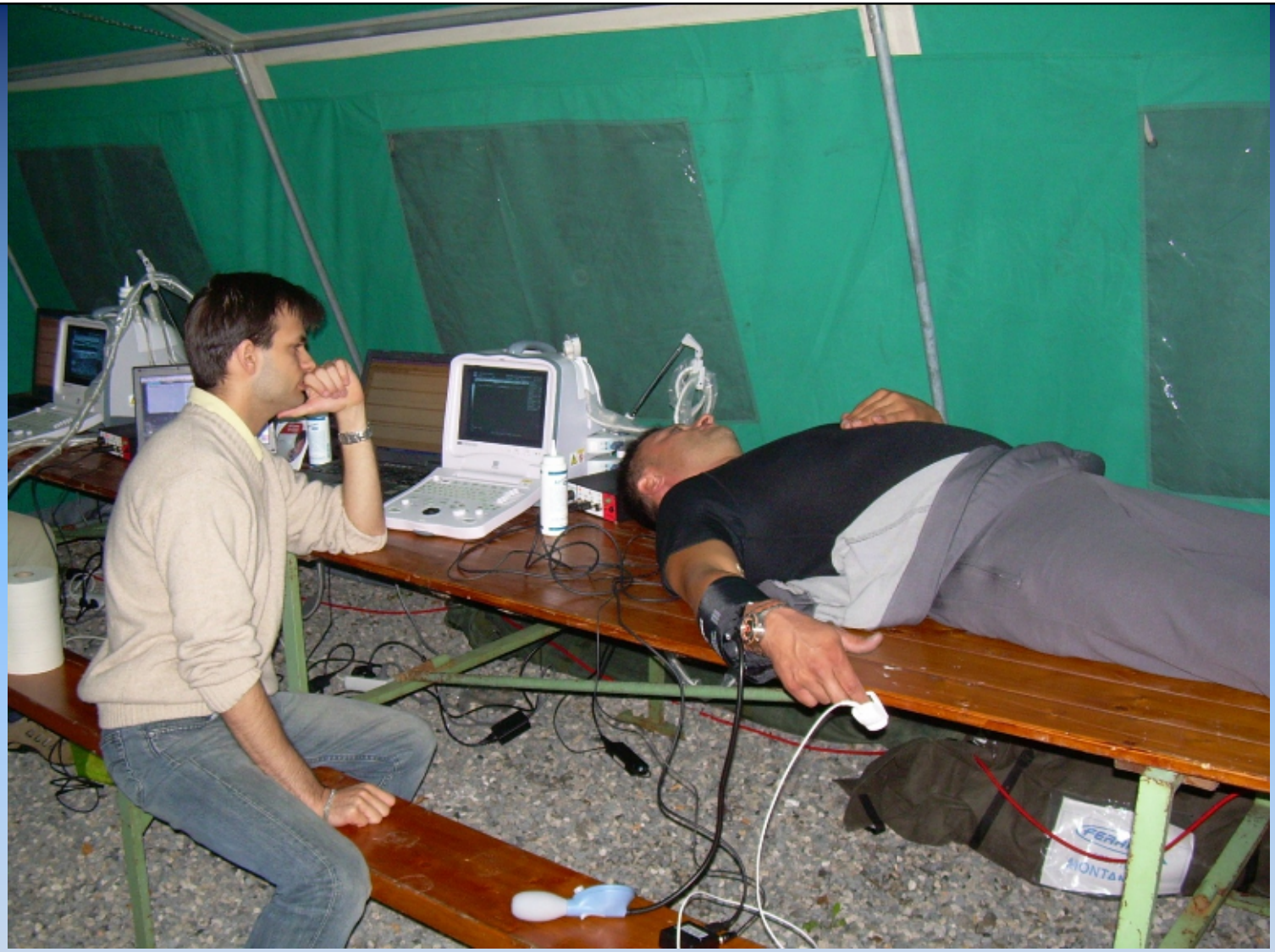




Post-dive Dopplering



Total Body Impedence
&
Infra-red Pre-Heating



Post-Dive Flow Mediated Dilation measurement

Urine Specific Gravity measurement

Haematocrit measurement

“Field Tools”

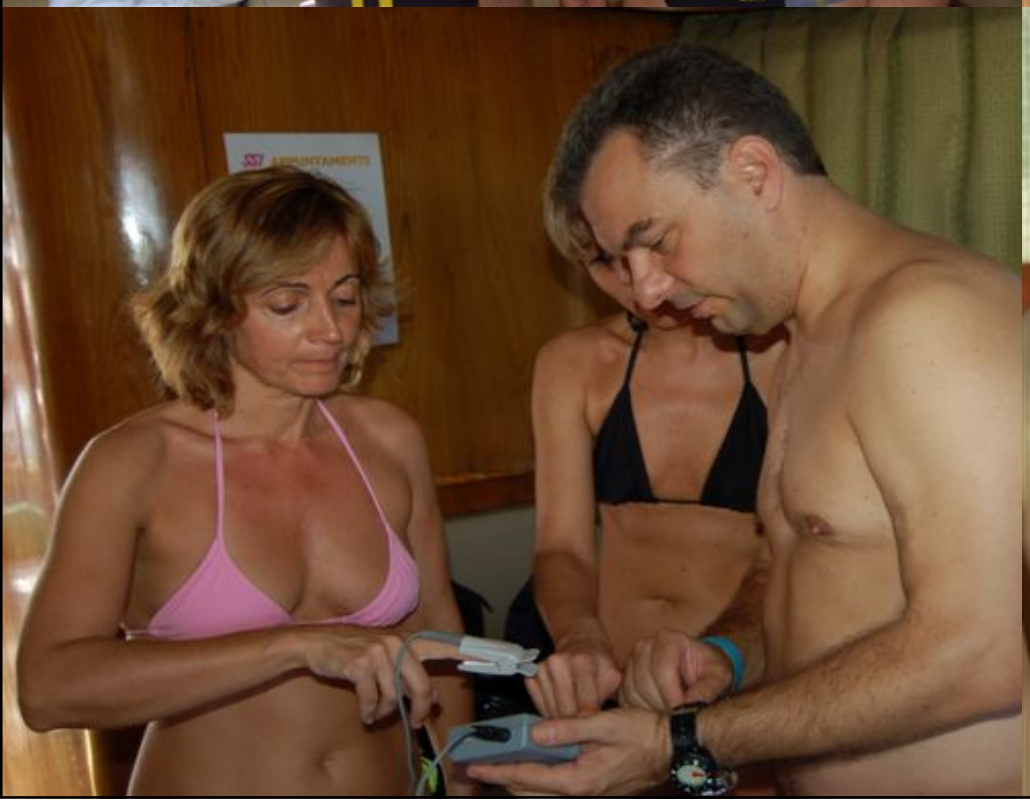
Field Tools Development

Advanced Research Kit

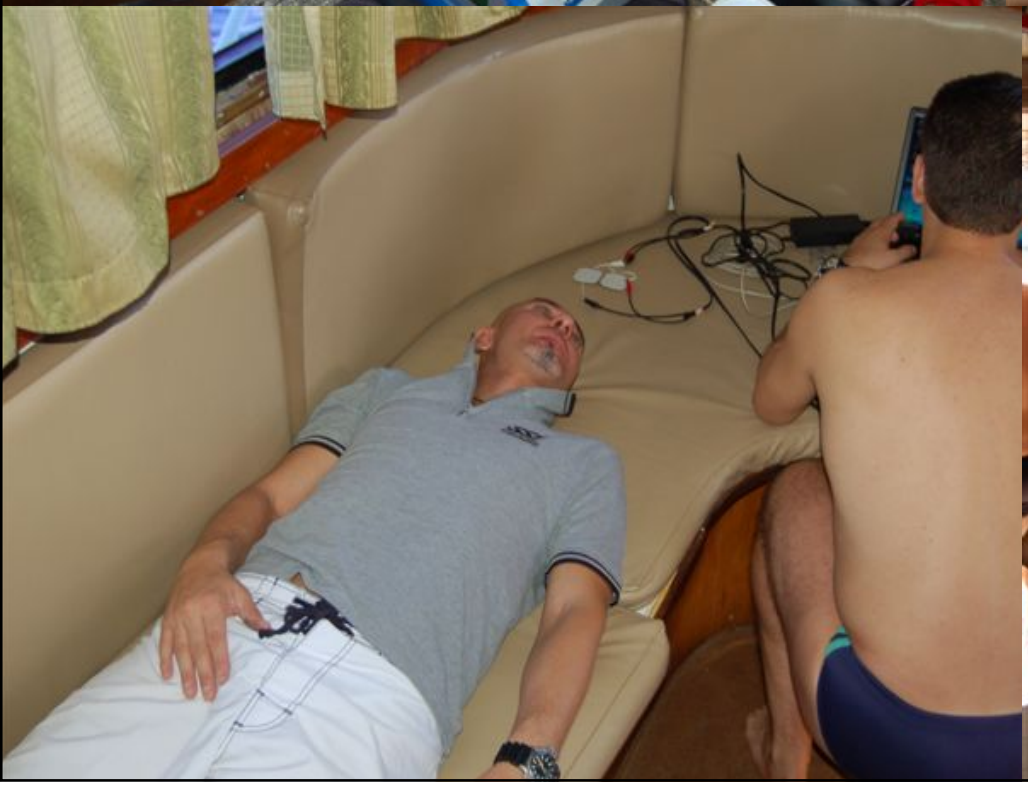
ARK - Advanced Research Kit
DAN Europe's new Field Lab

ARK - Advanced Research Kit
DAN Europe's new Field Lab

Sharm El Sheikh , 0ctober 2007

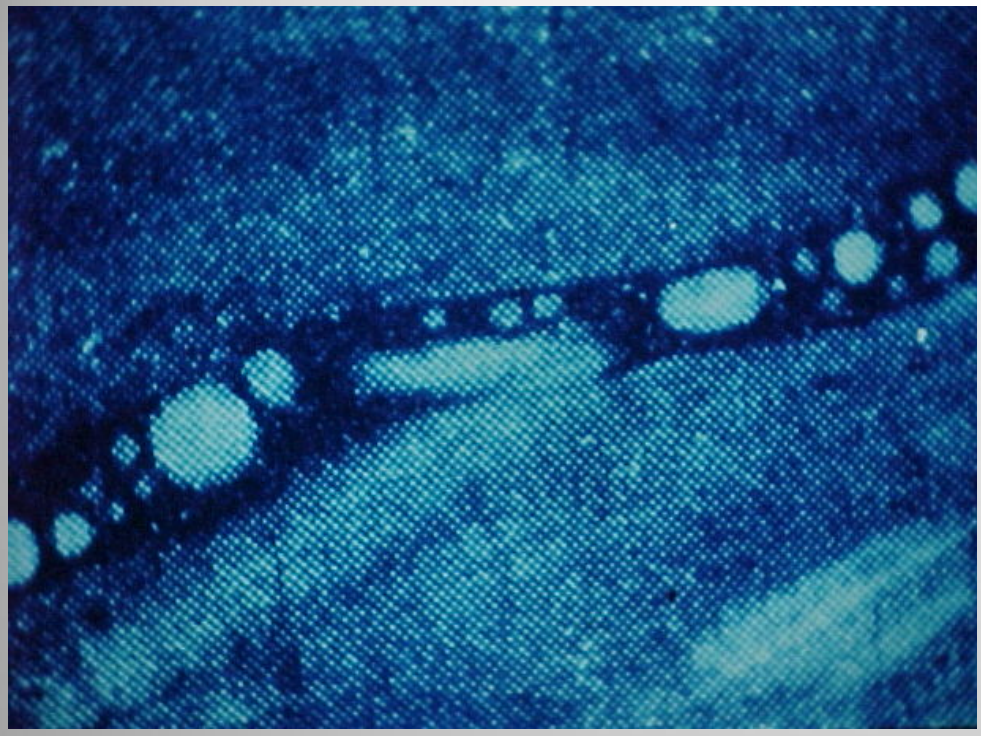


Sharm El Sheikh , 0ctober 2007



PDE & DSL

- > 200,000 dives 1998-2008
- > 25,000 divers
- 50 DCI cases



The Common Enemy !

Bubble Busters at work!

Lateral Thinking Required….


Thank You

Abstract A1

The Ruffini type-2 corpuscle
an explanation for pain-only decompression sickness

Michael B. Strauss, M.D

The Ruffini Type-2 Corpuscle

an explanation for

Pain-only Decompression Sickness

UF

Michael B. Strauss, M.D.
Stuart S. Miller, M.D.
Alan J. Lewis, M.D.
Jeff E. Bozanic, M.D.
Igor, Aksenov, M.D., Ph.D.

LBMMC

Long Beach Memorial Medical Center

and

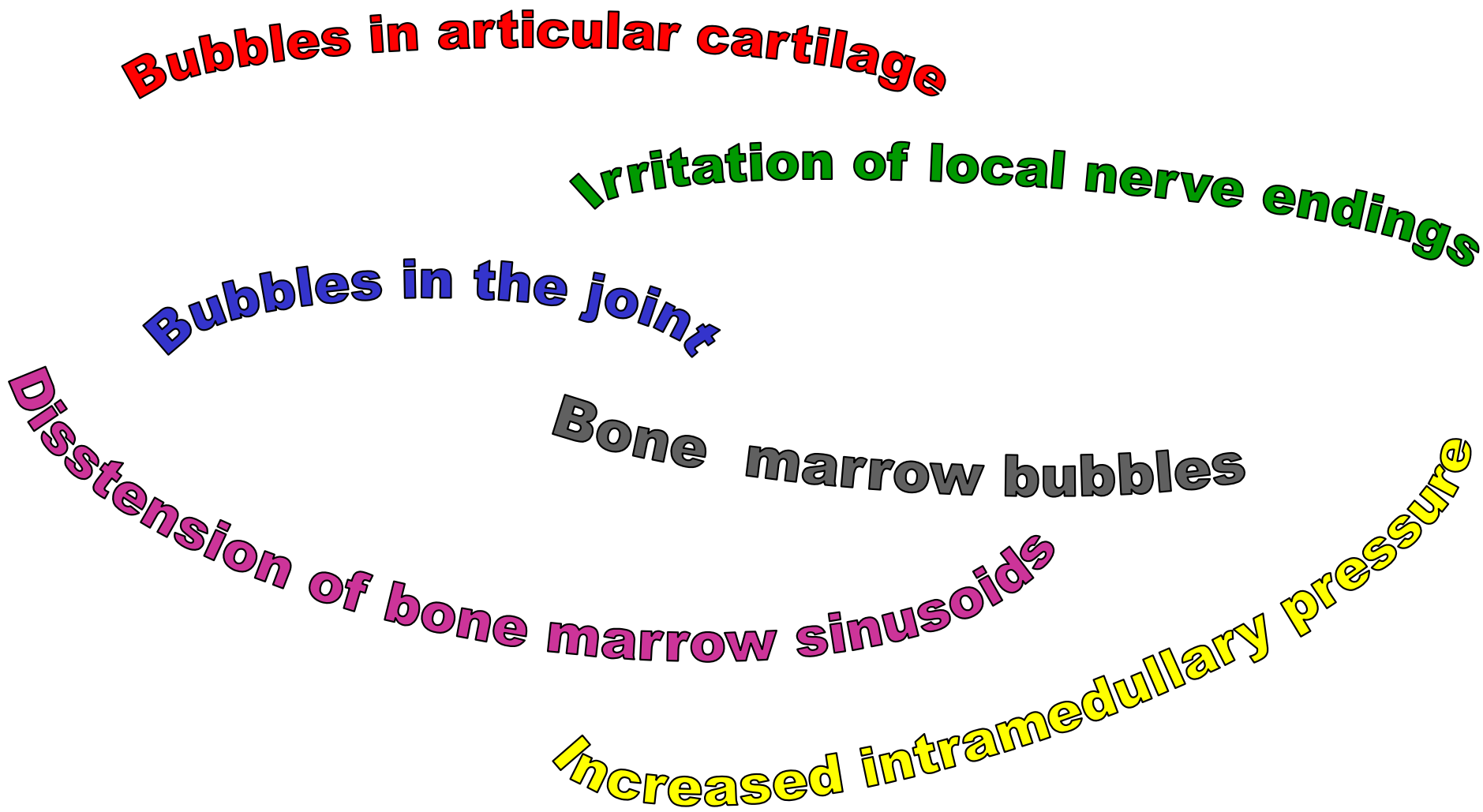
University of Florida, Gainesville

Introduction

- The cause of ain in Type-1(pain only) DCS remains elusive
- Unequivocal absence of physical signs…
- Immediate, dramatic pain relief with recompression
- Joint pain is the predominant manifestation of DCS in saturation divers and aviators

Invalid Hypotheses

(To explain the pathophysiology of pain only DCS)



Invalid Hypotheses-2

- All focus on an autochthonous (in situ, spontaneous) mechanism [for bubble formation]
- …There is no agreement on the actual site (Francis & Mitchell)

Evolution of the Ruffini Hypothesis

Hills-1970

- Pain in DCS is a mechanical problem
- Autochthonous bubble formation
- Immediate relieve with recompression

Evolution 2

Strauss-1980 (The dislocated joint model)

- Potential (orthopaedic) sources of pain

  -Nerve stretch (e.g. sciatica)
  -Periostial elevation
  -Muscle ischemia
  -Tendon and ligament stretch

~~Golgi tendon~~

~~Muscle spindle~~

- Pain in sensory organelles embedded in avascular structures

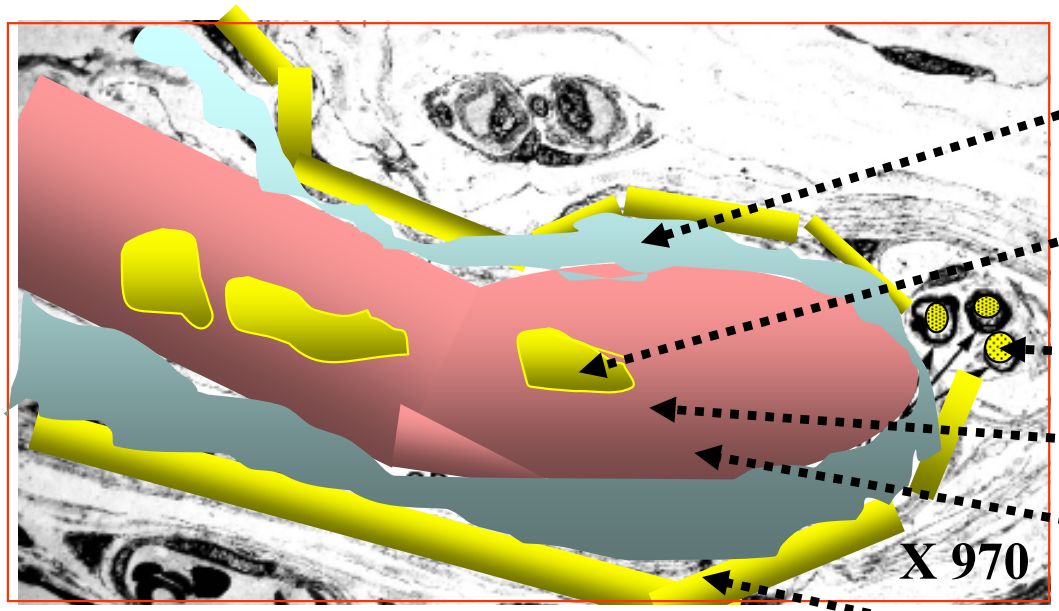
What is the avascular structure?

Evolution 3

Halata-1984 (The Ruffini type-2 corpuscle)

- A slow reacting pain sensor
- Embedded in joint capsules with afferent C-fiber innervation
- Stretching of the organelle generates the severe type of pain associated with dislocations, sprains, etc.

Ruffini Type-2 Corpuscle



Intracapsular Fluid-filled Space

Nerve Terminals

Myelinated Nerve Fibers

Collagen Fibrils

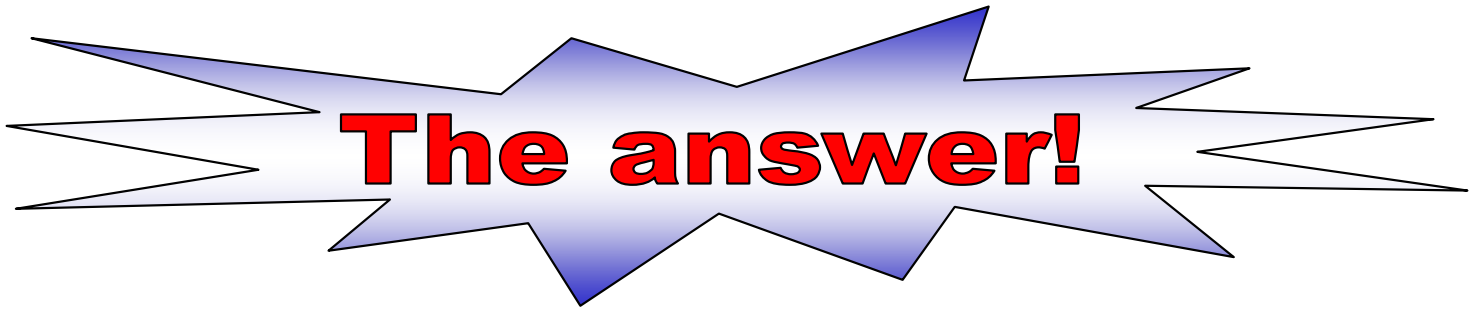
Fibroblasts

Perineurium
(Unmyelinated Nerve Fibers)

Evolution 4

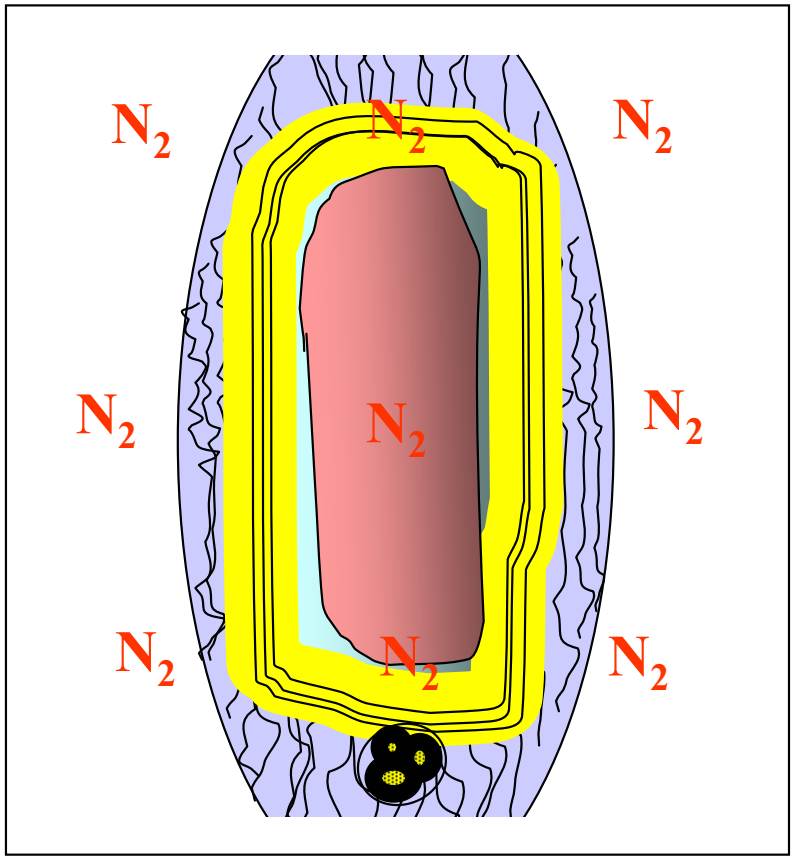
Strauss-1990

- Autochthonous bubbles in relatively avascular structures (slow tissues) such as the joint capsule diffuse into the Ruffini Type-2 corpuscle (RT2C)
- Distention of the perineurium of The RT2C from within—in contrast to external stretch (from a dislocated joint)
- Dramatic pain relief—like the reduced joint after a dislocation—with mechanical reduction (pressurization ala Boyle's law) of the intra-organelle bubble



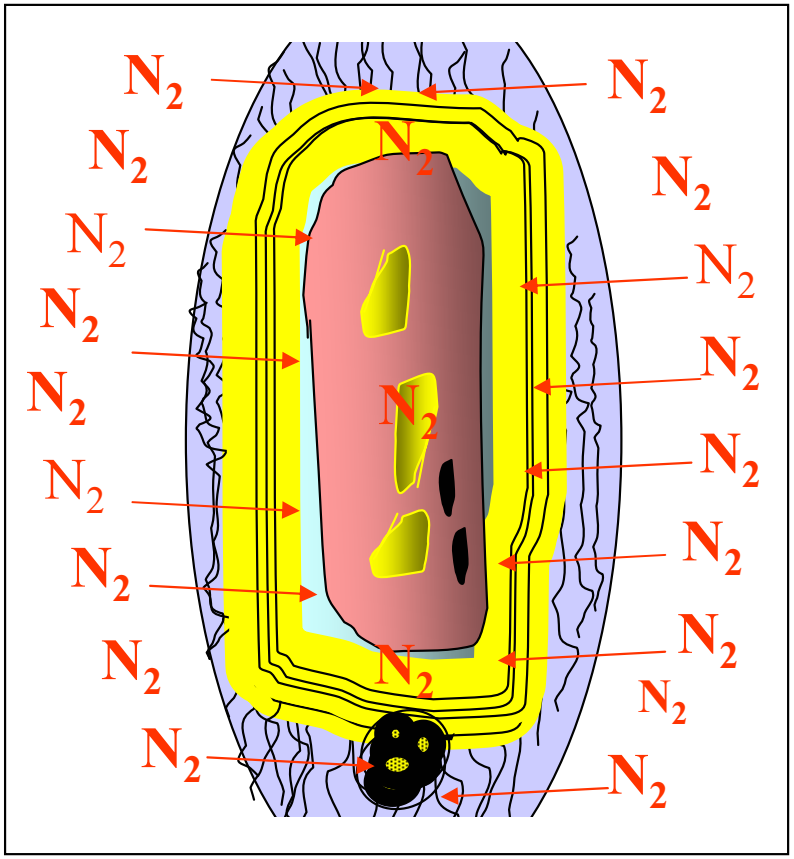
A "Perfect Fit"

On the Surface



Equilibrium

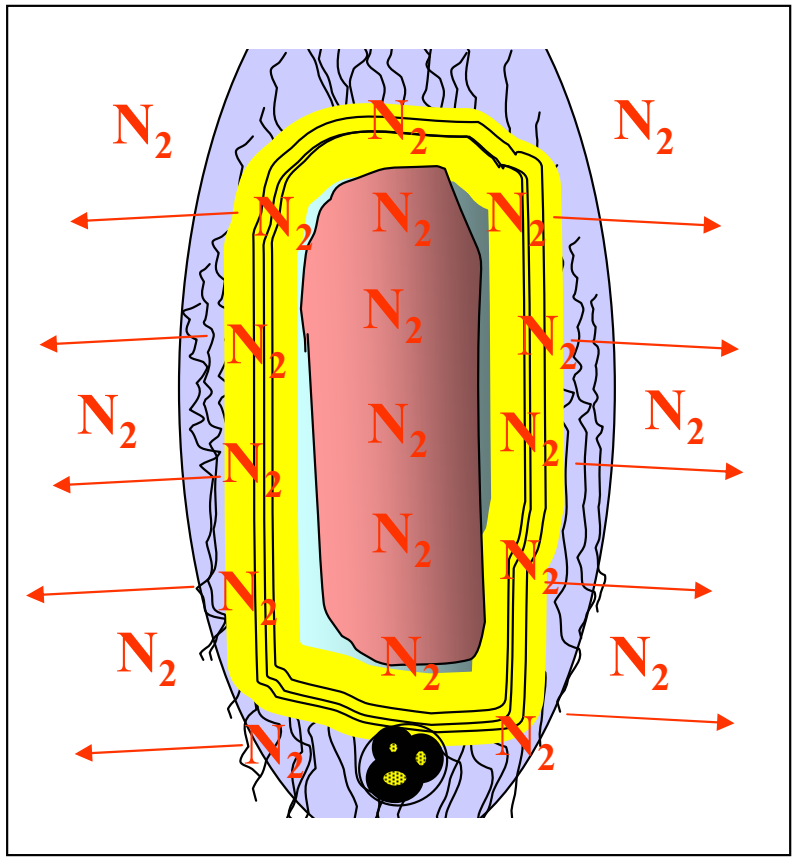
During the Dive



On-gassing

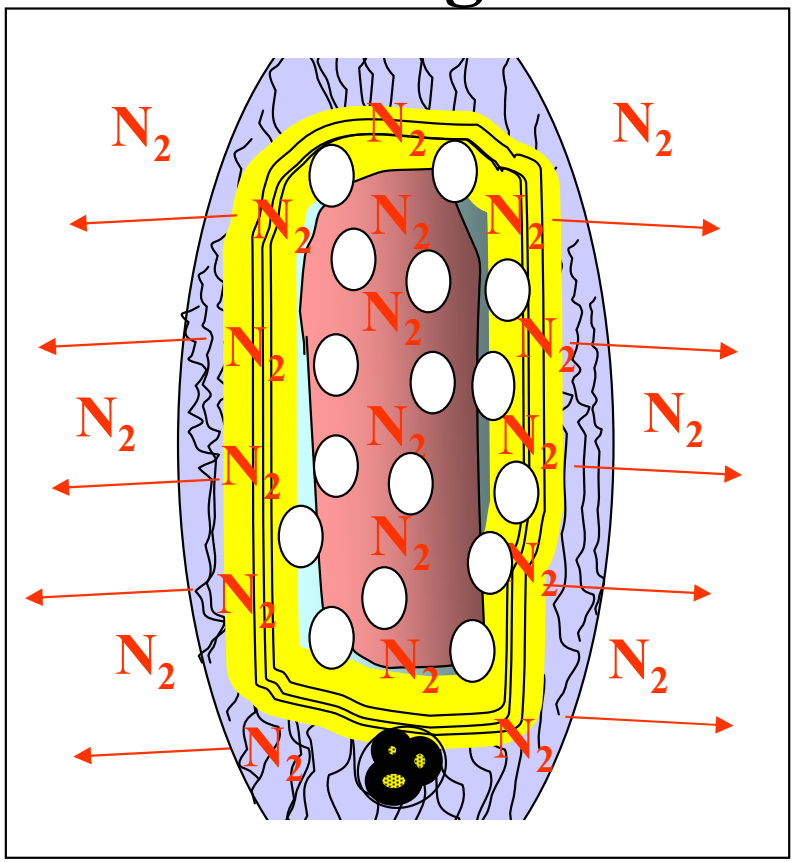
A "Perfect Fit" 2

Return to the Surface



Supersaturation with Off-gassing

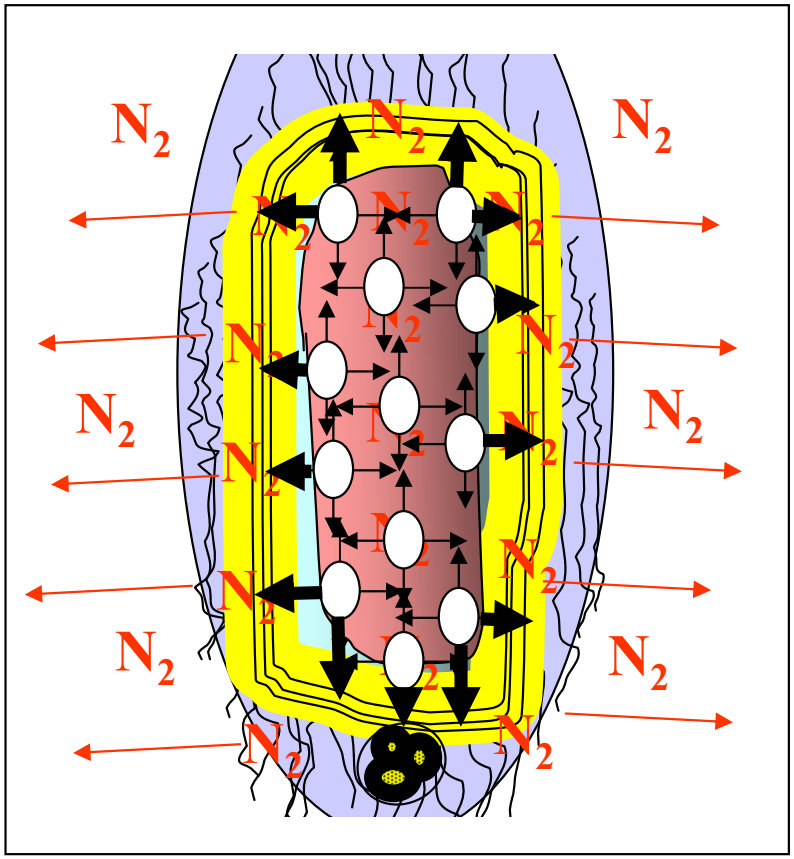
Overwhelming Gradient



Autochthonous bubbles form in Ruffini Type-2 Corpuscle

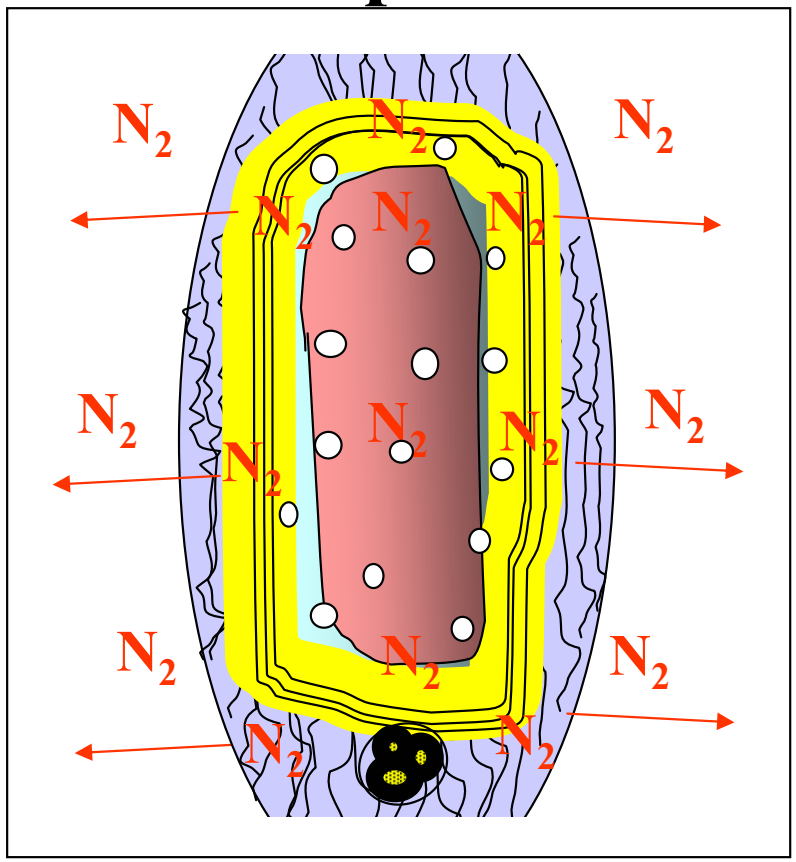
A "Perfect Fit" 3

Pain Symptoms



Stretch response from bubbles distending perineurium

Recompression



Bubble reduction (Boyle's law) with resolution of pain

Conclusions

- Ruffini Type-2 Corpuscle Explains
  - -The cause & character of pain…
  - -Uniformly good responses to recompression…

- Bubble evolution in the RT2C fits the SPR (Super-saturation Perfusion Rate) Model explanation for autochthonous bubble formation

Conclusions 2

- With improved imaging techniques
  - "Silent" bubbles in the RT2C will become detectable
    (Analogous to intravascular bubble detection with Doppler)

- "Silent" bubbles in adventitial tissues around nerves (and serosal membranes around abdominal organs)
  - May explain other Type-1 DCS symptoms
    (Paresthesias, hypesthesias & fatigue)

Abstract A2

Ability to visualize circulating decompression-induced gas emboli by portable transthoracic echocardiography increases with increasing precordial doppler grade

Neal W. Pollock, Ph.D.

ABILITY TO VISUALIZE CIRCULATING DECOMPRESSION-INDUCED GAS EMBOLI BY PORTABLE TRANSTHORACIC ECHOCARDIOGRAPHY INCREASES WITH INCREASING PRECORDIAL DOPPLER GRADE

Neal W. Pollock, Ph.D.
Divers Alert Network and
Center for Hyperbaric Medicine and Environmental Physiology
Duke University Medical Center
Durham, NC

Undersea and Hyperbaric Medical Society
Salt Lake City, UT - June, 2008

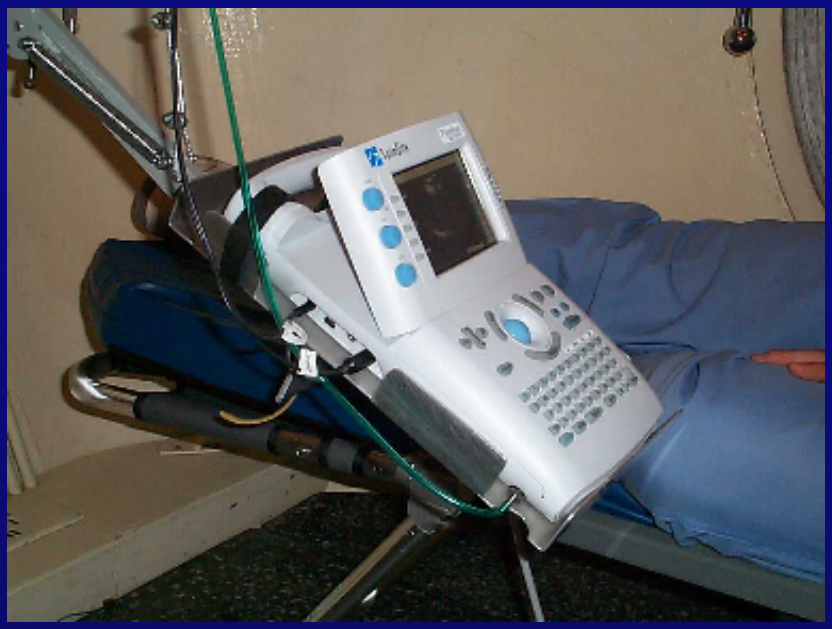
METHODS

- Subjects in our decompression studies are routinely evaluated with precordial Doppler and TTE
  - Doppler signals scored on 0-IV grade Spencer scale
  - TTE scans focus on left heart but presence/absence of right heart bubbles is noted if field is interpretable
- This study compared monitoring periods for which precordial Doppler and right heart TTE data were available
- Chi squared analyses were used to test differences in TTE-identified bubbles across Doppler grade levels
  - significance accepted at $p<0.05$

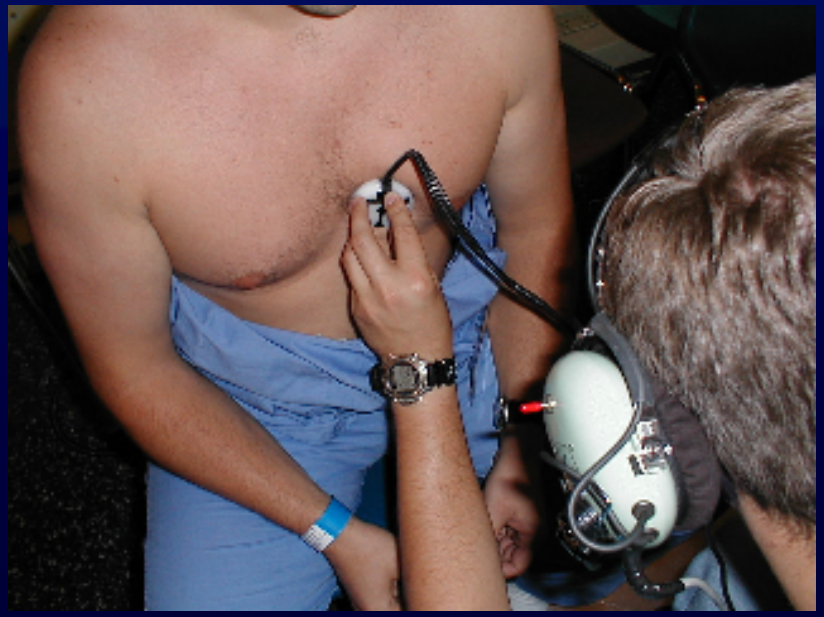
INTRODUCTION

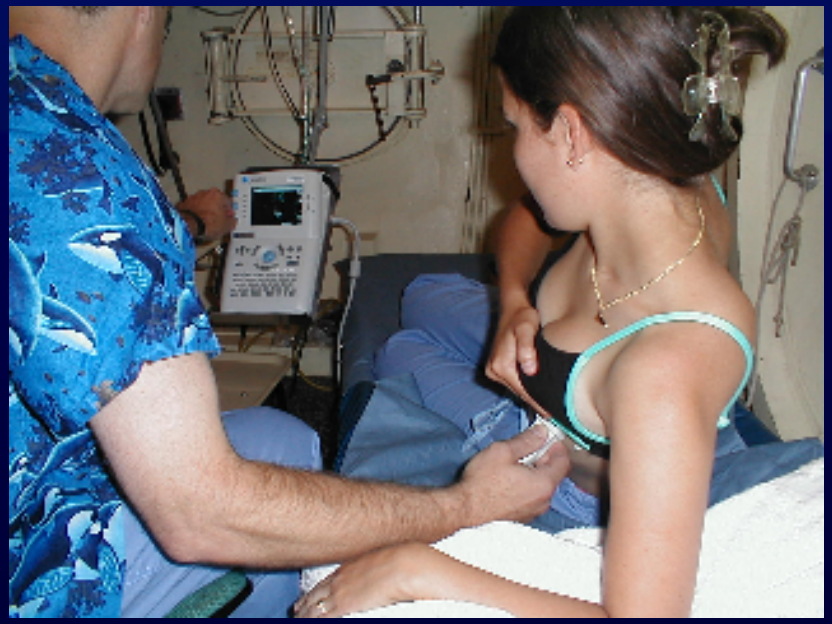
- Decompression is associated with gas emboli (bubble) formation
  - Doppler ultrasound is useful for monitoring bubbles
- Left ventricular gas emboli potentially create an elevated risk of neurological DCS
  - portable two-dimensional transthoracic echo imaging (TTE) systems facilitate left heart monitoring under laboratory or field conditions
- An unresolved question is whether portable TTE is as sensitive as Doppler to low bubble grades

TechnoScientific
Doppler Bubble Detector

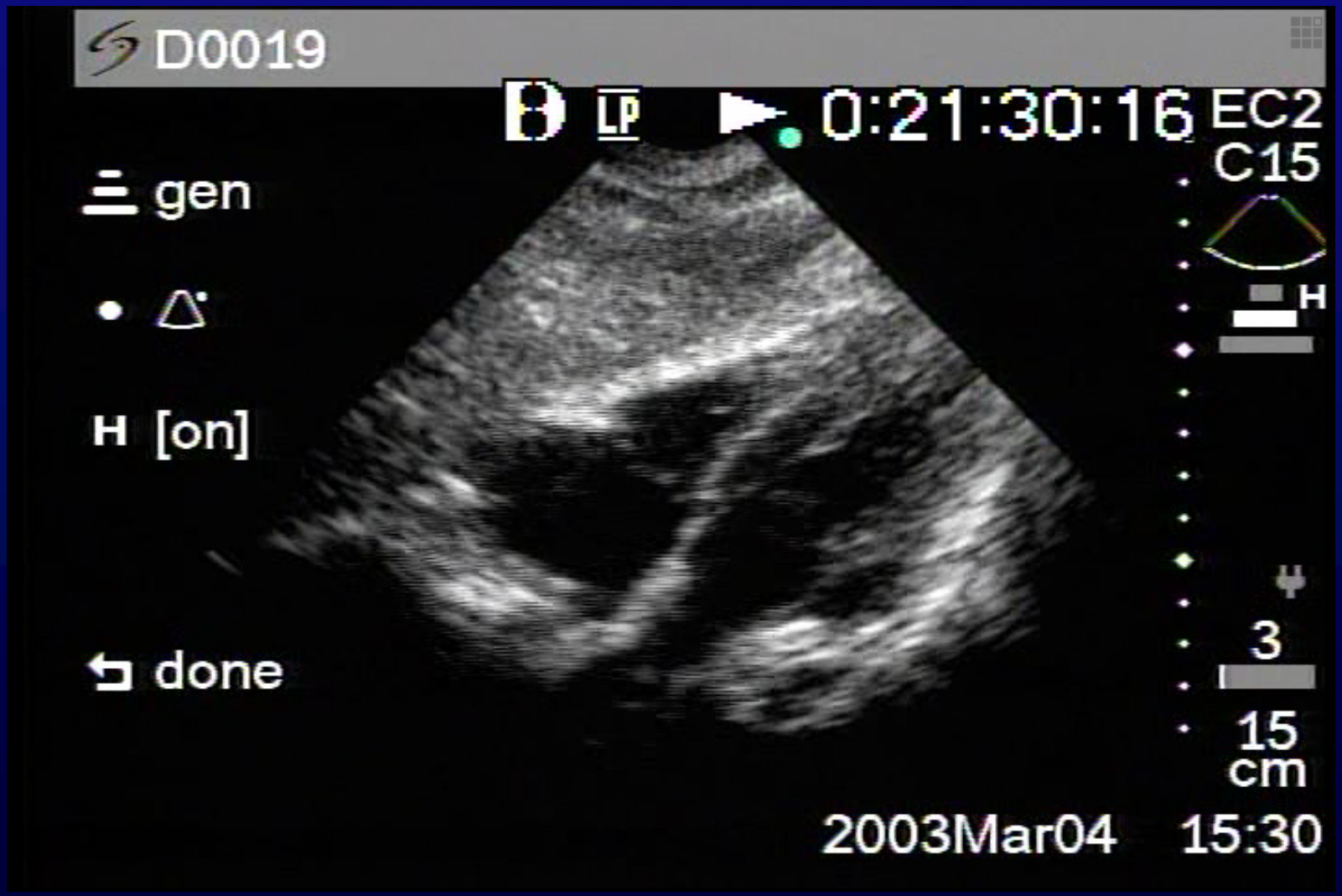


SonoSite SonoHeart Elite
Transthoracic Echo (TTE)





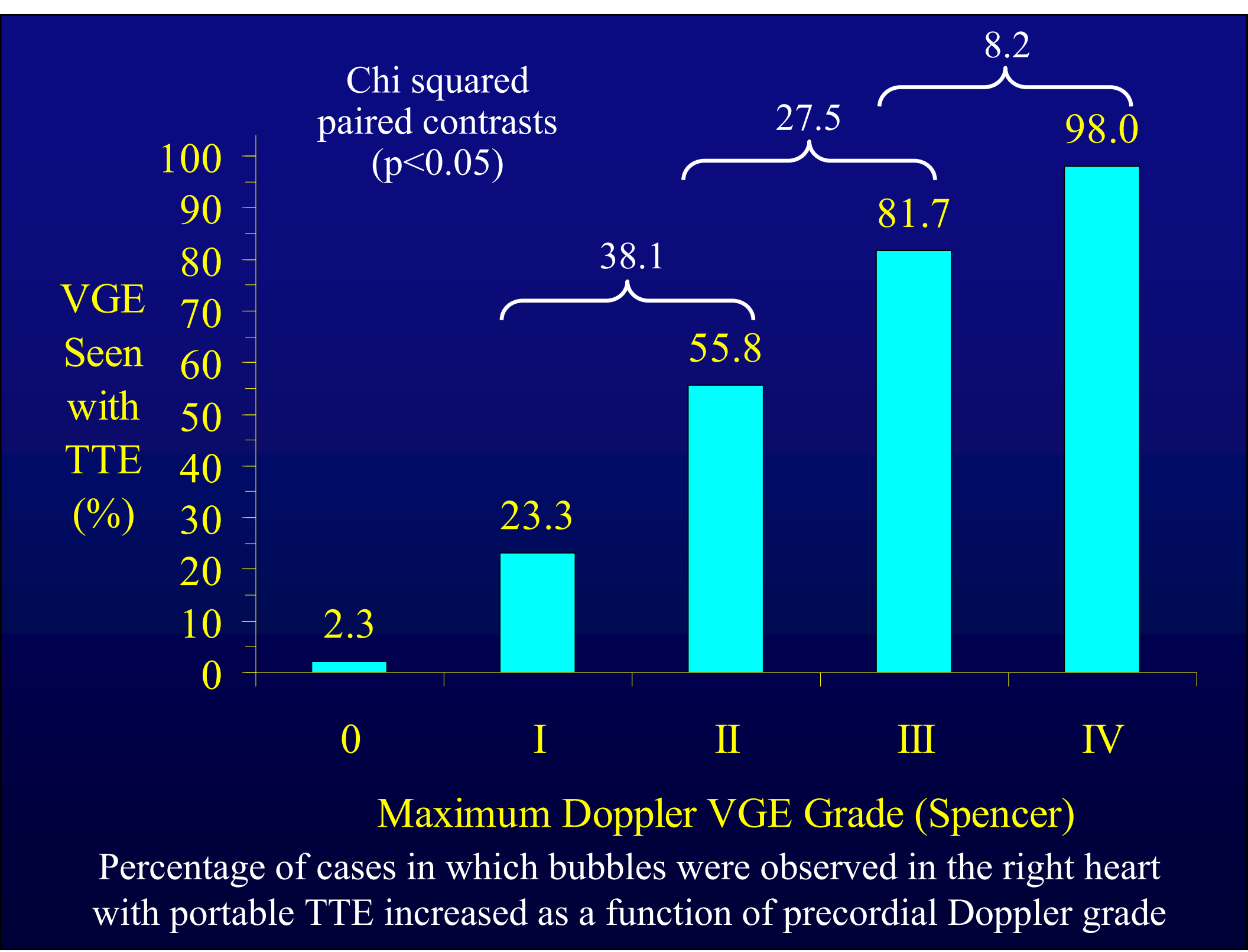
30,000 FT ALTITUDE EXPOSURE
Subcostal TTE View



N.W. Pollock, Ph.D.

RESULTS

- Note: Our TTE monitoring has identified two cases of LVGE
  - both were immediately compressed; no symptoms
- For the current study, a total of 2,734 records were reviewed for non-zero scores
  - 575 Doppler (21%)
  - 383 TTE (14%)
- The ability to identify bubbles with TTE progressively increased with increasing non-zero Doppler grades



Percentage of cases in which bubbles were observed in the right heart with portable TTE increased as a function of precordial Doppler grade

FUTURE INITIATIVES

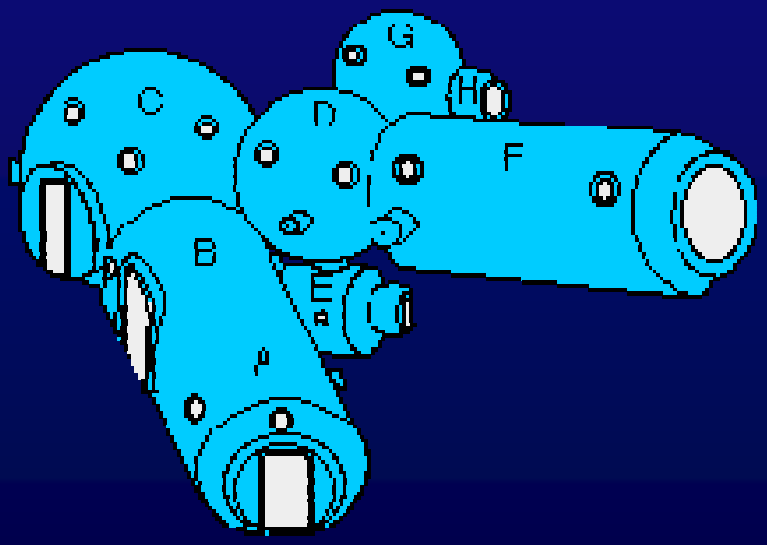
- Compare the agreement between Doppler and each of our three standard views
  - apical, parasternal and subcostal
- Grade right heart bubbles observed with TTE to compare with standard precordial Doppler scores
- Evaluate new TTE imaging devices

CONCLUSIONS

- Portable TTE devices facilitate left heart monitoring during decompression studies not feasible with precordial Doppler
- Portable TTE devices appear to be more able to detect right heart bubbles when precordial Doppler-detected grades are higher
- The relative insensitivity of portable TTE to lower bubble grades indicates that scoring provided by the different technologies may not be fully comparable

ACKNOWLEDGMENTS

- Equipment purchased through U.S. Navy Coastal Systems Grant N61331-02-C-0007 and NASA Cooperative Agreement NCC9-83



Center for Hyperbaric Medicine and Environmental Physiology

Website: http://hyperbaric.mc.duke.edu

E-mail: neal.pollock@duke.edu

Abstract A3

Pulmonary oxygen toxicity: PO2, not FIO2

B.E. Shykoff

Pulmonary Oxygen Toxicity: PO_2, not F_IO_2

B.E. Shykoff

Navy Experimental Diving Unit,

Panama City, FL

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Navy Experimental Diving Unit

Background

- The presence of inert gas in a breathing mixture should help to prevent alveolar collapse.
- Atelectasis is seen in head-out immersion with oxygen breathing.
- As little as 20% N_2 is protective in anesthetized patients, and as little as 5% in aviators.

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Navy Experimental Diving Unit

Hypothesis

- If absorption atelectasis contributes to the generation of pulmonary oxygen toxicity, at the same oxygen partial pressure (PO_2) dives would produce fewer toxic effects with lower inspired oxygen fraction (F_IO_2) than with 100% oxygen.

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Navy Experimental Diving Unit

Table 1.
Pulmonary Oxygen Toxicity Definition

Pulmonary function decreased from baseline by[3]

Forced vital capacity (FVC)	7.7%
Forced expired volume in 1 s (FEV_1)	8.4%
Mid forced expired flow (FEF_{25-75})	16.8%
Maximum forced expired flow (FEF_{max})	17%
Diffusing capacity of the lung for carbon monoxide (D_LCO)	14.2%

Symptoms reported

Cough	Chest tightness
Inspiratory burning	Shortness of breath

Methods

- Baseline: Pulmonary function tests (PFTs) within the week before diving, flow-volume loops again prior to diving
- Postdive: PFTs within 2 hours of surfacing, then daily for 3 days

  Collins CPL, Ferraris Respiratory

Eight-hour resting dives, PO_2 = 1.3 atm, 50%, 84%, and 100% oxygen

50% oxygen (Deep Dives)

- Navy Diving and Salvage Training Center (NDSTC) buoyant ascent tower
  - 17 divers – 50 feet deep
  - MK 16 Mod 1 rebreather underwater breathing apparatus (UBA), 50% N_2, 50% O_2

84% oxygen (Intermediate depth)

- Navy Experimental Diving Unit (NEDU) Ocean Simulation Facility wet pot
  - 31 divers, depth of 20 feet.
  - Open circuit 16% N_2, 84% O_2, [MK20, Aga mask]

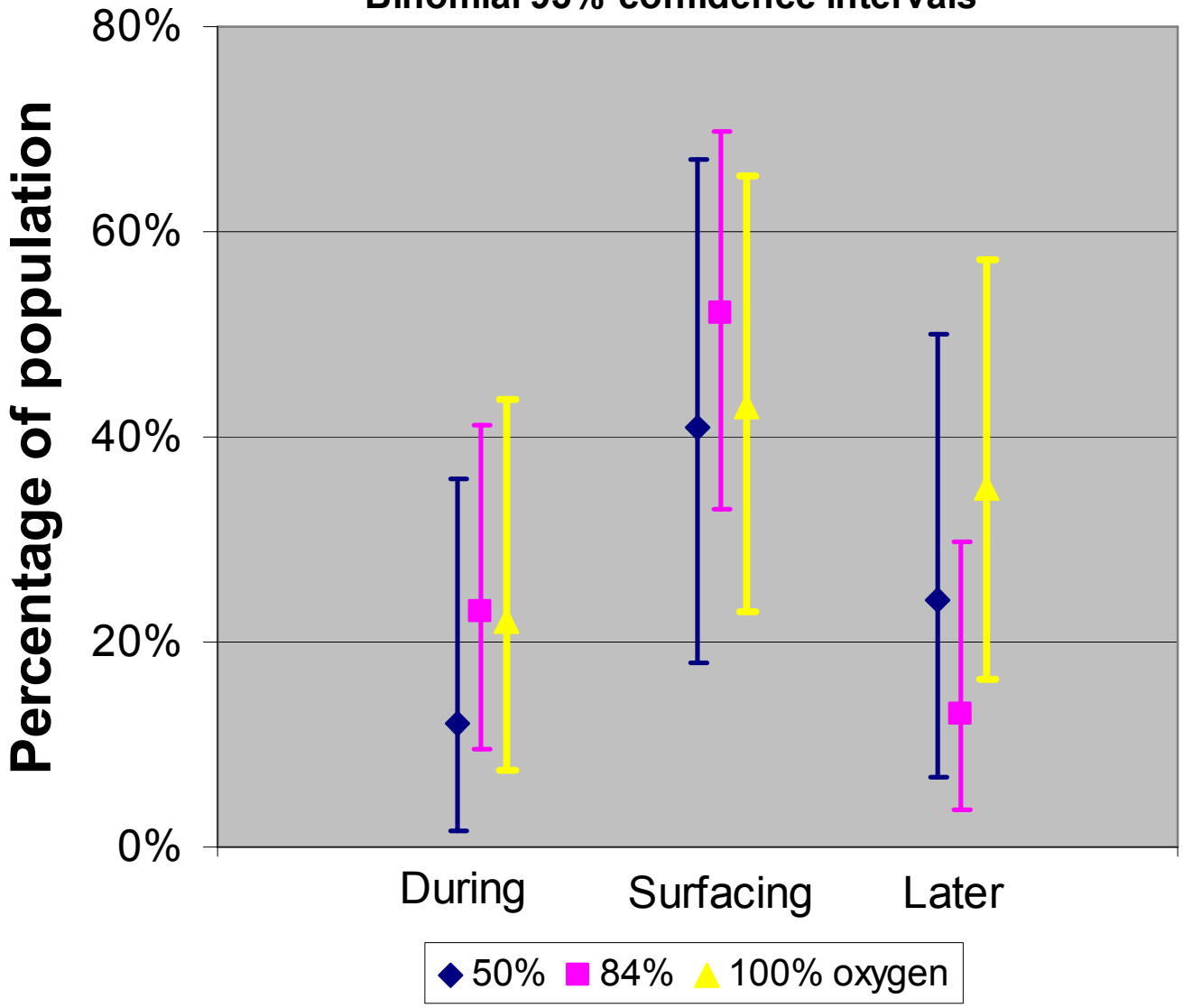
100% oxygen (Shallow dives)

- NEDU 15-foot deep test pool
  - 23 divers, 12 feet
  - Open circuit 100% oxygen [MK20, Aga mask]

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Navy Experimental Diving Unit

Symptoms

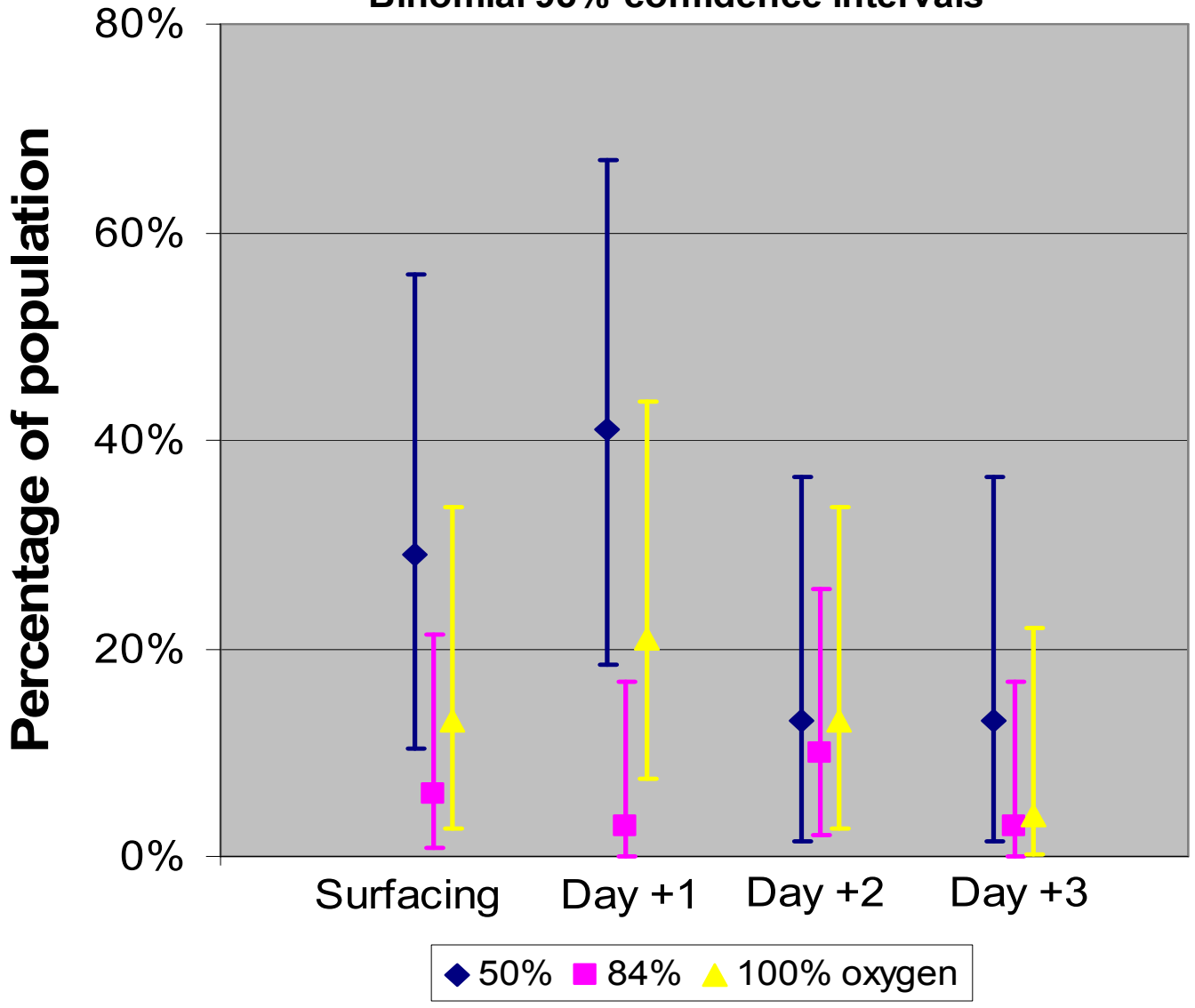
Binomial 95% confidence intervals



NAVSEA
NAVAL SEA SYSTEMS COMMAND
Navy Experimental Diving Unit

Decreased pulmonary function

Binomial 95% confidence intervals



NAVSEA
NAVAL SEA SYSTEMS COMMAND
Navy Experimental Diving Unit

Discussion

- Eight hours with PO_2 = 1.3 atm cannot be recommended, even for resting divers.
- Pulmonary oxygen toxicity appears to be a function of PO_2– that is, of chemical activity of oxygen, not F_IO_2.
- Atelectasis well-known with oxygen immersion Why might our results differ from others?
  - Use of the MK 16 UBA may have obscured some protective effects of nitrogen.
  - Alveoli that close on the bottom because of oxygen absorption may be reopened by gas expansion on ascent.

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Navy Experimental Diving Unit

Conclusions

- Pulmonary oxygen toxicity results obtained with 100% oxygen are applicable to diving situations with the same PO_2, regardless of the gas fraction.
  - Switching from 100% O_2 to Nitrox breathing while going deeper is not similar to taking a surface interval.
- Absorption atelectesis is at most a minor source of pulmonary oxygen toxicity in divers.

Abstract A4

The effect of exercise at 24 and 2 hours prior to diving on the evolution of venous gas emboli

M Gennser1, SL Blogg2, KM Jurd3, JC Thacker3,GA Loveman3, M Stansfield3 and FM Seddon3

The efect of exercise at 24 and 2 hours prior to diving on the evolution of venous gas emboli

M Gennser[1], SL Blogg[2], KM Jurd[3], JC Thacker[3], GA Loveman[3], M Stansfield[3] and FM Seddon[3]

1. Department of Defence Medicine, Swedish Defence Research Agency (FOI), Stockholm, Sweden
2. SLB Consulting, The Barn, Manor House Wynd, Winton, Cumbria, UK
3. QinetiQ, Fort Road, Gosport, Hampshire, UK.

QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

Background:

- Physical exercise prior to diving considered a risk factor (eg Harvey et al 1944, Evans & Walder 1969, Vann 1982)
- Exercise 20 h prior to diving reduces bubble formation & DCS in rats (Wisløff & Brubakk 1999)
- In rats exercise 2 h prior to diving has no effect per se and reduces the positive effects of exercise 20 h prior to diving (Loset et al 2006)
- In man exercise both 24 h (Dujic et al 2004) and 2 h (Blatteau et al 2005) prior to diving has been shown to reduce decompression stress

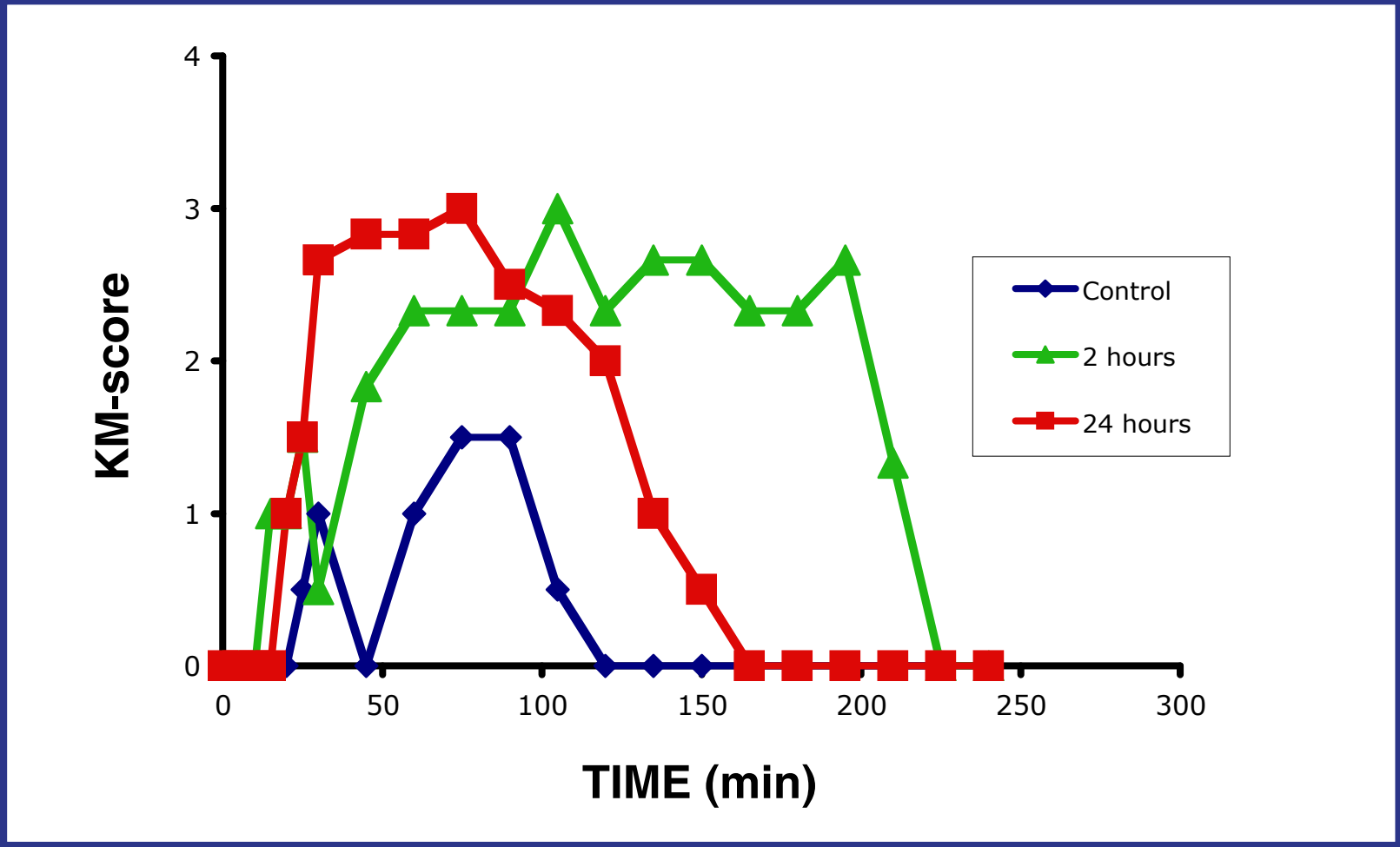
Aim:

Investigate whether exercise 24h our 2h prior to hyperbaric exposure is most effective in reducing bubble release in man

Methods:

- Ten men were compressed in hyperbaric chamber to 18 m (0.28 MPa) for 100 min and decompressed using Royal Navy Table 11 (modified).
- Each subject performed 3 dives; the first was a control dive, the latter two were preceded by 40 min sub-maximal exercise either 24 h or 2 h before diving.
- Venous gas emboli (VGE) were evaluated using pre-cordial Doppler ultra-sound rated on the Kisman-Masurel scale
- Doppler measurements were made immediately on surfacing, then at 5 min intervals for 30 min, and at 15 min intervals thereafter for at least 2h

Median Doppler scores post-decompression



- No difference between max-KM scores
- Significantly shorter period with bubbles in Control dive

Conclusions:

Contrary to recent studies, the number of VGE was not significantly lower in either the 2h or 24h exercise groups in comparison to the non-exercise control.

Methodological differences between this and previous studies exist. One obvious difference is the fact that the subjects in the present study were not professional divers.

Abstract A5

The effect of saturation decompression using oxygen on swine RNA

Malkevich N, McCarron RM, Mahon RT

Richard T. Mahon
CDR,MC,USN
and
Nina Malkevich, PhD
Richard McCarron, PhD

Naval Medical Research Center
(NMRC)
Silver Spring, MD

The effect of oxygen during saturation decompression on swine RNA

- Saturation Decompression from 132 fsw
- Why study in swine
- What we did
- What we found
- Microarray

NOAA

NOAA Air Decompression Table for Air Saturation at 50 fsw

Depth (fsw)	Rate of Decompression	Time (min)
50 to 30	6 min/ft	120
30 to 28	22 min/ft	44
28 to 26	23 min/ft	46
26 to 24	24 min/ft	48
24 to 22	25 min/ft	50
22 to 20	26 min/lt	52
20 to 18	27 min/ft	54
18 to 16	28 min/ft	56
16 to 13	29 min/ft	87
13 to 10	30 min/ft	90
10 to 8	31 min/ft	62
8 to 6	32 min/lt	64
6 to 4	33 min/ft	66
4 to 2	34 min/ft	68
Time at 1 fsw	**68 min**	**68**

Total time 975 min
16:15 hr:min
No oxygen

NOAA Air/Oxygen Decompression Table for Air Saturation at 42 fsw

Depth (fsw)	Rate of Ascent (fsw per min)	Time (min)	Breathing Gas
42 to 24	2	9	Air
24 stop	—	180	Air
24 to 20	1	4	Air
20 stop	—	180	Air
20 to 16	1	4	Air
16 stop	—	180	Air
16 to 12	1	4	Air
12 stop	—	75	Oxygen
12 to 8	1	4	Air
8 stop	—	80	Oxygen
8 to 4	1	4	Air
4 stop	—	90	Oxygen
4 to surface	1	4	Air

Total time 418 min
13:38 hr:min
Oxygen time 4.1 hr

NEDU

DIVE #	DEPTH ACTUAL (fsw)	EAD DEPTH (fsw)	DECO SCHEDULE	TOTAL TIME (hr:min)	PRE-BREATHE (hr:min)	TOTAL O_2 (hr:min)	# SUBJ	# DCS (class)
1,2,6	34	40	Phase I Schedule 1	4:10	None	3:55	23	1 (III)
3	42	50	Phase I Schedule I-2	5:53	None	5:28	8	5 (III, II, II, II, II)
4,5,7	42	50	Phase I Schedule I-2A	7:52	None	7:17	20	3 (III, II, II)
8,10, 12,14	42	50	Phase II Schedule A1	10:17	None	8:00	31	4 (II, I, I, I)
9,11, 15,16	42	50	Phase II Schedule A2	10:02	4:00	8:00	32	0
17,18	42	50	Phase II Schedule A3	8:47	3:00	7:00	16	0
19,20	42	50	Phase II Schedule A4	7:32	2:00	6:00	16	2 (II, II)
21,22	50	60	Phase III Schedule A	12:30	2:00	10:00	15	0
23	50	60	Phase III Schedule AA	11:20	1:00	9:00	6	2 (II,II)
24	50	60	Phase III Schedule AB	11:20	2:00	9:00	8	0

Latson 2000

50 fsw Equivalent Air Depth (42 fsw actual depth) (#cases DCS/#subjects)

Pre-Breathing Time (hrs)	Total Oxygen Time (hrs)				
	5.5	6.0	7.0	7.3	8.0
0	5/8			3/20	4/31
1					
2		2/15			0/8
3			0/16		
4					0/32

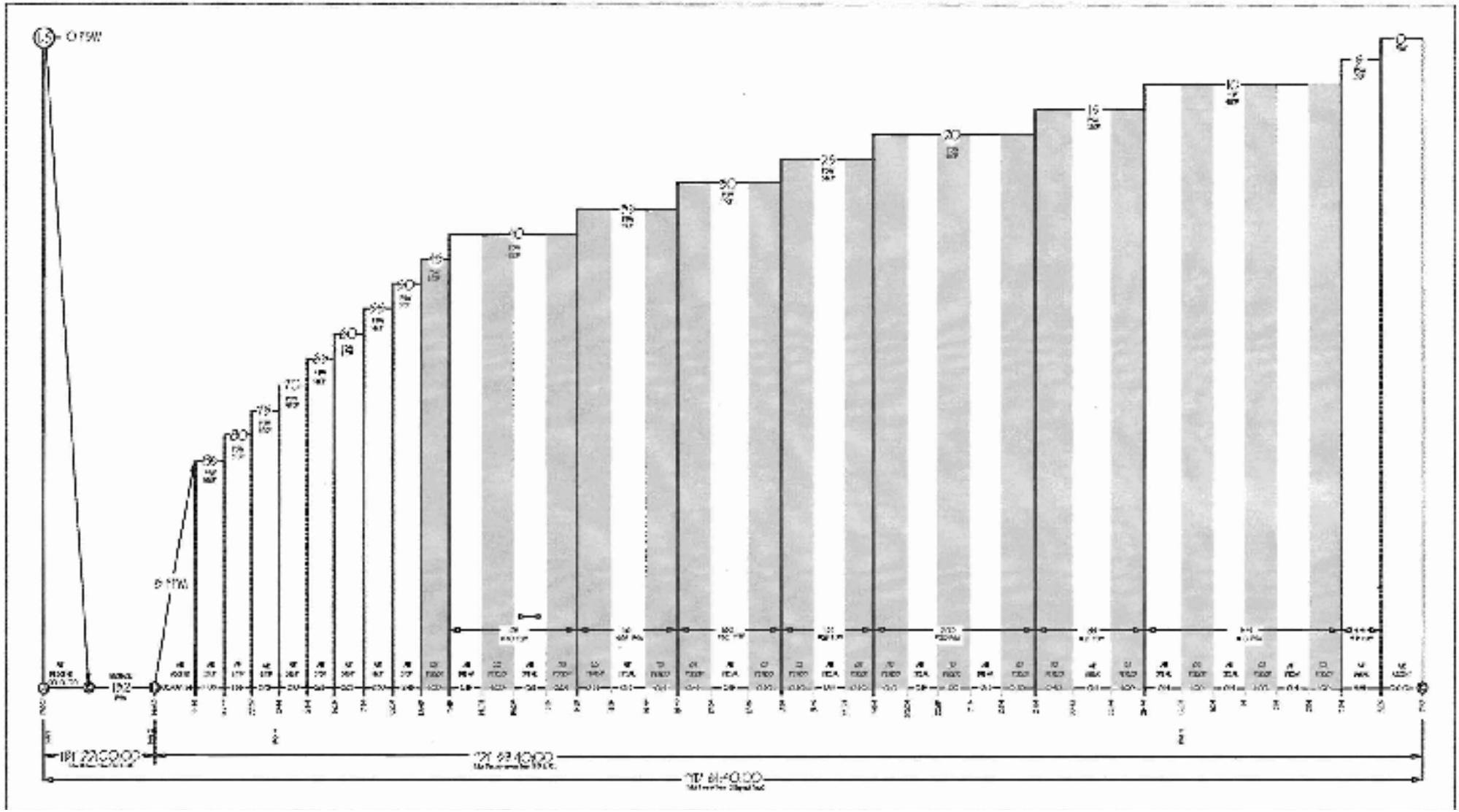
Latson 2000

EAD (fsw)	O_2 Time at Depth (O_2 Pre-breathe)(min)	Decompression Stop Depth (fsw)						Total O_2 Time (min)
		45	40	35	30	25	20	
20	0	Oxygen Breathing Times at Depth (min)						0
25	70							70
30	140							140
35	120					40	40	200
40	120				10	85	40	255
45	120			20	105	115	50	410
50	120			85	105	115	50	475
55	120		55	95	105	115	50	540
60	120	30	85	95	105	115	50	600

NOAA Air/Oxygen Decompression Table For Air/Normoxic
Saturation Between 0-100 fsw Standard (Formerly Table 12-7, 1975 Edition, Table 12-12, 1979 Edition)

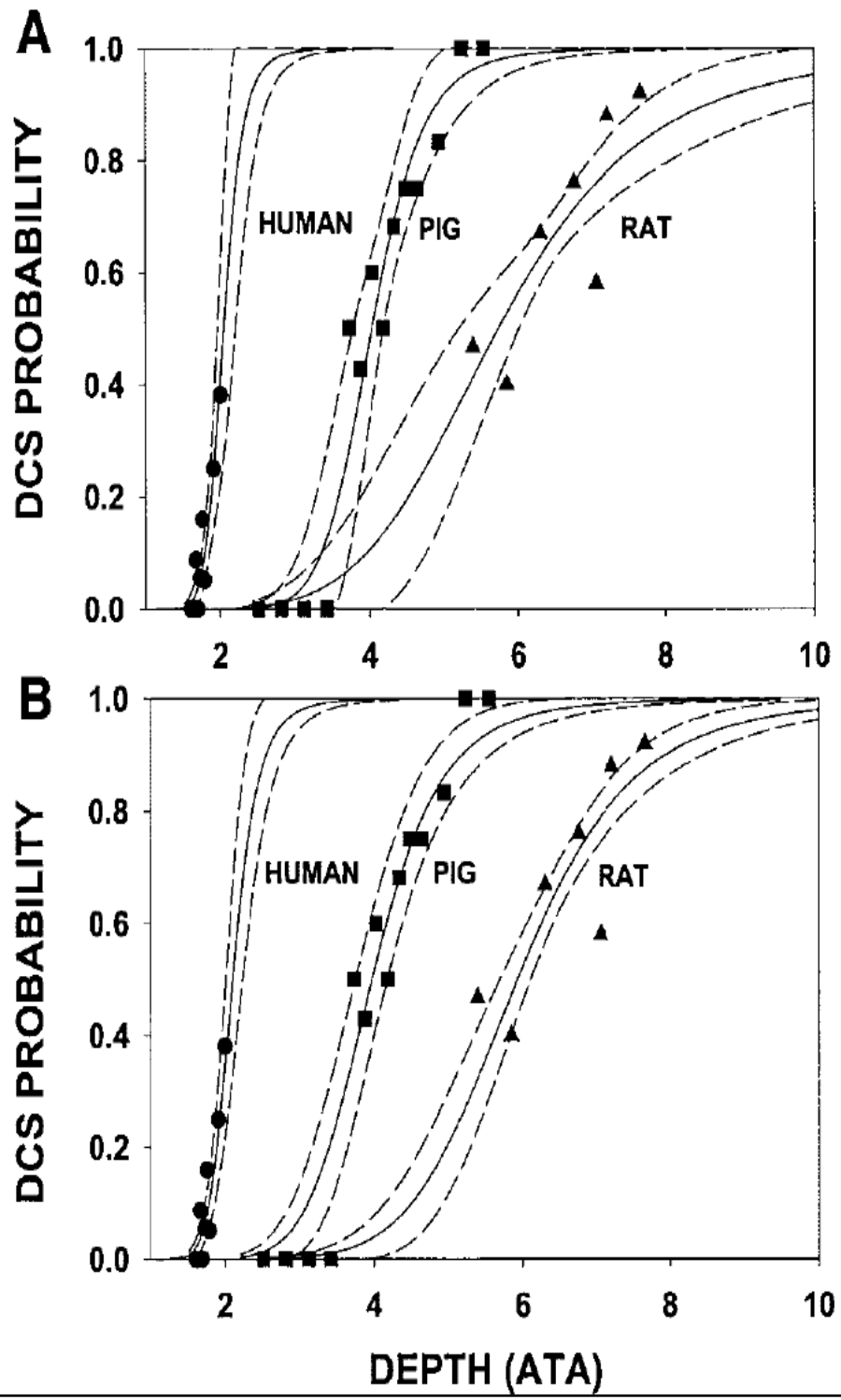
Decompression using Air and Oxygen after Nitrogen-Oxygen Saturations from 0 to 100 fsw						
	First Stop			Subsequent Stops		
A	B			C		
Saturation Depth Range (fsw)	Depth (fsw)	Gas	Time at Stop (hr:min)	Depth (fsw)	Gas	Time at Stop (hr:min)
96-100	80	Air	1:30	75	Air	2:15
91-95	75	Air	1:30	70	Air	2:25
86-90	70	Air	1:30	65	Air	2:30
81-85	65	Air	1:35	60	Air	2:35
76-80	60	Air	1:40	55	Air	2:40
71-75	55	Air	1:40	50	Air	2:45
66-70	50	Air	1:45	45	Air	2:45
61-65	45	Air	1:45	40	Air	2:00
56-60	40	Air	0:30	40	Oxygen	0:30
				35	Oxygen	1:00
51-55	35	Oxygen	0:45	30	Air	0:30
				30	Oxygen	1:00
46-50	30	Oxygen	0:45	25	Air	2:00
				25	Oxygen	1:00
41-45	25	Oxygen	1:00	20	Air	0:30
				20	Oxygen	1:00
36-40	20	Oxygen	1:00	15	Air	2:00
31-35	15	Oxygen	0:30	15	Oxygen	1:00
26-30	10	Oxygen	0:30	10	Air	0:30
				10	Oxygen	1:00
				5	Air	0:30
				5	Oxygen	0:30
22-25	5	Oxygen	0:30	30	Oxygen	0:30
0-21	No-Decompression			Surface		

33.5h/7.5h O2



Depth (FSW)	85	80	75	70	65	60	55	50	45	40	35	30	25	20	15	10	5
Time (min)	305	115	125	130	135	145	150	165	**60**	**65**	**70**	**75**	**80**	**90**	**100**	**180**	215

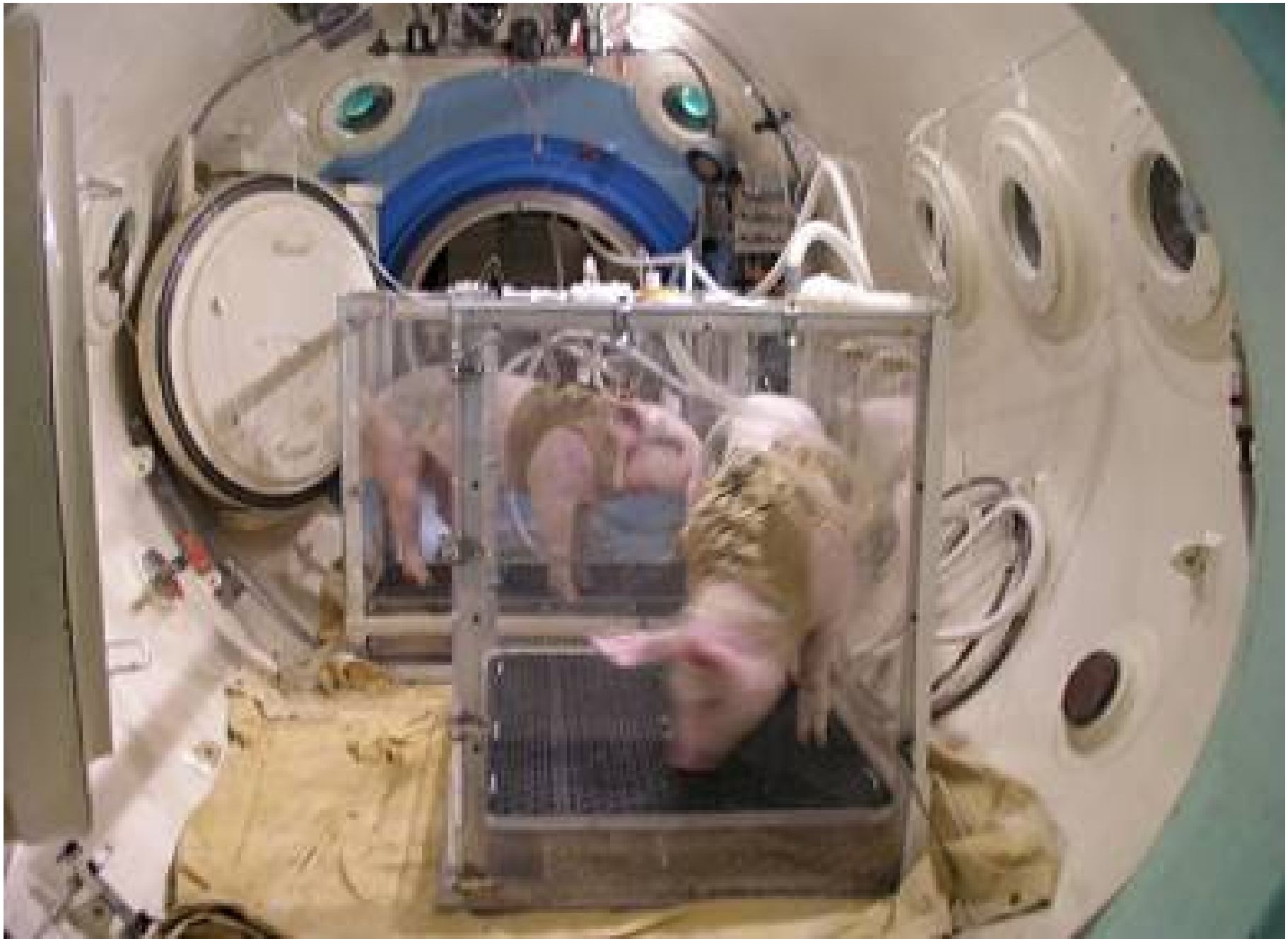
Total decompression time 29.5h; O2 8.5h

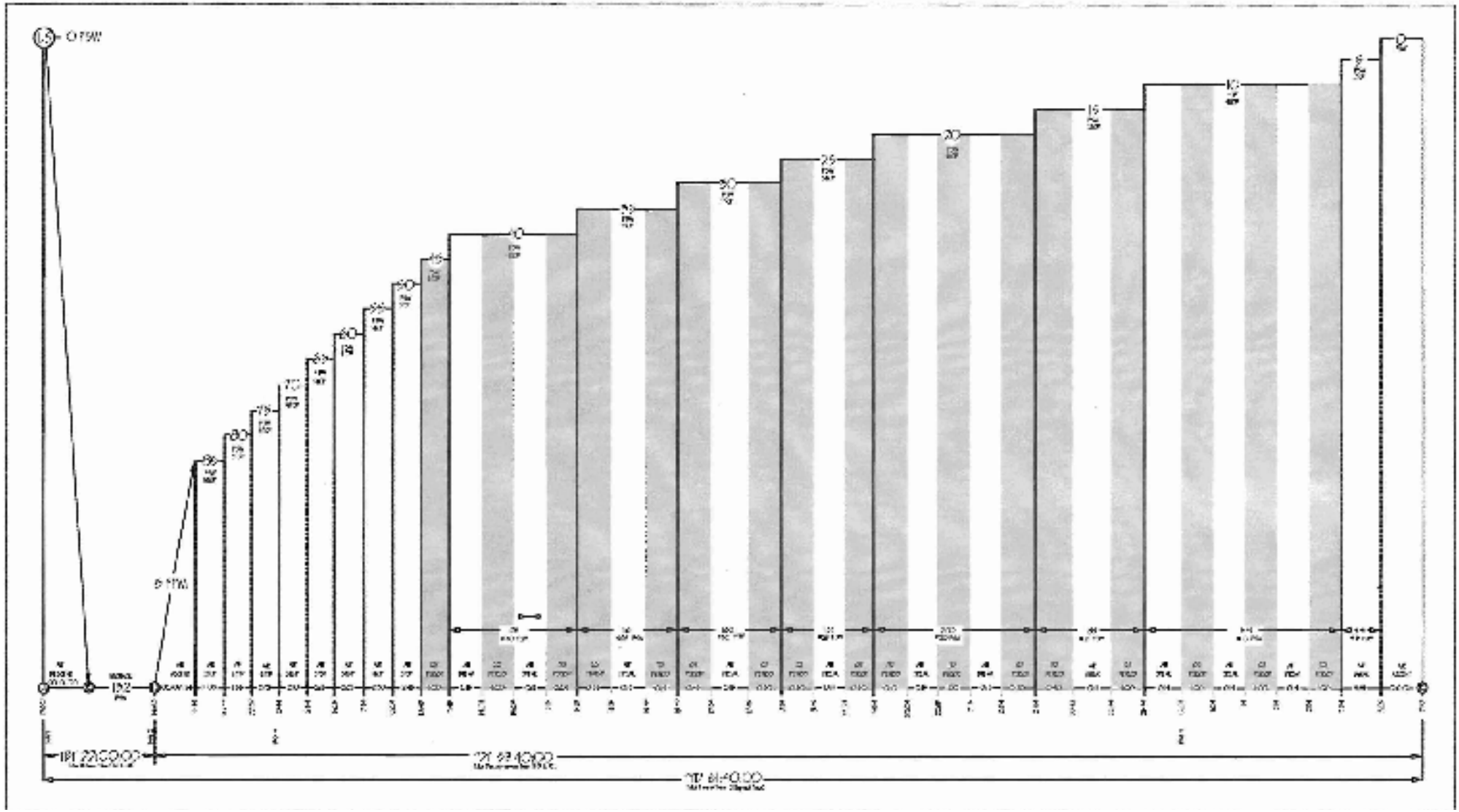

A
B
DCS PROBABILITY
DCS PROBABILITY
1.0
0.8
0.6
0.4
0.2
0.0
HUMAN
PIG
RAT
2
4
6
8
10
DEPTH (ATA)

Lillo 2000

Methods

- Central catheter
  - Overnight recovery
- Compression to 132 fsw
- 22h for saturation
- 250cc Normal Saline IV every 12h
- Decompression schedule
- Observe for 24h





Depth (FSW)	85	80	75	70	65	60	55	50	45	40	35	30	25	20	15	10	5
Time (min)	305	115	125	130	135	145	150	165	**60**	**65**	**70**	**75**	**80**	**90**	**100**	**180**	215

Total decompression time 29.5h; O2 8.5h

Observations

- Cutis
- Pain
- Cardiopulmonary
- Neurologic
  - Nystagmus
  - Sensory
  - Gait (Tarlov)

Modified TARLOV

- 0-complete paralysis
- 1- Minimal Movement
- 2- Stands with assistance
- 3- Stands Alone
- 4- Weak Walk
- 5- Normal Gait

Tarlov Outcomes

	O2 Profile	Air Control	Sham
N	10	9	9
Tarlov Surface	5(8) 4(2) *	5(9)	5(9)
Tarlov 24h	5(9) 4(1)	5(9)	5(9)

* p = 0.02

Decompression Conclusions

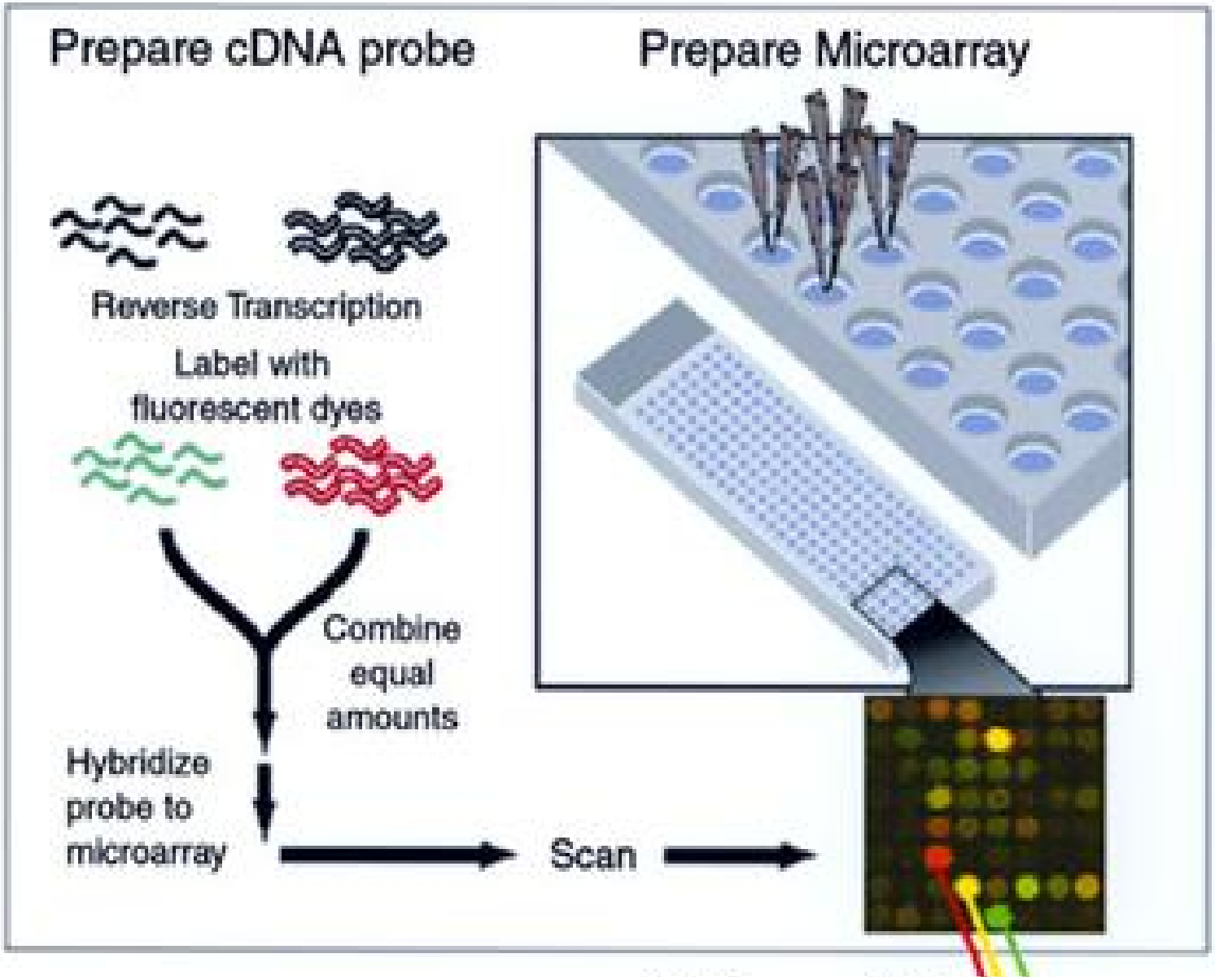
In this saturation decompression profile HBO during decompression is of no benefit

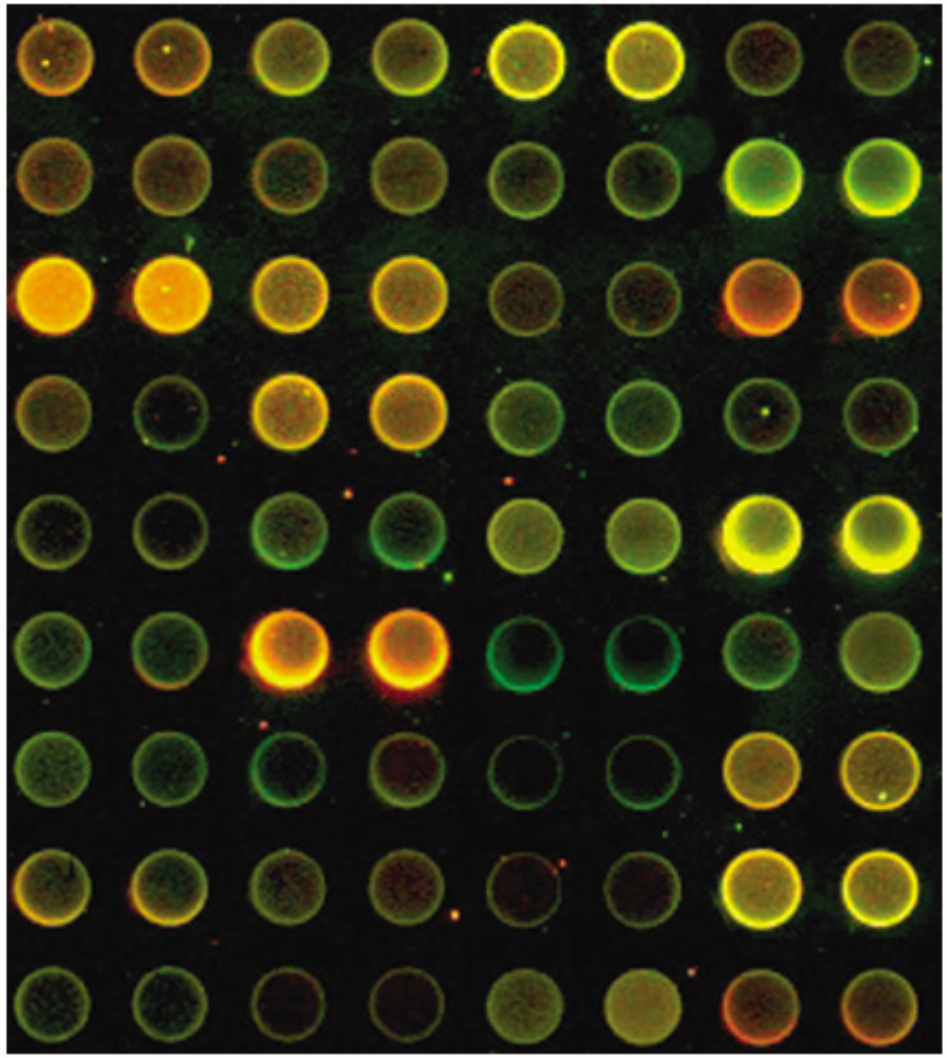
Microarray

- Lung sample of convenience
- 24 h post surface
- UPTD
  - Air decompression

    1380
  - O2 decompression

    3880


Prepare cDNA probe
Prepare Microarray
Reverse Transcription
Label with
fluorescent dyes
Combine
equal
amounts
Hybridize
probe to
microarray
Scan

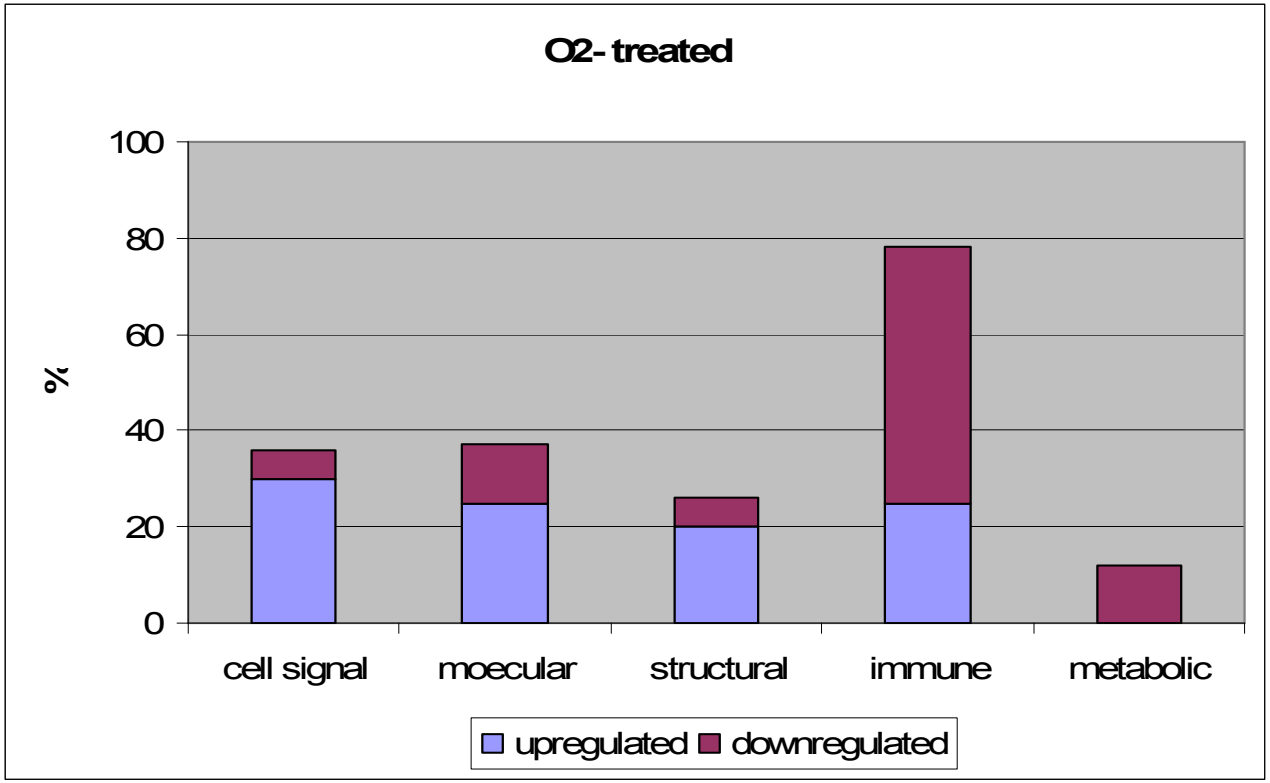


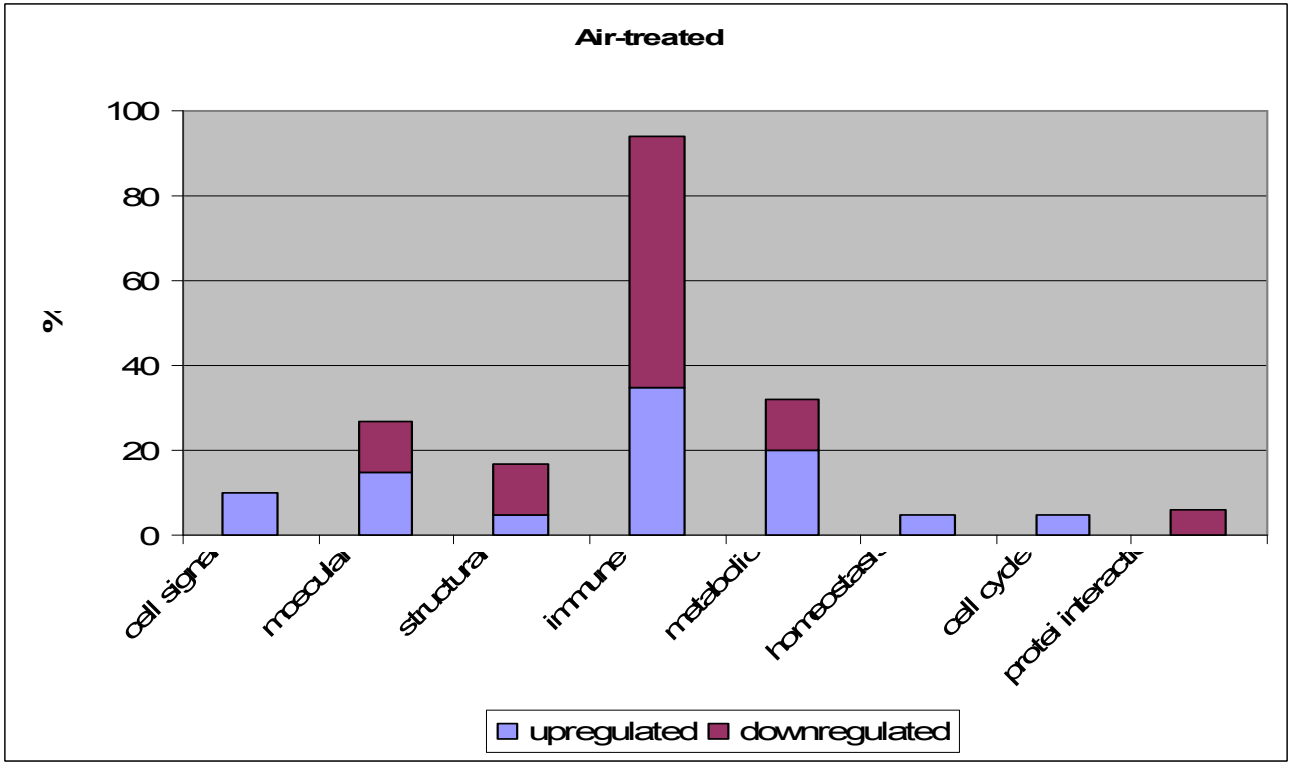
100% oxygen

	GENE DESCRIPTION	ACCESSION CODE	No. pos. animals1
upregulated	nidogen 2	CN156760	8
	prostate stromal protein ps20	CF363052	8
	prostate stromal protein ps20	CF361753	8
	scr.msk.p1.Contig2, mRNA sequence	CF364971	8
	Chimerin 1 (GTPase-activating protein, rho, 2)	BQ597587	8
	reticulon 1 isoform A; neuroendocrine-specific protein	CK457674	8
	a disintegrin and metalloproteinase with thrombospondin motifs	CO989594	8
	alpha 1 type XVIII collagen isoform 1 precursor; endostatin	CN155194	8
	calcitonin receptor-like receptor	NM_214095	7
	pentaxin-related gene, rapidly induced by IL-1 beta	CN153343	7
	melanoma cell adhesion molecule	BQ605024	7
	alpha 2 type IV collagen preproprotein; canstatin	CO950243	7
	Sus scrofa cDNA 5', mRNA sequence.	BG609032	7
	scr.msk.p1.Contig1, mRNA sequence	BQ601005	7
	chimerin 1	CD572334	7
	scr.msk.p1.Contig1, mRNA sequence	BF710490	7
	similar to collagen alpha 1(IV) chain precursor	BI183311	7
	matrix metalloproteinase 1 (type I collagenase)	CA779388	7
	heat shock protein 47	CN160329	7
	enabled homolog	AJ653947	7
downregulated	immunoglobulin kappa light chain variable region O11	AF334741.1	-8
	TN3	NM_214147	-8
	Immunglobulin VDJ region	U38212.1	-8
	scinderin	CO989361	-8
	alveolar macrophage-derived chemotactic factor-I	NM_213867	-8
	chemokine (C-X-C motif) ligand 13 (B-cell chemoattractant)	CF787657	-8
	immunoglobulin mu heavy chain constant region	S42881.1	-8
	platelet basic protein	NM_213862	-7
	cytochrome P450 3A26	CO990609	-7
	Immunglobulin VDJ region	U38217.1	-7
	Clone G502 immunoglobulin kappa light chain VJ region	CF180359	-7
	porcine inhibitor of carbonic anhydrase	NM_213847	-7
	tetranectin (plasminogen binding protein); tetranectin (plasmino	BI186214	-7
	similar to RIKEN cDNA 2010001M09	BX916934	-7
	371602 MARC	BI343446	-7
	Ig gamma 2b chain constant region	M81771.1	-7
	uncoupling protein 2	NM_214289	-7

Air

DESCRIPTION	ACCESSION CODE	No. pos. animals 1
caspase 7 isoform delta, large subunit; ICE-like apoptotic protease 3; apoptotic protease	BX929078	3
cytoskeletal beta actin	BI182788	3
chemokine	DT192019	3
heterogeneous nuclear ribonucleoprotein	DC801990	3
nidogen 2 (predicted)	CN156760	2
WAP four-disulfide core domain 1 precursor; WAP four-disulfide core domain 1 homolog	CF363052	2
WAP four-disulfide core domain 1 precursor; WAP four-disulfide core domain 1 homolog	CF361753	2
calcitonin receptor-like receptor	NM_214109	2
pentaxin-related gene, rapidly induced by IL-1 beta	CN153343	2
haloacid dehalogenase like hydrolase domain containing 2	CF784578	2
Clone rtoc27b_h3 y1 abd_ mRNA sequence	CF364971	2
ICN2	CO989727	
placenta specific 8	BI401223	2
optimedin form A	CD572350	2
IRRE like 3	CF360110	2
Growth arrest and DNA-damage-inducible protein GAI II45 beta (Negative growth-regul	CF167278	2
cytochrome P450 2H22	NM_214441	2
Growth arrest and DNA-damage-inducible protein GAI II45 beta (Negative growth-regul	BF708594	2
myolubulerin related protein 3, myolubulerin related protein 0	DT000090	2
KI I domain containing, RNA binding, signal transduction associated 3, Sam68 like phosp	CK459702	2
similar to immunoglobulin kappa light chain variable region O11	AF334741	-4
platelet basic protein	NM_213862	-4
TN3	NM_214111	-3
immunglobulin VDJ region mRNA	U38212.1	-3
cytochrome P450 3A26	CO990609	-3
immunglobulin VDJ region mRNA	U38217.1	-3
immunoglobulin kappa light chain VJ region	CF180359	-3
eosinophil chemotactic cytokine, likely ortholog of mouse chitinase, acidic	CF360680	-3
interleukin 2 receptor gamma	NM_214098	-3
MHC class II antigen (SLA-DRB) mRNA for SLA-DR1 beta 1 domain	AB016740	-3
RING finger protein 13 isoform 1	BI184073	-3
immunoglobulin kappa light chain VC region	AF334730	-3
immunoglobulin kappa light chain VJ region	BI399688	-3
nucleolin	AJ657247	-3
bA338I4.1 (novel lipase)	CB474828	-3
nucleolin	DT157351	-3
secreted phosphoprotein-I	NM_214002	-3


O2- treated
100
80
60
40
20
0
%
cell signal
moecular
structural
immune
metabolic
upregulated
downregulated


Air-treated
100
80
60
40
20
0
%
upregulated
downregulated

Microarray Conclusions

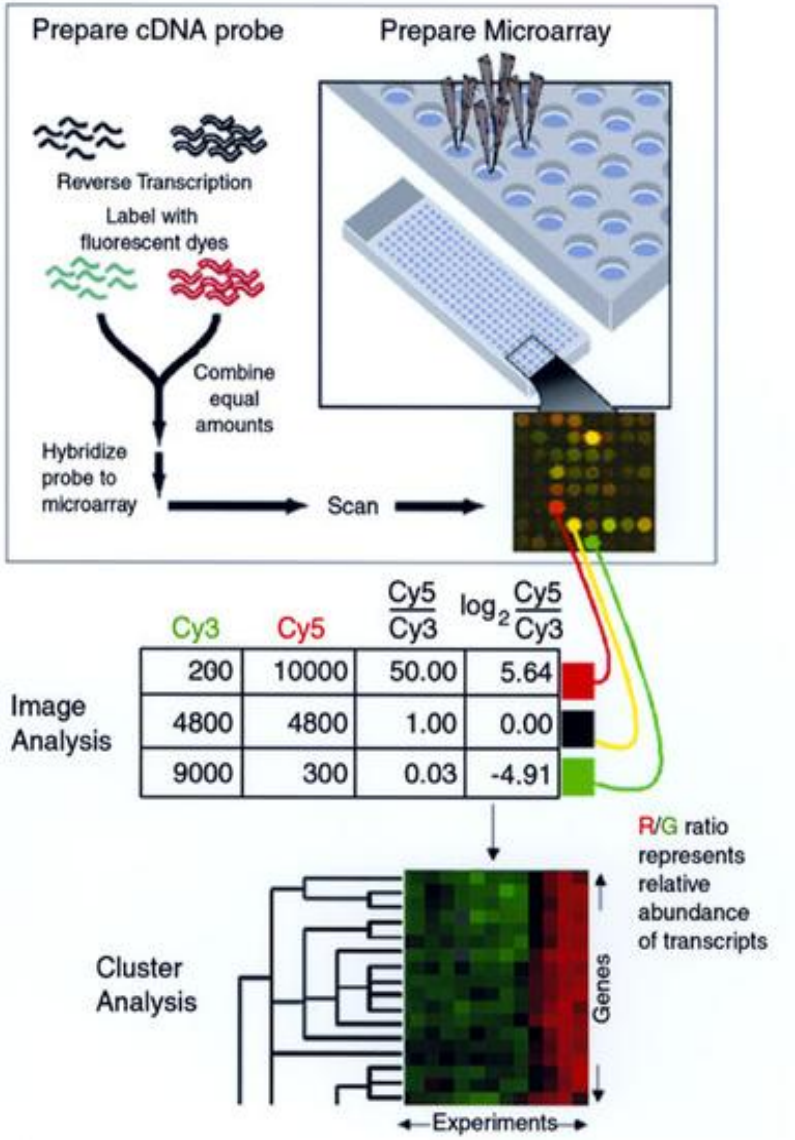
Saturation and Decompression with or without HBO has a broad effect on Gene Transcription in the lungs of swine

?

	100% oxygen		
	GENE DESCRIPTION	ACCESSION CODE	No. pos. animals1
upregulated	nidogen 2	CN156760	8
	prostate stromal protein ps20	CF363052	8
	prostate stromal protein ps20	CF361753	8
	scr.msk.p1.Contig2, mRNA sequence	CF364971	8
	Chimerin 1 (GTPase-activating protein, rho, 2)	BQ597587	8
	reticulon 1 isoform A; neuroendocrine-specific protein	CK457674	8
	a disintegrin and metalloproteinase with thrombospondin motifs	CO989594	8
	alpha 1 type XVIII collagen isoform 1 precursor; endostatin	CN155194	8
	calcitonin receptor-like receptor	NM_214095	7
	pentaxin-related gene, rapidly induced by IL-1 beta	CN153343	7
	melanoma cell adhesion molecule	BQ605024	7
	alpha 2 type IV collagen preproprotein; canstatin	CO950243	7
	Sus scrofa cDNA 5', mRNA sequence.	BG609032	7
	scr.msk.p1.Contig1, mRNA sequence	BQ601005	7
	chimerin 1	CD572334	7
	scr.msk.p1.Contig1, mRNA sequence	BF710490	7
	similar to collagen alpha 1(IV) chain precursor	BI183311	7
	matrix metalloproteinase 1 (type I collagenase)	CA779388	7
	heat shock protein 47	CN160329	7
	enabled homolog	AJ653947	7
downregulated	immunoglobulin kappa light chain variable region O11	AF334741.1	-8
	TN3	NM_214147	-8
	Immunglobulin VDJ region	U38212.1	-8
	scinderin	CO989361	-8
	alveolar macrophage-derived chemotactic factor-I	NM_213867	-8
	chemokine (C-X-C motif) ligand 13 (B-cell chemoattractant)	CF787657	-8
	immunoglobulin mu heavy chain constant region	S42881.1	-8
	platelet basic protein	NM_213862	-7
	cytochrome P450 3A26	CO990609	-7
	Immunglobulin VDJ region	U38217.1	-7
	Clone G502 immunoglobulin kappa light chain VJ region	CF180359	-7
	porcine inhibitor of carbonic anhydrase	NM_213847	-7
	tetranectin (plasminogen binding protein); tetranectin (plasmino	BI186214	-7
	similar to RIKEN cDNA 2010001M09	BX916934	-7
	371602 MARC	BI343446	-7
	Ig gamma 2b chain constant region	M81771.1	-7
	uncoupling protein 2	NM_214289	-7

Microarray methodology:

The main use of the microarray technology (DNA chips)- is to determine which genes are activated and which genes are suppressed when cells are compared from control and test swine lungs. Every gene is measured simultaneously.



For that purpose: mRNA is extracted from samples.

↓

Labelled colored (c)DNA is made through reverse transcription of a portion of the lung samples RNA and labeled with Cy (Cy3 green is for test cDNA and Cy5 red is for control cDNA).

↓

Labeled cDNA (from control and test cells) is placed on the microarray chip to hybridize overnight, 37C. Every spot on the chip represents a different coding sequency from different genes (DNA that can base pair with cDNA).

↓

Unbound DNA is washed away to avoid non specific binding.

↓

Plate is placed in the scanner where 2 lasers pass over the slide and read the intensity emitted by Cy5 Red (control) and Cy3 green (test) flour chromes. The 16-bit-scale image is generated after all wells are read.

Abstract A6

Inflammatory gene expression in the leukocytes of naive subjects and experienced divers following acute hyperbaric stress

BA Cameron, TC McLellan, DJ Eaton
and SG Rhind

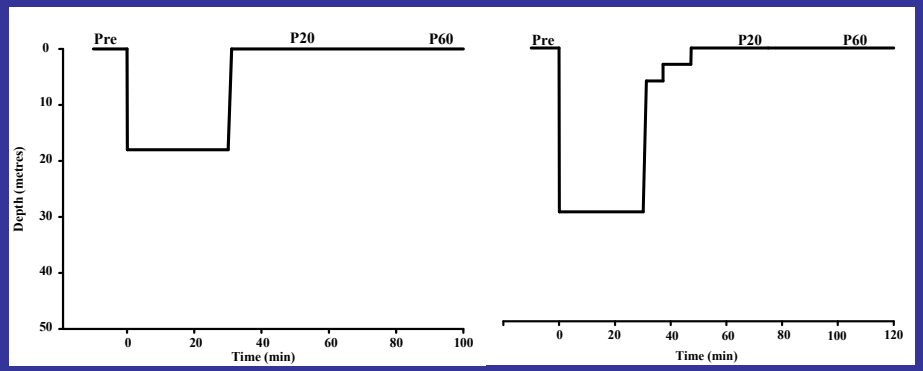
BMSC

Inflammatory Gene Expression in the Leukocytes of Naive Subjects And Experienced Divers Following Acute Hyperbaric Stress

BA Cameron, TC McLellan, DJ Eaton and SG Rhind.
Defence Research and Development Canada, Toronto, Ontario, and the Bamfield Marine Sciences Centre, Bamfield, British Columbia

Methods

First Two Dives in Series

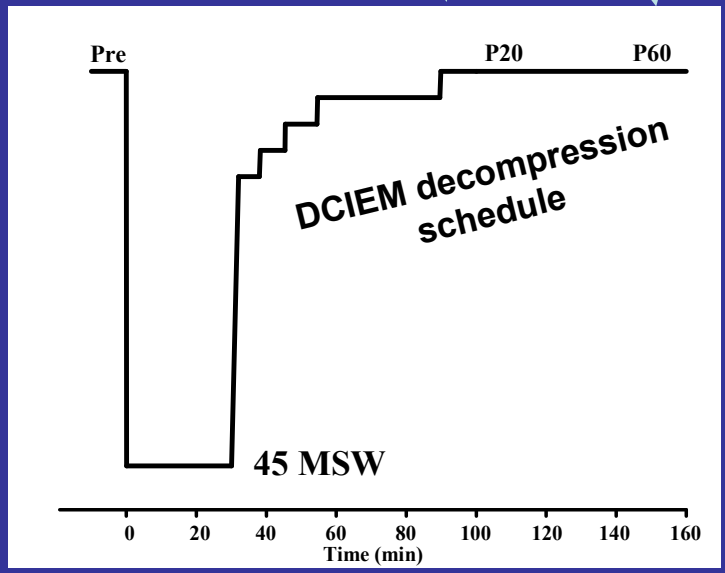


Venipuncture

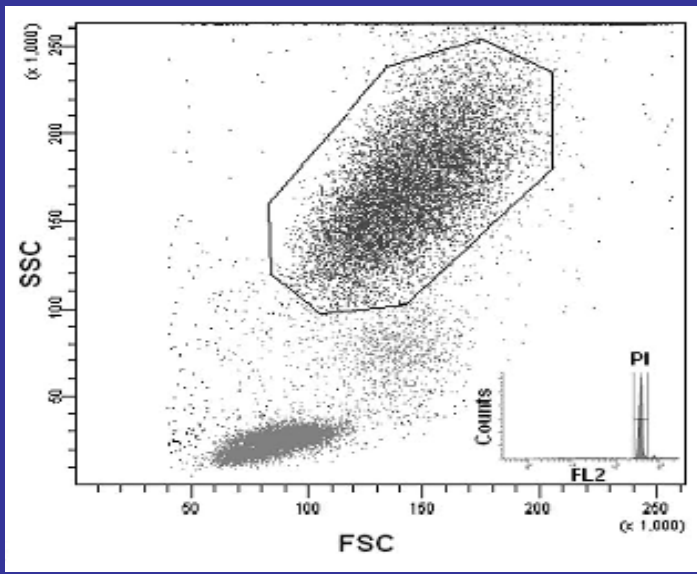
Pre Dive Blood Draw

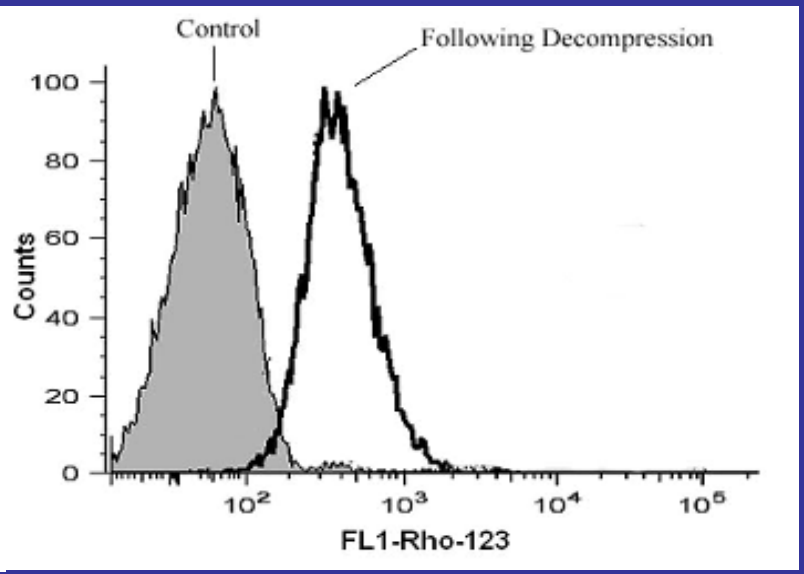
Post 20 min Blood Draw

Post 60 min Blood Draw



Reactive oxidant generation and % HSP70 expression in PMNs and IL-1RA expression in monocytes was determined flow cytometrically using the fluorogenic substrate, dihydrorhodamine (DHR) 123 and fluorescence-labelled monoclonal antibodies.





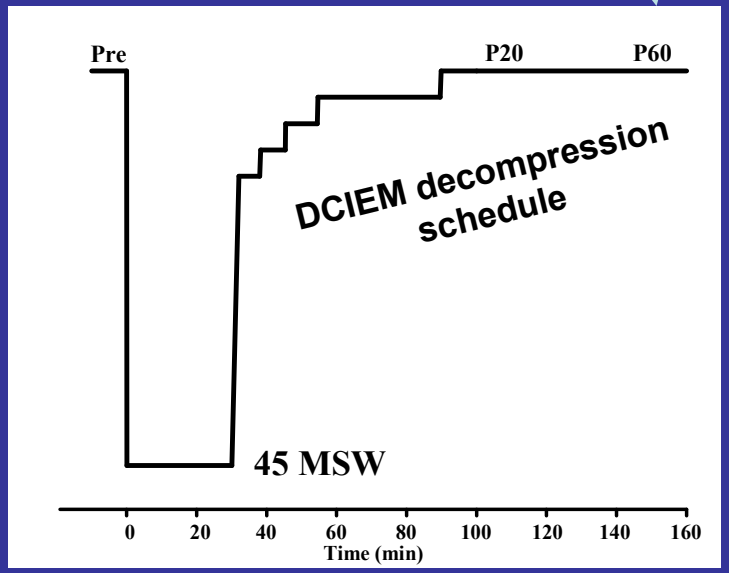
6 Experienced Divers

6 Naïve Subjects

Venipuncture

Pre Dive Blood Draw

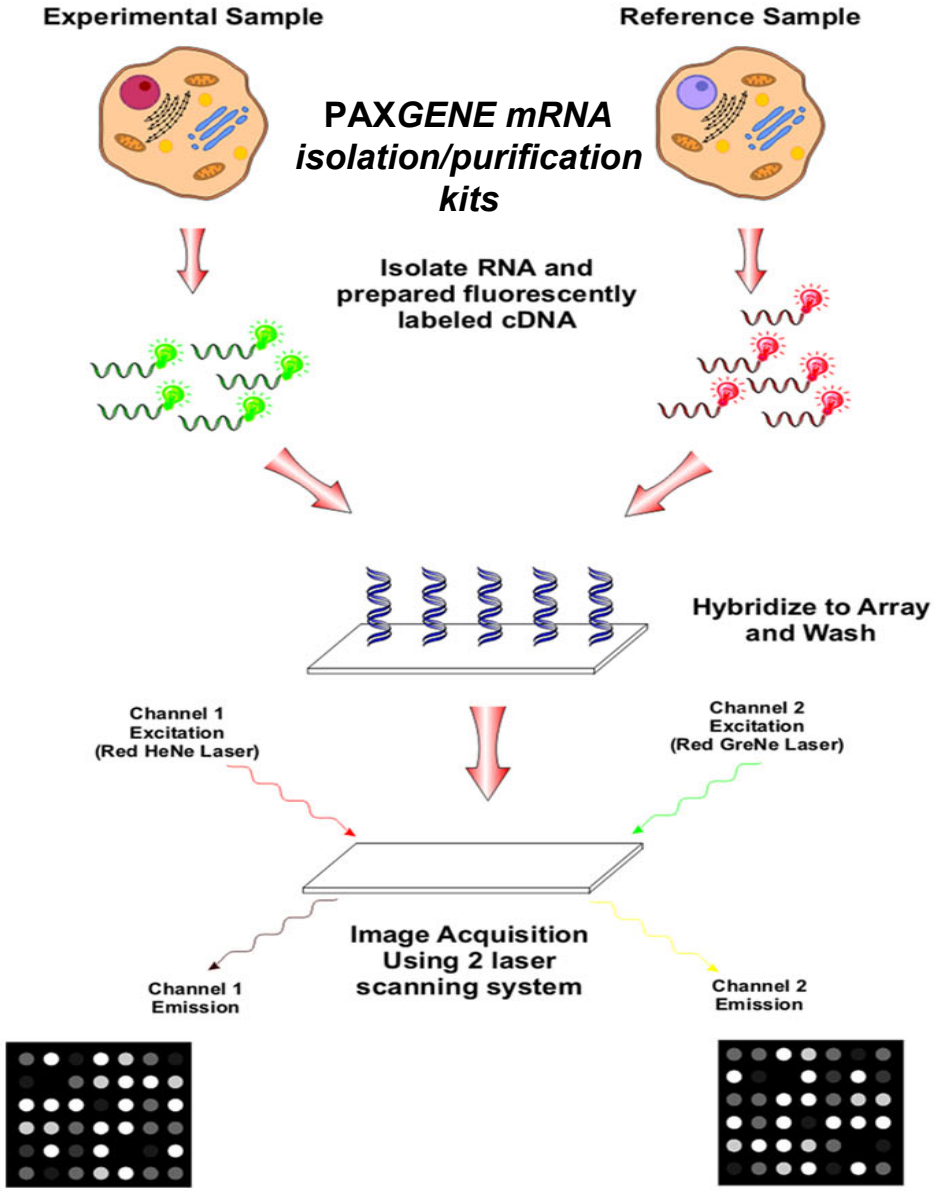
Post 60 min Blood Draw

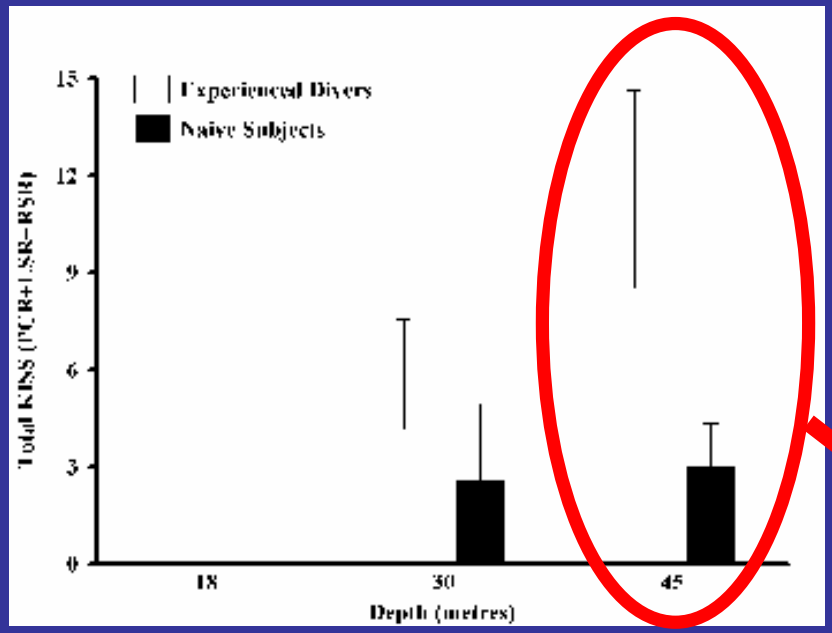


6 Experienced Divers and 6 Naïve Subjects

Fold changes in mRNA expression were calculated from two-colour array microchip displays and normalized to mRNA expression reference samples from ten different quiescent human cells.

mRNA Two Colour Micro-Array





Resting Doppler Ultrasound

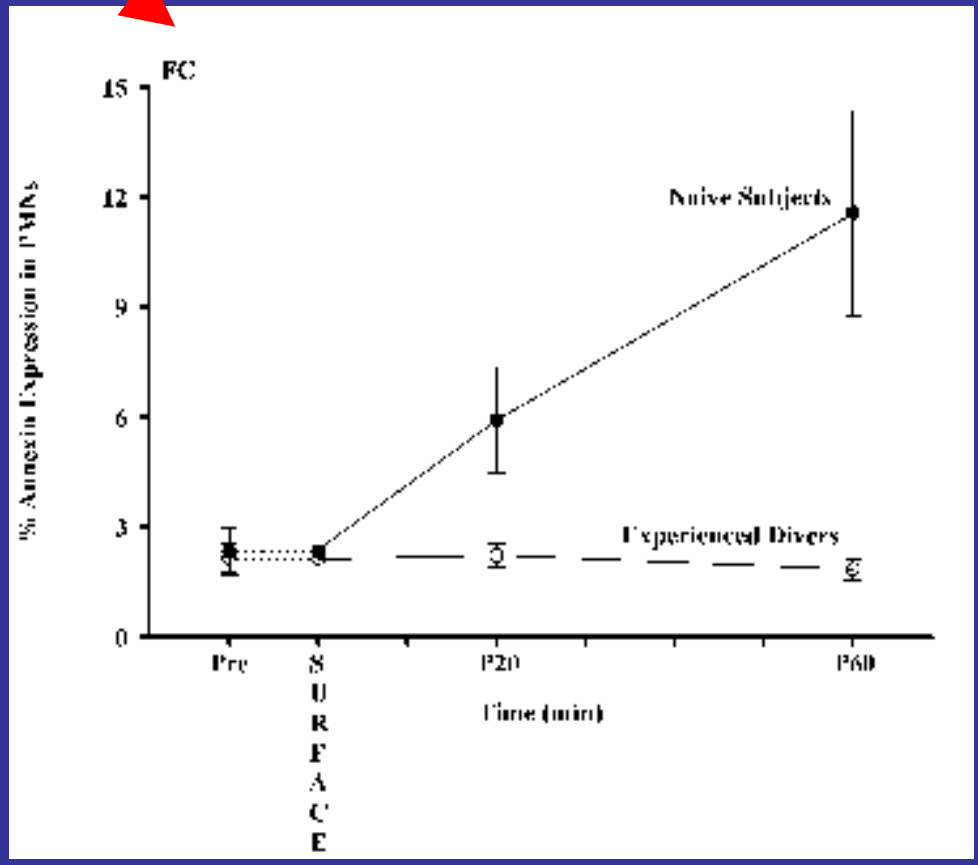
Summed the integrated 20, 40, 80 &120 minute Kisman-Masurel VGE scores (KISS) for the precordium and subclavian veins = tKISS

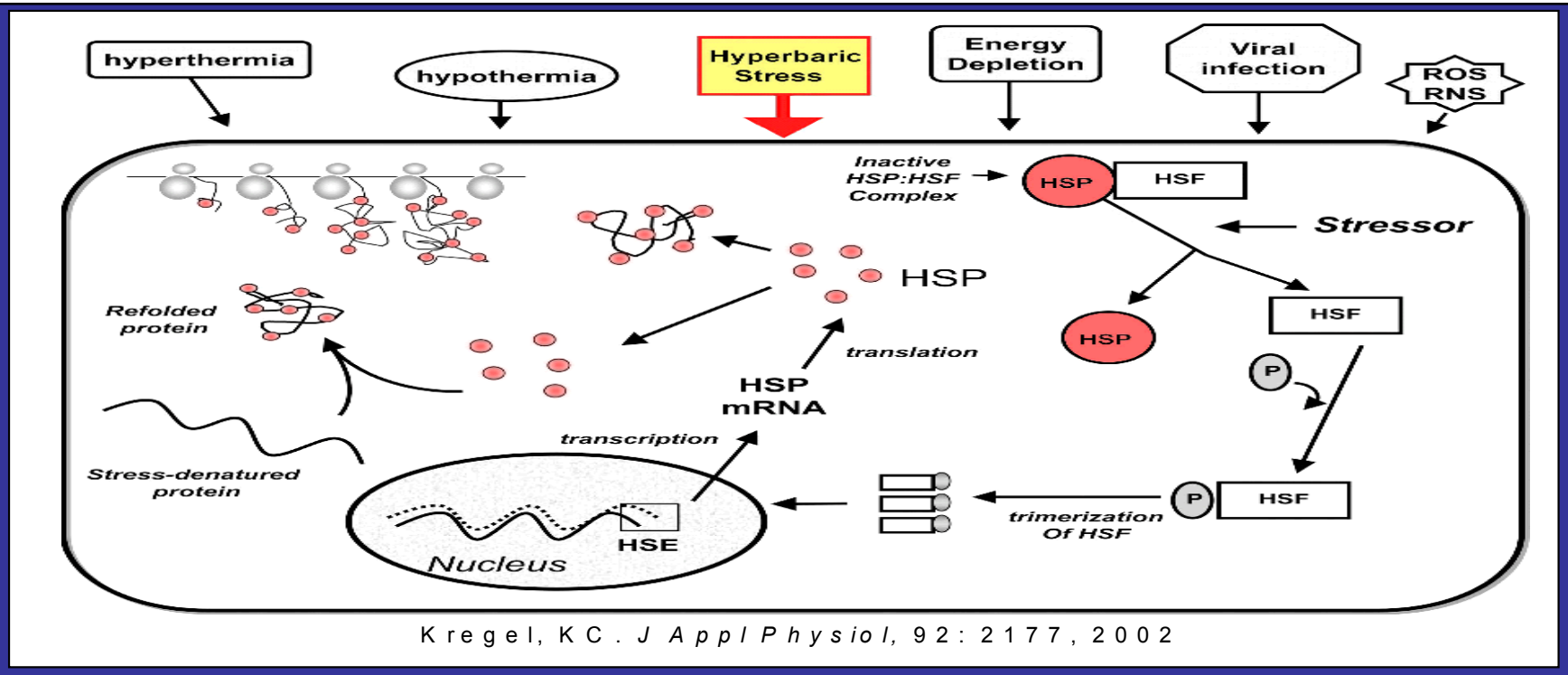
Examined flow cytometry and μarray data from the 45 meter dives

Apoptosis

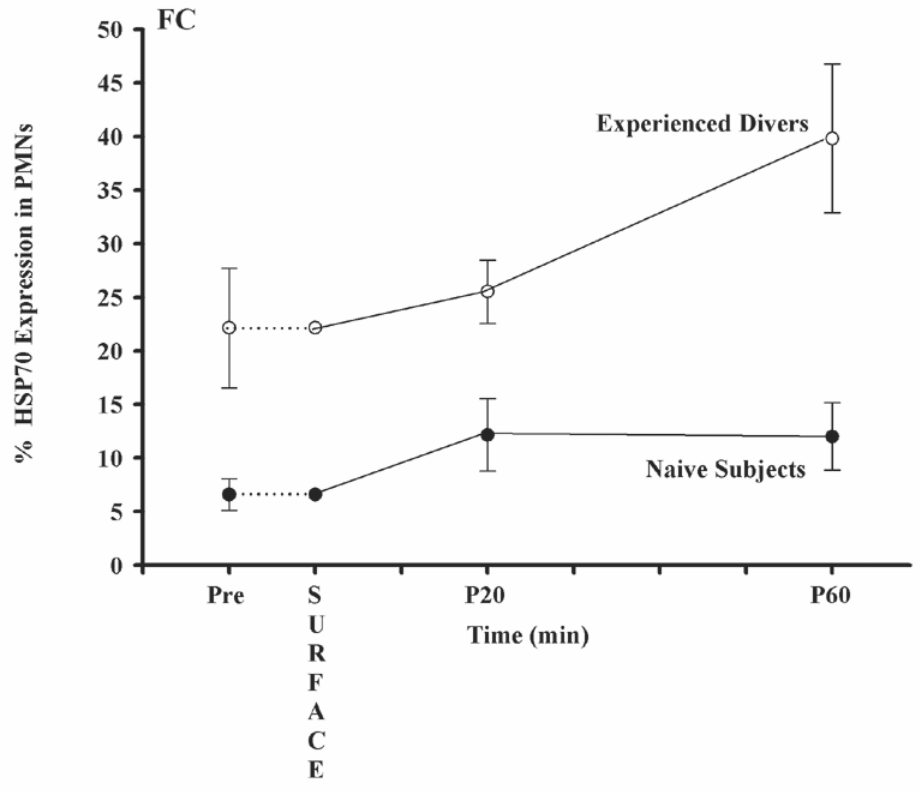
Controlled cell death prompted by many factors including increased cytokine release during inflammatory response.

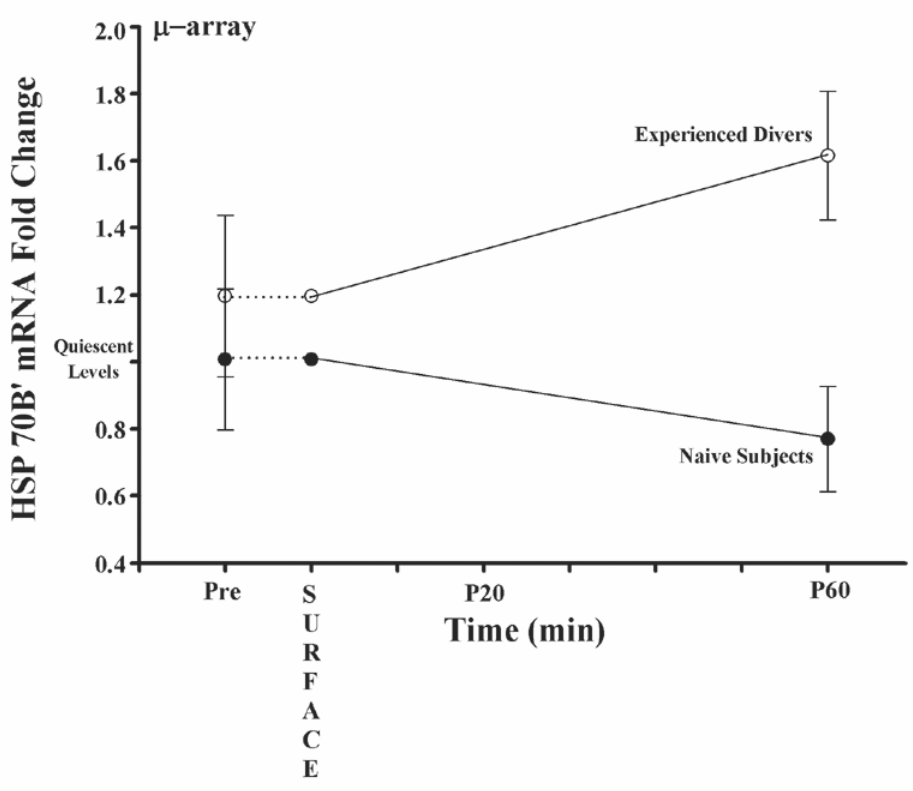
The PMNs of experienced divers showed reduced or delayed apoptosis following ascent from the 45 meter dive.



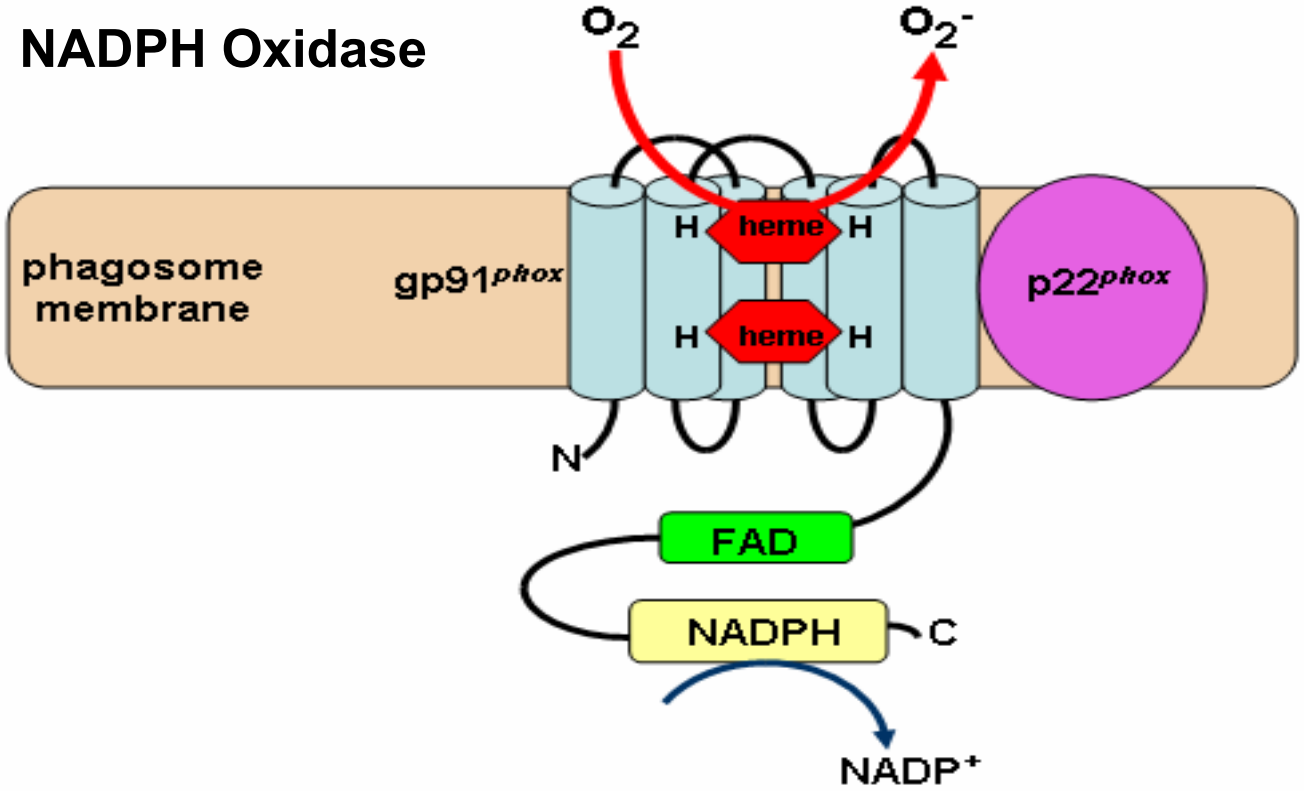


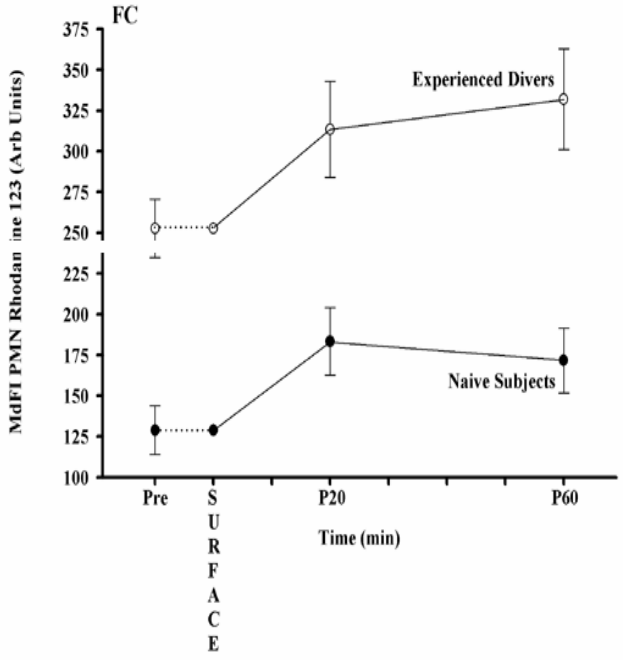
Kregel, KC. *J Appl Physiol*, 92: 2177, 2002

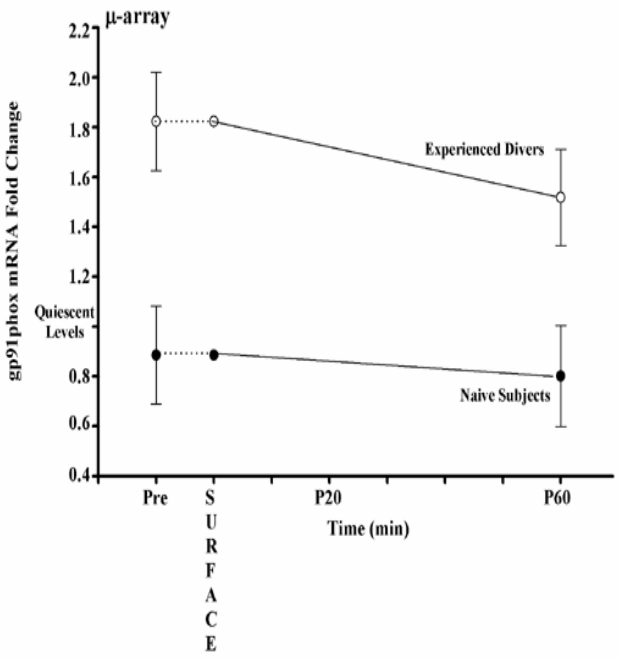


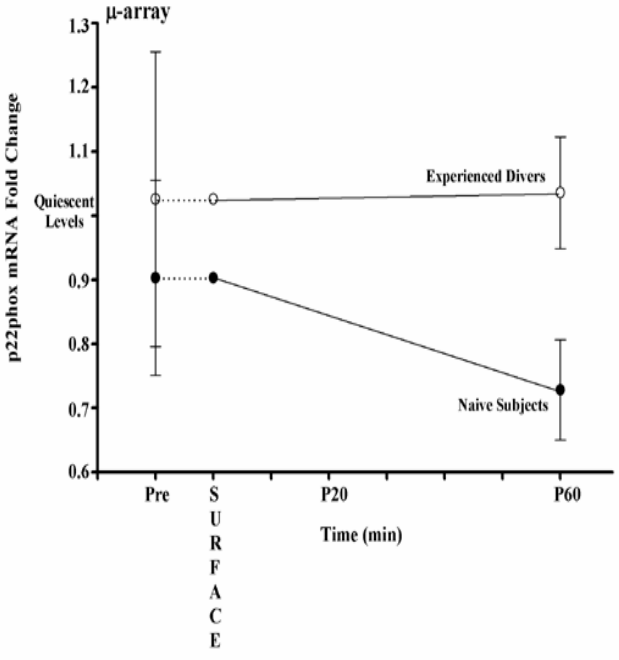


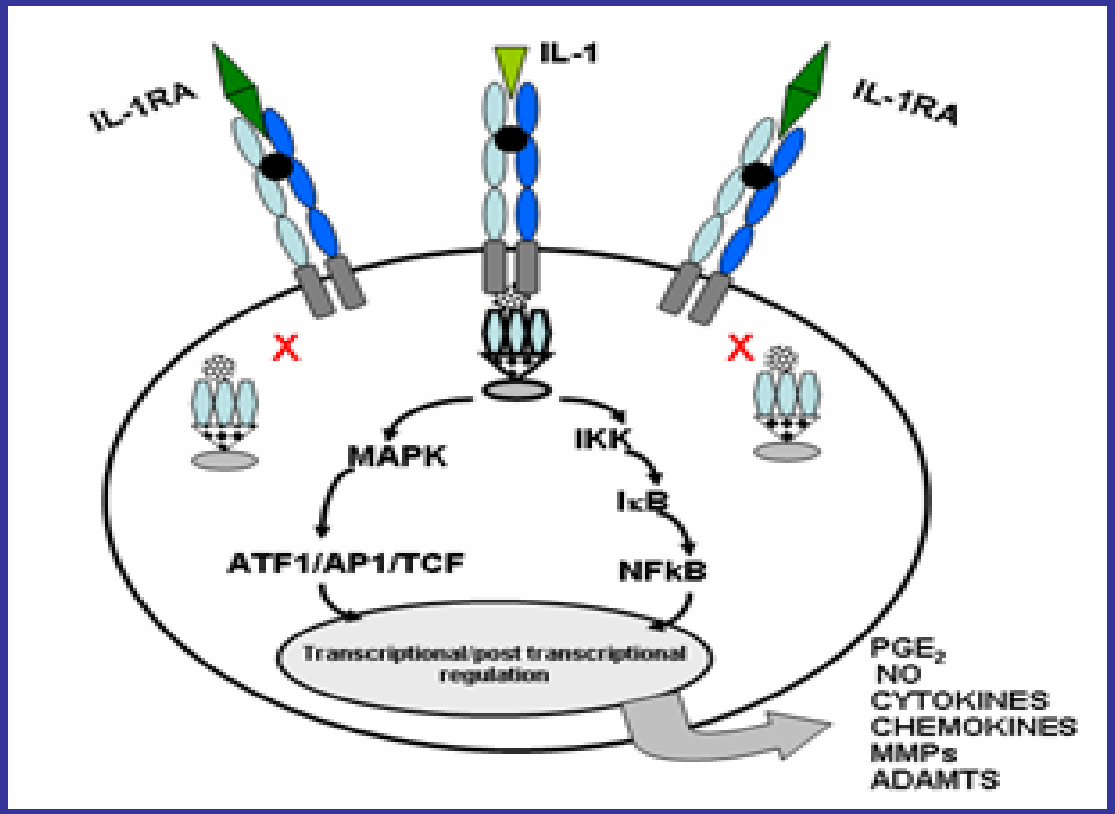
NADPH Oxidase

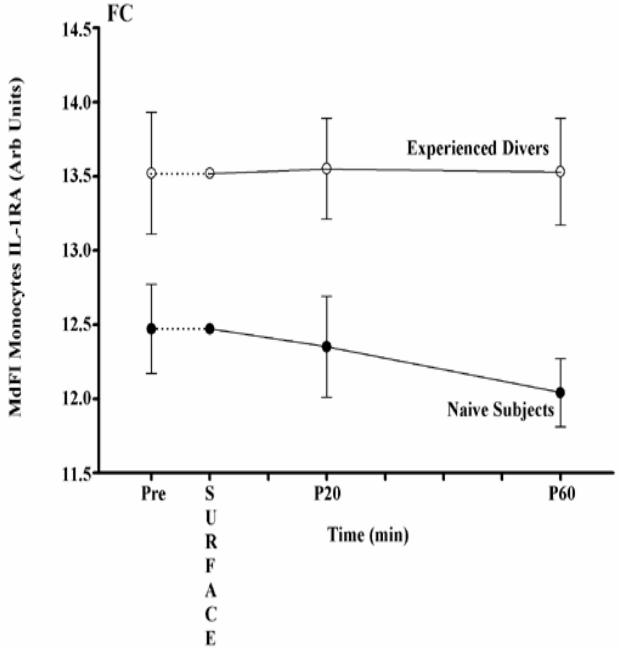


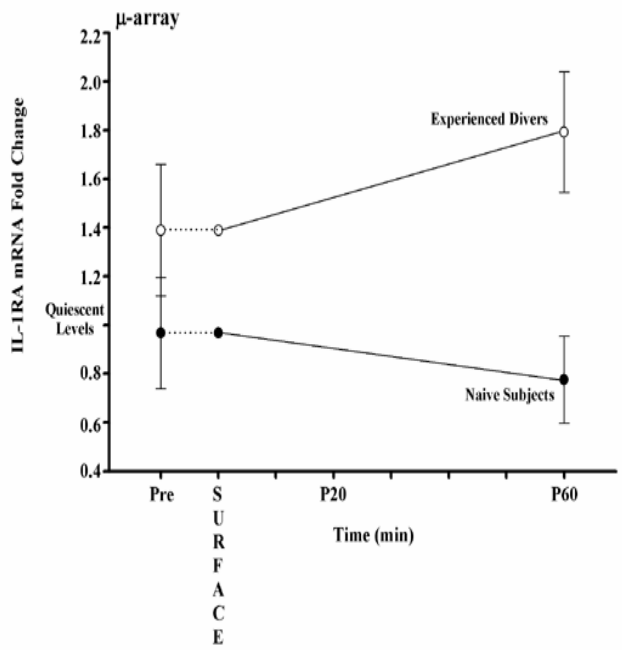


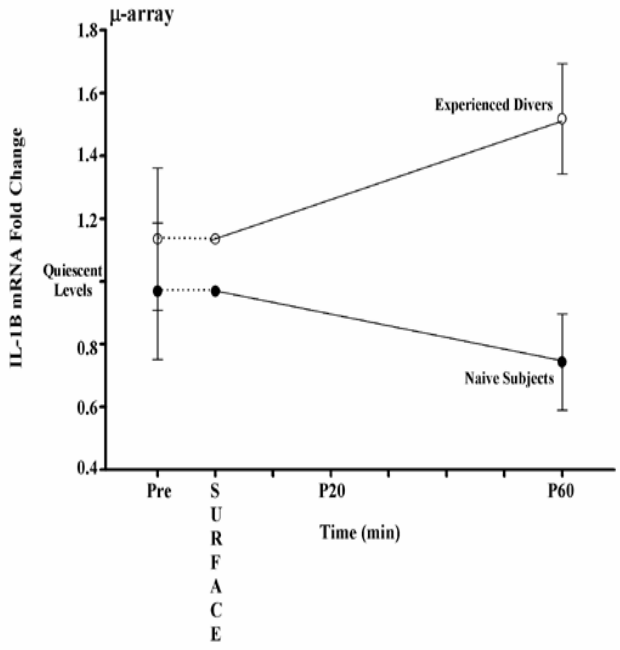




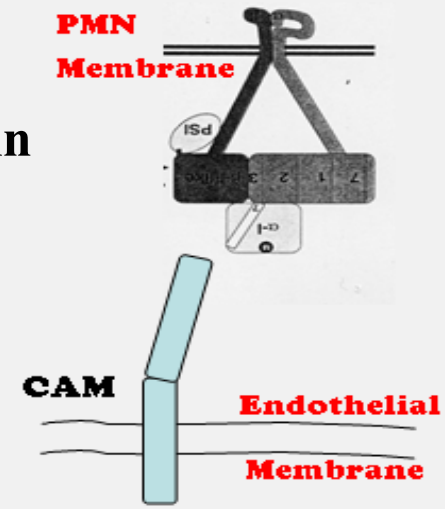

IL-1
IL-1RA
IL-1RA
X
X
MAPK
IKK
IκB
ATF1/AP1/TCF
NFkB
Transcriptional/post transcriptional regulation
PGE2
NO
CYTOKINES
CHEMOKINES
MMPs
ADAMTS

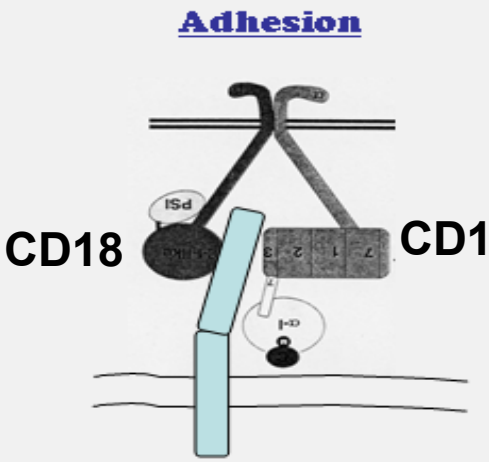

FC
MdFI Monocytes IL-1RA (Arb Units)
14.5
14.0
13.5
13.0
12.5
12.0
11.5
Experienced Divers
Naive Subjects
Pre
SURFACE
P20
P60
Time (min)

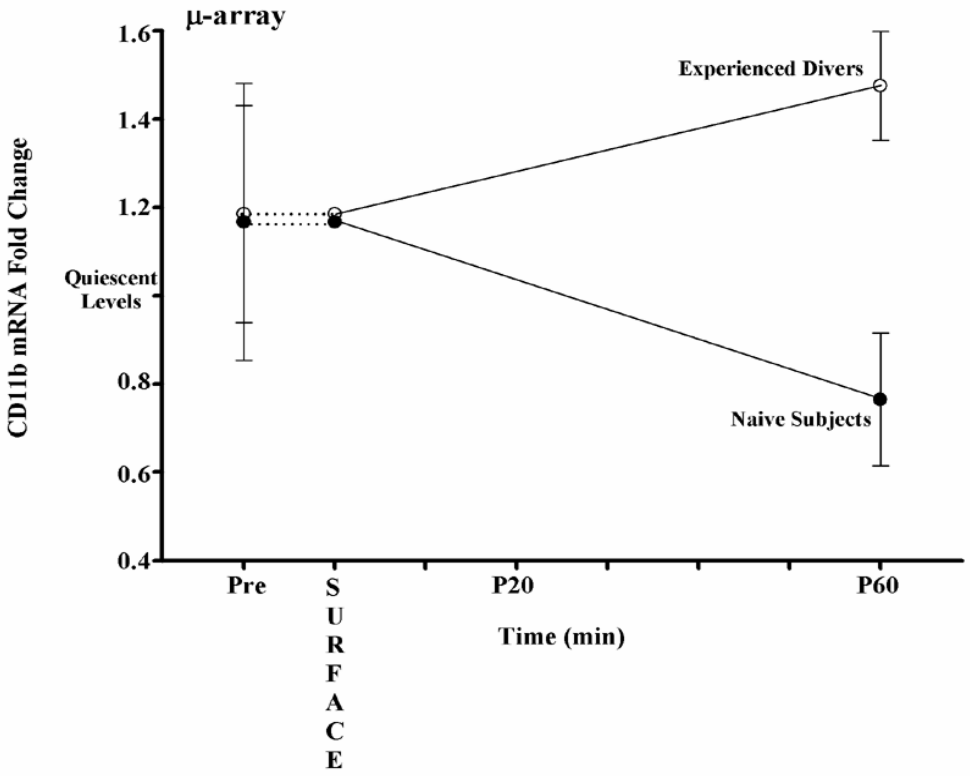

μ-array
IL-1RA mRNA Fold Change
2.2
2.0
1.8
1.6
1.4
1.2
0.8
0.6
0.4
Quiescent Levels
Experienced Divers
Naive Subjects
Pre
SURFACE
P20
P60
Time (min)

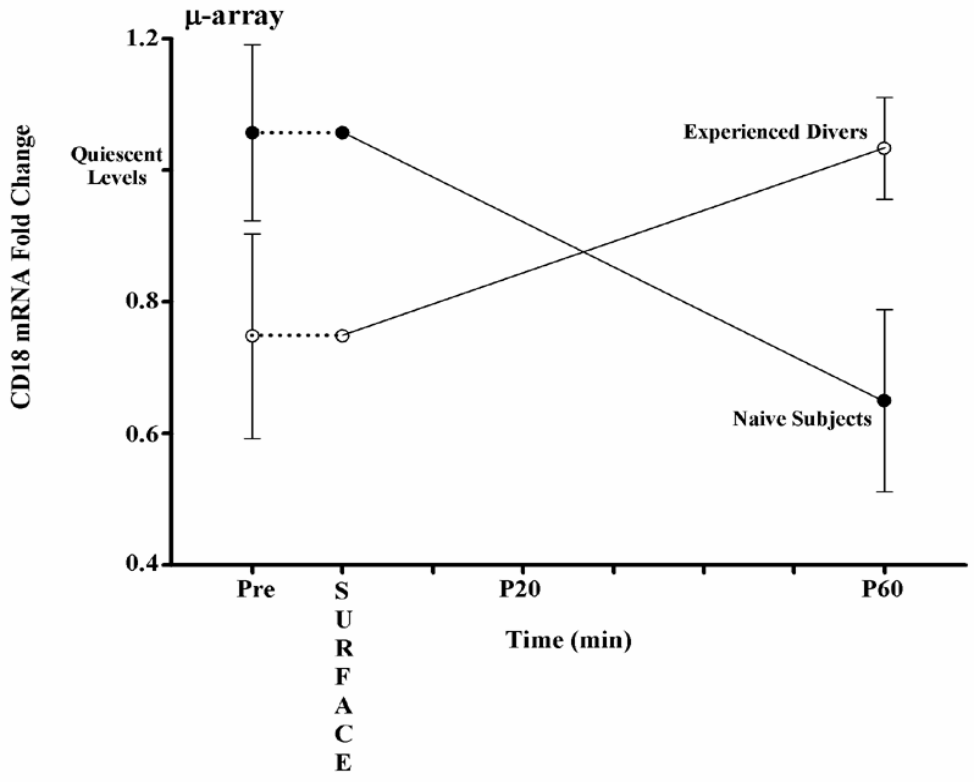

μ-array
IL-1B mRNA Fold Change
1.8
1.6
1.4
1.2
0.8
0.6
0.4
Quiescent Levels
Experienced Divers
Naive Subjects
Pre
SURFACE
P20
P60
Time (min)

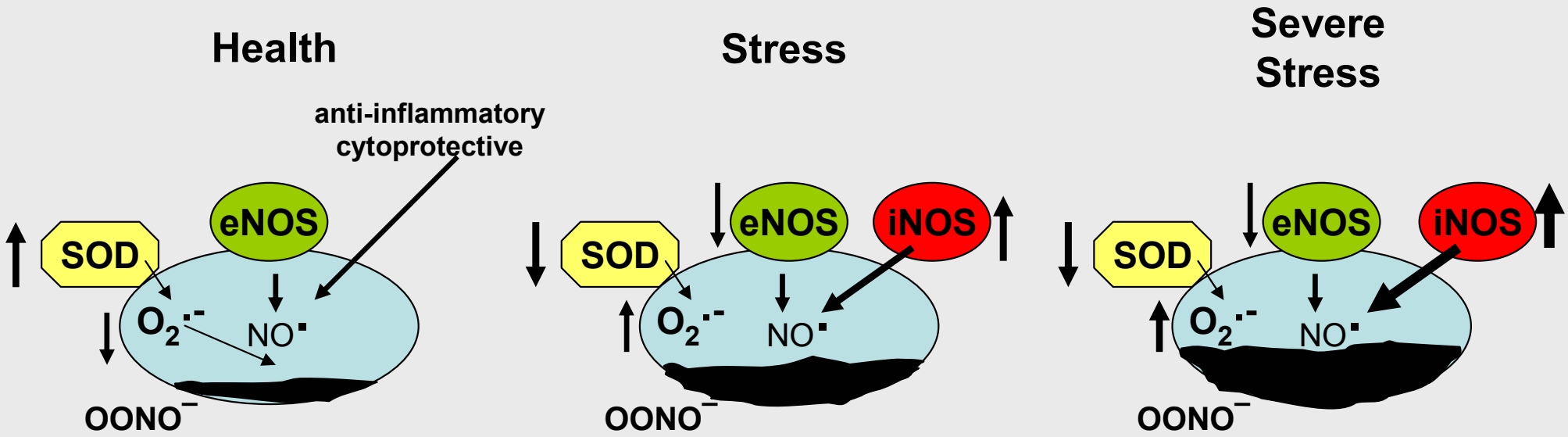
β2-integrin complex

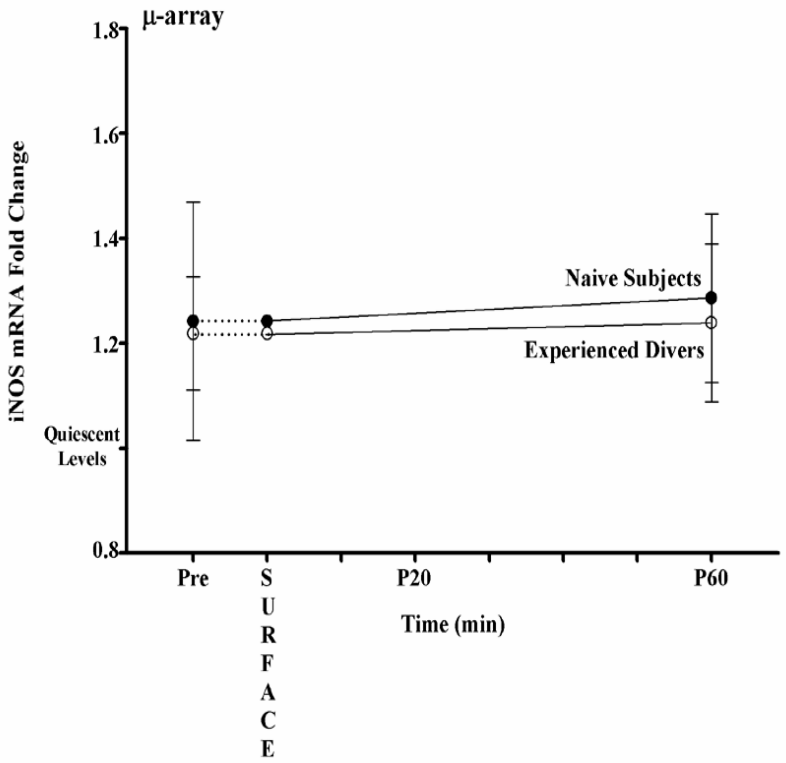


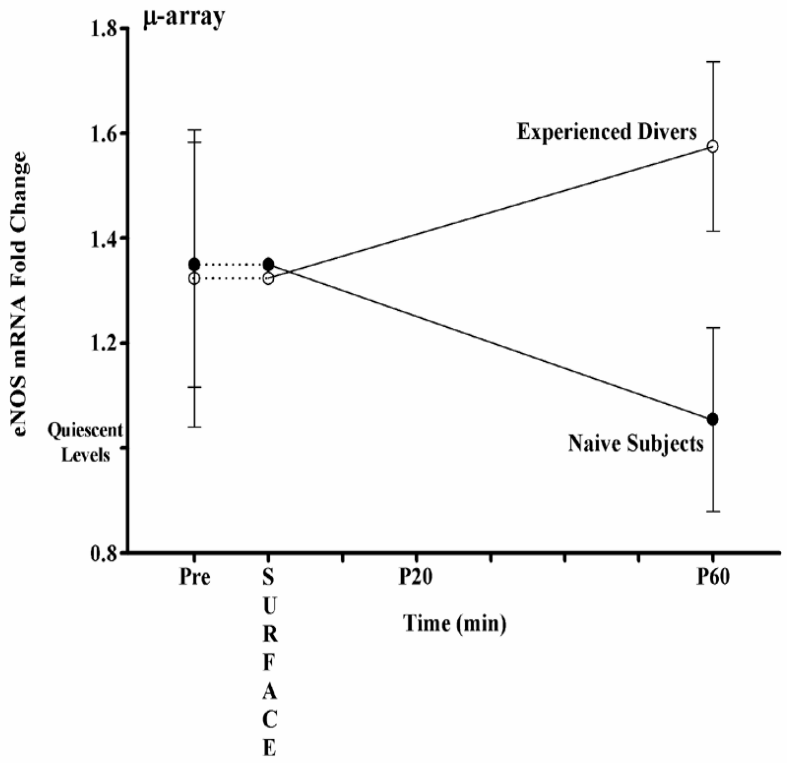







Health
Stress
Severe Stress
anti-inflammatory
cytoprotective
SOD
eNOS
iNOS
$O_2^{\cdot-}$
NO·
OONO⁻


μ-array
iNOS mRNA Fold Change
1.8
1.6
1.4
1.2
Quiescent Levels
0.8
Naive Subjects
Experienced Divers
Pre
SURFACE
P20
P60
Time (min)


μ-array
eNOS mRNA Fold Change
1.8
1.6
1.4
1.2
Quiescent Levels
0.8
Experienced Divers
Naive Subjects
Pre
SURFACE
P20
P60
Time (min)

Summary

Close experimental relationship between protein and mRNA expression measured by flow cytometry and micro-array analysis, respectively.

Several pro- and anti-inflammatory cytokines that were expressed and activated in the experienced divers remained inactive in the naïve subjects following the dive.

The absence of iNOS transcription coupled with the higher levels of eNOS mRNA suggests a controlled inflammatory response to VGE in the experienced divers not observed in the naïve divers.

This controlled inflammatory response may have influenced the delay in apoptosis in the PMNs of the experienced divers.

Micro-array analysis acts as a molecular roadmap to biochemical pathways involved in the inflammatory response due to venous gas emboli following decompression.

Acknowledgements:
United States Navy, Office of Naval Research
Defense Research and Development, Canada
The Natural Sciences and Engineering Research Council of Canada.

Session A

1030-1100: BREAKS/EXHIBITS
1100-1130: POSTERS

Abstract A7

Enhanced nuclear factor (NF)-KB activation in experienced divers in response to acute hyperbaric stress

Rhind SG, Cameron BA, Eaton DJ, McLellan TM

DEFENCE R&D DÉFENSE

ENHANCED NUCLEAR FACTOR (NF)-κB ACTIVATION IN EXPERIENCED DIVERS IN RESPONSE TO HYPERBARIC STRESS

Rhind SG, Cameron BA, Eaton DJ, McLellan TM

Defence Research & Development Canada, Toronto, Ontario, and

the Bamfield Marine Sciences Centre, Bamfield, British Columbia

2008 UHMS Annual Scientific Meeting

Salt Lake City, UT

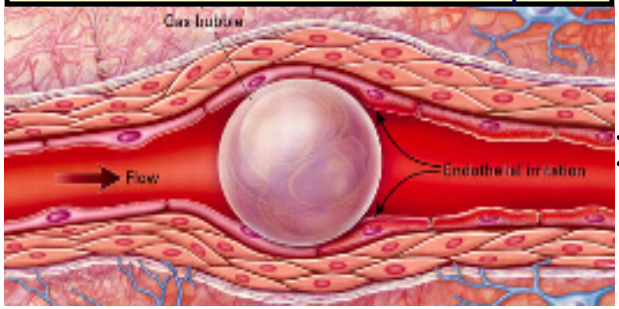
Defence Research and Development Canada | Recherche et développement pour la défense Canada

Canada

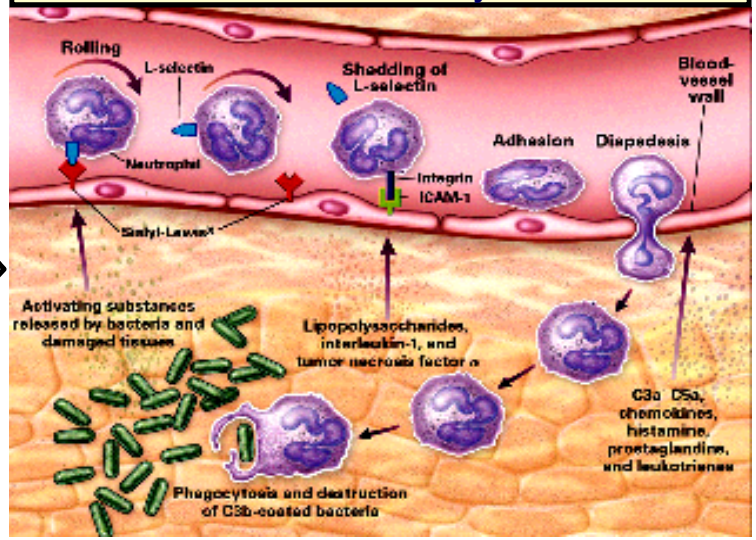
Immunopathology of DCS

Causative Agent

Vascular Endothelial Disruption



Immuno Inflammatory Cascade



- Decompression causes bubble formation in the circulation & tissues
- *Main cause of DCS clinical symptoms*

- Bubbles lead to direct endothelial disruption
- Functional stripping of endothelial cells
- Vascular leakage
- Occlusion of blood flow, reduced shear stress

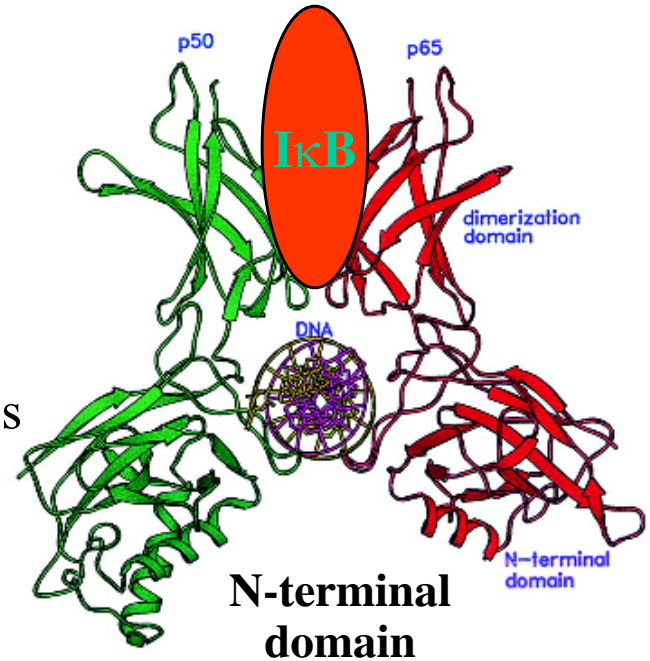
- Neutrophil activation, adhesion, infiltration
- Activation of complement (C3a, C5a) and coagulation (tissue factor)
- Changes in cell signaling cascades
- Inflammatory cytokine (IL-1, TNF-α) and chemokine (IL-8) production
- Release of cytotoxins: oxygen/nitrogen radicals, proteases
- Changes in heat stress proteins and cellular apoptosis

What is NF-κB?

- NF-κB comprises a family of transcription factors regulating a large number of genes related to *immunity, inflammation, cell proliferation and survival*.
- Consists of several different combinations of subunits in the cytoplasm, *most common being a heterodimer of p50/p65 (Rel A)* and the *IκBα inhibitory subunit*.
- In resting cells, NF-κB is sequestered in the cytoplasm complexed to IκB in a non-DNA-binding form – IκB serves as a cytoplasmic tether to keep NF-κB out of the nucleus.

Responsible for dimerisation + nonspecific DNA- phosphate contact

C-terminal domain



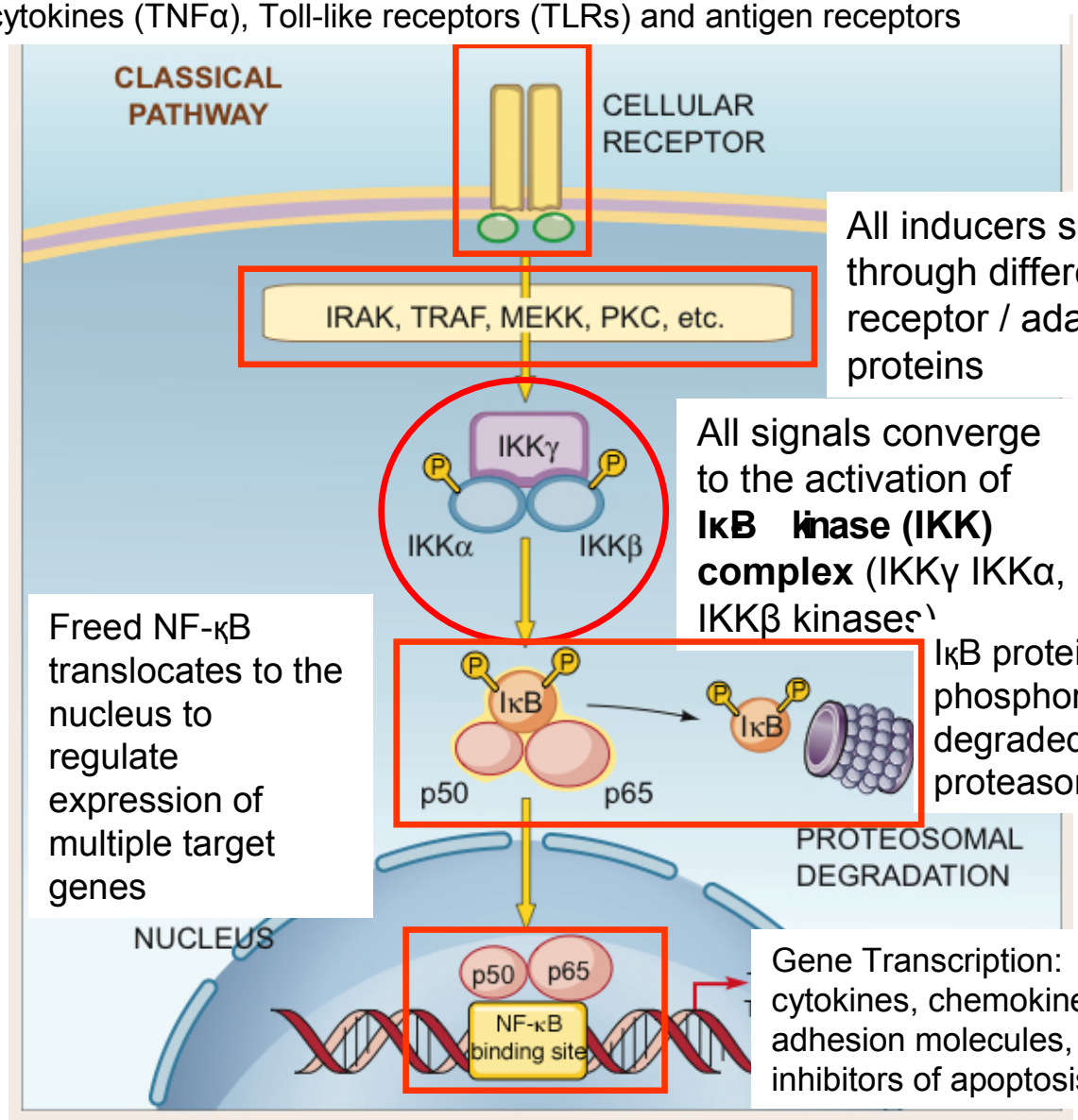
N-terminal domain

Specific DNA contact

NF-κB Signaling Pathway

NF-κB-activating pathway induced by a variety of mediators: pro-inflammatory cytokines (TNFα), Toll-like receptors (TLRs) and antigen receptors

- *Central regulator of the cellular stress response*



All inducers signal through different receptor / adaptor proteins

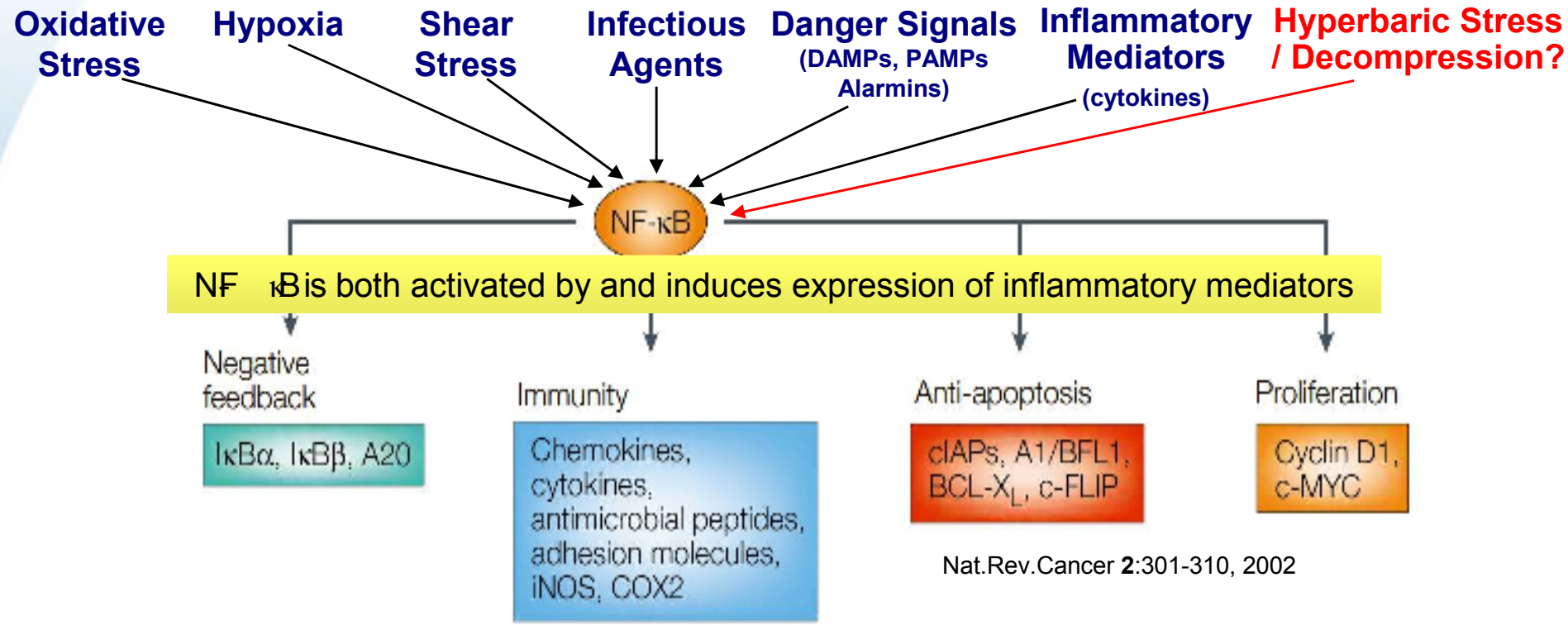
All signals converge to the activation of **IκB kinase (IKK) complex** (IKKγ IKKα, IKKβ kinases)

IκB proteins rapidly phosphorylated & degraded by the proteasome

Freed NF-κB translocates to the nucleus to regulate expression of multiple target genes

Gene Transcription: cytokines, chemokines, adhesion molecules, inhibitors of apoptosis

NFκB Induction & Target Gene Regulation



Nat.Rev.Cancer **2**:301-310, 2002

- NF-κB modulates development, activation, effector functions of both innate and adaptive immunity via regulation of target genes:
  - cytokines, adhesion molecules, immune receptors, acute phase proteins, other immune modulators
- Anti-Apoptotic genes and cell cycle regulators
  - protecting cells from undergoing apoptosis in response to DNA damage or cytokine treatment
- Negative Feedback Loop: IκB-α under direct control of NF-κB
  - NF-κB activates IκB gene expression – newly synthesized IκB inactivates NF-κB in the cytoplasm

Purpose

- ***To our knowledge there has been no documentation about the impact of acute hyperbaric and decompression stress on the intracellular activation of NF-κB and whether repeated exposure to hyperbaric stress leads to an adaptive response in the immune signaling pathways.***
- ***With the use of a cross-sectional design, examine the effects of repeated hyperbaric and decompression stress on the NF-κB activation in PMN neutrophils and PBMN monocytes.***

Experimental Design

- One grouping (between) factor, ***hyperbaric experience***
- Two levels (naive (n = 9) vs experienced (n = 11))

Naive had never experienced hyperbaric stress whereas experienced had experienced the stress at least once per month during the past 6 months.

	Age (y)	**Height (cm)**	**Weight (kg)**
Naive	36.9 (11.4)	177.5 (7.8)	80.0 (14.8)
Experienced	40.6 (4.9)	175.3 (6.6)	85.3 (11.9)

Experimental Design

- Two repeated factors, *time* (pre, 20, 60 min post exposure) and *decompression stress* following hyperoxic hyperbaric exposure to three levels:
  - Level 1 (Low): 180 kPa (18 msw) for 30 min
  - Level 2 (Moderate): 300 kPa (30 msw) for 30 min
  - Level 3 (High): 450 kPa (45 msw) for 30 min

  Pressurization rates were 18 $kPa \cdot min^{-1}$ and decompression rates were in accordance with established DCIEM dive tables and represented 1, 15 and 55 minutes for the low, moderate and high levels of hyperbaric stress.

  - Order of exposures proceeded from low through with 7 days intervening between each exposure.

Flow Cytometric Analysis of Intranuclear NF-κB

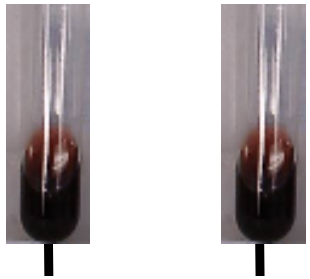
Whole blood collected *pre-dive, 20- & 60-min post-dive* into 3 mL sodium heparin vacutainers.

Spontaneous
(fresh WB)

LPS Stimulation
(100ng/mL, 37°C, 30min)

(50 μL)

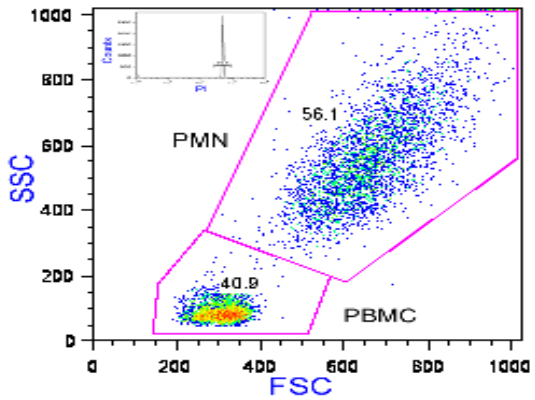
Preparation of isolated nuclei



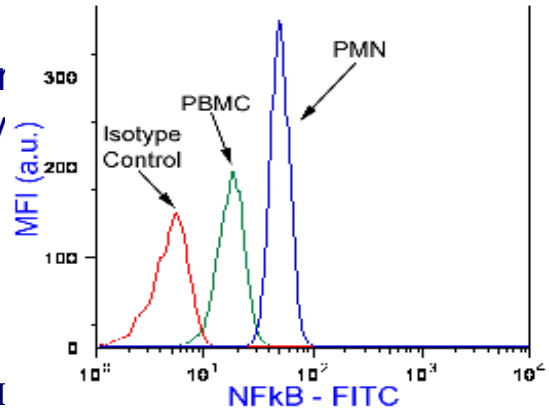
- Lysed aliquots processed with CycleTest Plus DNA kit
- Cells washed in citrate buffer
- 125μL Soln A (trypsin+spermine tetrahydrochloride)
- 100μL Soln B (trypsin inhibitor–RNase buffer+ spermine tetrahydrochloride buffer).

Flow Cytometric Analsysis

Isolated nuc

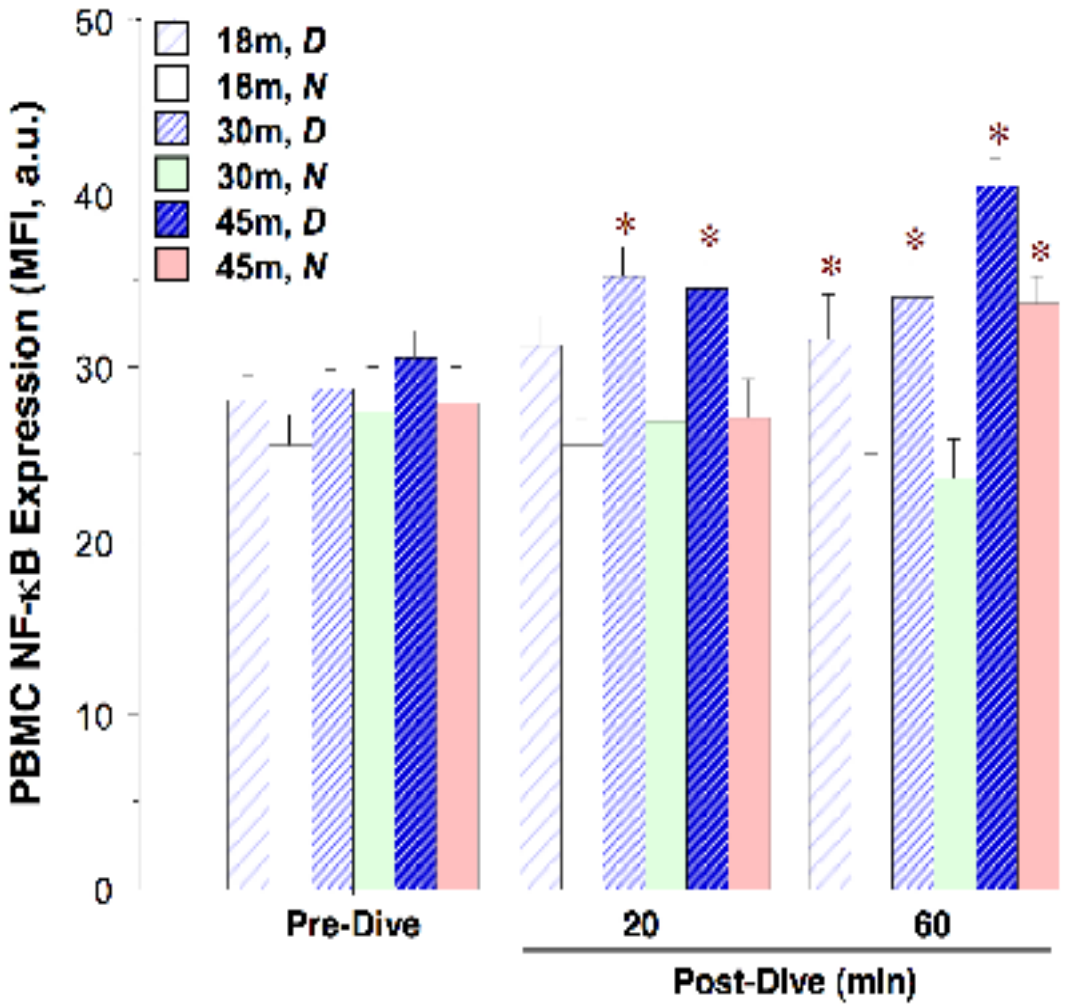


G_1 isotype co
ated antibody



RESULTS
Spontaneous PBMC NF-κB Expression

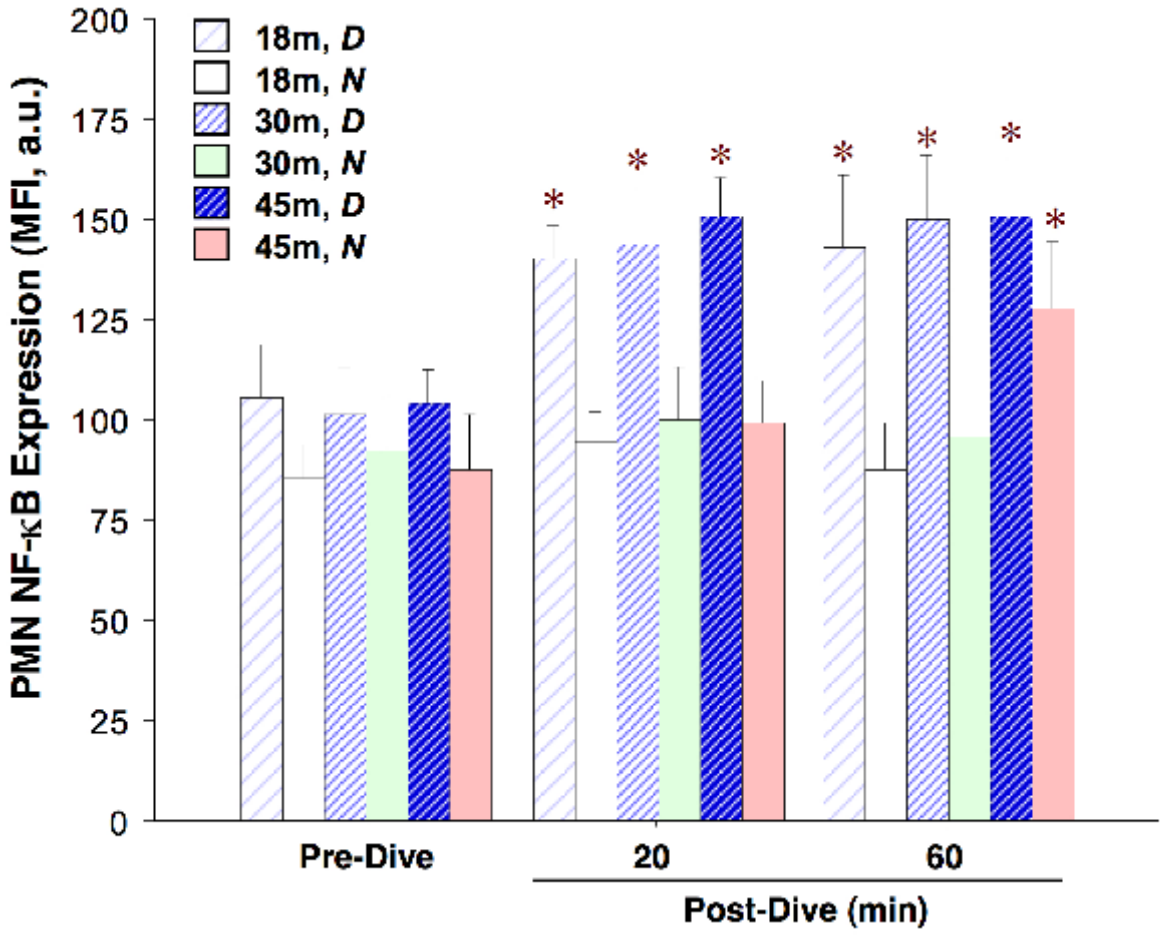
- Resting spontaneous NF-κB expression in PBMC was similar between *Naive (N)* subjects and *Divers (D)*.
- After acute hyperbaric stress, *D* exhibited a time-dependent elevation (up to 60%) of intranuclear NF-κB in PBMC at all depths.
- Significant translocation occurred only after the 45 m dive at 60-min post-dive in *N*.



*p <0.05 post dive *vs* pre dive values by ANOVA.

RESULTS
Spontaneous PMN NF-κB Expression

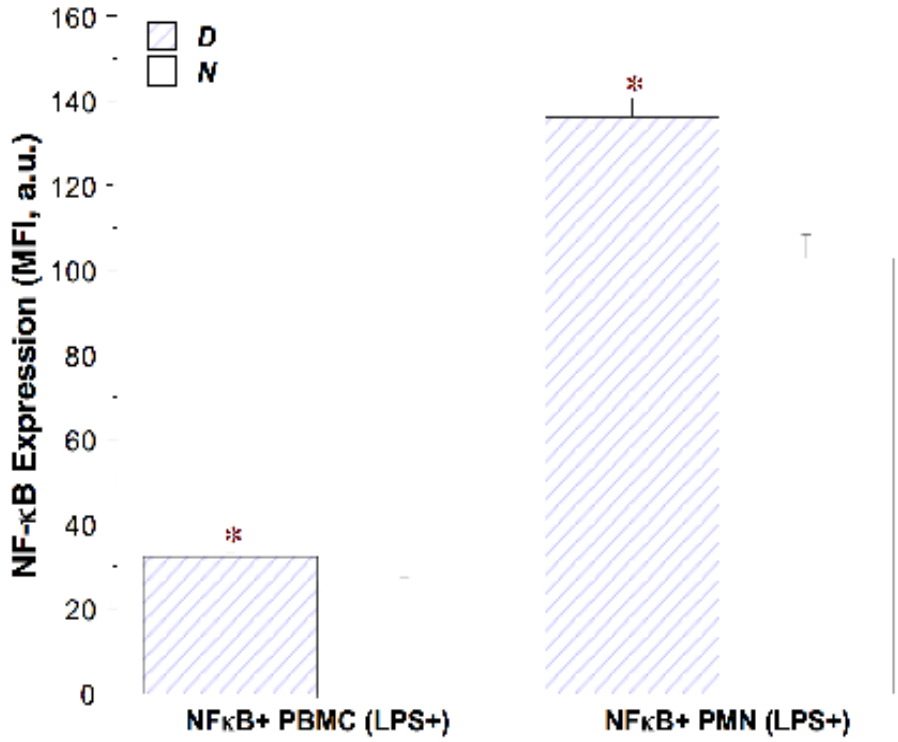
- As with PBMC, pre-dive levels of NF-κB in PMNs were similar between *N* and *D* groups.
- Constitutive NF- κB expression was higher in resting PMNs compared to PBMC.
- Acute hyperbaric stress elicited a similar pattern of intranuclear NF-κB translocation at all depths in *D*
- Significant translocation occurred only after the 45 m dive at 60-min post-dive in *N*.



*p <0.05 post dive *vs* pre dive values by ANOVA.

RESULTS
LPS-Stimulated NF-κB Expression

- Compared to spontaneous expression, LPS stimulation induced significant increases in NF-κB translocation by PBMC and PMNs in both groups.
- LPS-induced NF- κB translocation was greatest (up to 45%) in *D* compared to *N* responses.



*p <0.05 divers versus naive subjects.

Conclusions

- This study demonstrates enhanced nuclear translocation of NF-κB in both PBMC and PMNs from humans exposed to acute hyperbaric exposure, that is greatest in experienced divers following repetitive episodes of hyperbaric stress.
- These results suggest that modulation of NF-κB-dependent inflammatory gene expression pathways may contribute to diving acclimatization and susceptibility to decompression sickness in individuals undergoing chronic hyperbaric stress.
- The complex regulatory mechanisms governing NF-κB activation/deactivation by acute/chronic hyperbaric stress/decompression are currently under investigation.

Acknowledgements

This research was supported by a DRDC Technology Investment Fund and the US DoN Office of Naval Research.

Thank you.

Abstract A32

Annual Diving Fatality Rates Among Insured DAN Members

Denoble PJ, Vaithyanathan P, Vann RD

ANNUAL DIVING FATALITY RATES AMONG INSURED DAN MEMBERS

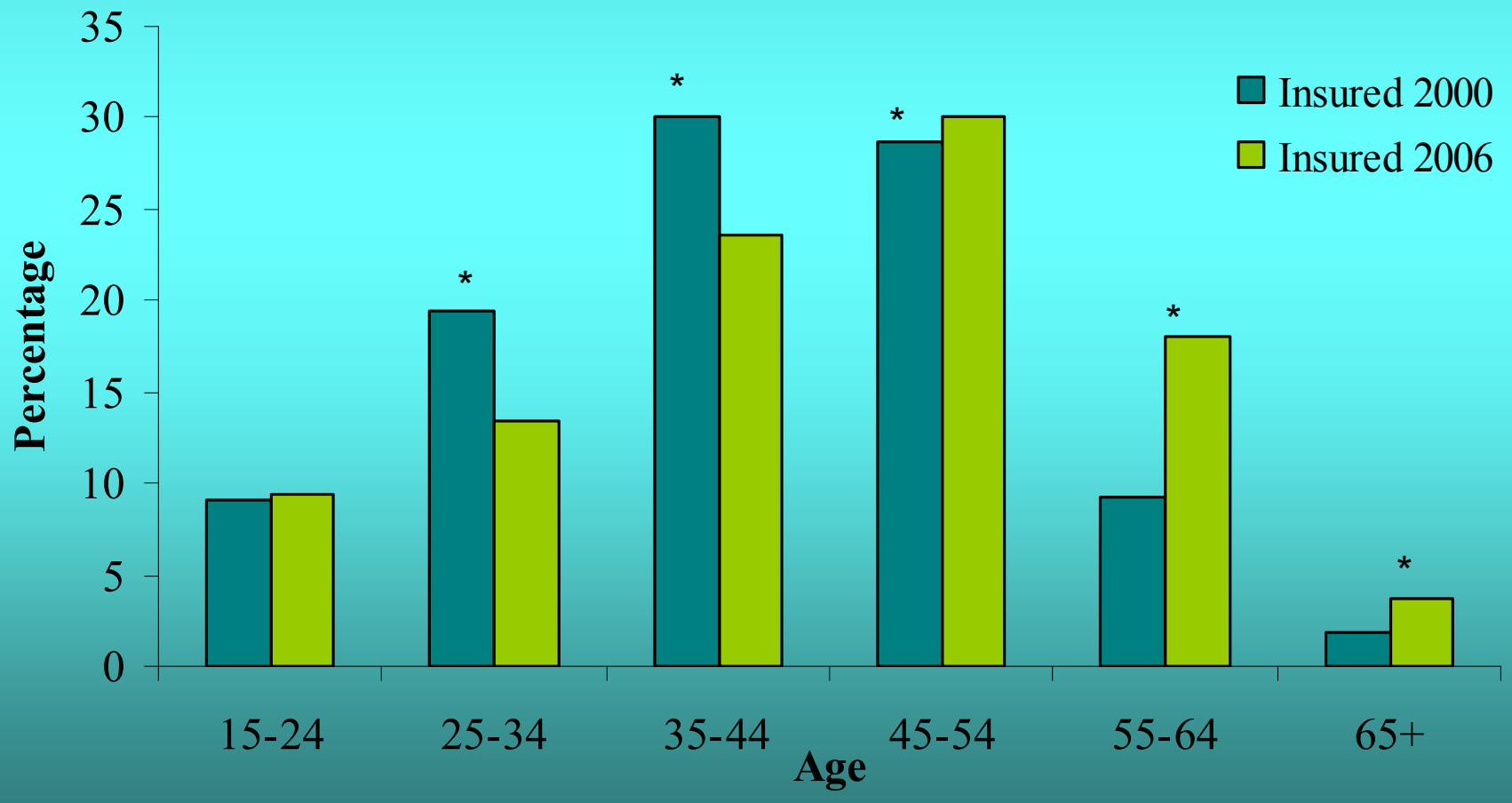
Denoble PJ[1,3], Vaithyanathan P[1], Vann RD[1,2]

[1]Divers Alert Network (DAN), Durham NC; [2]Center for Hyperbaric Medicine and Environmental Physiology, Duke University, Durham NC; [3]Department of Anesthesiology, Duke University Medical Center. Durham, NC

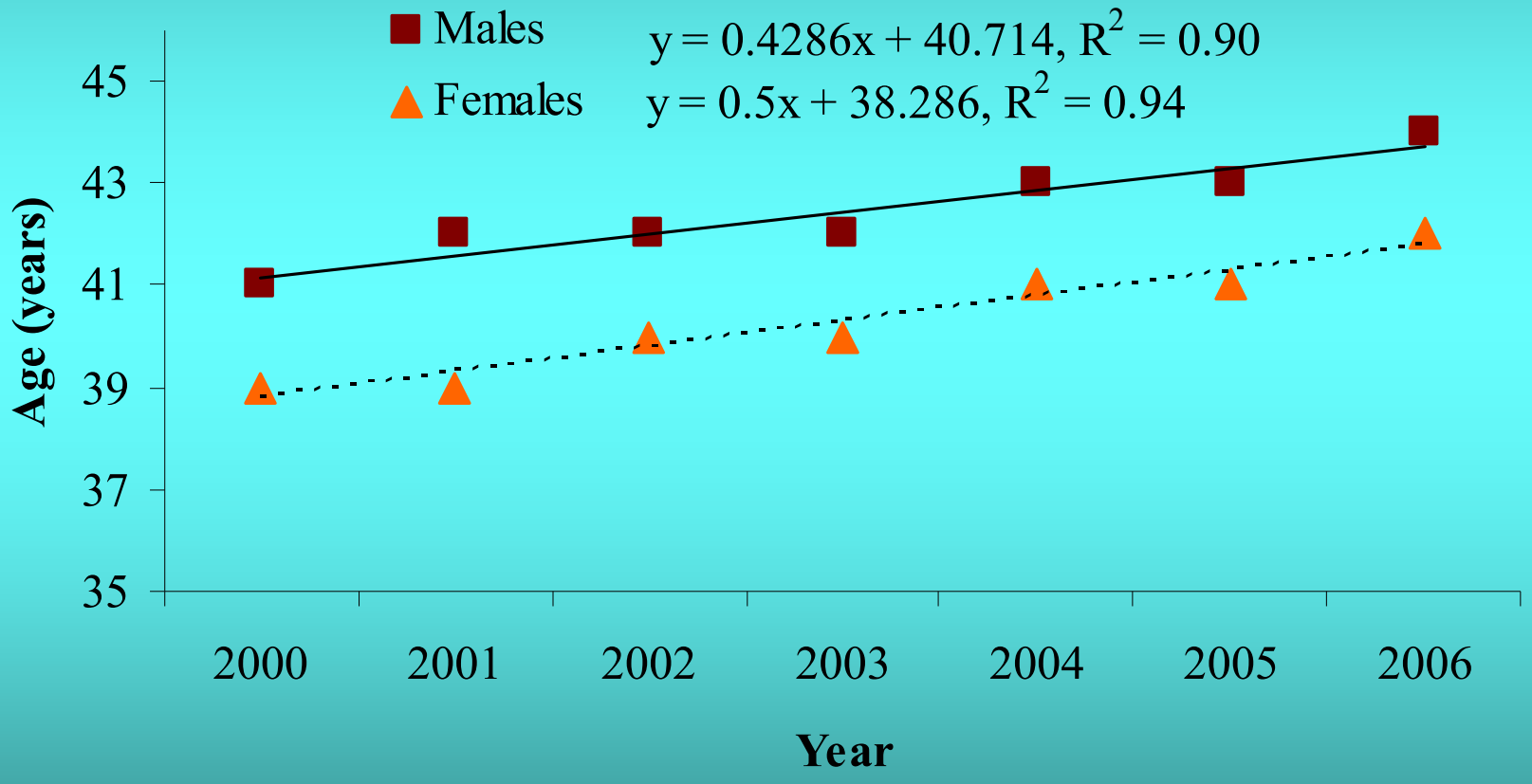
2008

Age Distribution of Insured DAN Members

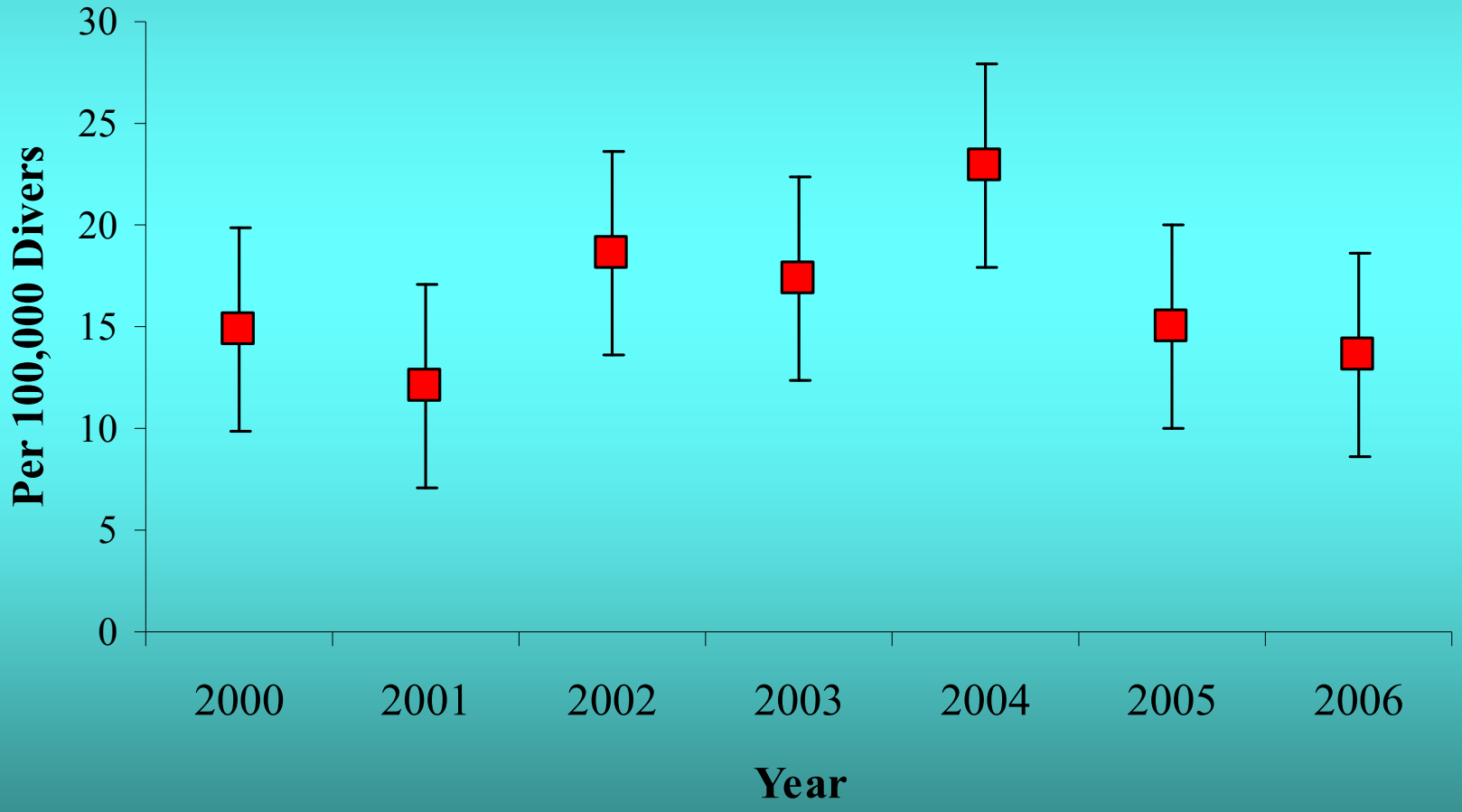
(n = 1,141,347 member years)



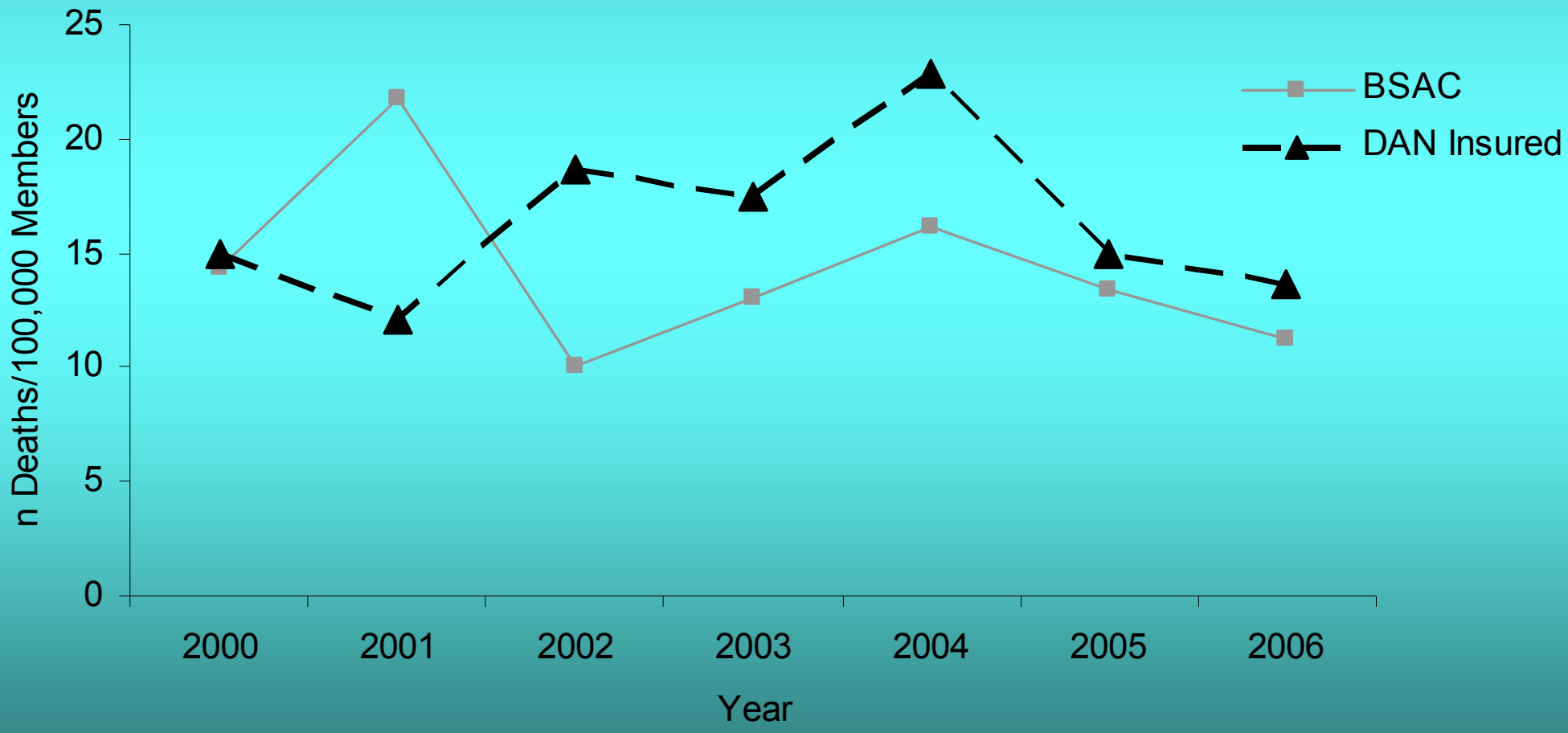
Mean Age of Insured DAN Members



Annual Fatality Rates



DAN vs. BSAC

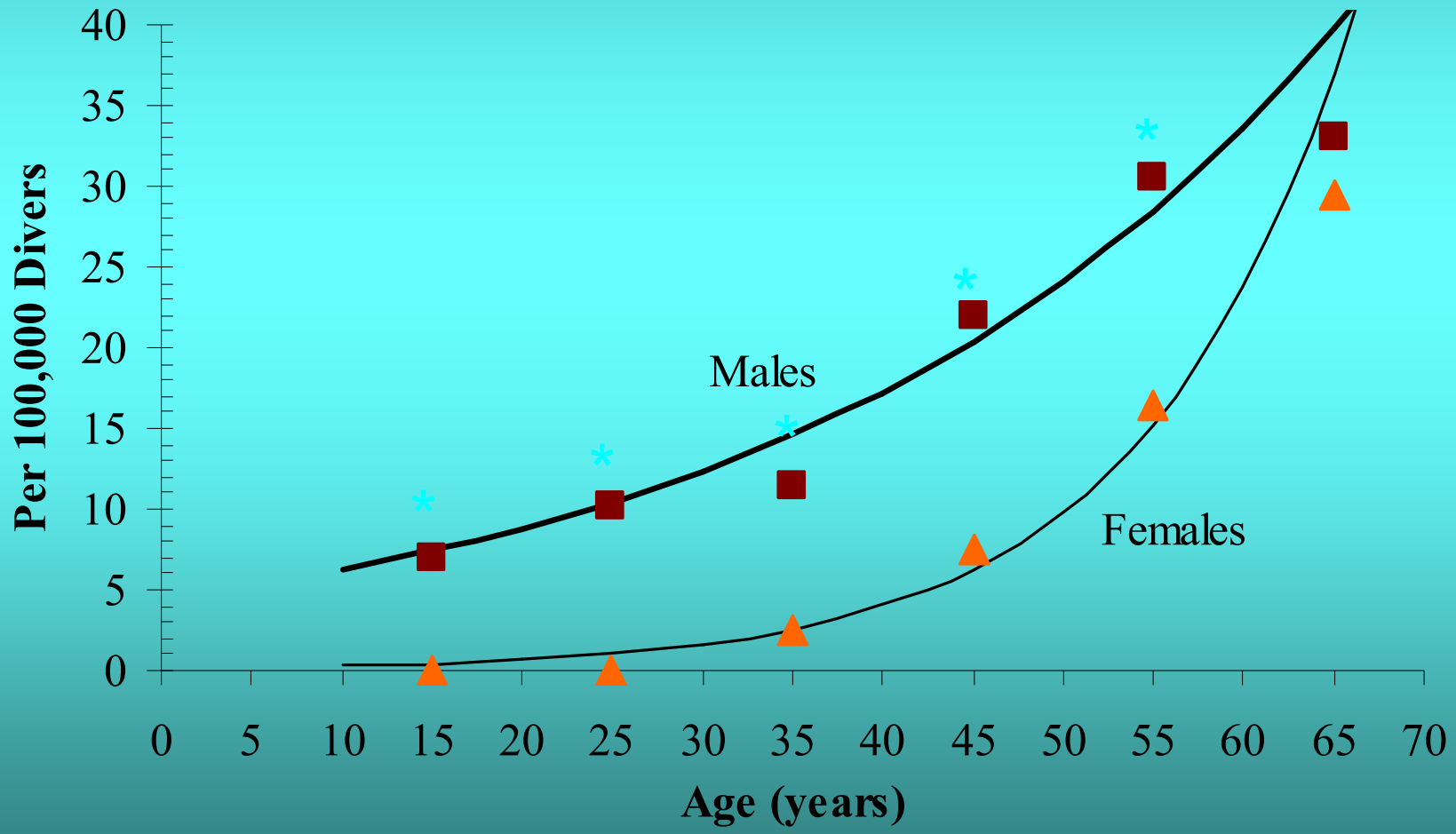

25
20
15
10
5
0
n Deaths/100,000 Members
2000
2001
2002
2003
2004
2005
2006
Year
BSAC
DAN Insured

Comparison of Fatality Rates

Subpopulation	Denominator	Time period	Rate	
			per 100,000 participants	per 100,000 dives
BSAC	estimated # dives	1999	17.4	1.1
BSAC	facts	2000/2006	14.4	
Australia	estimates	1989	34	1.7 to 3.4
USA	estimates	1989	16.7	0.8 to 1.6
DEMA	estimates	1990	3.2 to 4.2	
BC, Canada	tank count	1999/2000		2.04*
Orkney	facts	1999/2000		3 to 5.4*
Japan	tank count estimates			1 to 2.4
DAN	facts	2000/2006	16.4	0.8 to 1.6

Fatality Rates By Age

DAN Insured Members (2000-2006)



Cause of Death and Relative Risks With Age

Cause	<50 years	>=50 years	RR
Cardiac	5	29[1]	12.9
AGE	8	14	3.9
Drowning	15	17	2.5
Unknown	15	16	1.93
Other	7	3	0.96
Total	788,489	352,878	

[1] Rate: 8/100,000 (1/12,000)

Conclusions

- DAN insured members have overall scuba related death rate similar to other subgroups of recreational divers.
- The death rate is higher in males and increases with age for both genders.
- Excess death rate in older divers is associated with health related causes.
- Person with risk factors for heart diseases should seek medical evaluation prior to diving.