Recent advances in diving medicine research

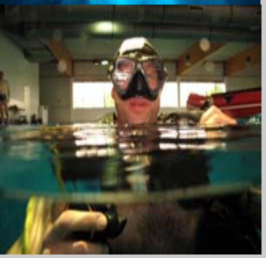
DAN Europe VGE Studies

A Century of Diving Medicine Research

- 1908 : J.S. Haldane – staged decompression prevents DCS
-
-

- 2003 : D. Elliott
  “After nearly 100 years of diving medicine research, we are almost certain of one thing: that bubbles have something to do with it”





Approaches in diving medicine research

- Epidemiological
  - DAN Accident Report, BSAC, DOSA, ...
- Biochemical research
  - Endothelial function (NO)
  - Heat Shock Proteins (HSP)
- Biopysical research
  - Bubble generation (decompression schedules)
  - Bubble dynamics (gas exchange tissue-bubble)
  - Bubble release
  - Bubble trajectory (PFO, pulmonary shunts)

Biochemical approach

- Physical exercise 24 hrs before the dive decreases bubble formation after the dive
- Diving decreases Flow Mediated Dilation, even when no bubbles are detected (endothelial MP)
- External NO suppletion decreases the FMD alterations after diving
- External heating before the dive decreases FMD alterations after dive (sauna, HSP)

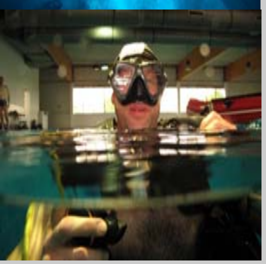
Venous Gas Emboli

- Present after up to 75-80% of "sports dives"
- Prevalence linked to "risk for DCS"
- Even if no "clinical DCS", possibly harmful (endo-thelial damage ?)

Bubbles vs decompression illness for compressed air dives: precordial bubbles at rest (from Spencer & Johanson, 1974; graded according to Spencer Code).

	Bubble grades				
	0	**I**	**II**	**III**	**IV**
No. of subjects (n=174)	110	27	18	14	5
No. with DCI (n=12)	1	1	3	6	4
Per cent incidence	1	4	17	43	80

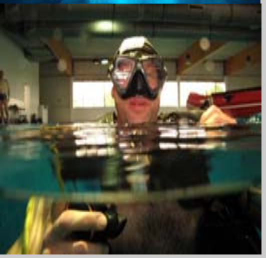




Quantification of VGE:

- Spencer scale (1974)
- Kisman-Masurel scale (1976)
- Ikeda scale (1989)
- DAN Bubble grade scale (2004)
- Eftedal-Brubakk scale (1997)

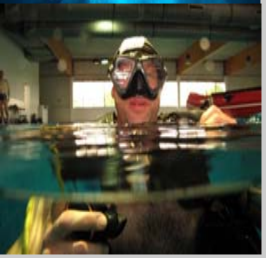
- Difficult, often subjective
- Semi-quantitative



Spencer Scale

- Grade 0 – complete lack of bubbles
- Grade 1 – occasional bubble signal, vast majority of cardiac cycles bubble-free
- Grade 2 – many, but less than half, of cardiac cycles contain bubbles, singly or in groups
- Grade 3 – all cardiac cycles contain bubbles in showers, but not overriding heart signals
- Grade 4 – bubbles sounding continuously during systole and diastole, overriding amplitude of normal heart signals





Kisman-Masurel Scale

Kisman-Masurel **frequency parameter** (bubbles per cardiac period)	
Code	**Frequency (*f*)**
0	0
1	1-2
2	Several, 3-8
3	Rolling, drumbeat ≥ 9
4	Continuous sound

Kisman-Masurel **percentage/duration parameter**		
Code	**Rest percentage (p)**	**Movement duration (d) cardiac periods**
0	0	0
1	1-10	1-2
2	10-50	3-5
3	50-99	6-10
4	100	>10

Kisman-Masurel **amplitude parameter**	
Code	**Amplitude (A)**
0	No bubbles discernible
1	Barely perceptible, A(b)<< A(c)
2	Moderate amplitude, A(b) < A(c)
3	Loud, A(b)= A(c)
4	Maximal, A(b)> A(c)

Kisman-Masurel Scale

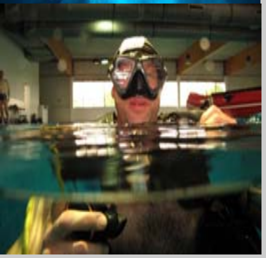
KM codes vs KM bubble grades							
ƒpA/ƒdA	Bubble grade	ƒpA/ƒdA	Bubble grade	ƒpA/ƒdA	Bubble grade	ƒpA/ƒdA	Bubble grade
111	I-	211	I-	311	I	411	II-
112	I	212	I	312	II-	412	II
113	I	213	I+	313	II	413	II+
114	I	214	II-	314	II	414	III-
121	I+	221	II-	321	II	421	III-
122	II	222	II	322	II+	422	III
123	II	223	II+	323	III-	423	III
124	II	224	II+	324	III	424	III+
131	II	231	II	331	III-	431	III
132	II	232	III-	332	III	432	III-
133	III-	233	III	333	III	433	IV-
134	III-	234	III	334	III+	434	IV
141	II	241	III-	341	III	441	III+
142	III-	242	III	342	III+	442	IV
143	III	243	III	343	III+	443	IV
144	III	244	III+	344	IV-	444	IV

Eftedal & Brubakk Scale

2D Echocardiography videos, 20-30 seconds

- Grade 0 – No observable bubbles
- Grade 1 – Occasional bubbles
- Grade 2 – At least one bubble every 4 cycles
- Grade 3 – At least one bubble every heart cycle
- Grade 4 – at least one bubble every cm^2
- Grade 5 – « white-out », single bubbles can not be discriminated



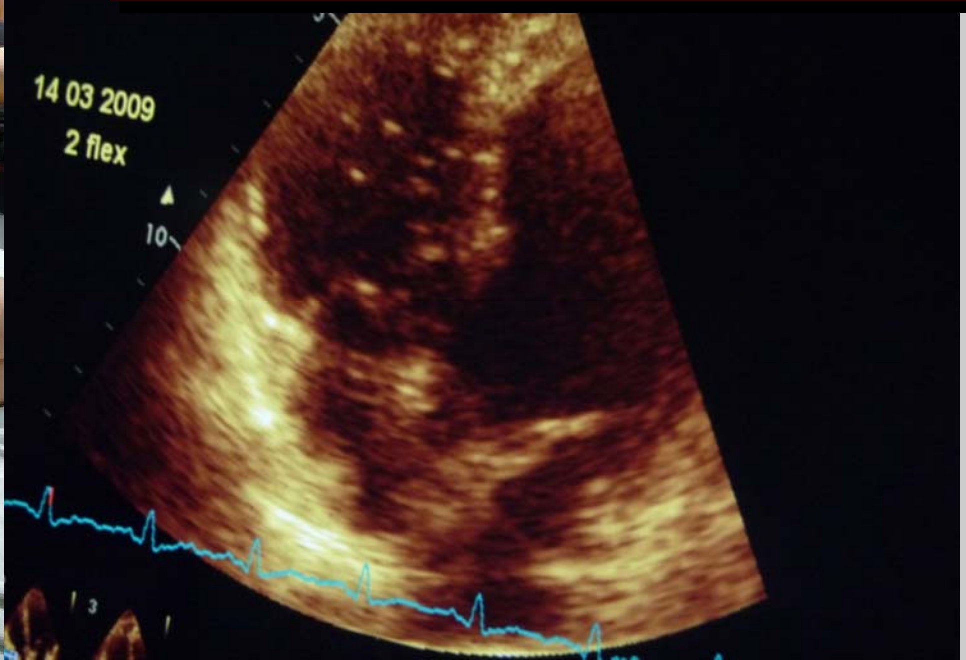


2010 : Echographic Bubble Counting

- Objective
- Reproducible
- Quantitative

ECHOGRAPHIC BUBBLE COUNT: AN OBJECTIVE MEASURE OF VENOUS GAS EMBOLI IN DIVING RESEARCH

Peter Germonpre, Costantino Balestra, Julie Merle, Pierre Lafere, Georges Obeid, Alessandro Marroni

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- Nitrogen bubbles are present after many (deeper) dives
- Individual variation in bubble “production”
- More bubbles = statistical higher risk for DCS
- Certain “interventions” before the dive can apparently reduce the risk for bubbles

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- Period : January-May 2009
  - 24 divers participated
  - “Standard” divers:
    - Male, 25-45 y, non smokers
    - BMI 20-25
    - Healthy, never DCS
  - One "standard"dive per week, Nemo33
  - 12 weeks, 7-8 dives / ps
  - Before and after dive: biometrics, echocardiography, blood sampling

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- 12 weeks of research

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- 198 “standard”dives

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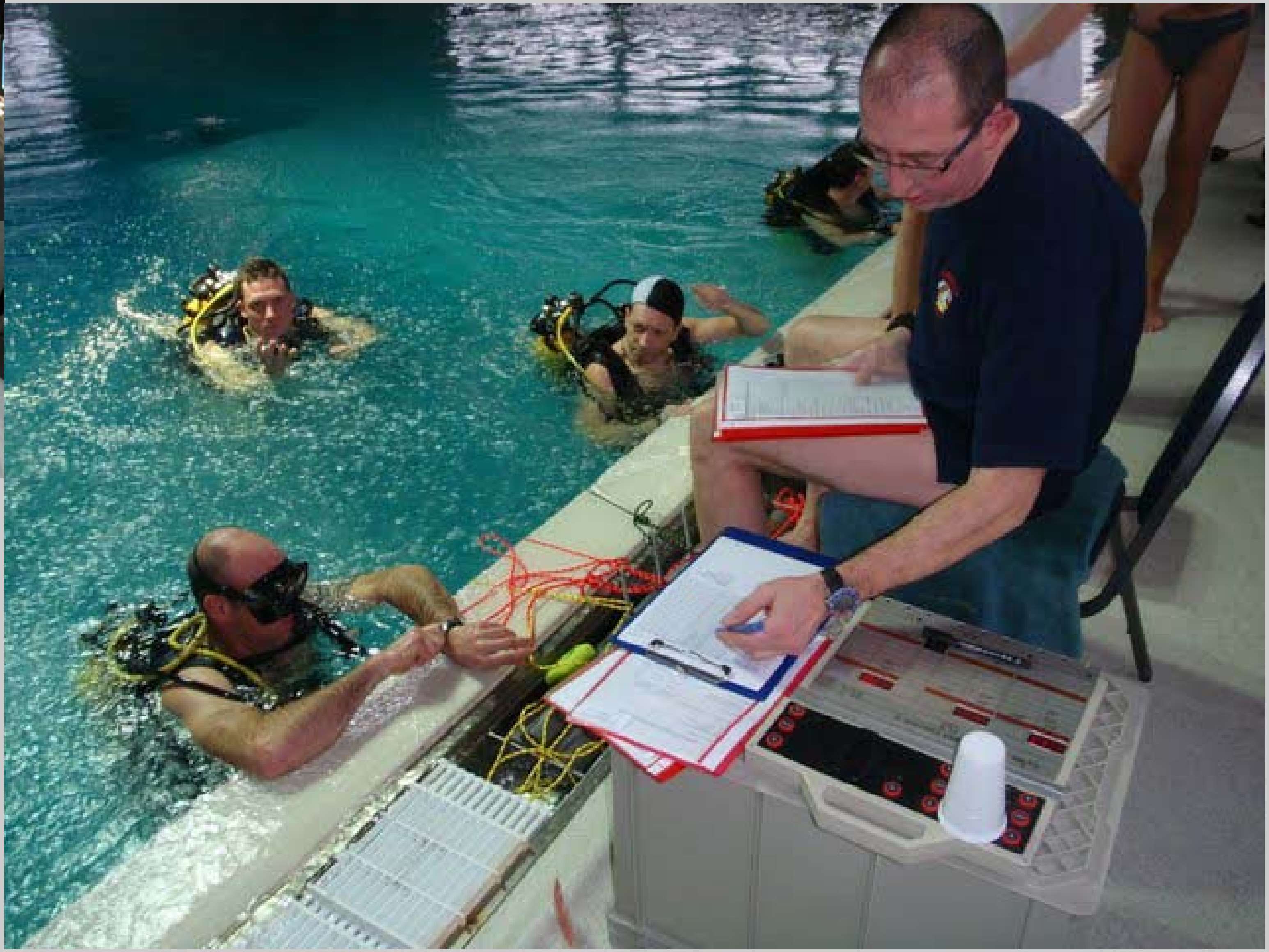
- 198 “standard”dives



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- 4050+ measurements

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- 4050+ measurements

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- 4050+ measurements

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- 4050+ measurements

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- 1188 echocardiographies

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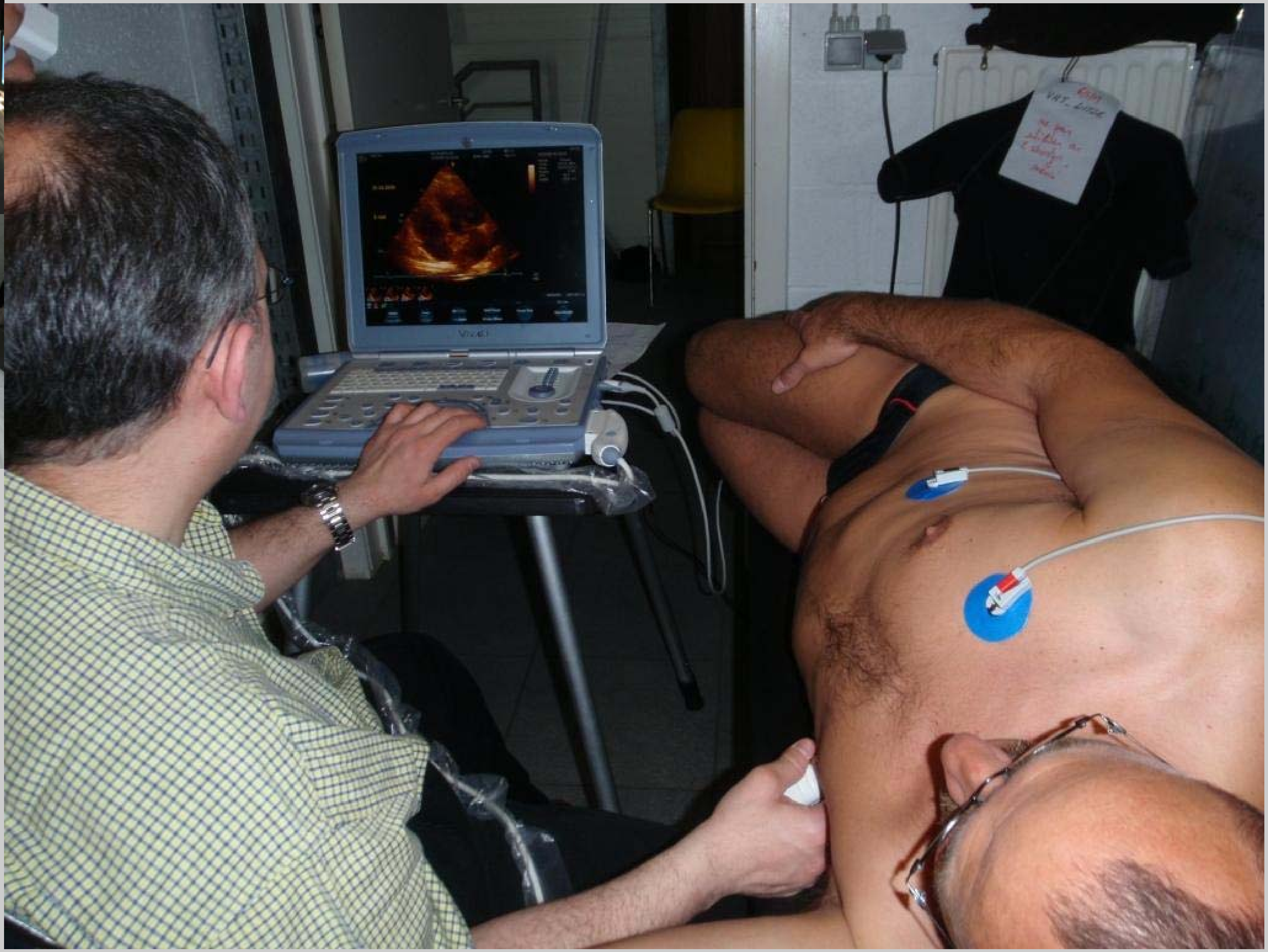
- 1188 echocardiographies



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Effect of preconditioning

- Vibration
- Heating (sauna)
- (dark) chocolate
- Anti-oxidants

- Bubbles
- Flow Mediated Dilation

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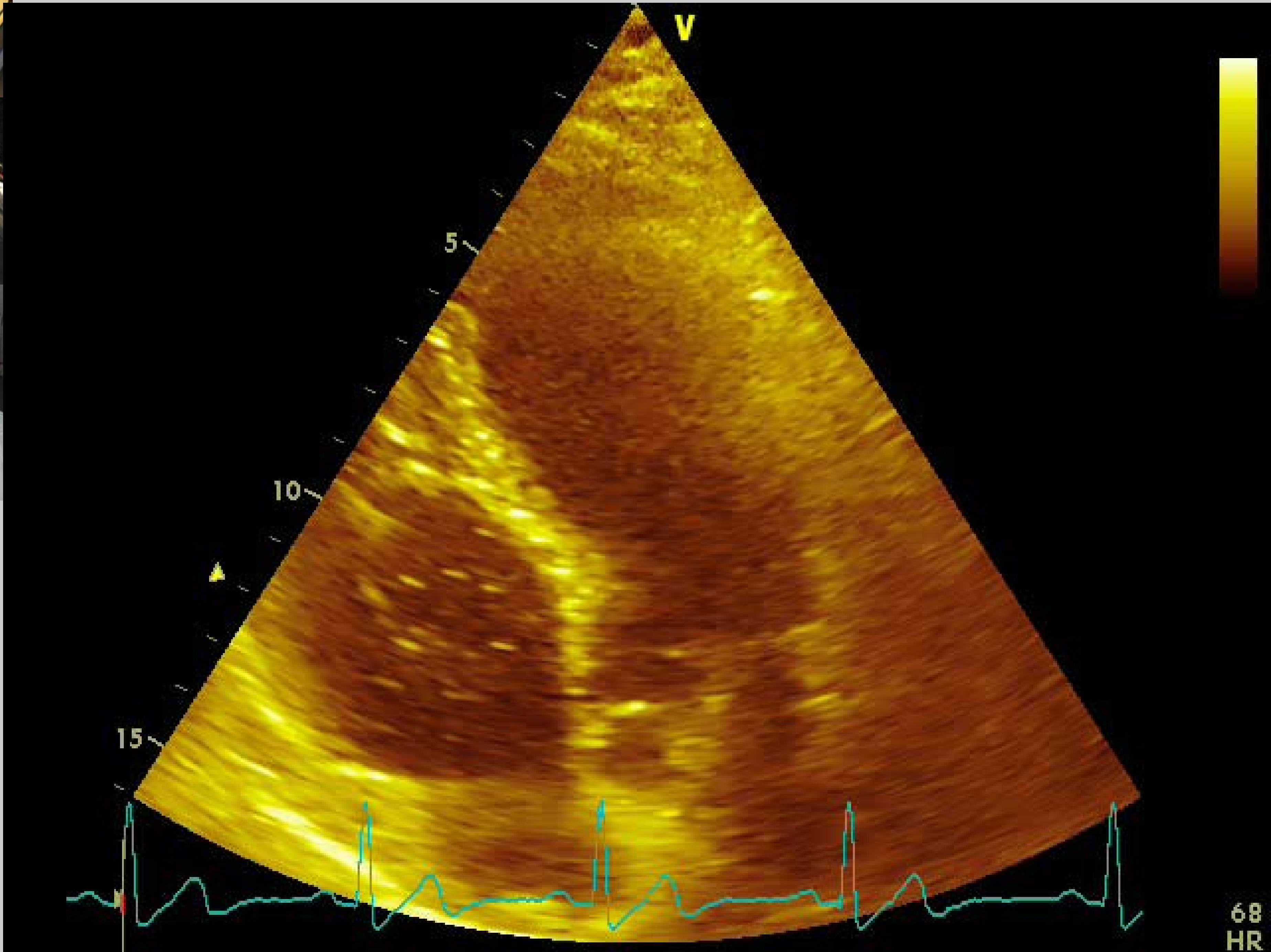

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- Intervention: vibration

RESEARCH ARTICLE

Pre-Dive Vibration Effect on Bubble Formation After a 30-m Dive Requiring a Decompression Stop

PETER GERMONPRÉ, JEAN-MICHEL PONTIER,
EMMANUEL GEMPP, JEAN-ERIC BLATTEAU,
STEFAAN DENEWETH, PIERRE LAFÈRE, ALESSANDRO MARRONI,
AND COSTANTINO BALESTRA

GERMONPRE P, PONTIER J-M, GEMPP E, BLATTEAU J-E, DENEWETH S, LAFÉRE P, MARRONI A, BALESTRA C. *Pre-dive vibration effect on bubble formation after a 30-m dive requiring a decompression stop.* Aviat Space Environ Med 2010; 81:1–5.

Introduction: The preconditioning of divers to reduce post-dive decompression sickness (DCS) has gained increased interest in diving medical research over the last few years. The beneficial effects of physical exercise, oxygen breathing, hyperbaric exposure, heat exposure, hyperhydration, or nitroglycerin administration before the dive are only a few examples of ongoing research. In this work, we investigated the effects of pre-dive whole-body vibration on post-dive bubble formation. ***Methods:*** Following French Navy standard dive procedures, 14 healthy male military divers performed 2 identical dives 1 wk apart to 30 m of seawater (msw) for 30 min. One of the dives was randomly preceded by a 30-min whole-body vibration session (frequencies 35-40 Hz), 1 h before the dive. Post-dive bubbles were measured precordially 30, 60, and 90 min after the dive and were graded according to the Kissman Integrated Severity Score (KISS) protocol, with and without knee flexing. Arterial

beneficial effects of pre-dive exercise (5,14), oxygen breathing (9), pre-dive hyperbaric sessions (19,24), heat preconditioning (6), hydration (15), and nitric oxide (NO) donor administration (13). Most of these experiments try to influence bubble formation by modifying biophysical or chemical properties of the endothelial surface, on which gas bubbles or nuclei are presumed to be forming. In this paper, we report the possibility of reducing post-dive bubble formation by a short bout of mechanical low-frequency vibrations of the whole body 1 h before the dive.

METHODS

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- Intervention: vibration

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- Intervention: sauna

RESEARCH ARTICLE

Predive Sauna and Venous Gas Bubbles Upon Decompression from 400 kPa.

Jean- È ric Blatteau, Emmanuel Gempp,
Costantino Balestra, Tony Mets, and Peter Germonpre

Blatteau J-È, Gempp E, Balestra C, Mets T, Germonpre P. *Predive sauna and venous gas bubbles upon decompression from 400 kPa.* Aviat Space Environ Med 2008; 79:1–6.

Introduction: This study investigated the influence of a far infrared-ray dry sauna-induced heat exposure before a simulated dive on bubble formation, and examined the concomitant adjustments in hemodynamic parameters. ***Methods:*** There were 16 divers who were compressed in a hyperbaric chamber to 400 kPa (30 msw) for 25 min and decompressed at 100 kPa · min^{-1} with a 4-min stop at 130 kPa. Each diver performed two dives 5 d apart, one with and one without a predive sauna session for 30 min at 65°C ending 1 h prior to the dive. Circulating venous bubbles were detected with a precordial Doppler 20, 40, and 60 min after surfacing, at rest, and after flexions. Brachial artery flow mediated dilation (FMD), blood pressure, and bodyweight measurements were taken before and after the sauna session along with blood samples for analysis of plasma volume (PV), protein concentrations, plasma osmolality, and plasma HSP70. ***Results:*** A single session of sauna ending 1 h prior to a simulated dive significantly reduced bubble formation [−27.2% (at rest) to 35.4% (after flexions)]. The sauna session led to an extracellular dehydration, resulting in hypovolemia (−2.7% PV) and −0.6% bodyweight loss. A significant rise of FMD and a reduction in systolic blood pressure and pulse pressure were observed. Plasma HSP70 significantly increased

from decompression (23). It has been suggested that the protective effect of heat exposure against DCS in rats could be related to biochemical processes involving heat shock proteins (HSP) of the 70-kDa range (9,23), and such HSP70 induction could also be involved in the mechanisms responsible for diving acclimatization after repeated compression-decompression cycles (37). Moreover, it has been demonstrated that heat-inducible proteins are also able to interact with the endothelial nitric oxide (NO) pathway (20), which may influence the degree of bubble formation in hyperbaric conditions (40,41).

It is well recognized that high environmental temperatures lead to sweat response, resulting in dehydration. In a previous work, we have also shown that moderate dehydration resulting in stroke volume reduction induced by a predive exercise could decrease venous cir-

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- Intervention: sauna

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- Intervention: chocolate

Cocoa Reduces Blood Pressure and Insulin Resistance and Improves Endothelium-Dependent Vasodilation in Hypertensives

Davide Grassi, Stefano Necozione, Cristina Lippi, Giuseppe Croce, Letizia Valeri, Paolo Pasqualetti, Giovambattista Desideri, Jeffrey B. Blumberg, Claudio Ferri

Abstract—Consumption of flavanol-rich dark chocolate (DC) has been shown to decrease blood pressure (BP) and insulin resistance in healthy subjects, suggesting similar benefits in patients with essential hypertension (EH). Therefore, we tested the effect of DC on 24-hour ambulatory BP, flow-mediated dilation (FMD), and oral glucose tolerance tests (OGTTs) in patients with EH. After a 7-day chocolate-free run-in phase, 20 never-treated, grade I patients with EH (10 males; 43.7±7.8 years) were randomized to receive either 100 g per day DC (containing 88 mg flavanols) or 90 g per day flavanol-free white chocolate (WC) in an isocaloric manner for 15 days. After a second 7-day chocolate-free period, patients were crossed over to the other treatment. Noninvasive 24-hour ambulatory BP, FMD, OGTT, serum cholesterol, and markers of vascular inflammation were evaluated at the end of each treatment. The homeostasis model assessment of insulin resistance (HOMA-IR), quantitative insulin sensitivity check index (QUICKI), and insulin sensitivity index (ISI) were calculated from OGTT values. Ambulatory BP decreased after DC (24-hour systolic BP −11.9±7.7 mm Hg, $P<0.0001$; 24-hour diastolic BP −8.5±5.0 mm Hg, $P<0.0001$) but not WC. DC but not WC decreased HOMA-IR ($P<0.0001$), but it improved QUICKI, ISI, and FMD. DC also decreased serum LDL cholesterol (from 3.4±0.5 to 3.0±0.6 mmol/L; $P<0.05$). In summary, DC decreased BP and serum LDL cholesterol, improved FMD, and ameliorated insulin sensitivity in hypertensives. These results suggest that, while balancing total calorie intake, flavanols from cocoa products may provide some cardiovascular benefit if included as part of a healthy diet for patients with EH. (***Hypertension*. 2005;46:398-405.**)

Key Words: endothelium ■ insulin ■ hypertension, essential

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- Intervention: chocolate

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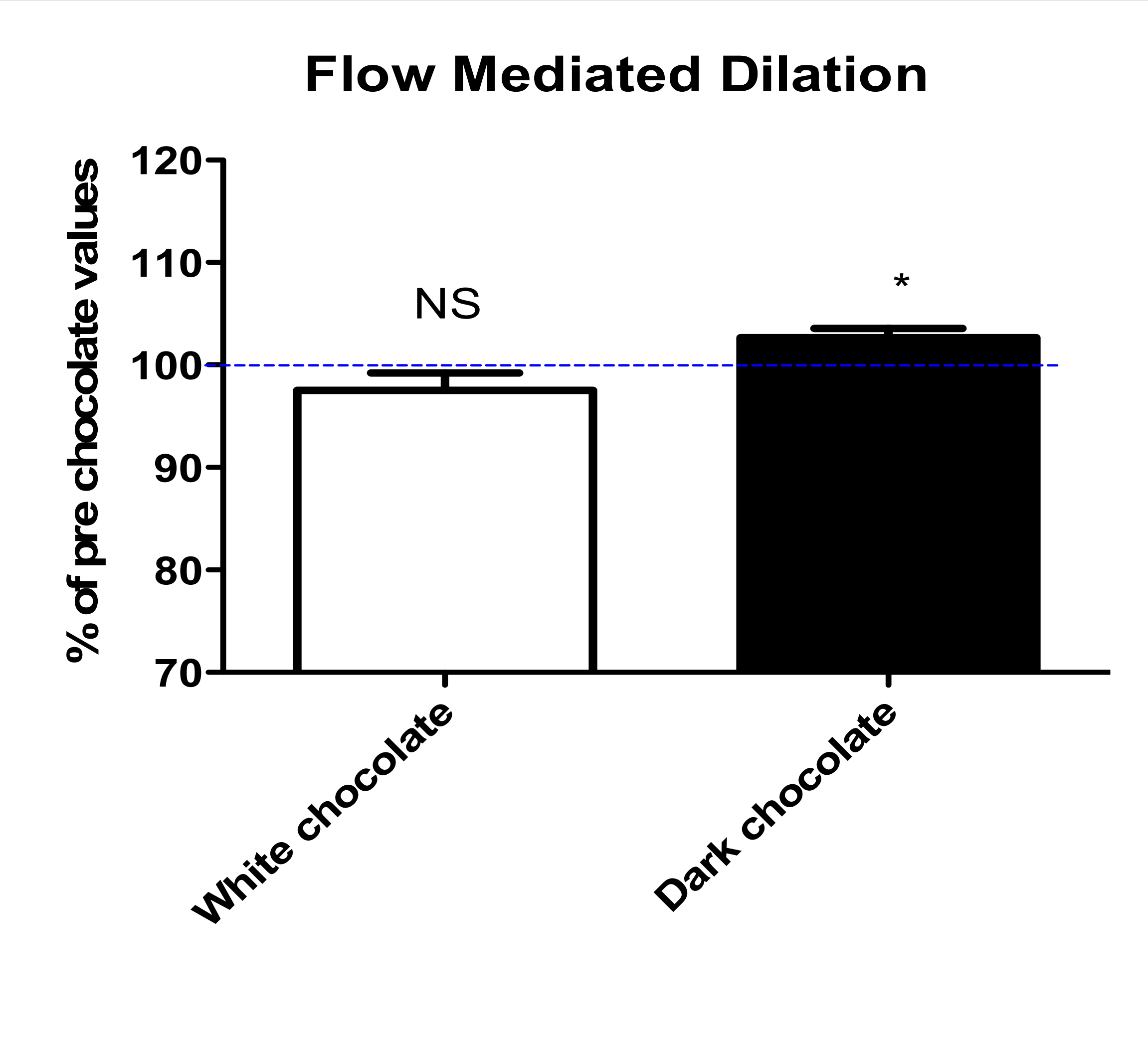
- Intervention: chocolate



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- Intervention: anti-oxydants

J Physiol 578.3 (2007) pp 859–870 859

The effects of acute oral antioxidants on diving-induced alterations in human cardiovascular function

Ante Obad[1], Ivan Palada[1], Zoran Valic[1], Vladimir Ivančev[1], Darija Baković[1], Ulrik Wisløff[2], Alf O. Brubakk[2] and Željko Dujić[1]

[1]*Department of Physiology, University of Split School of Medicine, Split, Croatia*
[2]*Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway*

Diving-induced acute alterations in cardiovascular function such as arterial endothelial dysfunction, increased pulmonary artery pressure (PAP) and reduced heart function have been recently reported. We tested the effects of acute antioxidants on arterial endothelial function, PAP and heart function before and after a field dive. Vitamins C (2 g) and E (400 IU) were given to subjects 2 h before a second dive (protocol 1) and in a placebo-controlled crossover study design (protocol 2). Seven experienced divers performed open sea dives to 30 msw with standard decompression in a non-randomized protocol, and six of them participated in a randomized trial. Before and after the dives ventricular volumes and function and pulmonary and brachial artery function were assessed by ultrasound. The control dive resulted in a significant reduction in flow-mediated dilatation (FMD) and heart function with increased mean PAP. Twenty-four hours after the control dive FMD was still reduced 37% below baseline (8.1 *versus* 5.1%, $P = 0.005$), while right ventricle ejection fraction (RV-EF), left ventricle EF and endocardial fractional shortening were reduced much less (∼2–3%). At the same time RV end-systolic volume was increased by 9% and mean PAP by 5%. Acute antioxidants significantly attenuated

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- Intervention: anti-oxydants

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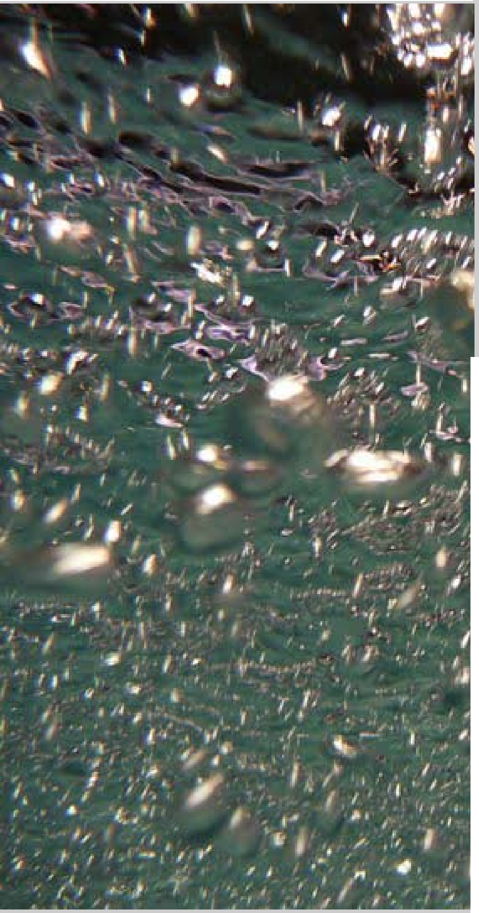
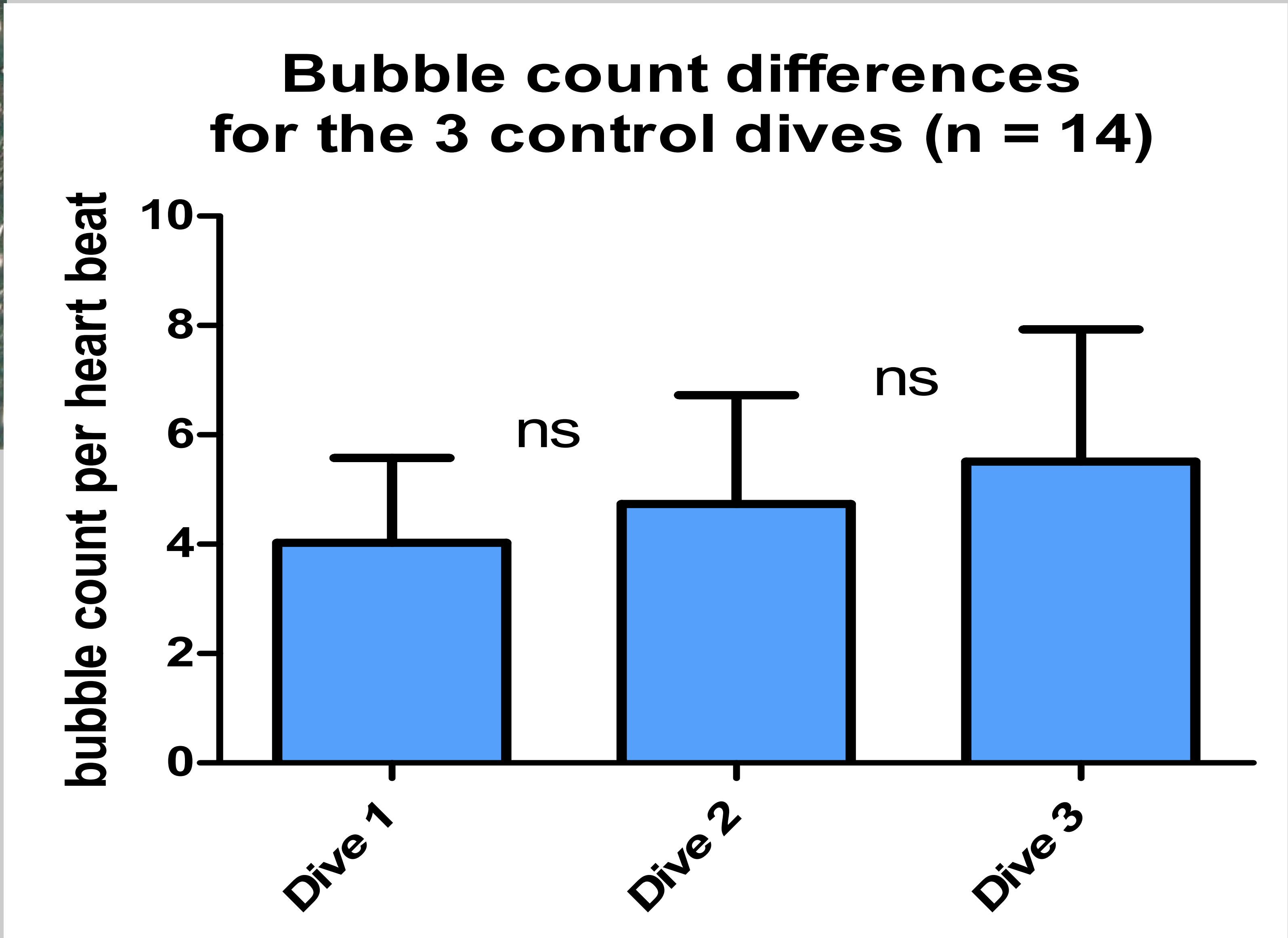
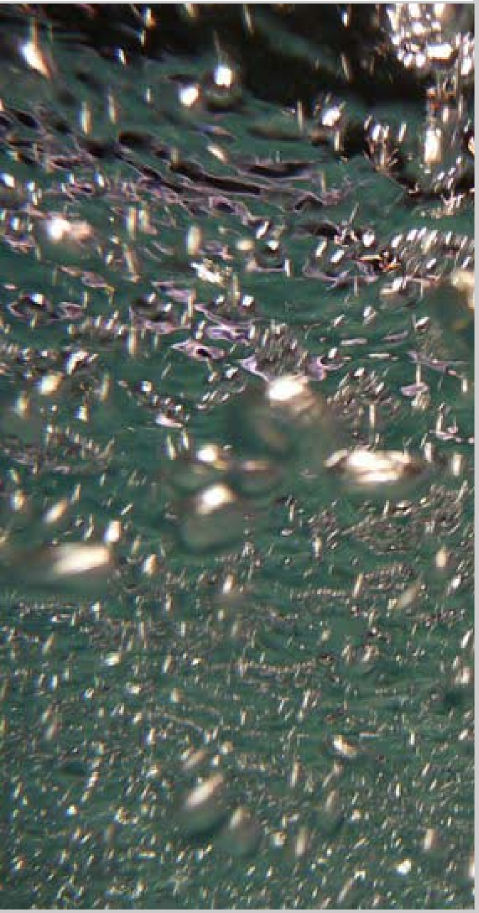
- Results : bubbles







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- Results : bubbles

- Three « standard » dives (with no pre-dive intervention) in randomised order
- 14 of the 24 divers were « bubbling »
- Stability of « bubblers » : OK for « interventional » studies

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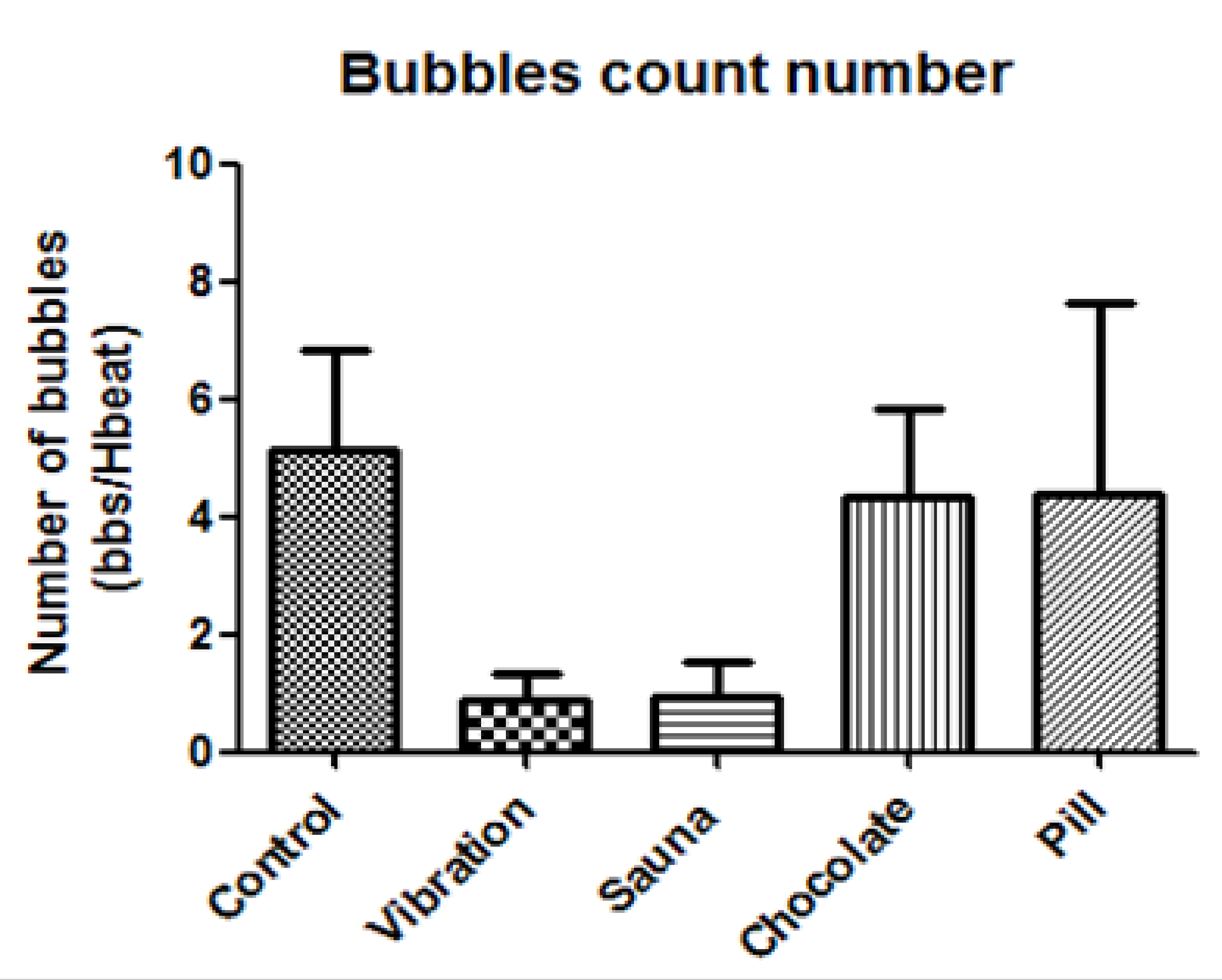
- Results : preconditioning



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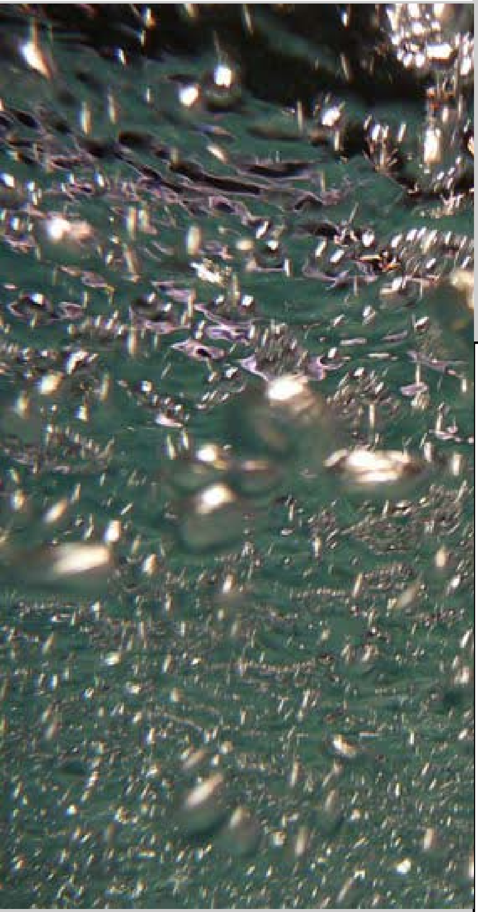

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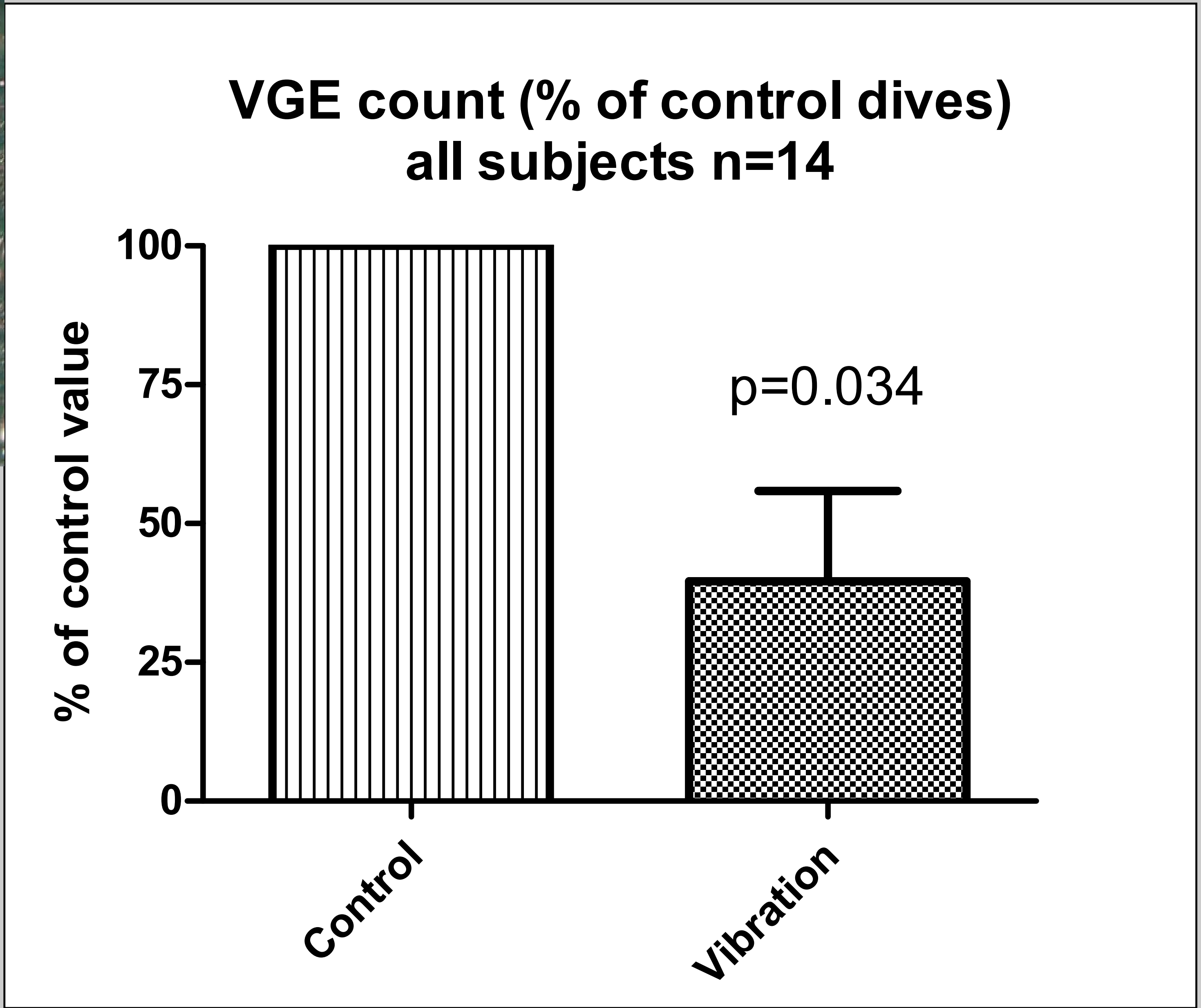
- Results : vibration



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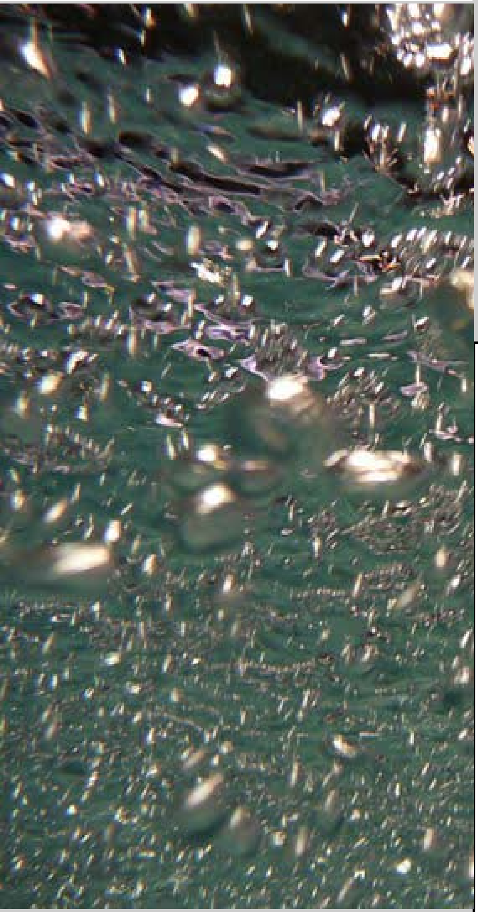
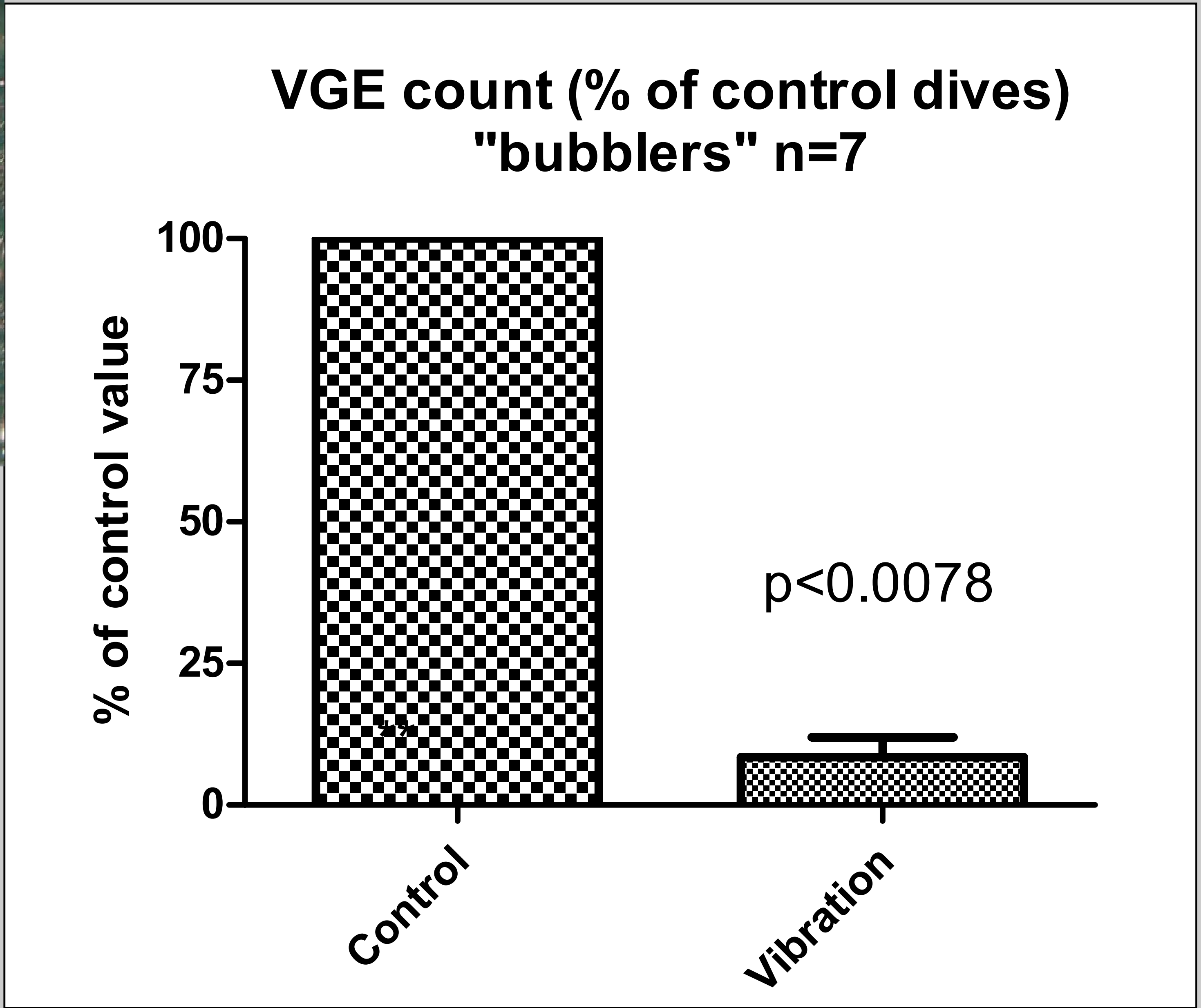
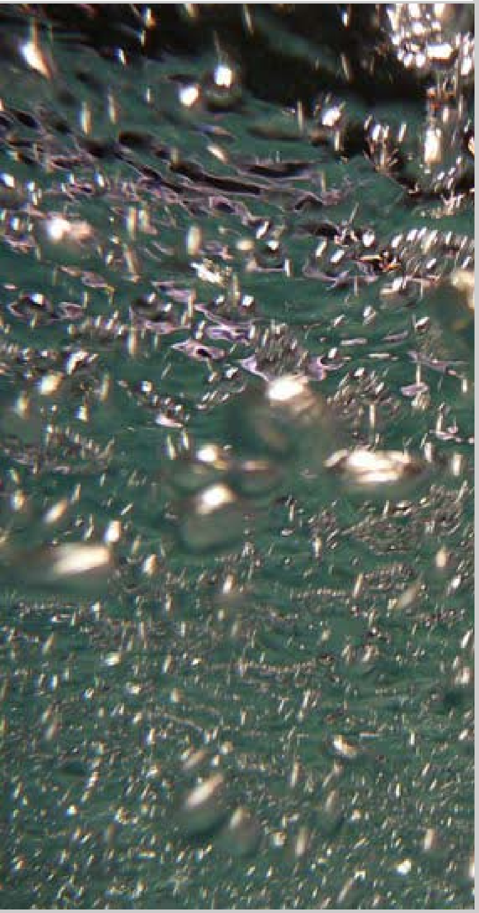
- Results : vibration







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- Conclusions : vibration

- Significant reduction in number of bubbles after the dive
- Verification of other parameters : no significant differences between dives, so effect attributable to vibration only

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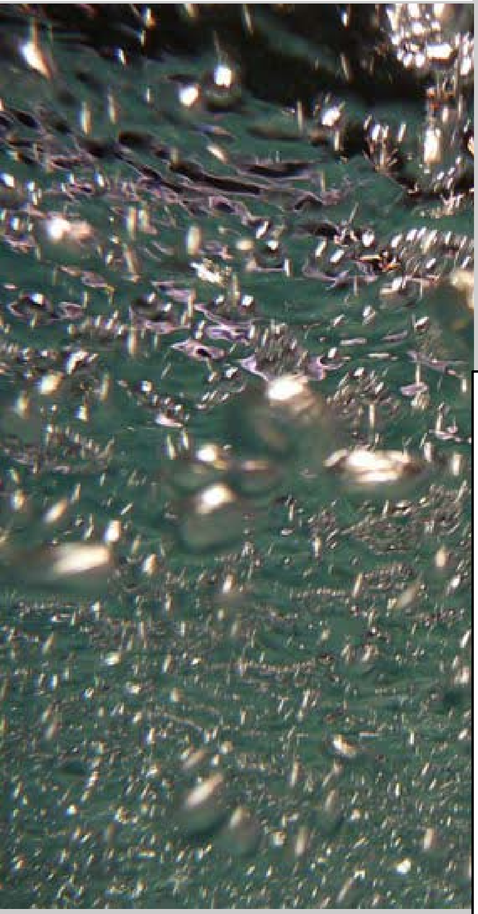
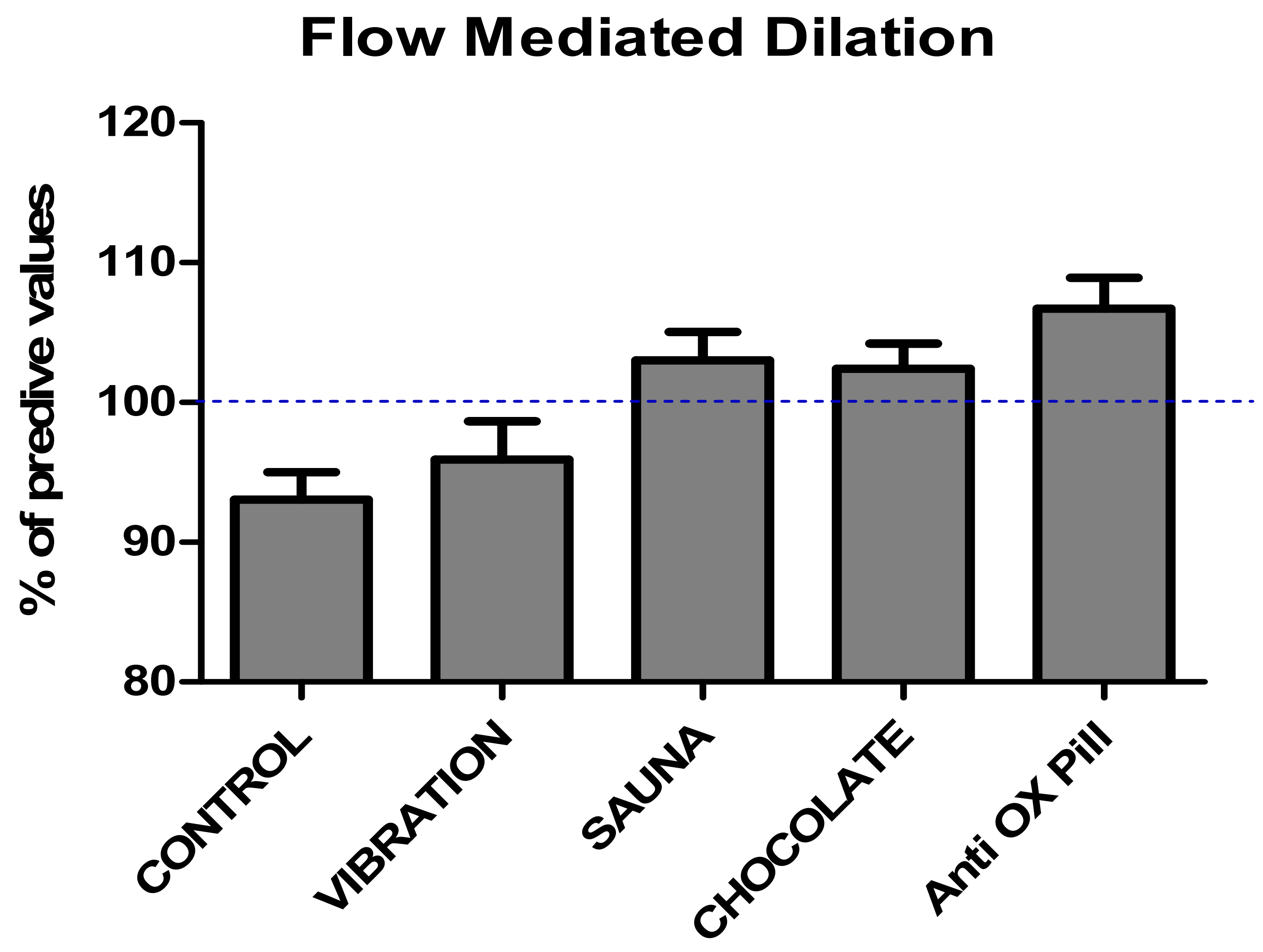
- Results : FMD





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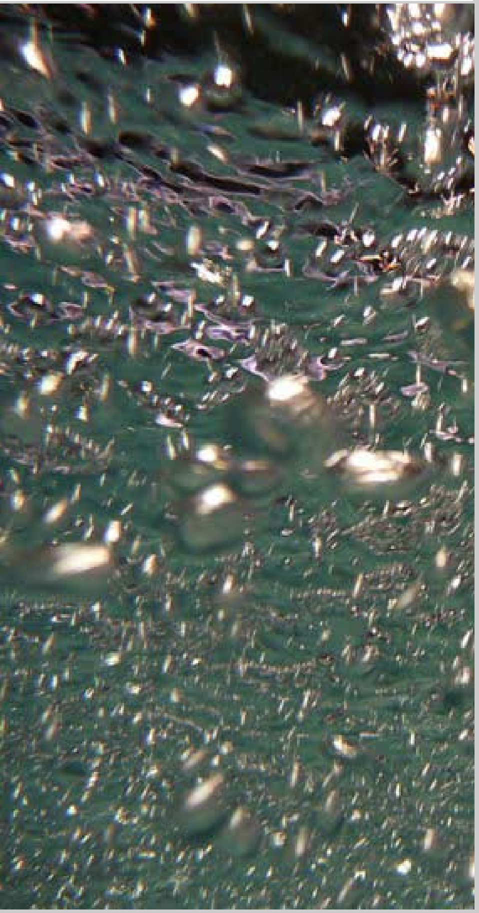

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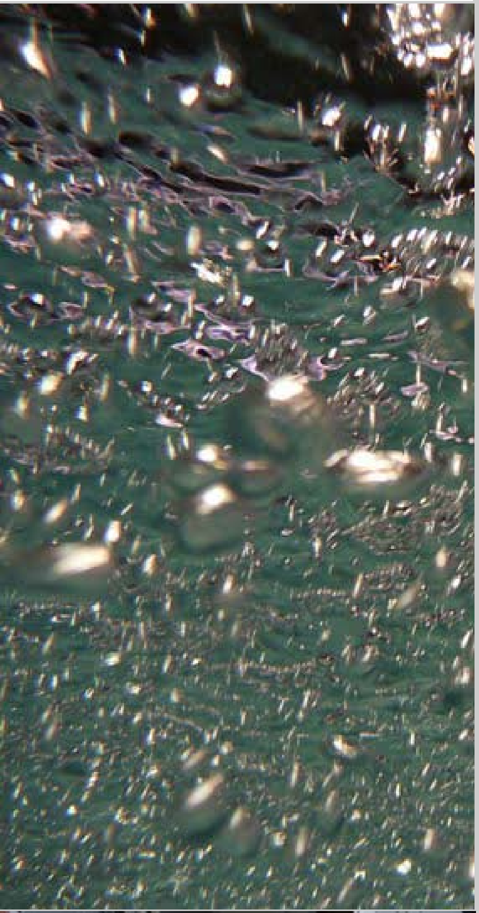
- Results : FMD

- Sauna, chocolate and anti-oxidants all restored FMD values
- Chocolate and anti-oxidants: no influence on bubbles
- Generally: no correlation between FMD and bubbles → NO-mediated hypothesis more prominent

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- Still to be analysed and "crossed"
  - ? Lipid levels in blood before the dive
  - ? Alimentary habits (saturated/unsaturated lipid profile)
  - ? Urinary density and dehydratation
  - ? Physical fitness
  - ? WBC / platelets / …

- To be continued…

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