Mechanistic and Monitoring Studies in Experimental Decompression Sickness (DCS) Utilizing Novel Treatments with Perfluorocarbon (PFC) Emulsions

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UHMS / ONR Undersea Medicine Review, June, 2011, Fort Worth, TX #A7

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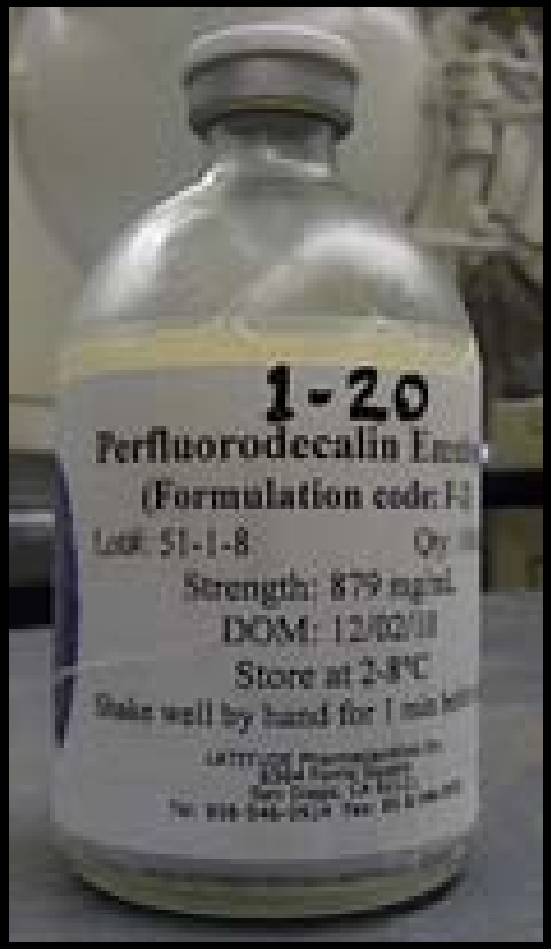
Dept of Anesthesiology

PHER-O_2 (87.9% w/v, Perfluorodecalin, 7.9% Phospholipon)

Sanguine Life Sciences
101 East Green Street, #6
Pasadena, California 91105



Active Ingredient: Perfluorodecalin, 879 mg/ml

- Osmolarity: 513 mOsm/L
- Viscosity: 23.3 cp (at 25° C)
- pH: 5.65
- 0.11 um (average particle size)

Inactive Ingredients: Phospholipon

- Glycine
- EDTA, disodium dihydrate
- Sodium phosphate dibasic
- Sterile water for injection

PHER-O_2 product's final pH: 7
Sterile method: 121° C for 15 minute
Storage: 2-8 ° C

Preliminary Data of Testing PHER-O_2 in Rodents

1. **Acute Protocol:**
   PHER-O_2 intravenous infusion in normal Rats
   - **Blood O_2 analysis**
   - **Hemodynamic analysis**

2. **Chronic Survival Protocol:**
   Treatment with PHER-O_2 after Cerebral Arterial Gas Embolism (CAGE)
   - **Behavioral Assessment: Beam-Walk, Morris Water Maze**

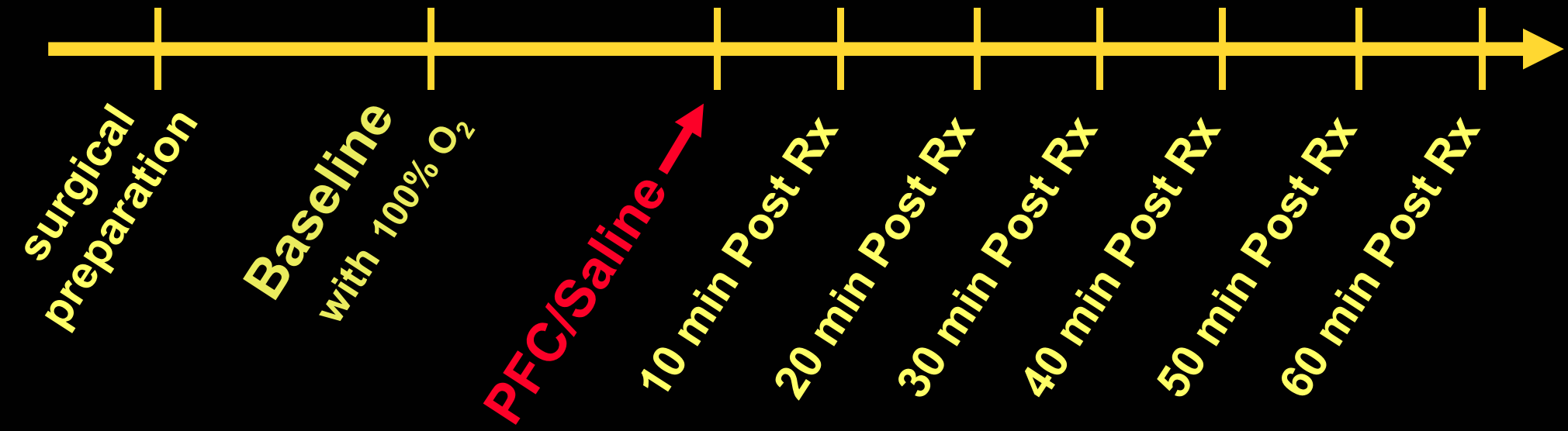
Intravenous PHER-O_2 Infusion Protocol

Tracheal intubed, Jugular vein, Tail Artery and Vein cannulated

Stabilization Baseline blood samples

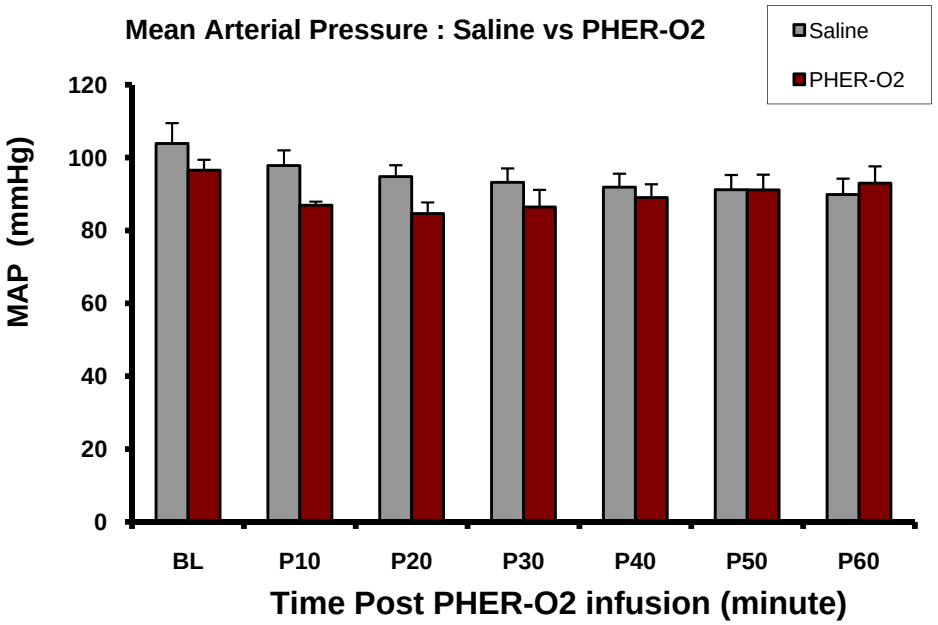
Saline/PFC, iv 4 ml/kg for 15 m (3.52g/kg)

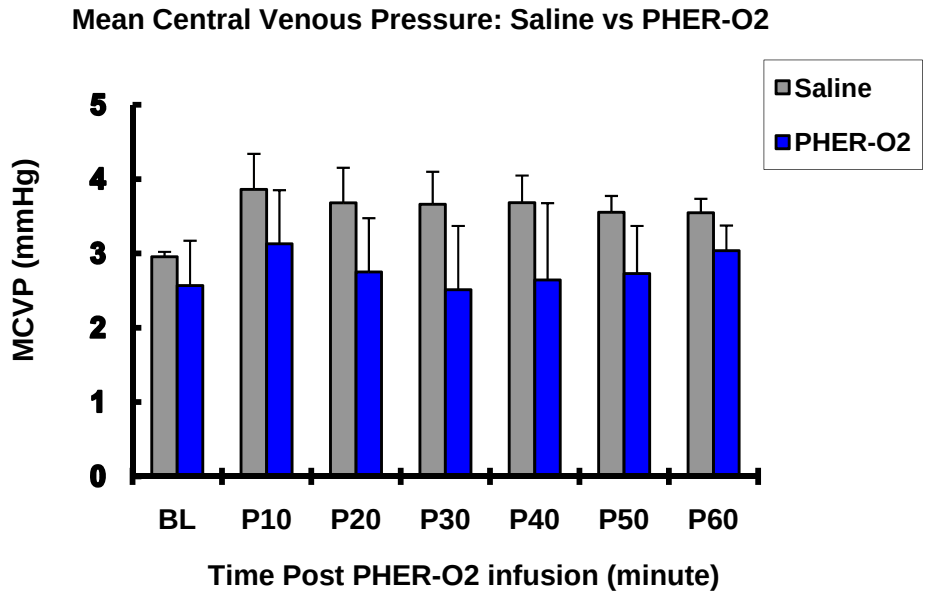
Data collecting:
Blood Gases
AP,CVP, ECG



SD Rat, PHER-O_2 (n=6), Saline (n=3)

Mean Arterial Pressure and Mean Central Venous Pressure after PHER-O_2 intravenous infusion





Heart Rate and Arterial Blood Chemistry were stable after PHER-O_2 intravenous infusion

ECG	BL	P10	P20	P30	P40	P50	P60
PHER-O2	343.33	358.33	353.00	349.33	348.33	335.00	338.33
Saline	353.33	350.00	353.33	340.00	343.33	350.00	333.33

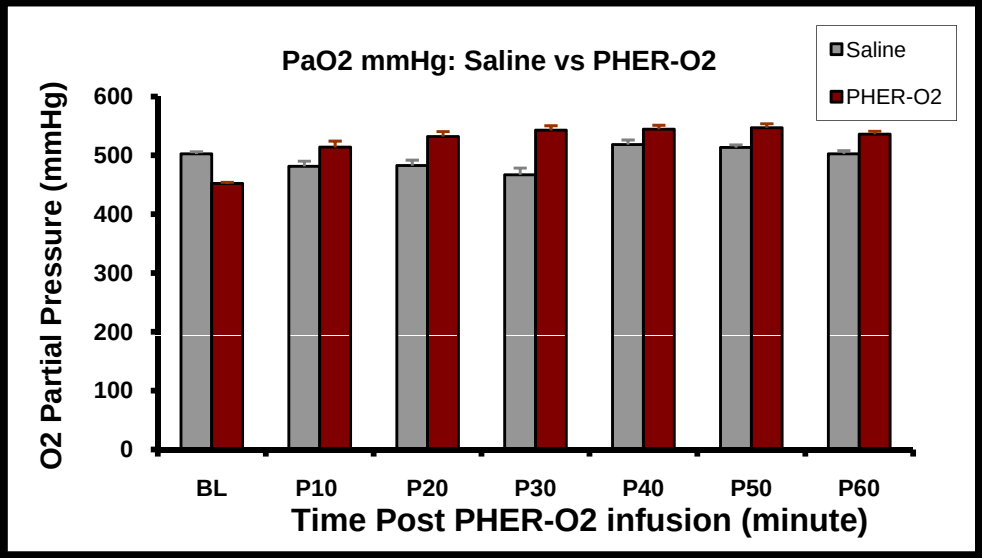
pH	BL	P10	P20	P30	P40	P50	P60
PHER-O2	7.42	7.42	7.39	7.38	7.37	7.36	7.36
Saline	7.44	7.43	7.41	7.41	7.39	7.39	7.40

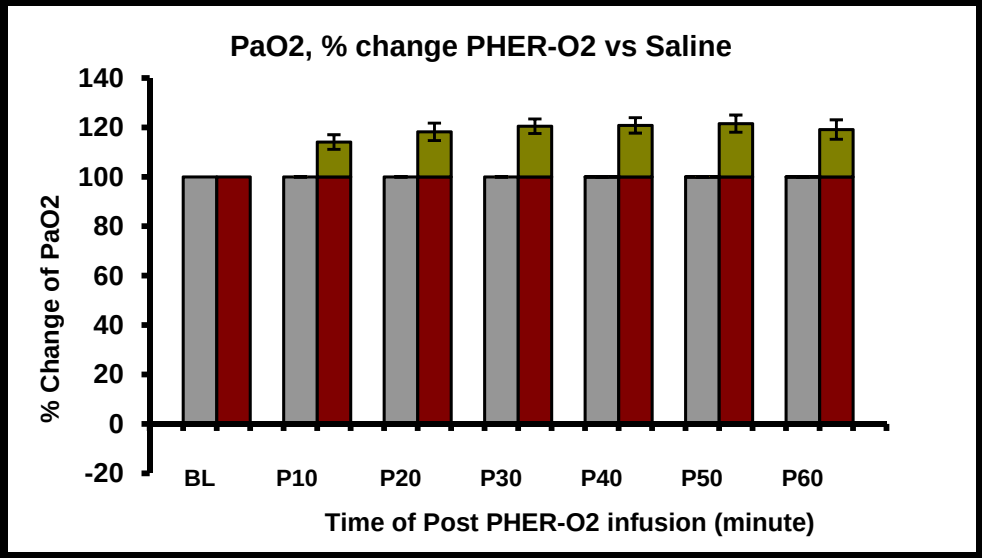
CO2	BL	P10	P20	P30	P40	P50	P60
PHER-O2	37.27	37.73	38.93	39.48	41.03	40.90	40.88
Saline	36.03	36.30	37.73	37.03	37.77	38.33	36.33

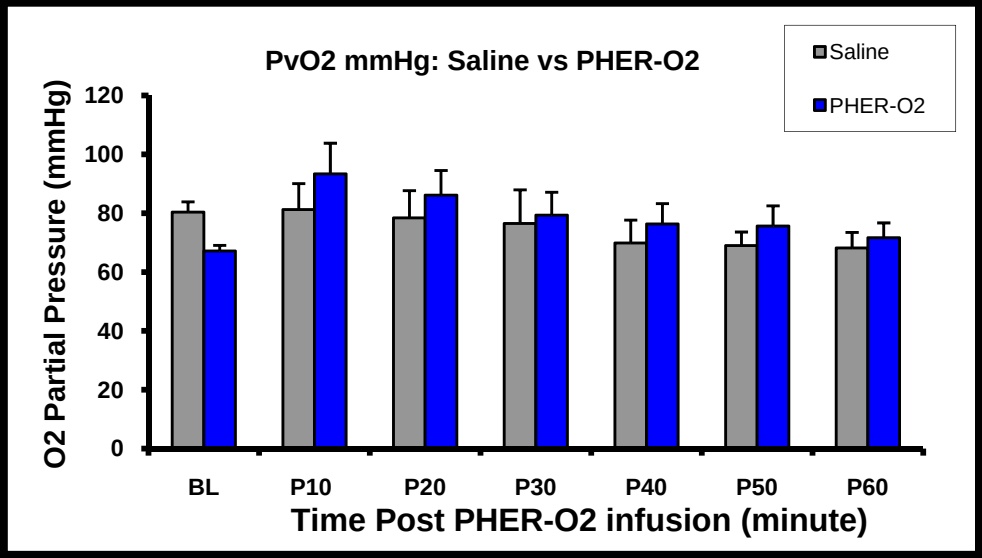
K+	BL	P10	P20	P30	P40	P50	P60
PHER-O2	3.90	4.12	4.02	3.88	3.92	3.92	4.05
Saline	3.83	4.00	3.93	4.00	3.87	3.90	3.97

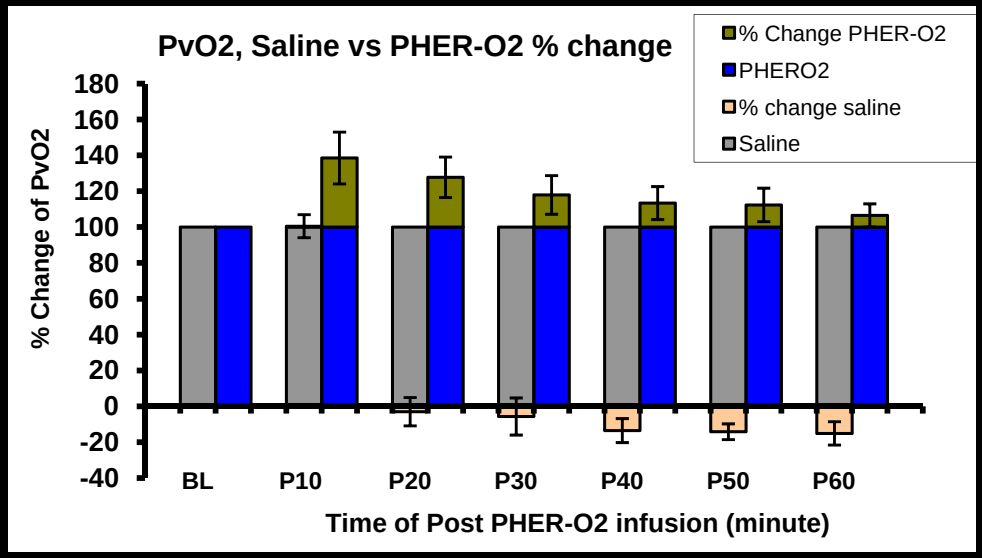
Glucose	BL	P10	P20	P30	P40	P50	P60
PHER-O2	**15.27**	**17.80**	**20.03**	**21.08**	**21.05**	**19.82**	**19.20**
Saline	16.07	15.40	15.03	14.93	14.57	14.63	14.63

Increase partial O_2 pressure in arterial and venous blood After PHER-O_2 intravenous infusion

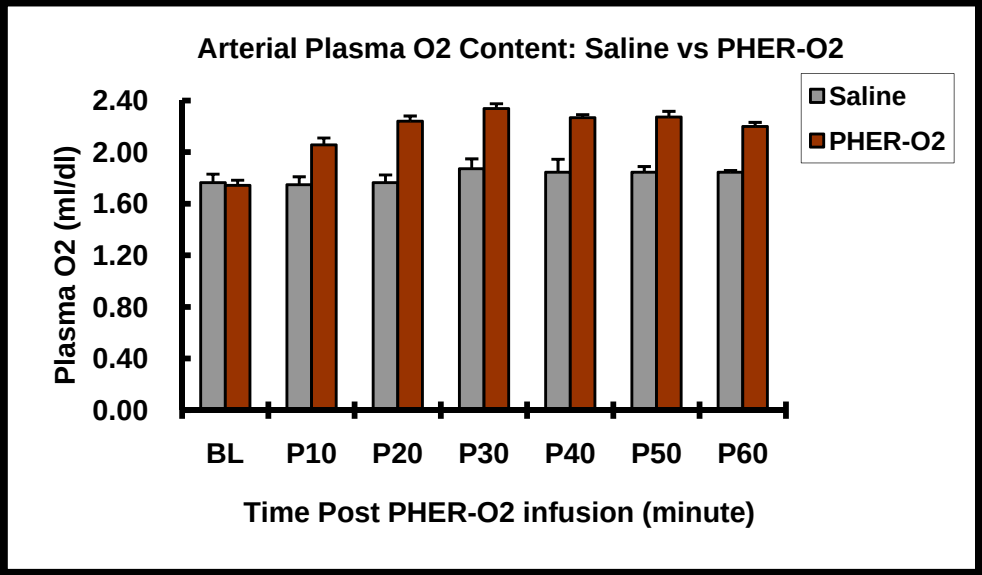


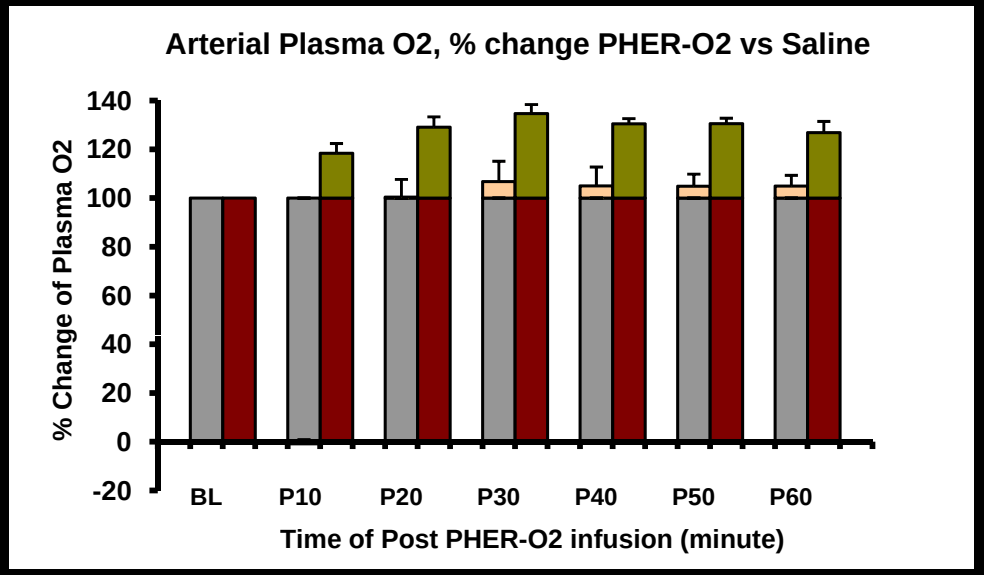


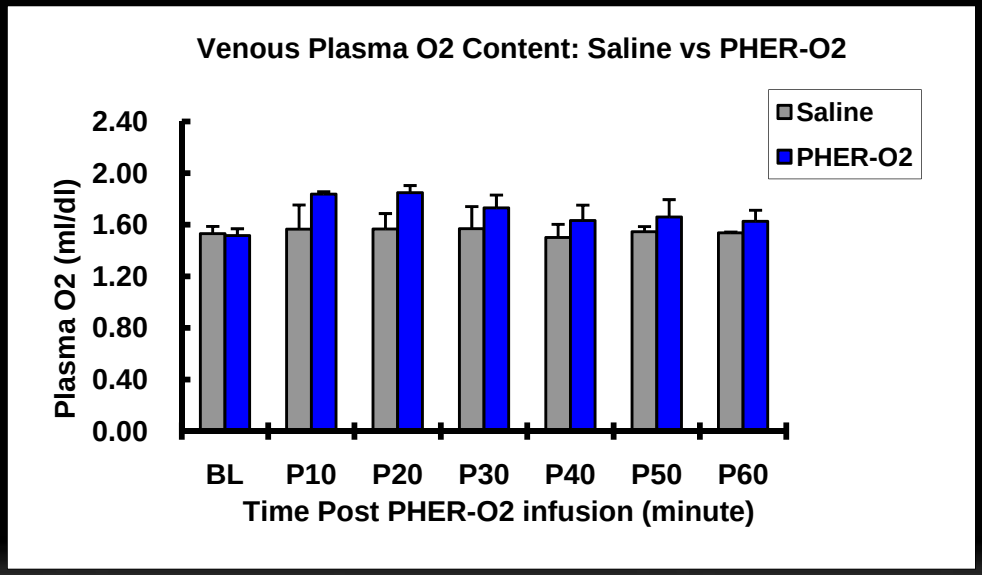


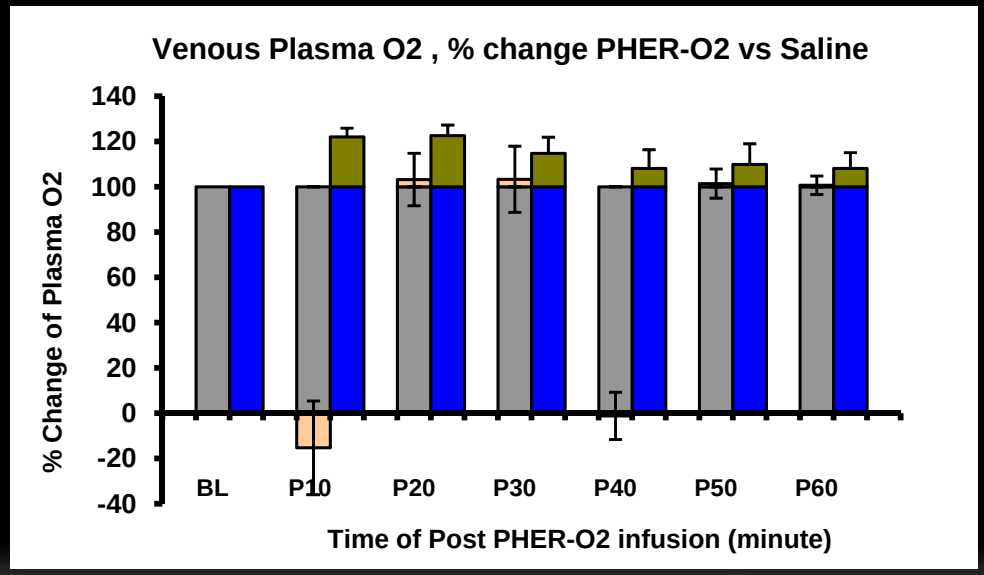


Increase Plasma O_2 Content in arterial and venous blood After PHER-O_2 intravenous infusion









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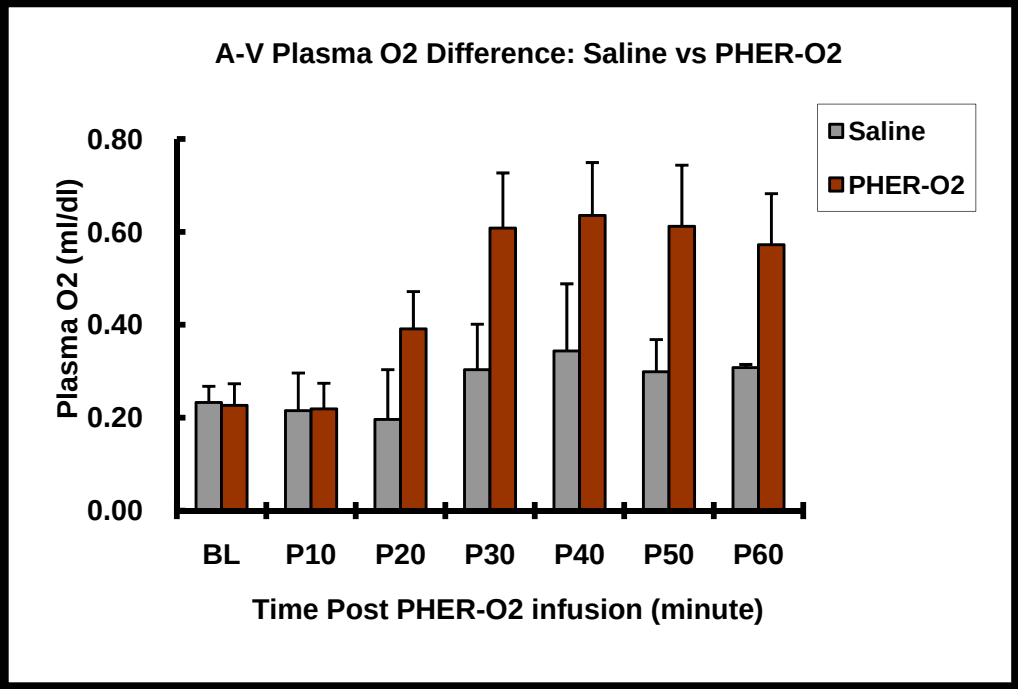
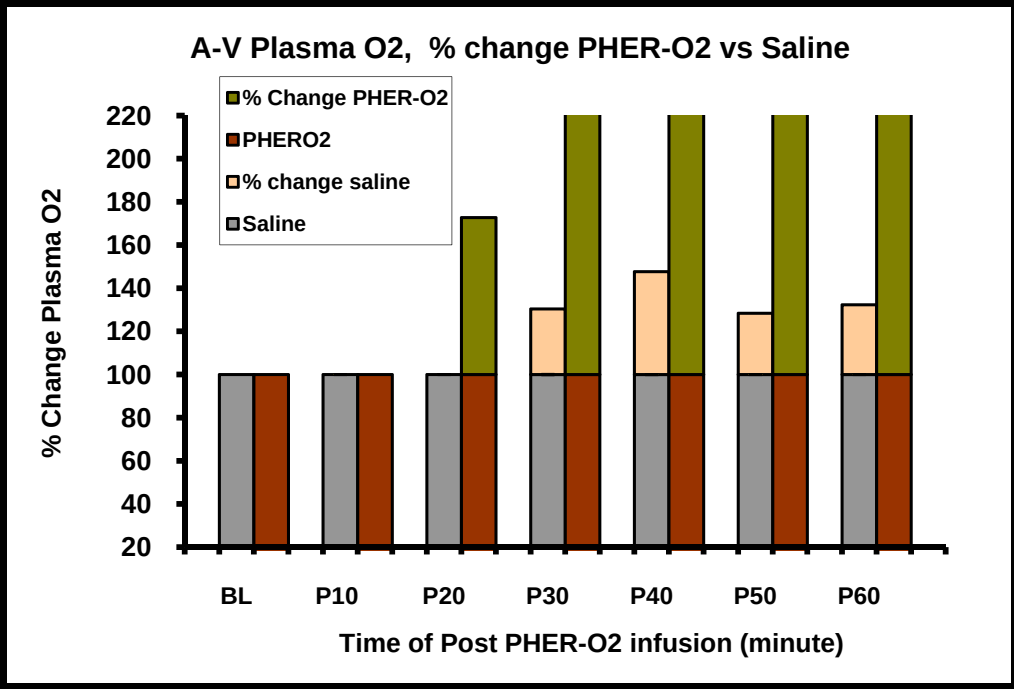
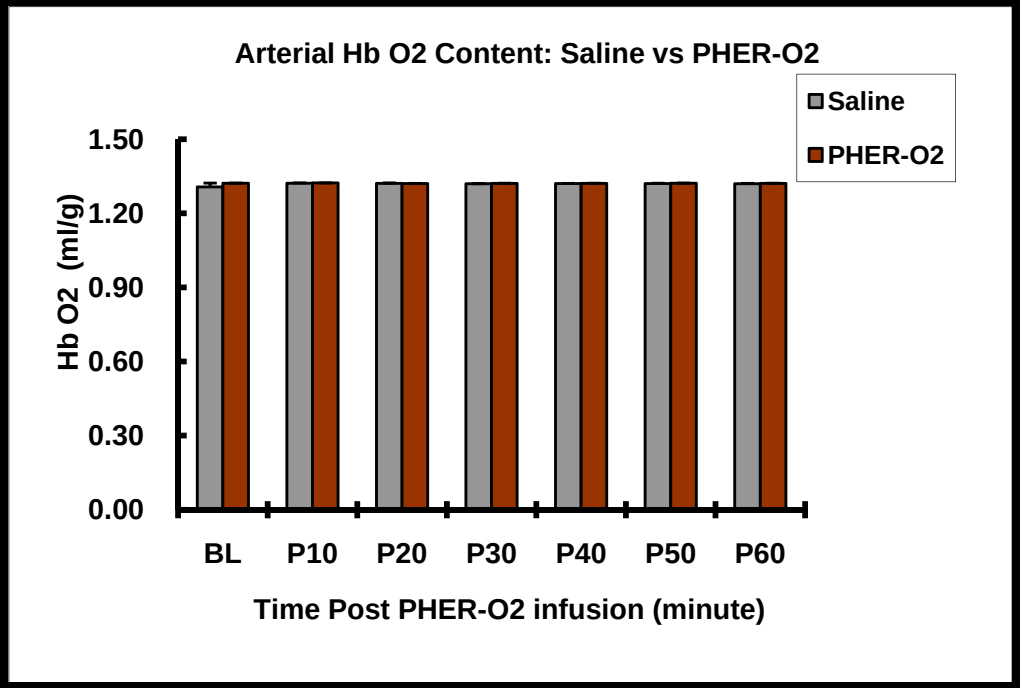
Increase Plasma O_2 Content Difference Between Arterial and Venous blood After PHER-O_2 intravenous infusion

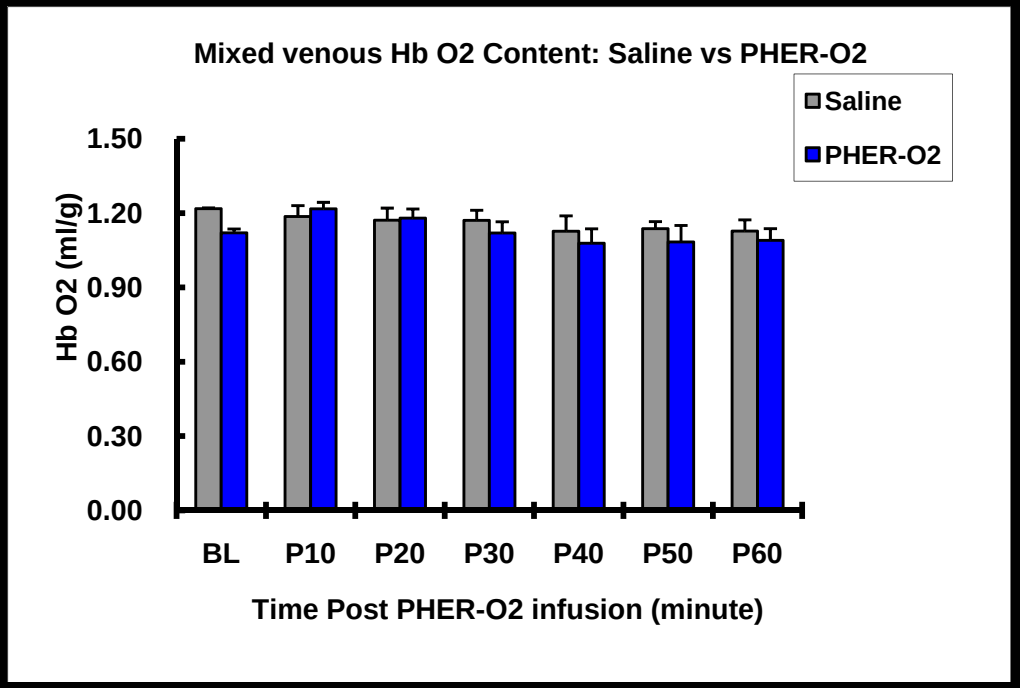




Hb O2 content = (Hb-MetHb)*1.33*Saturation/100
Hb O2/g content = ((Hb-MetHb)*1.33*Saturation/100)/(Hb-MetHb)
Plasma Oxygen Content Difference = Arterial plasma O2 – Venous plasma O2

There is no Change in Hemoglobin O_2 Content after PHER-O_2 intravenous infusion





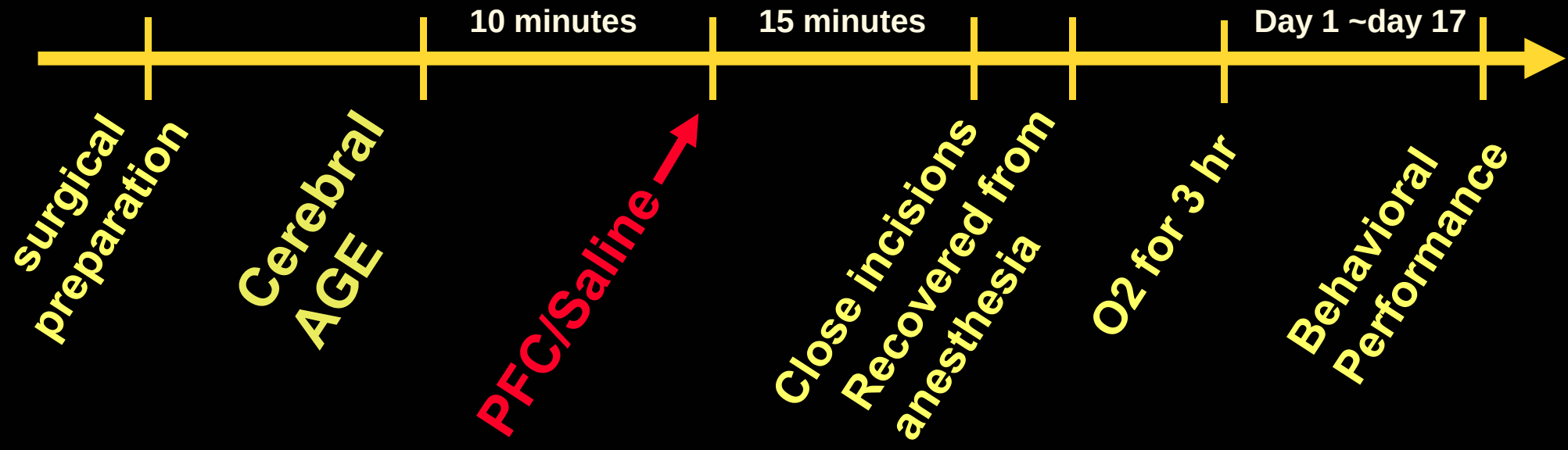
Survival Protocol: Intravenous PHER-O_2 Treatment after CAGE

Tracheal intubation, Tail vein cannulated External carotid artery cannulated

10 ul x2 air bolus was given

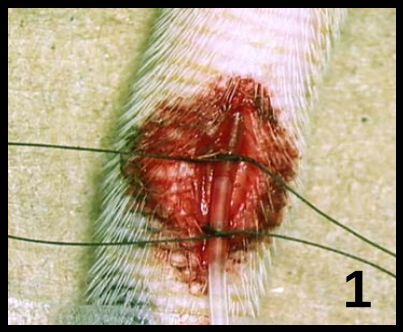
Saline/PFC, iv 4 ml/kg for 15 m (3.52g/kg), breath O2 for 3 hours

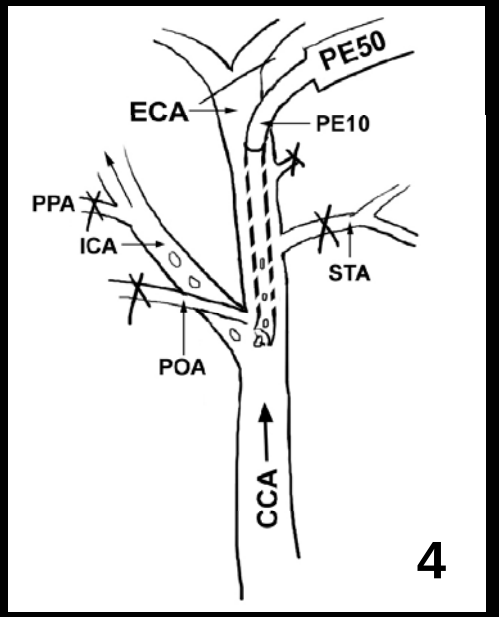
Beam Walk Morris Water Maze



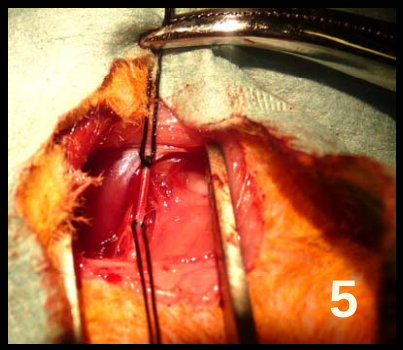
SD Rat, control (n=5), CAGE-saline (n=10), CAGE-PHER-O_2 (n=8)

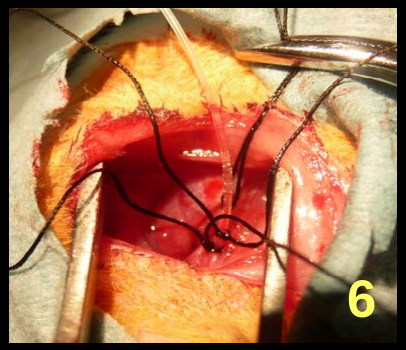
Tail vein catheterization with PE50 tube

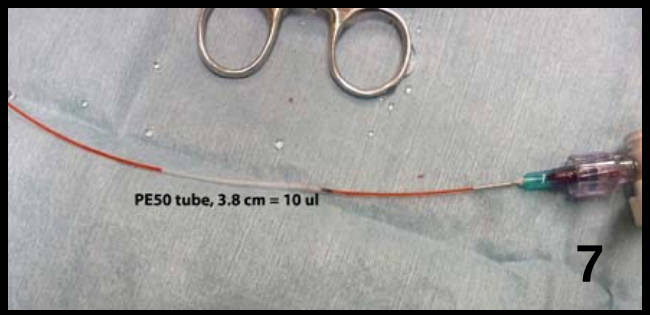


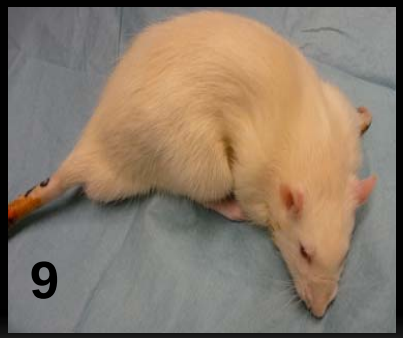


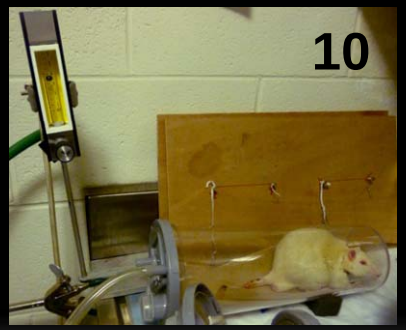
External Jugular Artery cannulation and air delivery (CAGE)

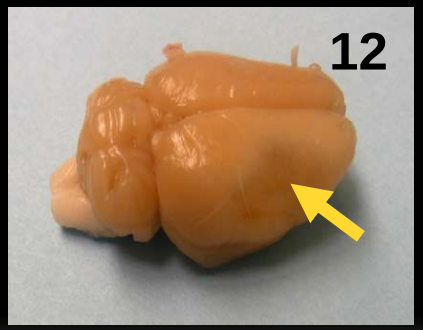






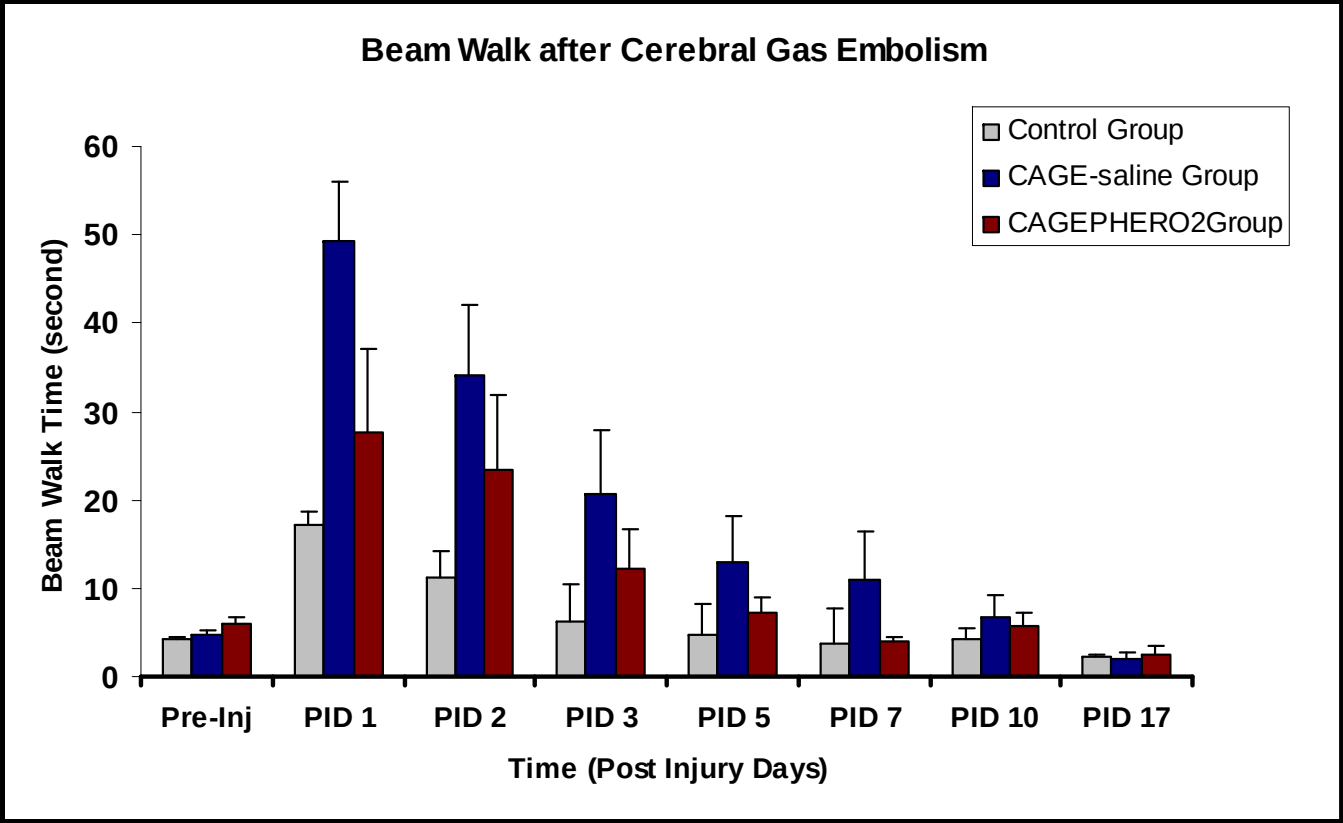






Behavioral Assessment

Beam Walk



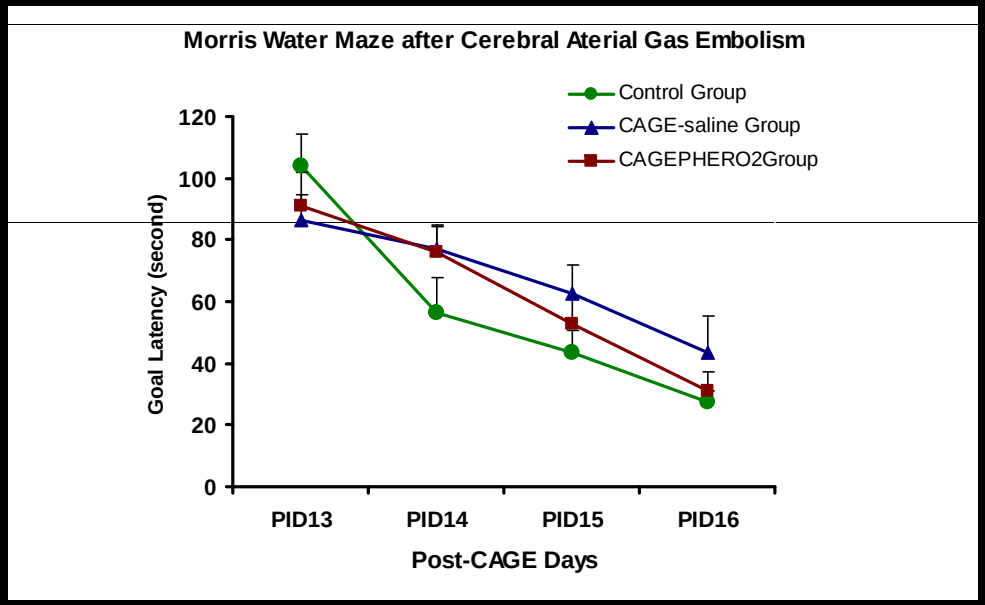
Beam Walk: assesses both balance and motor coordination

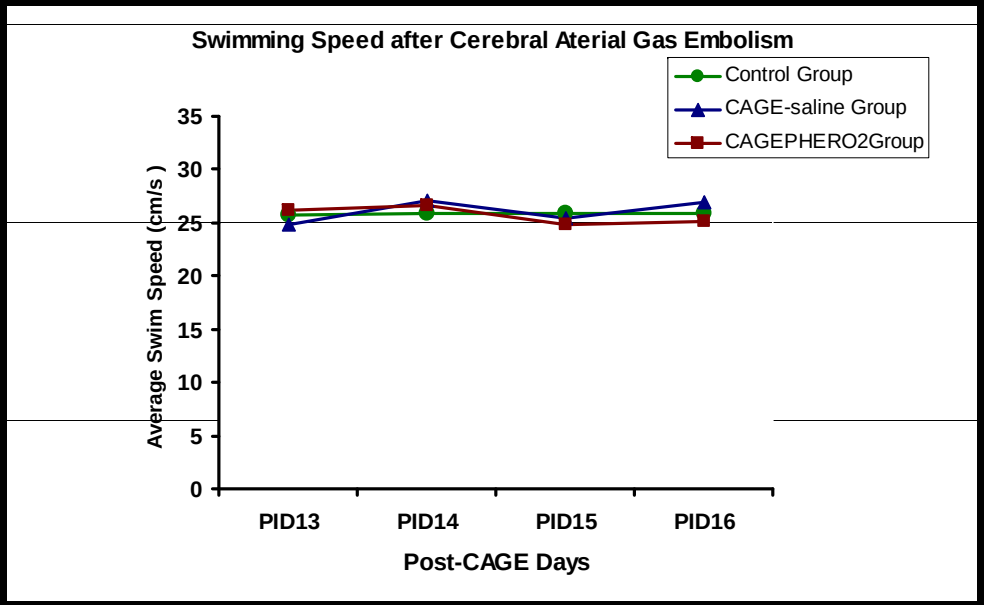
Cerebral AGE causes significant motor deficit compared with Sham group. In saline group, motor deficits lasted at least 7 days after cerebral AGE.

PFC treated animals showed that the earlier motor function recovery than those treated with saline after cerebral AGE.

Behavioral Assessment

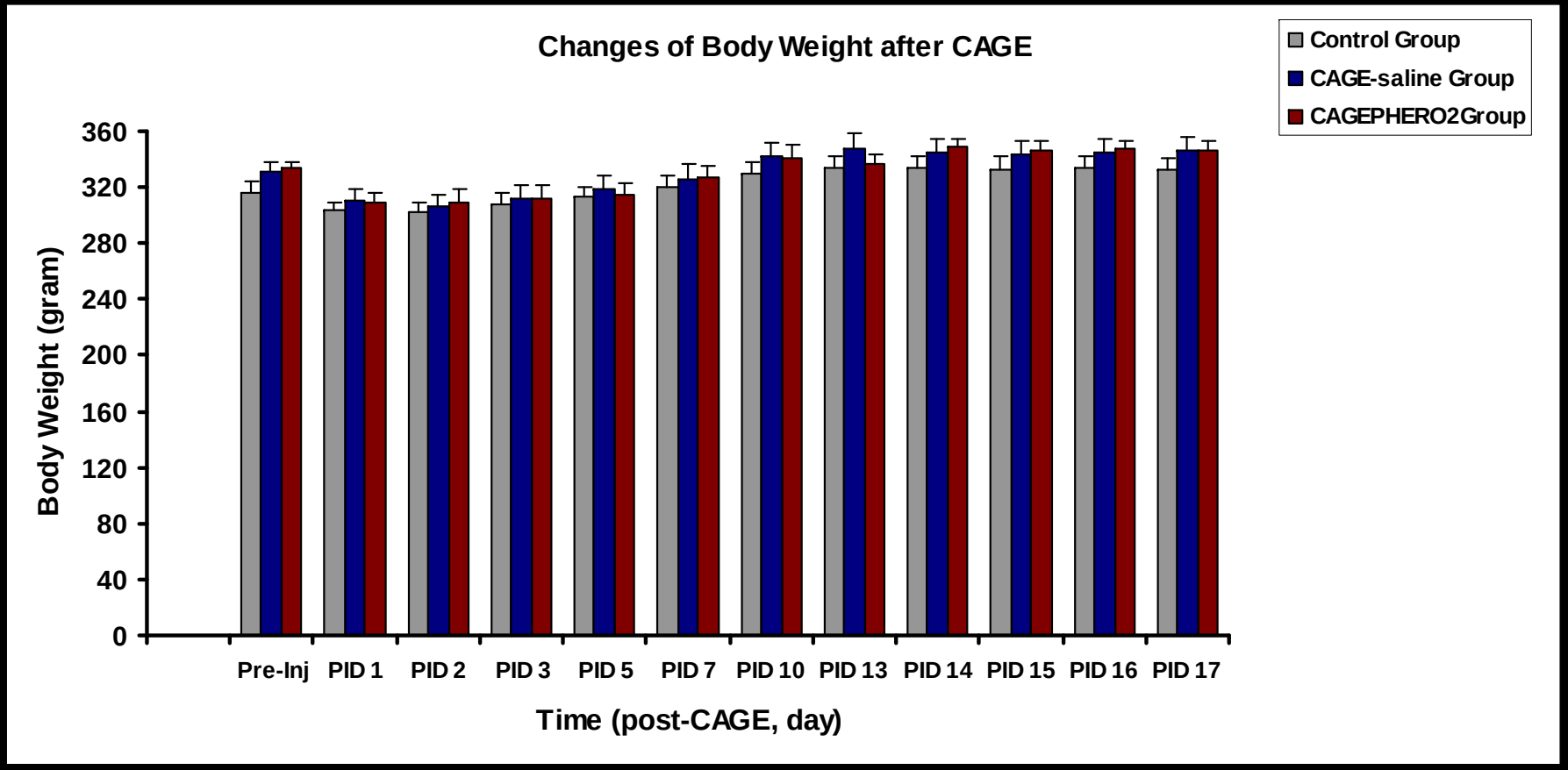
Morris Water Maze





Morris Water Maze (MWM): assesses cognitive learning function
Cerebral AGE causes significant cognitive deficit
PFC treated animals showed the early recovery of cognitive function compared with saline treated animals
Swim speed showed that there is no significant motor deficit among groups after 13 days of cerebral AGE

Body Weight



There is no significant changes in body weight after CAGE

Some Applications of PHER-O_2 (88% w/v, Perfluorodecalin)

DCS
AGE/VGE
TBI
Hemorrhagic Shock (resuscitation)
Cardio bypass
Organ transplant (organ preservation)
Orthopedic surgery

Technologies to be Delivered

Research ***abstracts***, full ***manuscripts*** and ***intellectual property*** advancing the science and treatment of DCI/AGE, mechanisms of DCI/AGE evolution & resolution, monitoring capabilities, neurological biomarkers.

Data from this study will further support a potential United States FDA submission for an indication of the treatment of DCI/AGE with PFC at surface. Such treatment could/would be useful in dive accident and DISSUB.

PFC represents an easily stored, simply transported, readily available pharmaceutical therapeutic option for non-compression treatment of DCI / AGE / VGE.

PFC represents a readily available, easily infused treatment for AGE emergency in surgery.