Overview:

- Early Studies
  - Concepts
  - Bench Data
  - Pre-Clinical Animal Studies

- Clinical Studies
  - Preterm Infant Studies
  - CDH Studies
  - Hypothermia
**Physicochemical Properties**

*(37°C @ 1 ATM)*

**Gas Solubility**

*Oxygen*  
33-66 ml/ 100 ml PFC

*Carbon Dioxide*  
140-166 ml/ 100 ml PFC

**Vapor Pressure**  
0.2-400 torr

**Density**  
1.58-2.0 g/ml

**Viscosity**  
0.8-8.0 cS

Transfusion

Control

Transfusion

1% Hb

Prevention of Decompression Sickness

Rapid Decompression

Gas Emboli in Microcirculation
"Mice as Men"

PREVENTION OF BENDS
RAPID DECOMPRESSION FROM 500 ATM.
AIR PRESSURE FOR 10 MINUTES
(34 obs. atm., 1000 ft below sea level)

<table>
<thead>
<tr>
<th>AIR</th>
<th>FLUOROCALFON BEND</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="air" alt="Mice" /></td>
<td><img src="fluorocarbon" alt="Mice" /></td>
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</tbody>
</table>

(Images of mice in different positions to illustrate the effects of different gases on decompression sickness.)
Mouse Movie

Schematic of Demand-Regulated Liquid Breathing System

Shaffer and Moskowitz, J. Appl Physiol. 1974

1989
Demand-Regulated Liquid Ventilation

*During TLV*

*Post TLV*

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Shaffer and Moskowitz, J. Appl Physiol. 1974

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![Image of a fetus in an egg shell](image-url)
Perfluorochemical Assisted Ventilation

- **Tidal Liquid Ventilation**
  1966 - Present

- **Partial Liquid Ventilation**
  1978 - Present

- **Aerosol Ventilation**
  1999 - Present
Liquid Ventilation in Preterm Lambs

Treatment → Oxygenation → Improvement

SF Treated Preterm Lambs: 120 days Gestation


Non-Respiratory Support Applications:

- Drug Delivery
- Imaging
- Lung Expansion
- Induction of Hypothermia
PERFLUOROCHEMICALS
AS PULMONARY CONTRAST AGENTS

- **Plain film x-ray**
  limited perspective to assess distribution
- **Computerized tomography (CT)**
  3D imaging along X,Y, and Z axes
  qualitative and quantitative analysis
- **High resolution CT**
  thin section 3D imaging along X,Y, and Z axes
  qualitative and quantitative analysis
Clinical Studies

- Preterm Infants
- CDH Infants
- Hypothermia

Greenspan JS et. al. Lancet (2)8671:1095, 1989
Preterm MultiCenter Trial

- 24-34 wks GA or BW=600-2000 gms.
- < 48 hrs of Age
- At least 2 doses of SF
- < 30 days old
- a/A < 0.2
- MAP > 10 cmH₂O
- Compliance < 0.3 ml/cmH₂O/kg

Leach et al., NEJM, 1996.
Partial Liquid Ventilation in Premature Newborns

Lung Changes During Distension With PFC

0 Hrs Distension  48 Hrs Distension
Results

- **Survival:**
  PILG = 6 of 8 (75%)
  Control = 2 of 5 (40%)

- **VFD:**
  PILG = 6.3 ± 3.3 days,
  Control = 4.6 ± 4.6 days

- **Time on ECMO:**
  PILG = 9.8 ± 2.3 days,
  Control = 14.5 ± 3.5 days
Conclusions

• PILG can be performed safely
• PILG may be of benefit in the management of newborns with CDH who require ECLS.
• A definitive trial of this novel intervention in neonates with high mortality is ongoing.

RhinoChill approach: 
*The aim is the brain...*

• Brain is the target organ
• Heart is controlled by the brain
• Puppet on a string
• Myriad autonomic efferents

*Transnasal route:*
*Nasal cavity is a heat exchanger sitting right under the brain*
Comparison of Brain Cooling Rates

Design

• 11 sites
• 84 patients
• Single arm
• All arrests
• Sep 07- Aug 08

Primary objective

• Safety and feasibility of early post-ROSC cooling using RhinoChill

Secondary end-points

• Minutes to initiate cooling
• Minutes to target temperature
Cooling is quickly initiated

Therapeutic temperature (34°C) reached in 27 min.

33°C target temperature reached in 60 min.

Cooling in the ICU is easily managed
RhinoChill advantage

- Easy, non-invasive catheter placement
- Simple to integrate with other emergency procedures
- Portability enables continued cooling in various clinical environments & scenarios
- Fast brain with consecutive central cooling
- Pre-hospital use is a natural application…

Intra-Arrest Transnasal Evaporative Cooling
A Randomized, Prehospital, Multicenter Study (PRINCE: Pre-ROSC IntraNasal Cooling Effectiveness)

Maaret Castrén, MD, PhD; Per Nordberg, MD*; Leif Svensson, MD, PhD; Fabio Tacccone, MD; Jean-Louis Vincent, MD, PhD; Didier Desnuelles, MD; Frank Eichwede, MD; Pierre Mols, MD, PhD; Tilmann Schwab, MD; Michel Vergnion, MD; Christian Storm, MD; Antonio Pesenti, MD, PhD; Jan Pachl, MD, PhD; Fabien Guérissé, MD; Thomas Elste, MD; Markus Roessler, MD, DEA; Harald Fritz, MD; Pieterjan Durnez, MD; Hans-Jörg Busch, MD; Becky Inderbitzen, MSE; Denise Barbut, MD

(Circulation. 2010;122:729-736)
Design

- 15 sites/EMS systems
- 200 patients
- RCT
- Nov 08 – Jul 09

Primary objective
- Safety and feasibility of intra-arrest cooling using RhinoChill™

Secondary end-points
- ROSC rate
- Minutes to target temperature
- Survival to discharge
- Neurologically intact survival

RhinoChill Portable Device
Cooled head faster

Increased survival for admitted patients

RhinoChill on Systemic Cooling Started

RhinoChill off

3 hours faster

Increased survival for admitted patients

RhinoChill
No RhinoChill

N=30
N=42
FUTURE CARE !!!!