Re-Defining Blood Substitute Quality Metrics – the Concept of Oxygen Delivery Potency

Stephen C. Rogers, PhD[1,2], Mary Brummet, MS[1,2], Paisley Maloney, BS[1,2], Jacqueline Nguyen, BS[1,2], Zohreh Safari, PhD[1,2],
Regina Adao, PhD[1,2], Qihong Wang, MS, MD[1,2], Tobi Rowden, RN[1,2], Daniel Bennet, BS[1,2], *Antionio Renaldo, PhD[1,2], Allan Doctor, MD[1,2]
Department of Pediatrics[1] & Center for Blood Oxygen Transport and Hemostasis[2], University of Maryland; *Presenting Author

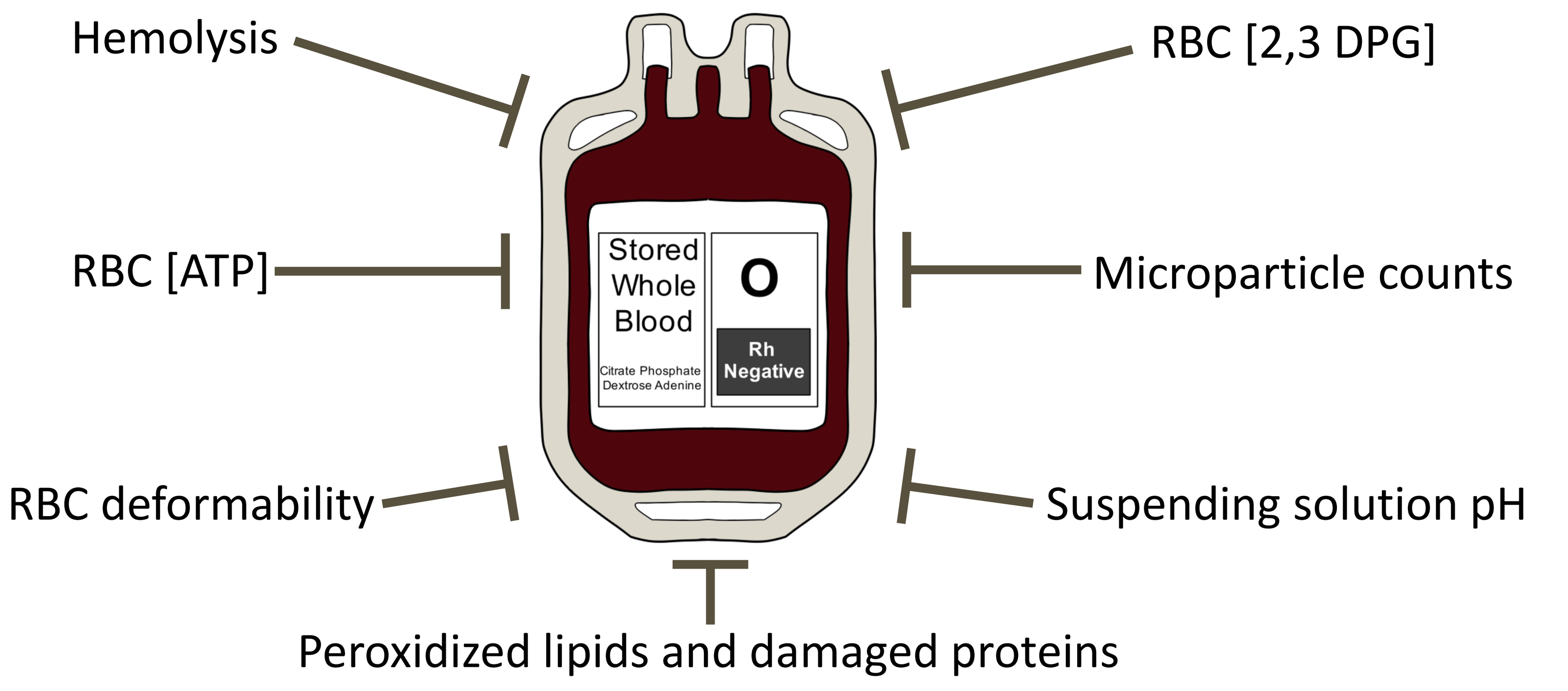
Aims

1. Develop a benchtop metric to quantify blood product performance
2. Create an *in vitro* model of human massive transfusion (HMT)
3. Benchmark oxygen (O_2) delivery of fresh whole blood (fWB) against conventionally prepared and stored human whole blood (sWB)

Background

How is blood product quality measured?

24-hour *in vivo* recovery*



Principal Therapeutic Function of Blood Transfusion:

Enhance O_2 CAPTURE in the LUNG & DELIVERY to TISSUE

Flaws with Current Criteria Defining Blood Product Quality:

- No metric to address the PRINCIPAL therapeutic function of a blood transfusion.
- U.S. Food and Drug Administration's PRIMARY CRITERIA for defining stored blood quality is ≥ 75% 24-hour post transfusion recovery of chromium 51 (^{51}Cr) labeled red blood cells* (RBCs).
- Problem: Current methods of assessing blood product quality are non-comprehensive.
- Proposed Solution: Determine blood product quality by their ability to enhance O_2 CAPTURE in the LUNG and DELIVERY to TISSUE.

Methods

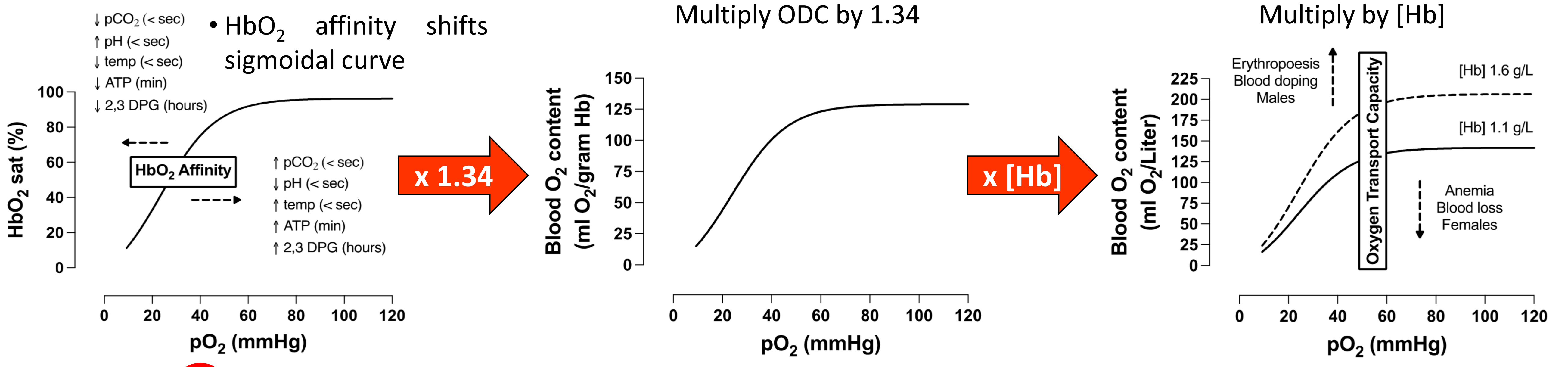
1. Develop a benchtop metric to quantify blood product performance

1a Converting O_2 dissociation and association curves to blood O_2 curves

I) Oxygen Dissociation Curves (ODC)
- Allosteric binding & release of O_2 to hemoglobin (Hb) is co-operative

II) Blood O_2 Content (mL O_2/gram Hb)
- Each gram of Hb can bind 1.34 mL of O_2

III) Blood O_2 Content (mL O_2/L Blood)
- Accounts for Hb concentration [Hb]



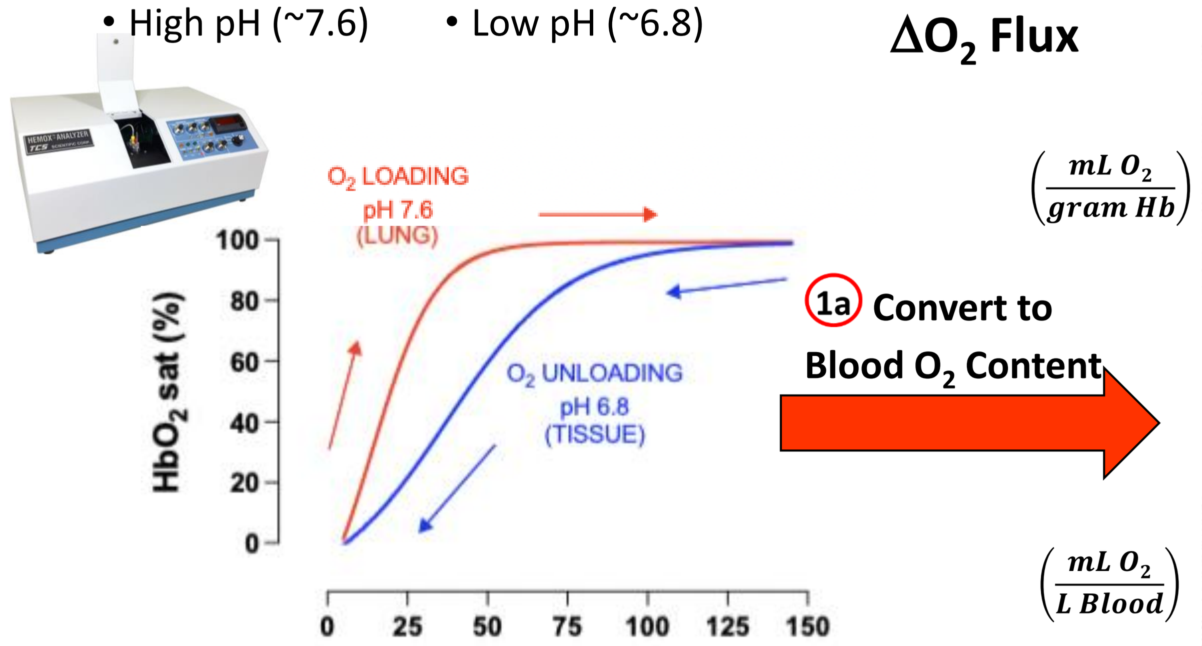
1b Determining O_2 Flux: Calculating maximal potential delivery potency

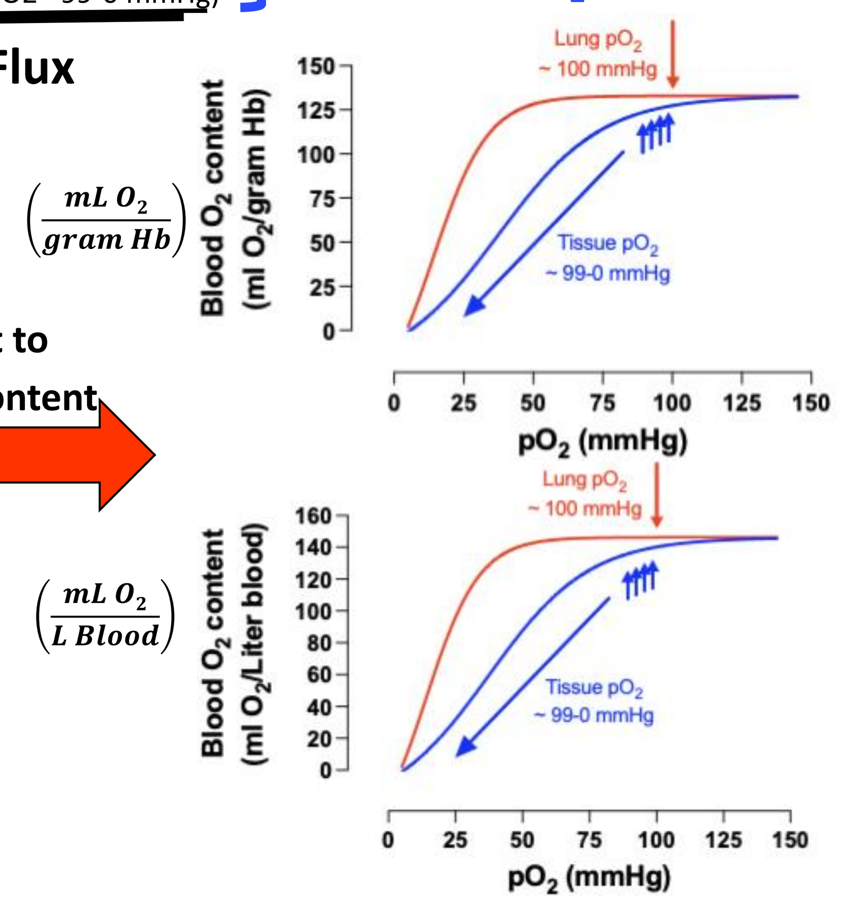
I) HEMOX analyzer: O_2 Association & Dissociation Curves (OAC & ODC)
- OAC: O_2 Loading
  - Lung
  - High pH (~7.6)
- ODC: O2 Unloading
  - Exercising Tissue
  - Low pH (~6.8)

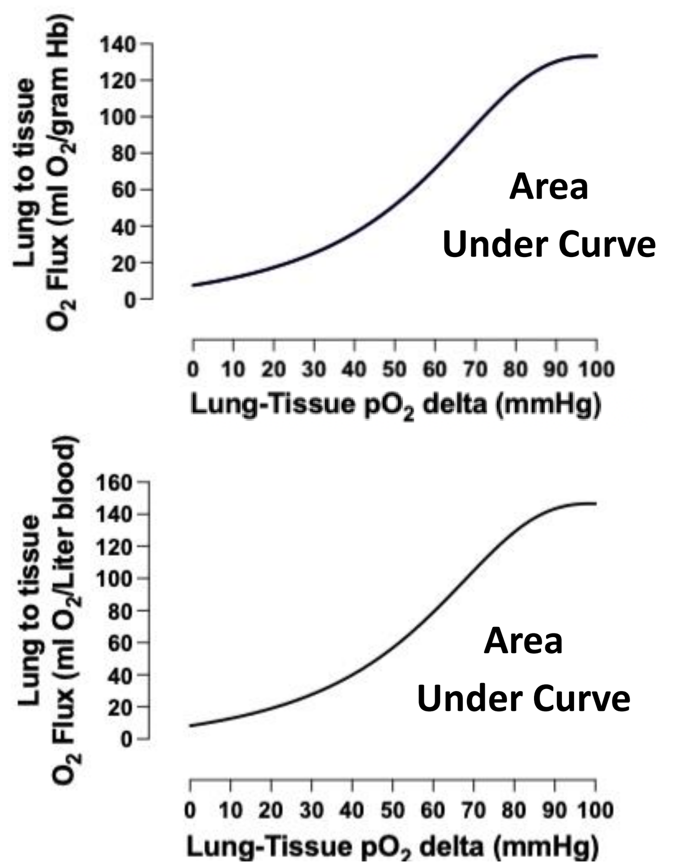
II) Calculate ΔO_2 Flux

$OAC_{(pO2=100\ mmHg)}$ } O_2 Content Leaving Lung
− $ODC_{(pO2=99\text{-}0\ mmHg)}$ } Max Tissue O_2 Offloading
ΔO_2 Flux

III) Integrate ΔO_2 Flux vs. ΔpO_2
- Y-axis: Max ΔO_2 Flux Potential
- X-axis: ΔpO2



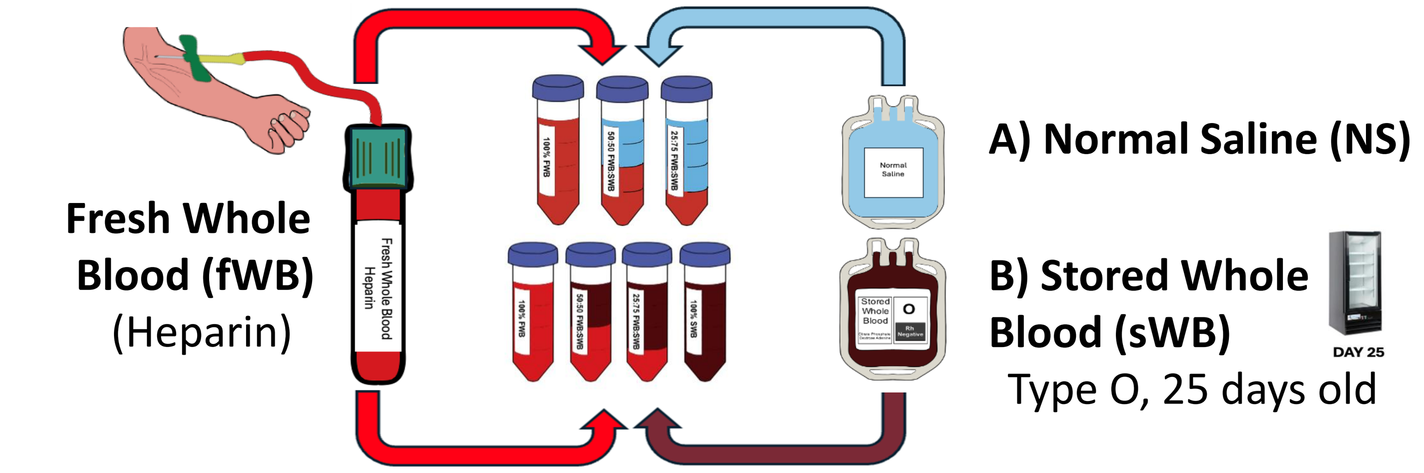




O_2 Flux: Metric incorporates Hb allostery, HbO_2 affinity, & [Hb]

2. Create an *in vitro* model of blood product performance (HMT)

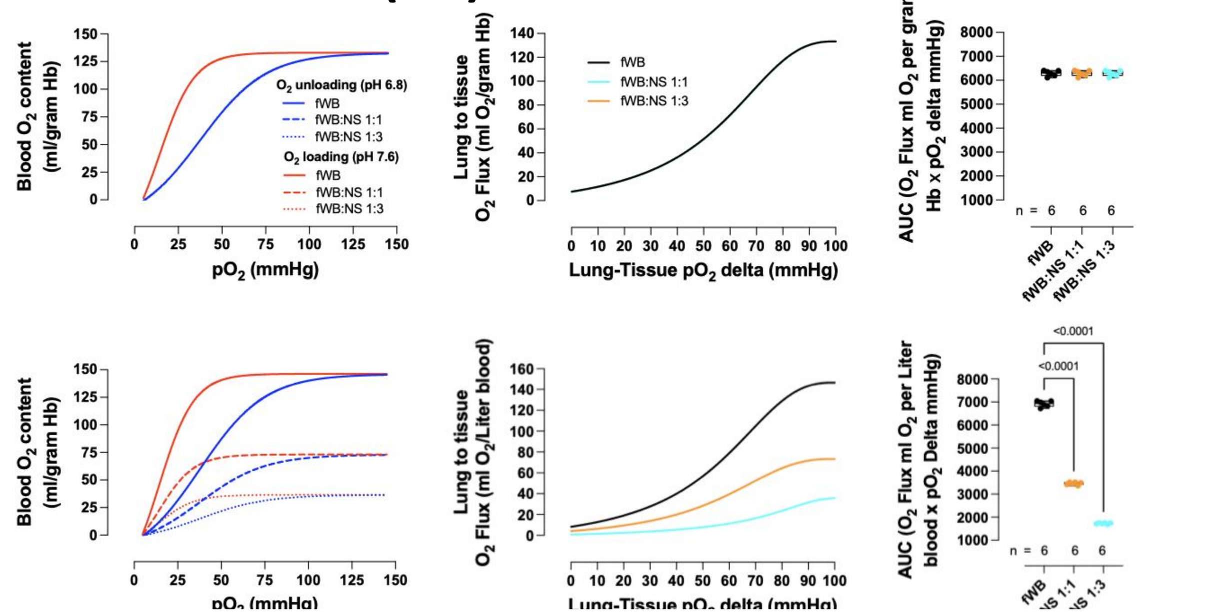
- Benchtop model replicating O_2 delivery profile of a human receiving massive transfusion (HMT)
- Fresh Whole Blood (fWB) was diluted to various ratios representing 50% or 75% transfusion with:
  - **A)** Normal Saline (NS)
  - **B)** Stored Whole Blood (sWB)



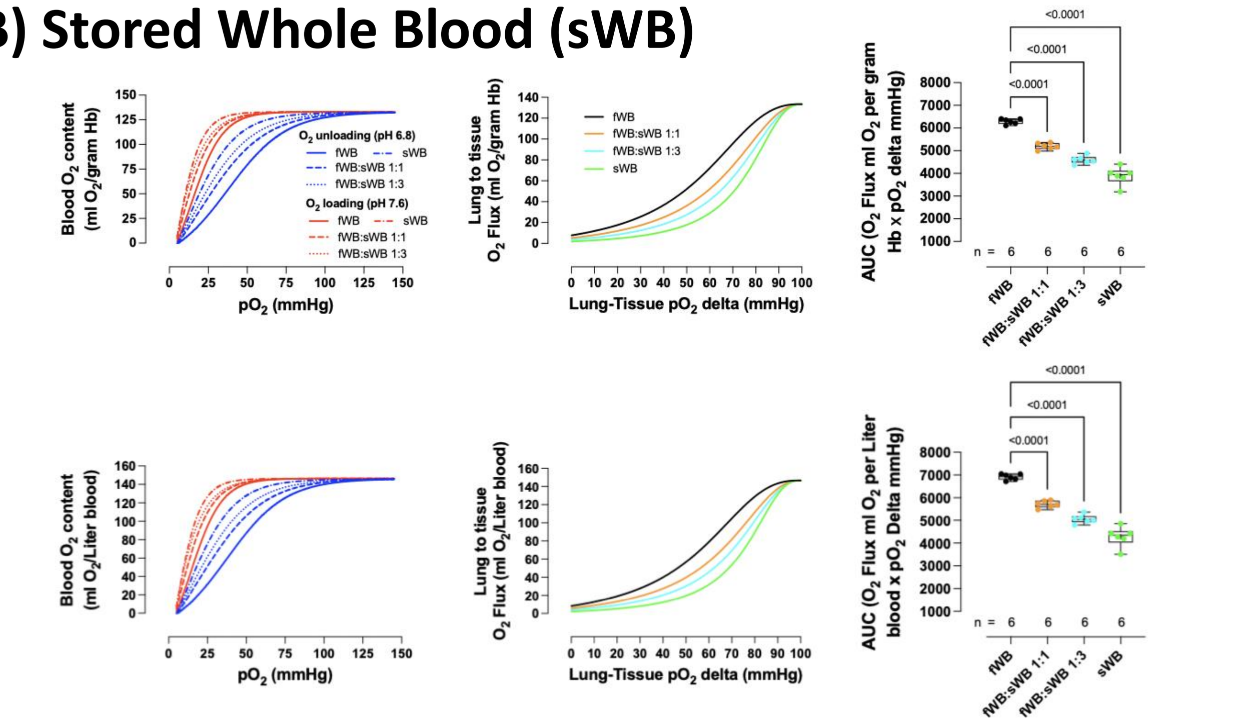
Results

3. Benchmark O_2 delivery of fresh whole blood (fWB) against conventionally prepared and stored human whole blood (sWB)

A) Normal Saline (NS)



B) Stored Whole Blood (sWB)



Conclusions

A) Normal Saline (NS):
- Blood O_2 Content per Liter demonstrates true effect of dilution and how necessary O_2 carrying capacity is to maintain sufficient O_2 delivery

B) Stored Whole Blood (sWB):
- sWB Blood O2 Content per gram Hb reflects well known trend in HBO2 affinity (left shift) reduction due to loss of 2,3 DPG
- sWB demonstrated a ~40 reduction in the O2 potency of RBCs compared to fWB

- fWB:NS demonstrated inferior O_2 Flux per Liter blood compared to fWB:sWB, due to loss of O_2 carrying capacity of NS

O_2 Flux: Functional metric to analyze RBC products by quantifying their O_2 potency (i.e. delivery capacity)