

# Biochemical defence mechanisms and decompression injury

PhD student Lise Fismen, UiB and NUI AS

Supervisors:

Professor Asbjørn M. Svardal, UiB  
dr. philos Rune Djurhuus, NUI AS

# Aims

- Establish tools and perform analyses to measure important biochemical factors
- Understand biochemical mechanisms that may prevent adverse effects of decompression stress in saturation diving

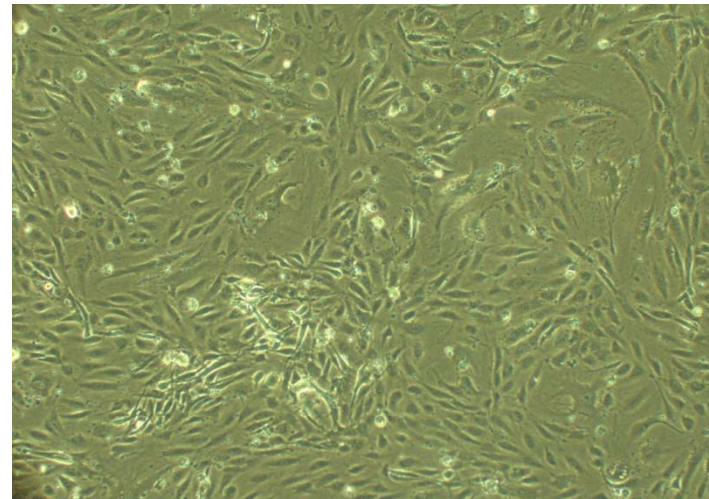
## Background

- Heavy exercise 20-24 hrs prior to diving reduced bubble formation and conferred protection against DCS (man and rat)
- Heat stress (42°C) 24 hrs prior to dive protected against injury due to decompression (rat)
- Possible role for nitric oxide (NO) in bubble formation and/or endothelial injury resulting from such bubbles

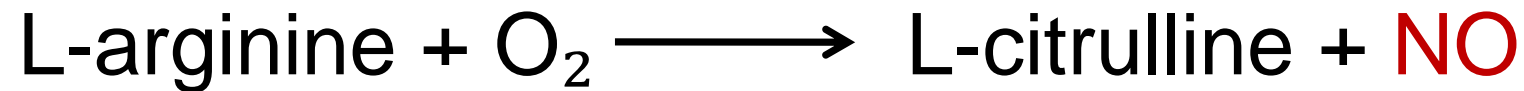
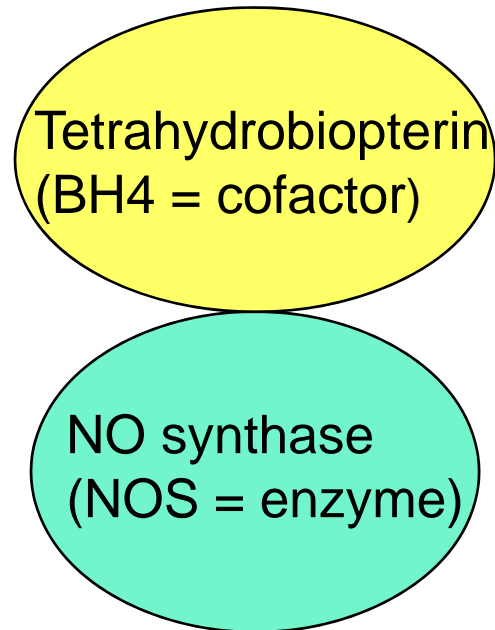
# Model system

Human endothelial cells exposed to:

- heat stress (45°C) to induce similar stress responses to those induced by heat (rat) and physical exercise (man and rat)
- simulated diving both at normal and increased oxygen levels



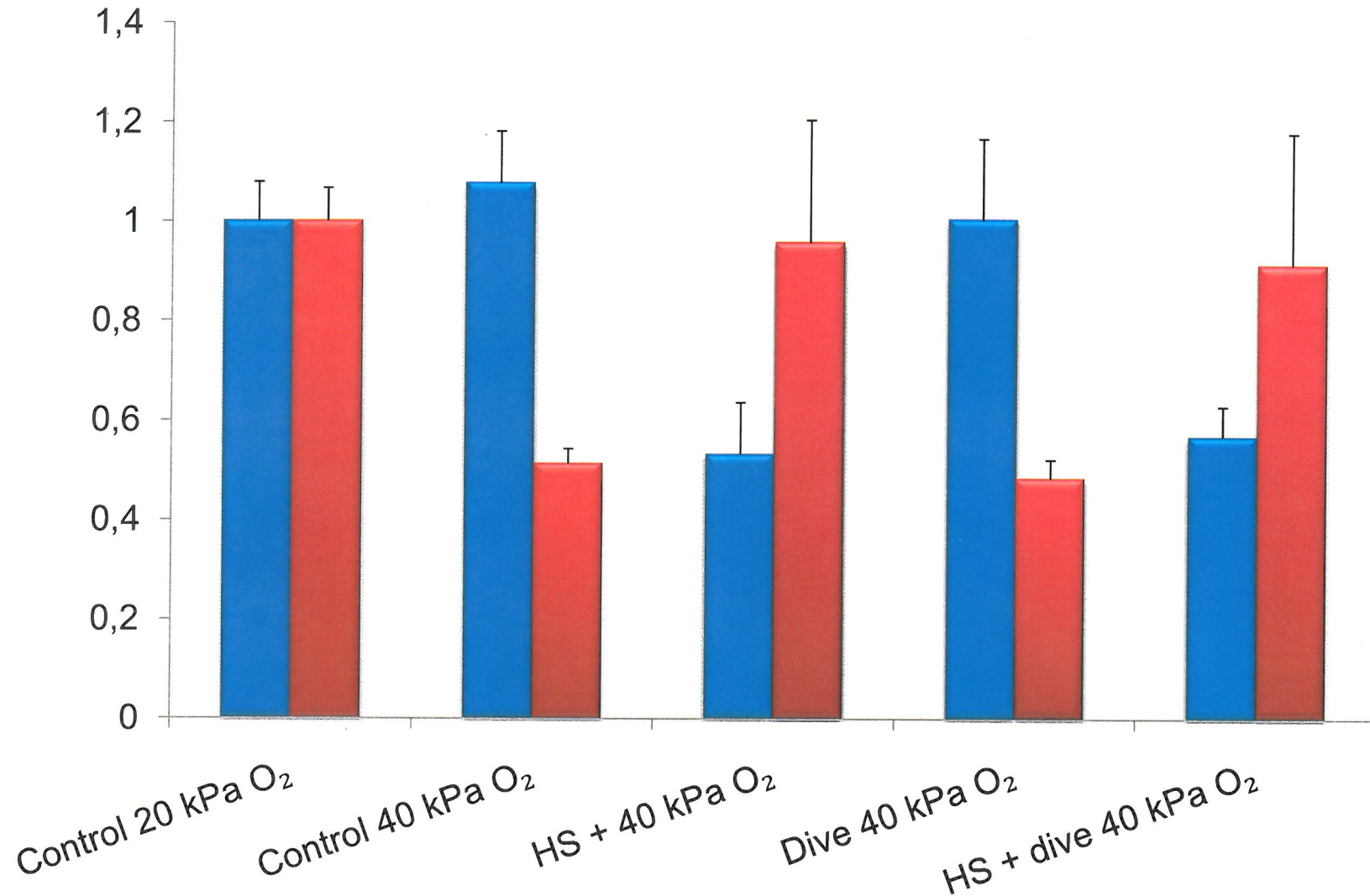
# Central biochemical reaction in the cells



# Results

■ NOS, relative to Control 20 kPa O<sub>2</sub>

■ BH4, relative to Control 20 kPa O<sub>2</sub>

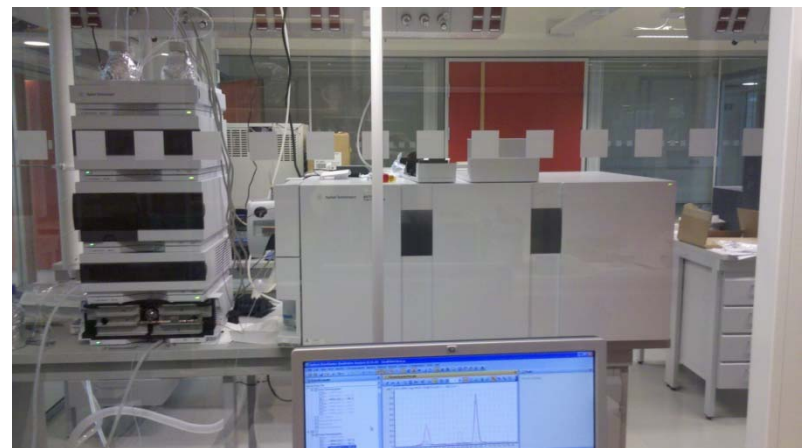


# Conclusions

- Decreased levels of BH4 may decrease endothelial generation of NO - increase risk of DCS?
- Pharmacological intervention to increase BH4 may sustain NO generation - reduce risk of DCS?

## Future potential of project

- BH4 method can be applied on plasma - opens for measurements in eg. rat/human models
- BH4 - also cofactor for enzymes producing neurotransmitters (dopamine, serotonin, melatonin, noradrenaline)
- BH4 improves endothelial function in diabetics, smokers and patients with hypercholesterolemia



# Marianne B. Havnes

PhD student

Supervisors:

Andreas Møllerløkken (NTNU),  
Alf Brubakk (NTNU) and Arvid Hope (NUI).



 Forskningsrådet

 **NTNU**  
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# Projects

- Central nervous system and diving
- Central nervous system sensitive biomarkers and diving
- Environmental factors during diving
  - Immune response to *Pseudomonas aeruginosa*



# Health challenges in saturation diving

- Health problems, such as skin and ear infections, in divers working on the Norwegian Continental Shelf have been systematically registered since 1985
- Reported to the Petroleum Safety Authority Norway (1990-2010)
  - 4 incidents of DCS and
  - 201 incidents of outer ear infection

(DSYS database, 2010).

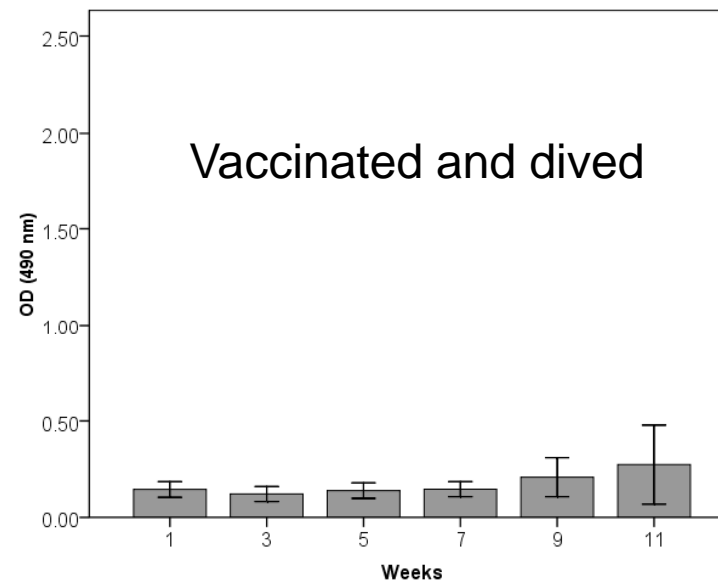
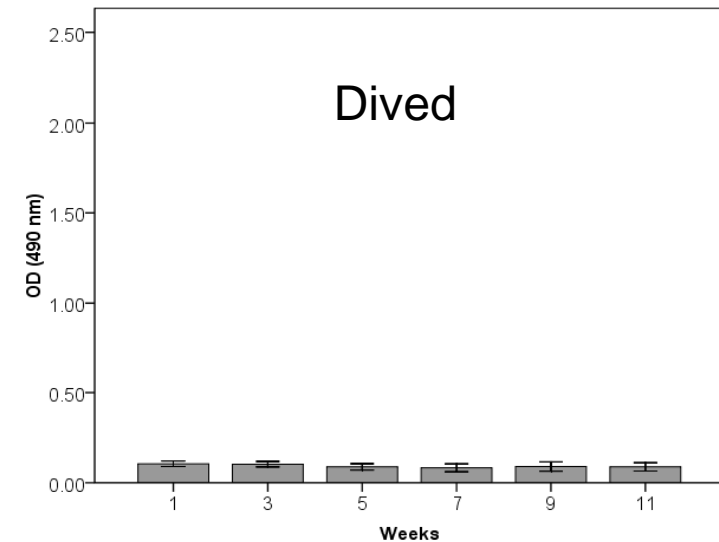
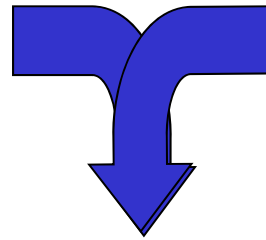
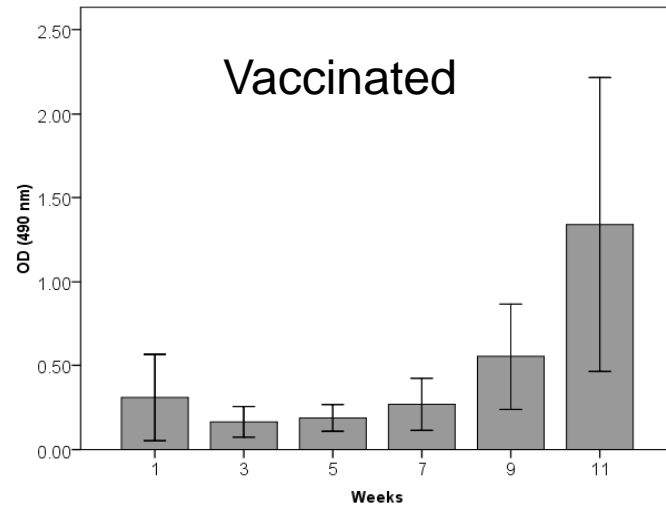


# *Pseudomonas aeruginosa* and anti-heat shock protein 60

- Skin infections in saturation diving are primarily caused by *Pseudomonas aeruginosa*.
- The sequence homology between human HSP60's and those of *P. aeruginosa* is about 50%
- Cystic Fibrosis patients infected by *P. aeruginosa* show high levels anti-Hsp60 compared to normal controls
- High level of anti-HSP60 have been considered to be a risk factor for atherosclerosis



# Experiment and results:



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# Results from animal experiments:

- Diving rats vaccinated with the bacteria *Pseudomonas aeruginosa* cause binding of cross reacting antibodies that can lead to an inflammatory response.



# Future projects

- Results from this animal study indicate that *Pseudomonas aeruginosa* exposure can have more than acute effects
- Study the long term effects of repeated exposure to *Pseudomonas aeruginosa*



# Nitric oxide in exhaled gas and exposure to hypoxia and hyperoxia



**MSc Cecilie Caspersen, UiB**

Supervisors: Einar Thorsen &  
Trine Stensrud

Dykkeseminar NOV 2011

## Background

- Diving and hyperbaric oxygen therapy is associated with the risk of pulmonary oxygen toxicity
- Oxygen toxicity contributes to the acute and long-term effects of diving on lung function
- New markers for early development of oxygen toxicity are required



# Background

- Nitric oxide
  - Mediator of inflammation
  - Vasodilator in the circulatory system
  - Signaling substance in the CNS



## Aim

- Characterise the dose-response relationship between inhaled  $PO_2$  and  $FE_{NO}$
- To see if changes in  $FE_{NO}$  are related to changes in pulmonary function variables

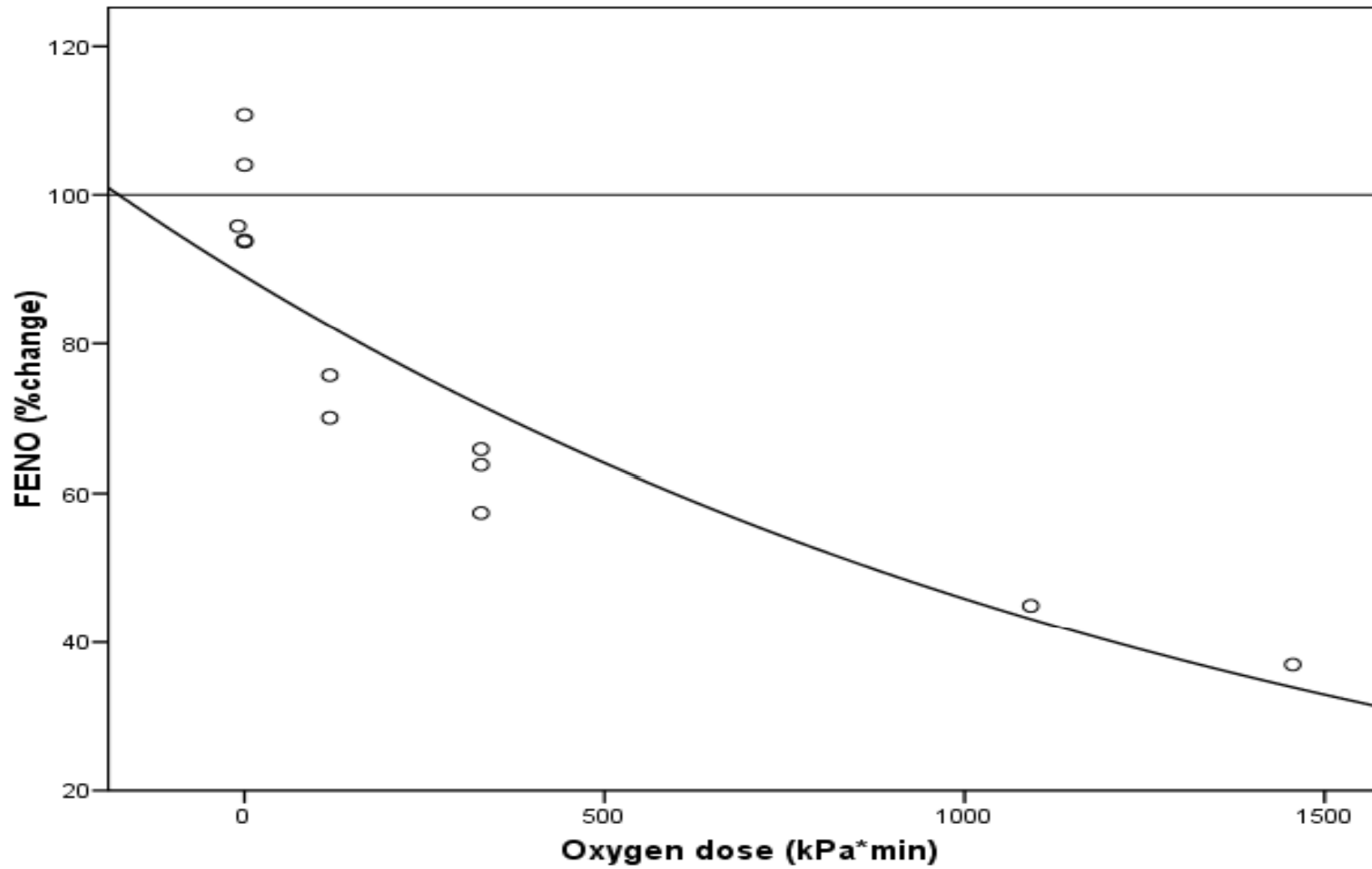


# Methods

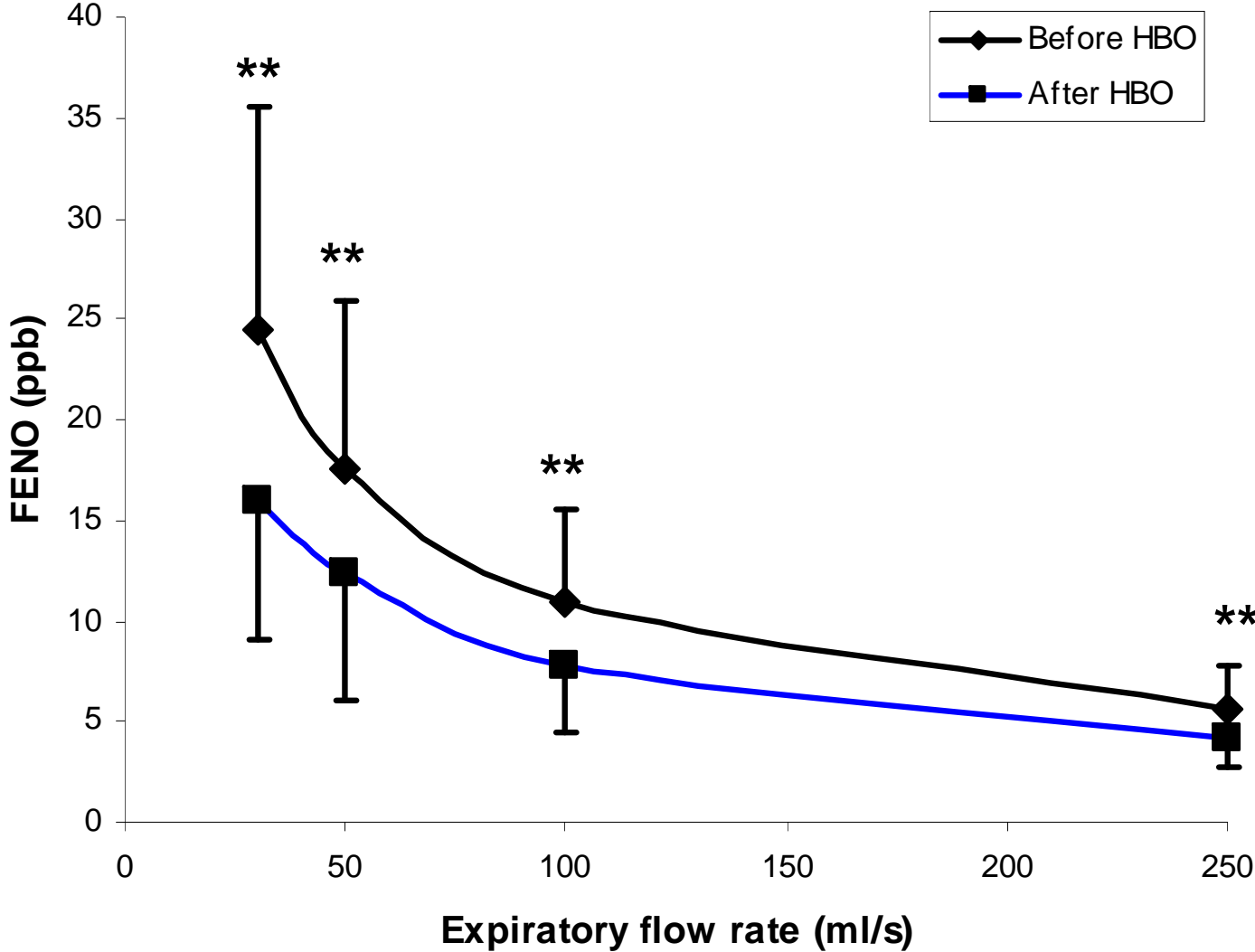
- Fraction of exhaled NO ( $FE_{NO}$ )
  - Dynamic lung volumes
  - Maximal expiratory flow rates
  - Static lung volumes
  - Diffusion capacity
  - Distribution of ventilation
  
- Hypobaric hypoxia at 2800m ( $PO_2=15$  kPa)
- Normobaric hyperoxia ( $PO_2=100$  kPa)
- Hyperbaric hyperoxia ( $PO_2=240$  kPa)
- Ambient air ( $PO_2=21$  kPa)



# Results: Dose-response



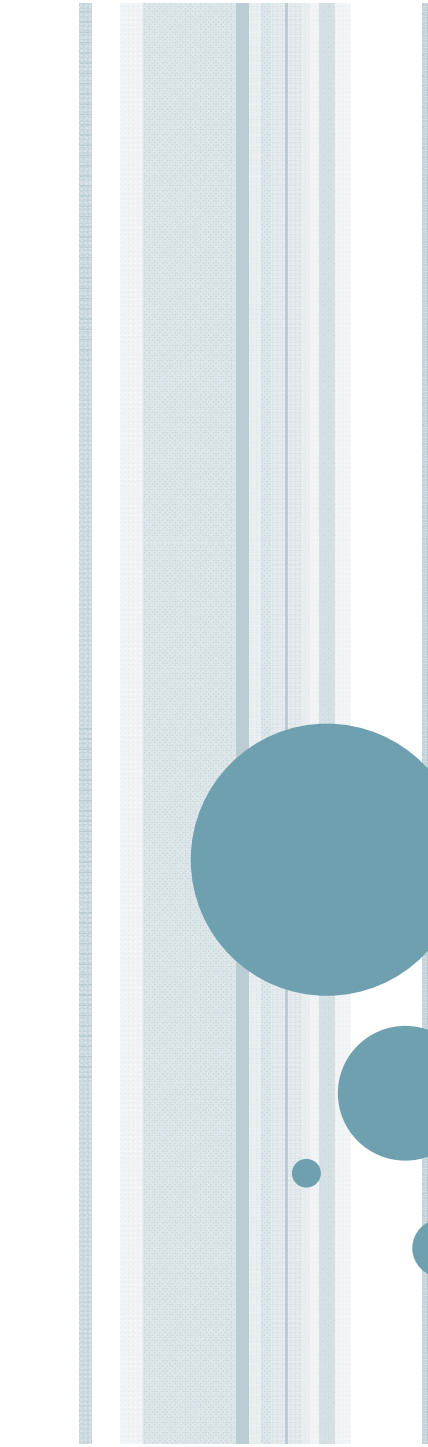
# Results: Alveolar and bronchial NO



## Future plans

- No association between the change in  $FE_{NO}$  and the changes in lung function variables after normobaric hyperoxia. Higher oxygen exposures required
- Investigate  $FE_{NO}$  after saturation diving and the association with venous gas microembolism



The left side of the slide features a decorative graphic consisting of several vertical bars of varying heights and widths, and a cluster of five teal-colored circles of different sizes. The largest circle is at the top left of the cluster, with four smaller circles of varying sizes positioned below and to its right.

# Experiencing Statoil's Competence Program within Diving Medicine and Physiology

MSc Marianne B. Havnes, NTNU  
MSc Lise Fismen, UiB and NUI  
MSc Cecilie Caspersen, UiB

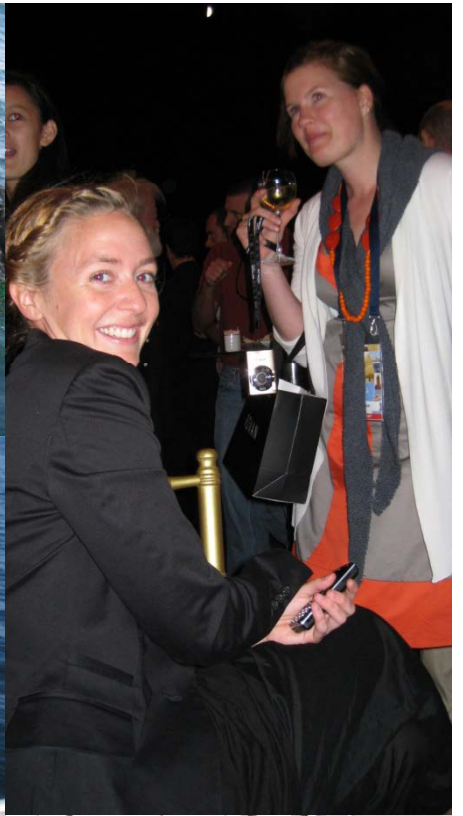
- A PhD education is the highest academic education
- 3 years to achieve the degree
- Consists of two parts; one educating and one independent research pathway
- Dissertation



## PHD-STUDENT IN THE COMPETENCE PROGRAM

- Arena for contact and exchange of ideas
- Insight into various aspects of diving related research
- Insight into the operational diving environment





## IDEAS FOR THE FUTURE

- Closer dialog with the diving industry
  - Interaction
  - Feedback
  - Problem solving
- Which topics do the researchers see, and which topics do the participating partners see?



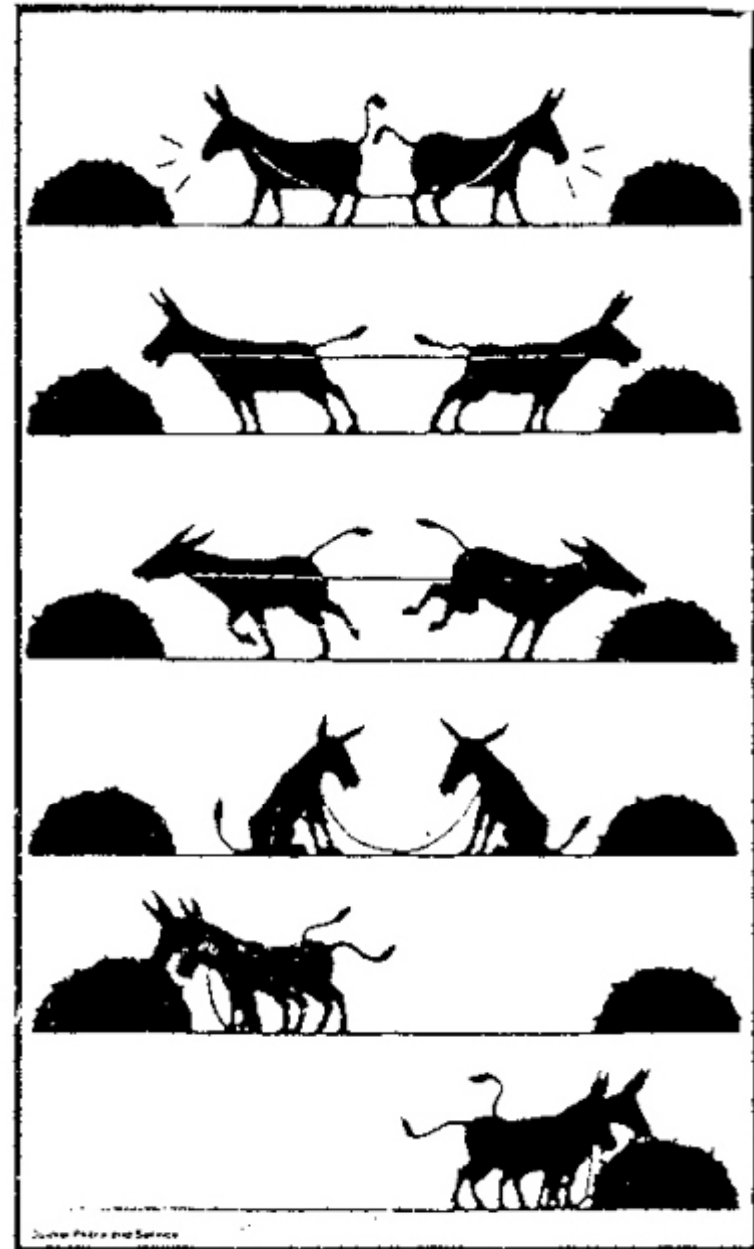
## IDEAS FOR THE FUTURE

- Consciousness about the difference between industry sponsored research and university initiated research
  - Economical
  - Philosophically



## IDEAS FOR THE FUTURE

- Co-operation!
- Research institutions
- Industry



# IDEAS FOR THE FUTURE

- Joint PhD program
  - Working alone vs working in a group
  - International exchange
  - Exchange between participating partners
  - Industry sponsored/buddy program
    - HR and/or HSE in different companies
    - Summerschool programs?
    - Other applied physiology aspects



## RECRUITMENT

- One of the main objectives of present Competence Program
- PhD only a academic degree?
  - Self-driven
  - Disciplined
  - Purposeful
  - Teamwork
  - Capable of finishing projects

