

Shipping Human Islets

ICR WORKSHOP

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Rationale for Shipment Equipment

- There is a need for shipment of human islets from isolation centers to other facilities for research or clinical transplantation
- Containers currently used for islet shipment are inadequate as they may allow exposure of the islets to “deadly” :
 - temperature and pressure variations
 - Oxygen limitations

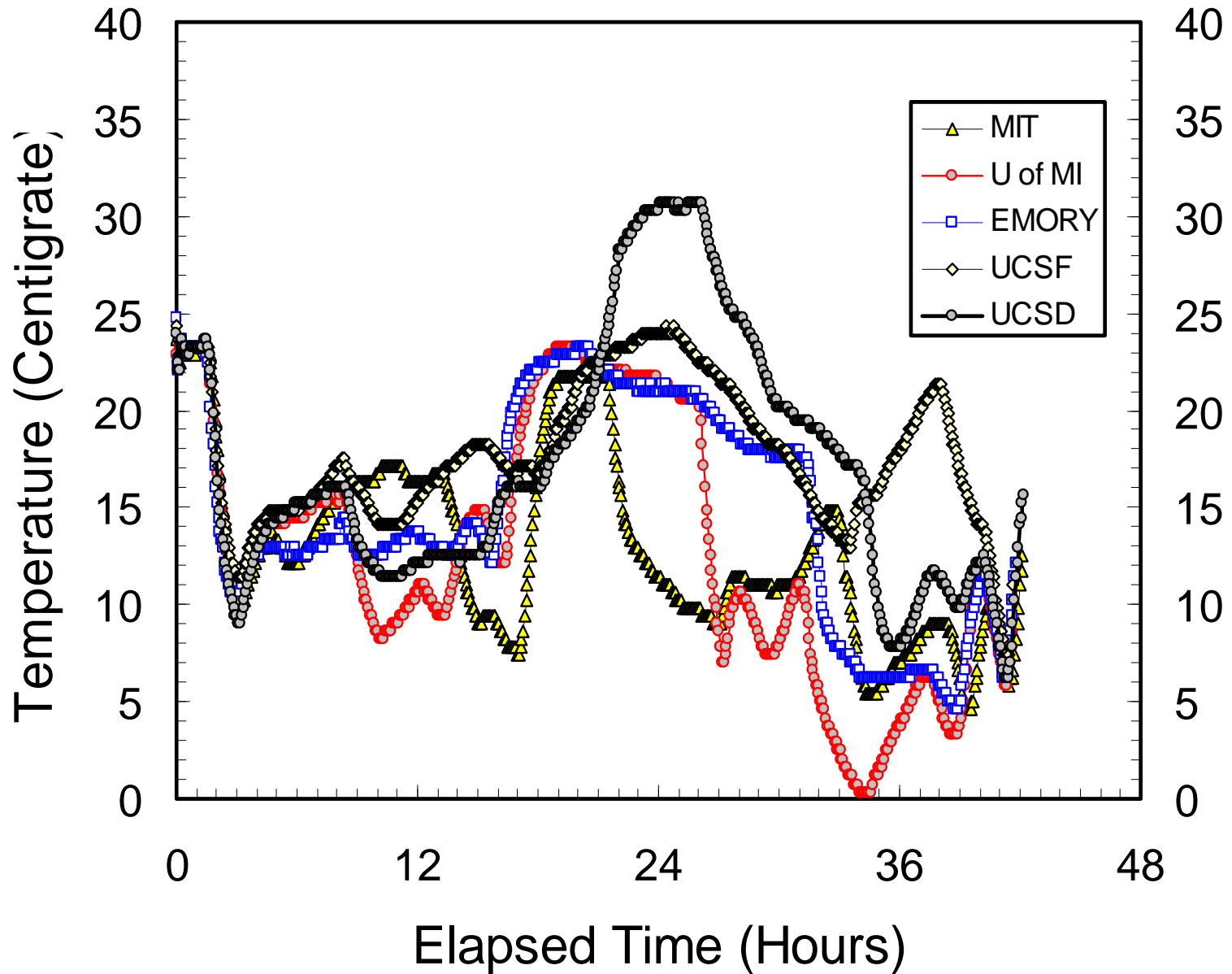
HUMAN ISLET SHIPPING

Important Parameters:

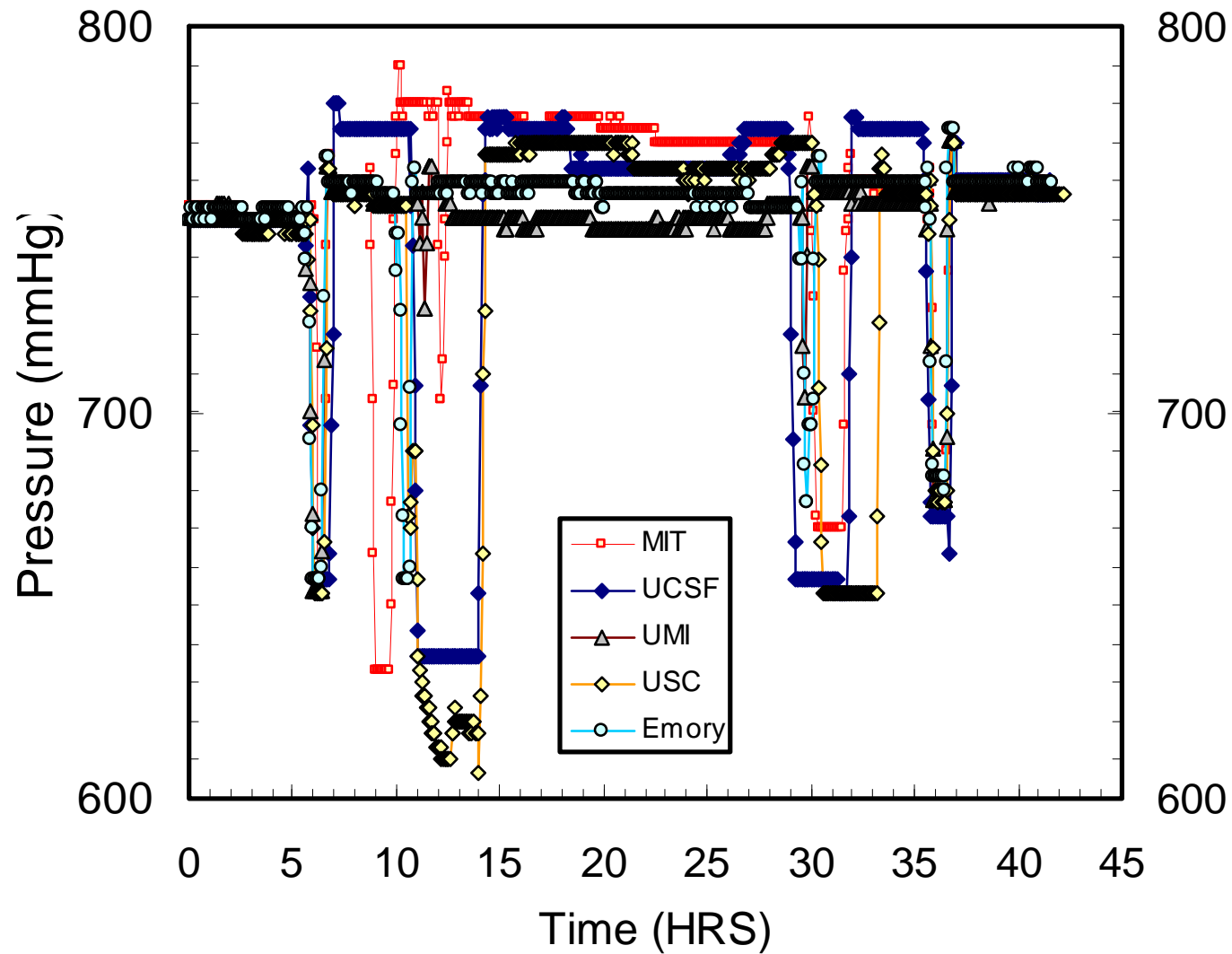
1. Temperature
2. Pressure
3. Oxygen

Data to support this?

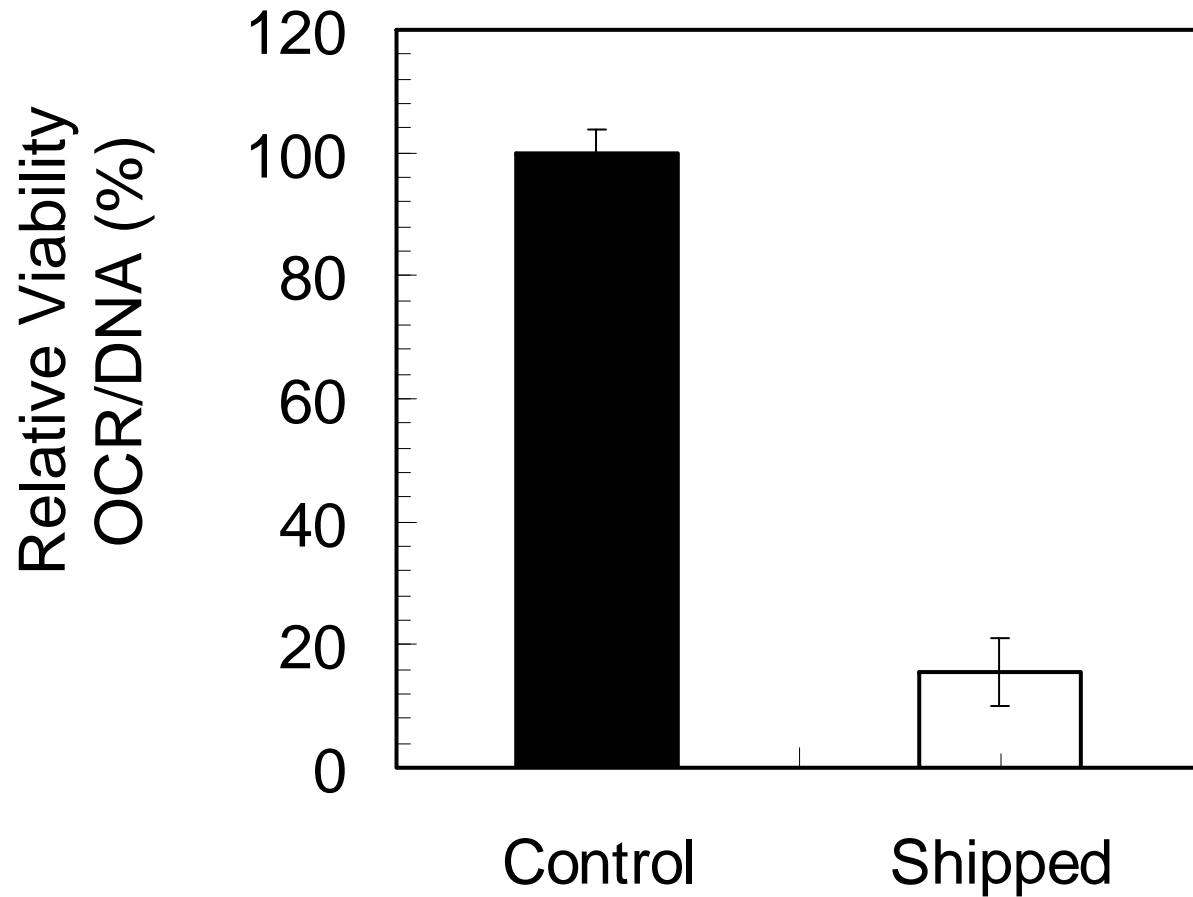
Temperature Measurements During Shipping (March 2004)



Pressure Measurements During Shipping (March 2004)



Effect of freezing temperature on viability

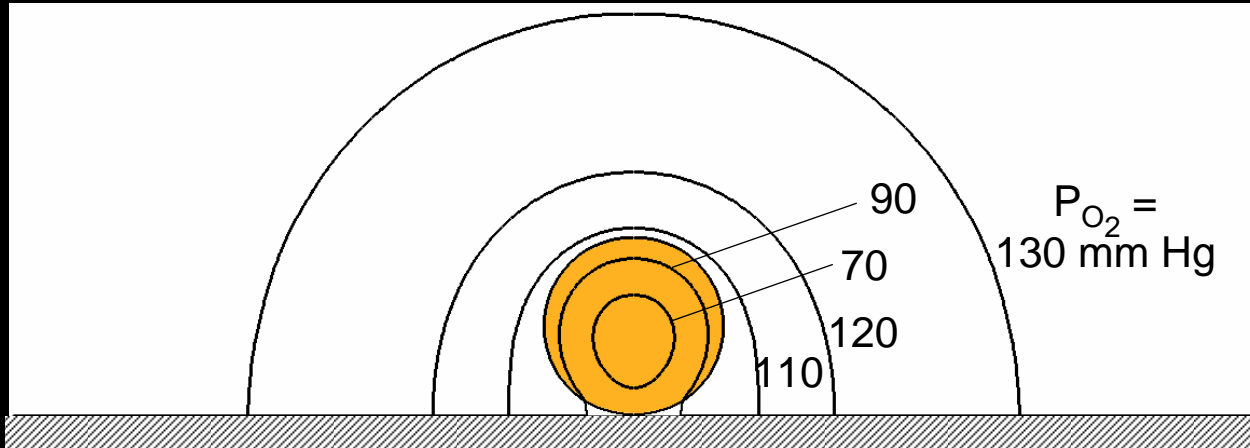


“Shipped” cells were exposed to temperatures below 0C for more than 1 hr

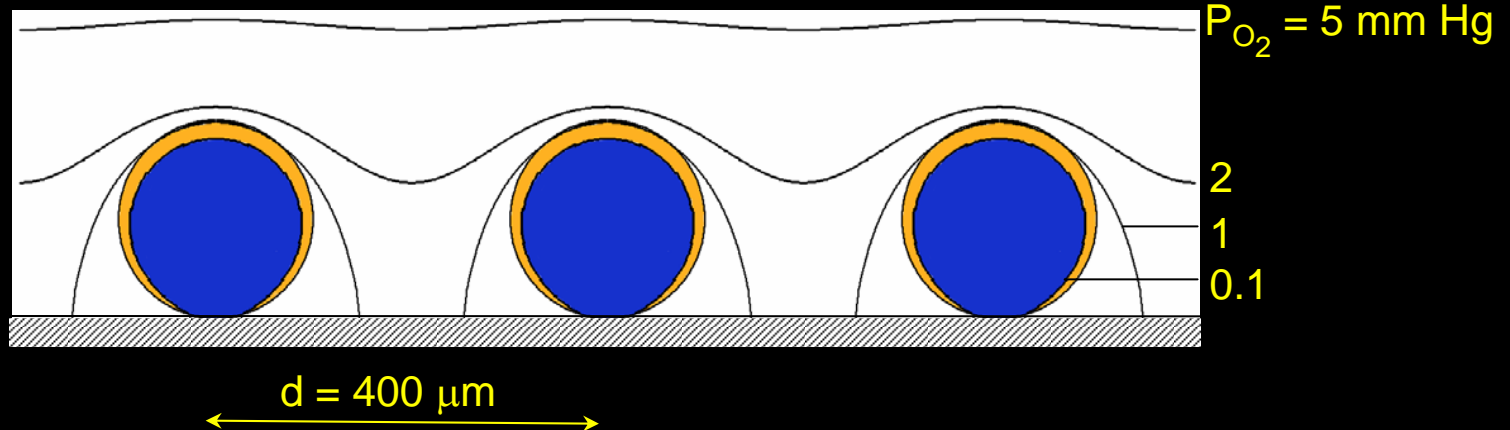
Islets in Culture

Single Islet

Ambient P_{O_2} = 142 mm Hg
Medium Depth = 6 mm
Islet Diameter, D = 200 μm

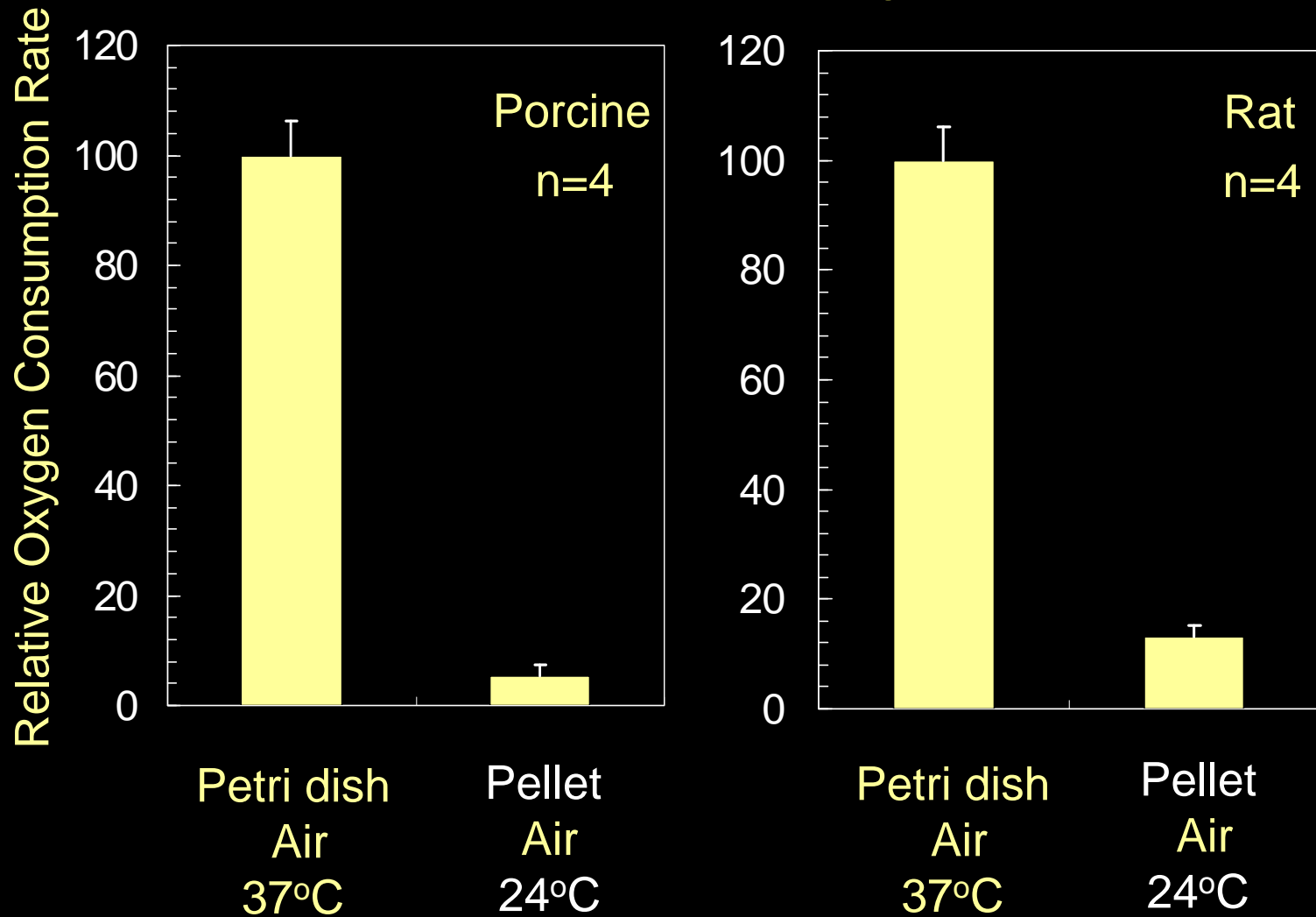


Multiple Islets



(Avgoustiniatos E.S., MIT, Ph.D. Thesis, 2001)

Islets shipped pelletized in the bottom of centrifuge tubes are severely damaged



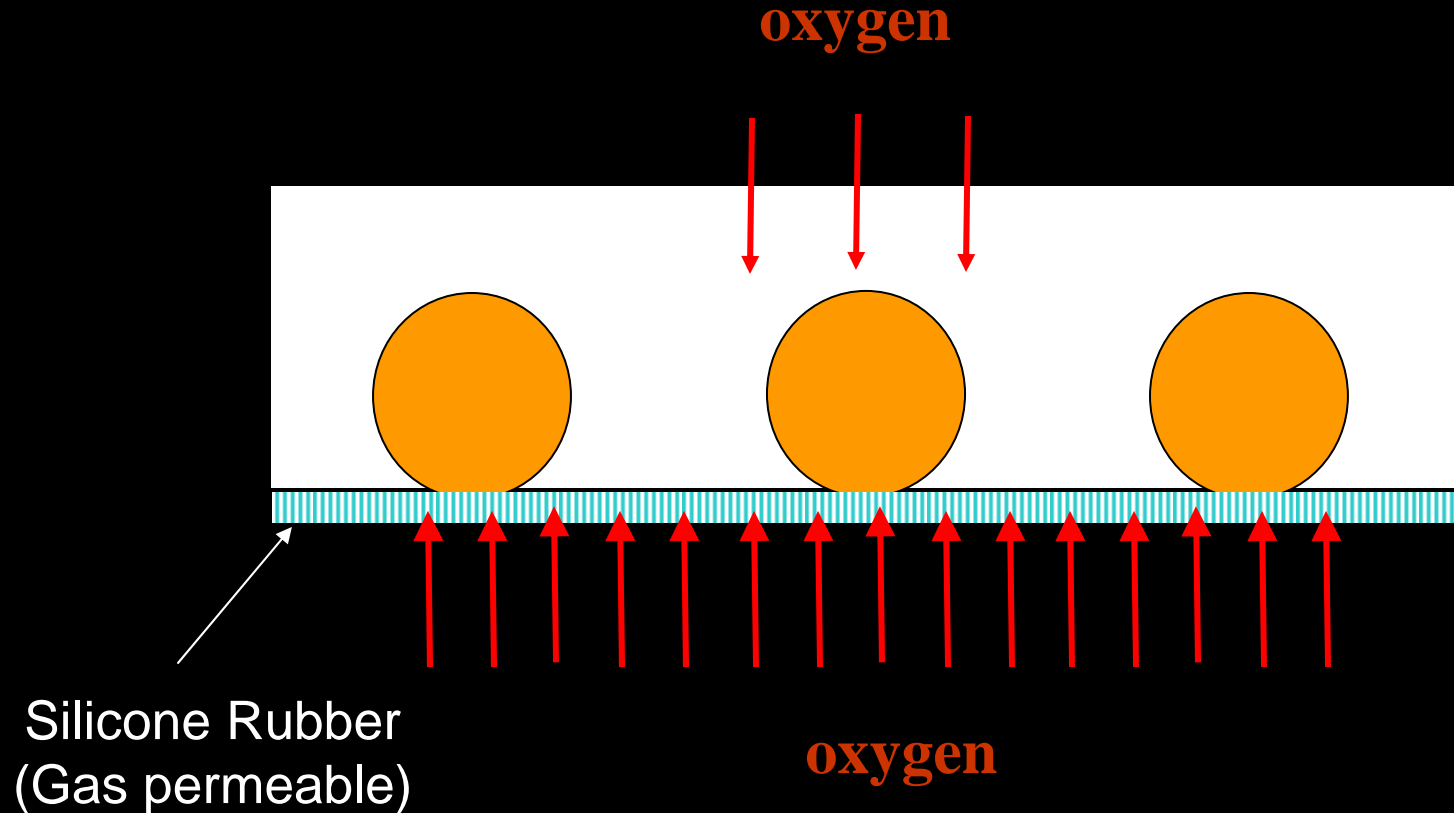
New Equipment for Islet Shipment

Hypothesis

Improving oxygenation by culturing islets on top of silicone rubber membranes will enable high-density culture (and shipment) without loss of viability

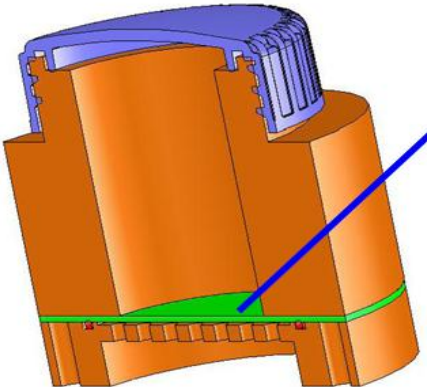
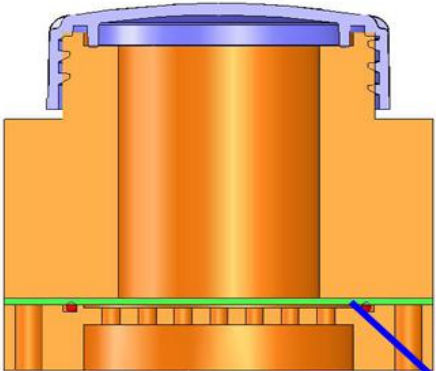
Hypothesis

Improving oxygenation by culturing islets on top of silicone rubber will enable high-density culture without loss of viability

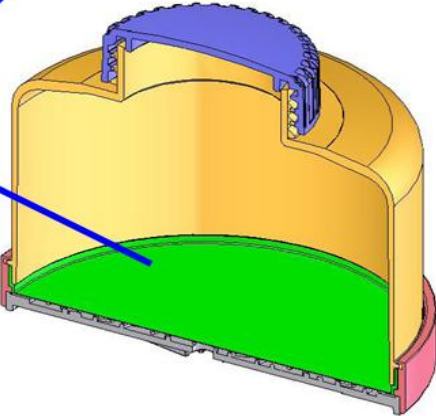
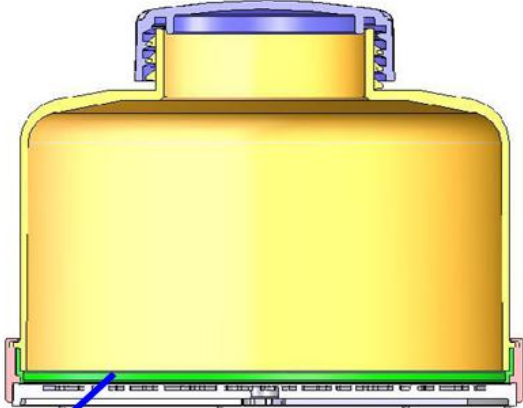


Culture Devices Based on Silicone Rubber

10 cm²
GP Device



100 cm²
GP Device



GP
Silicone
Rubber
Membrane

Gas Permeable Bags



American
Fluoroseal

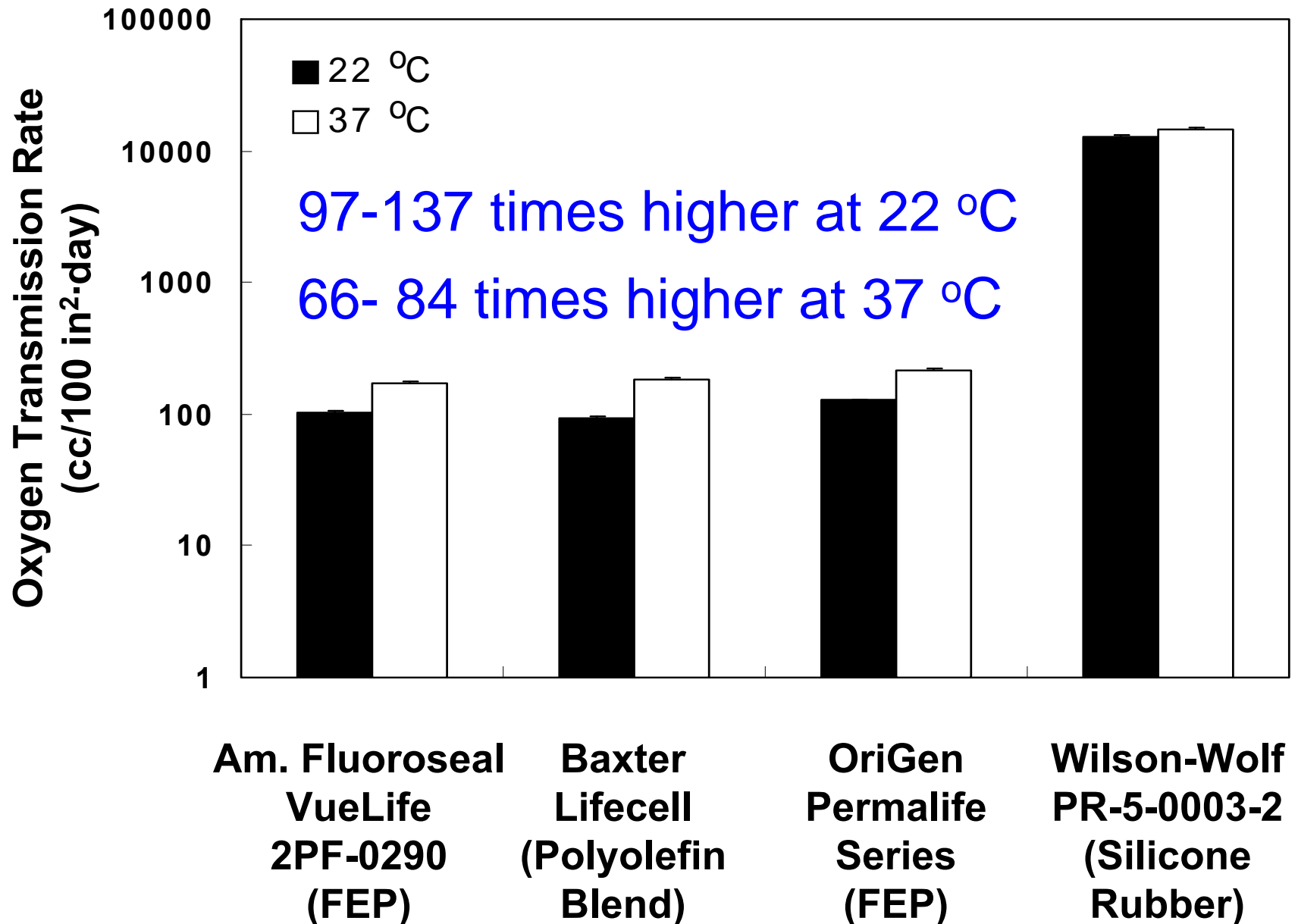
The image shows a clear plastic gas permeable bag with a red interior, connected to various tubes and connectors, set against a white background.

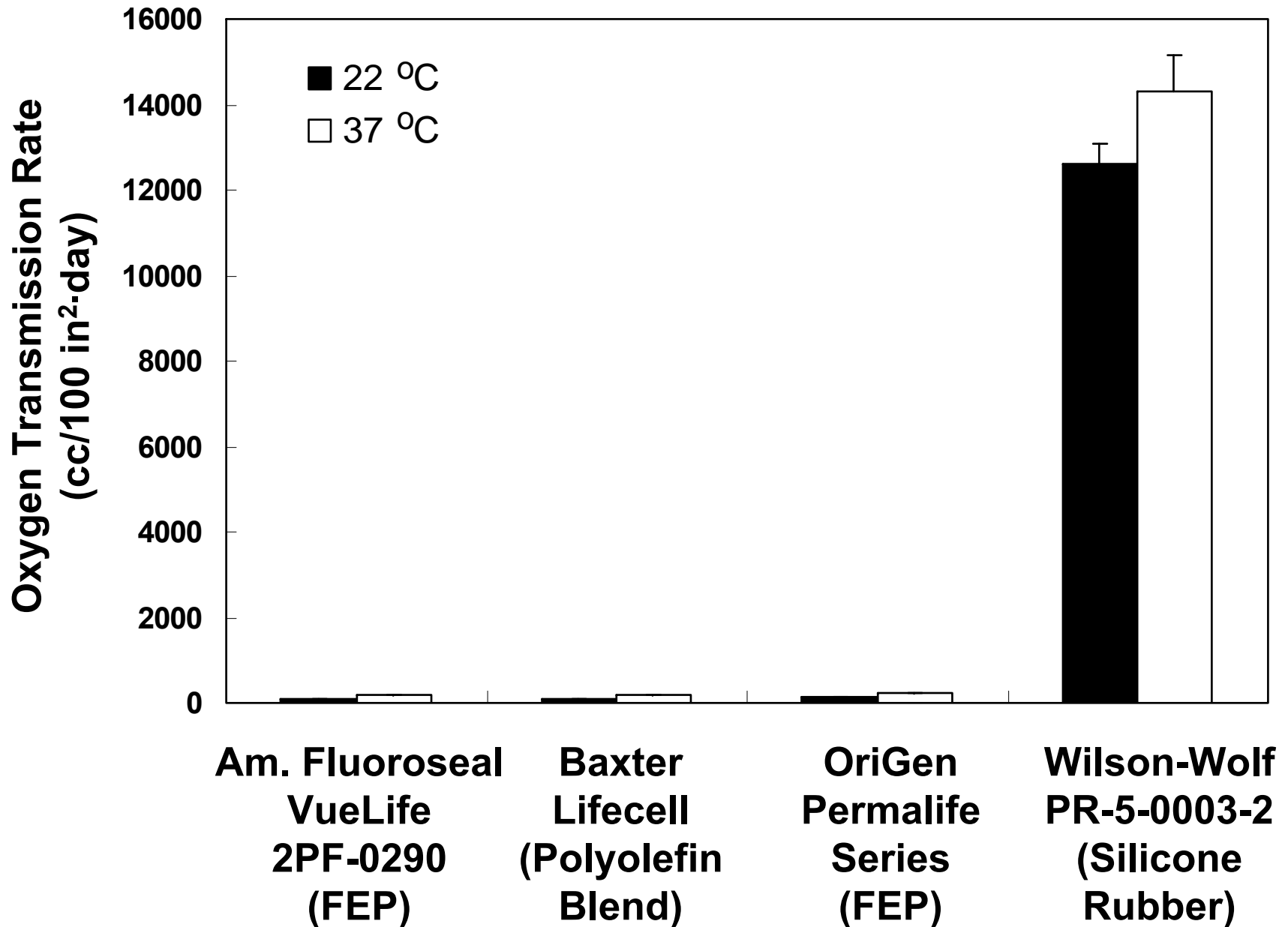


Origen

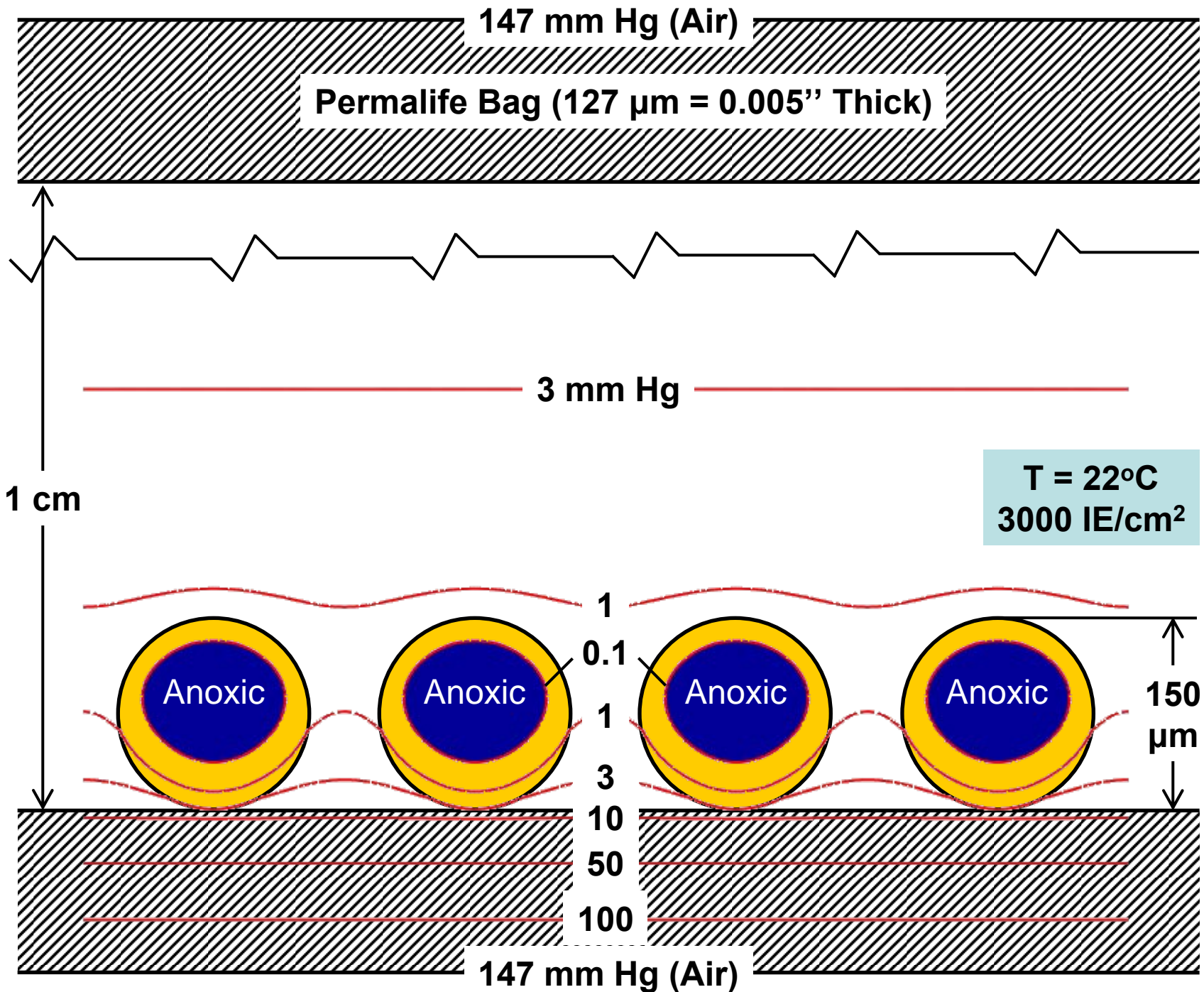
The image shows a person wearing a white glove holding a clear plastic gas permeable bag with a red interior, connected to a syringe and other tubing, set against a white background.

Gas permeable membranes differ.....

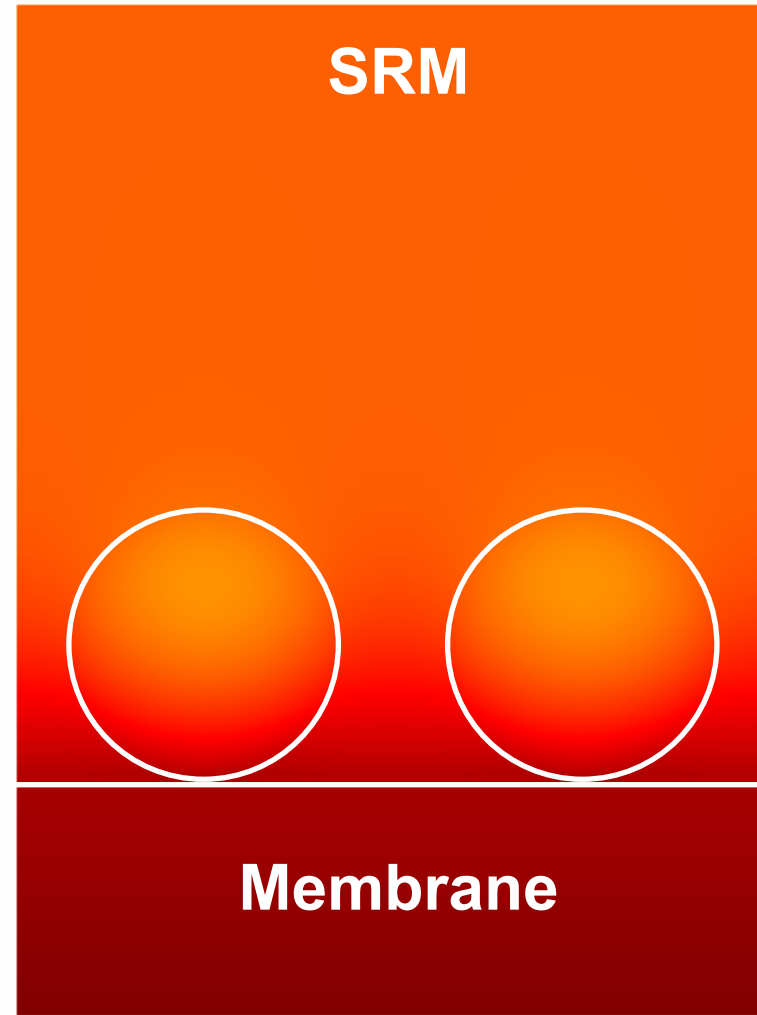




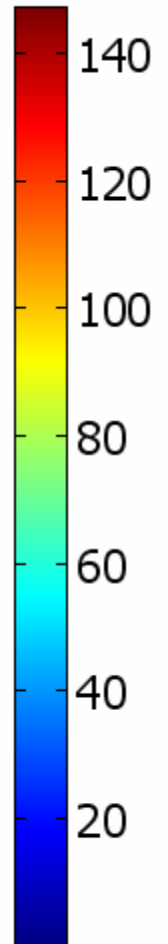
Does it matter?



$T = 22^{\circ}\text{C}, 3000 \text{ IE}/\text{cm}^2$

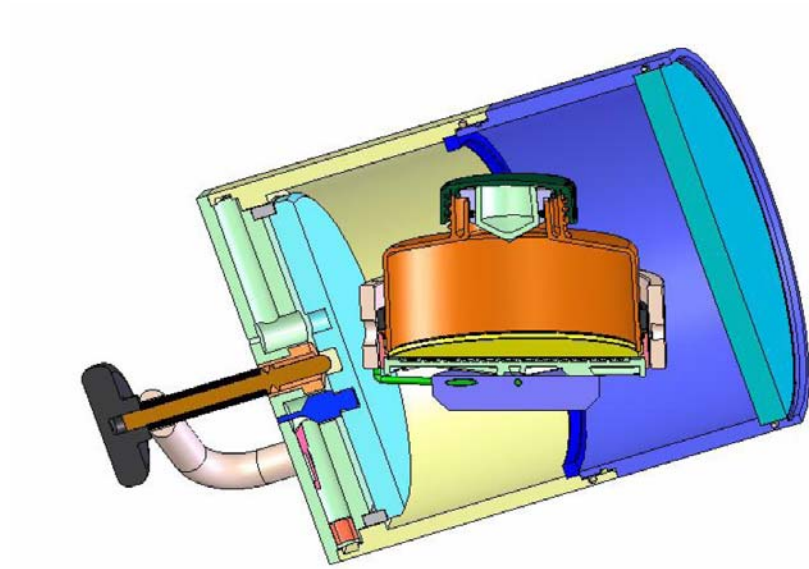
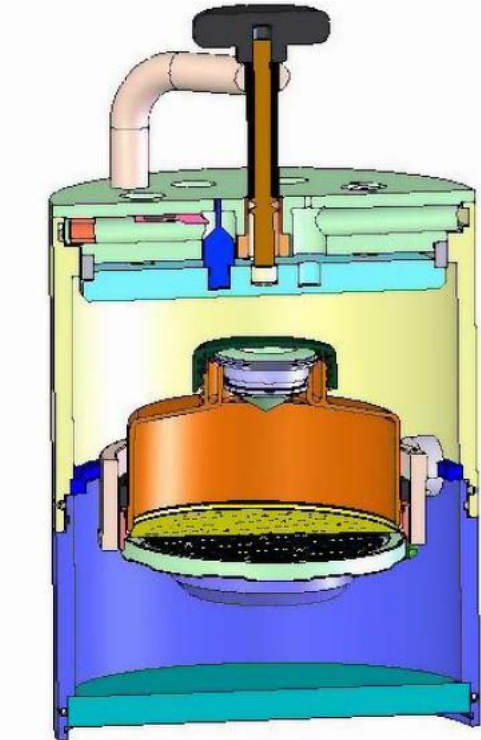


Max: 147



Min: 0.100

Pressure Regulated Gyroscopic Shipping Container for Silicone Rubber Vessels



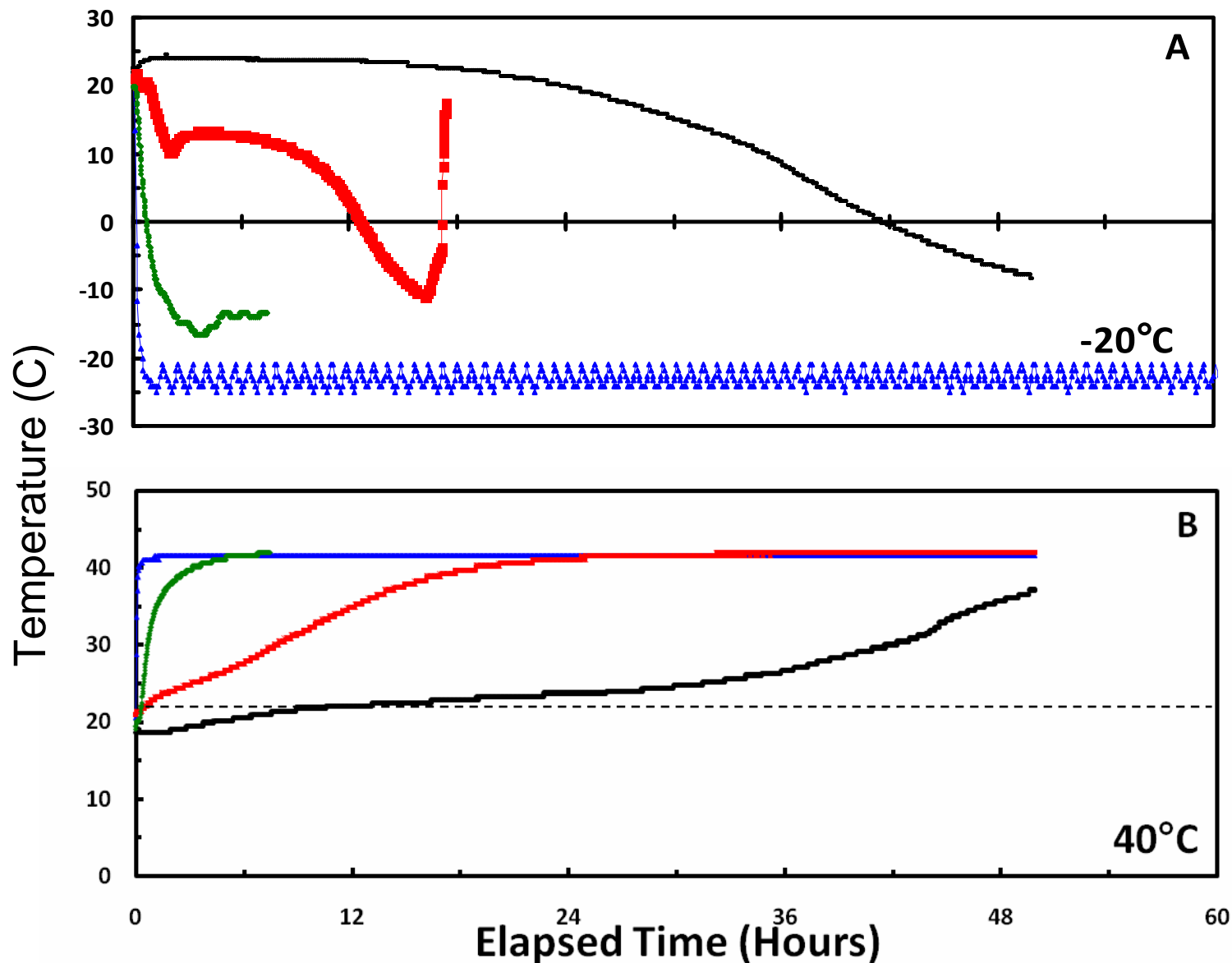
* Gyroscope can minimize chances of islet accumulation/aggregation

Pressure Regulated Gyroscopic Shipping Container Inside Styrofoam Box with Phase Change Material (PCM)*



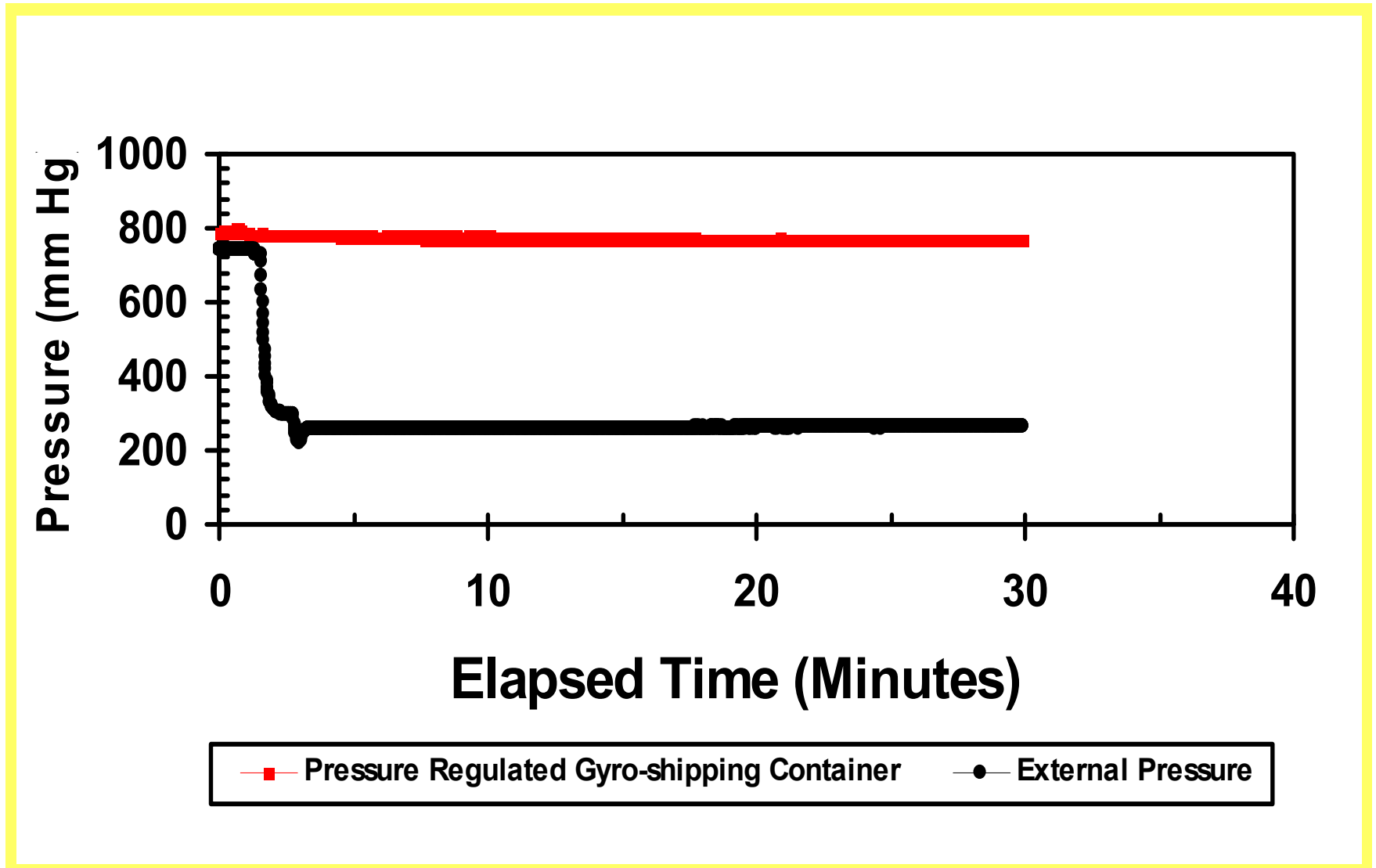
*For Temperature Regulation

Results with PCM Loaded Box

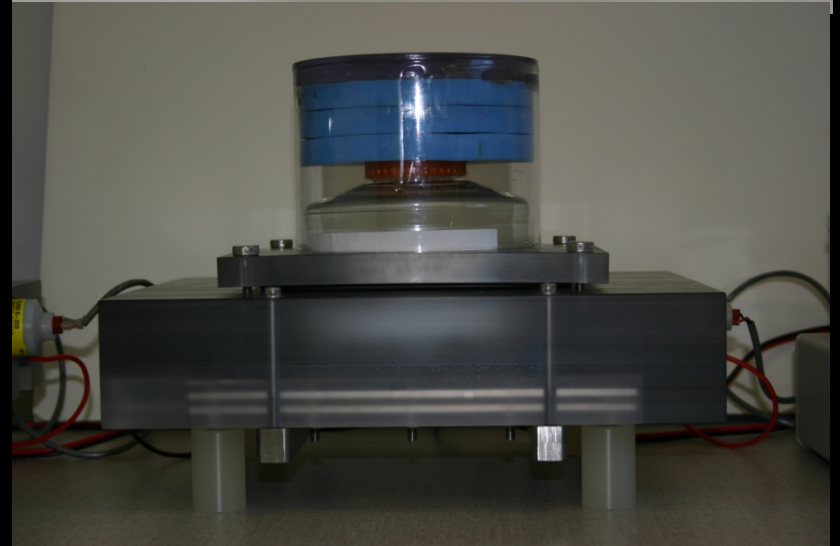
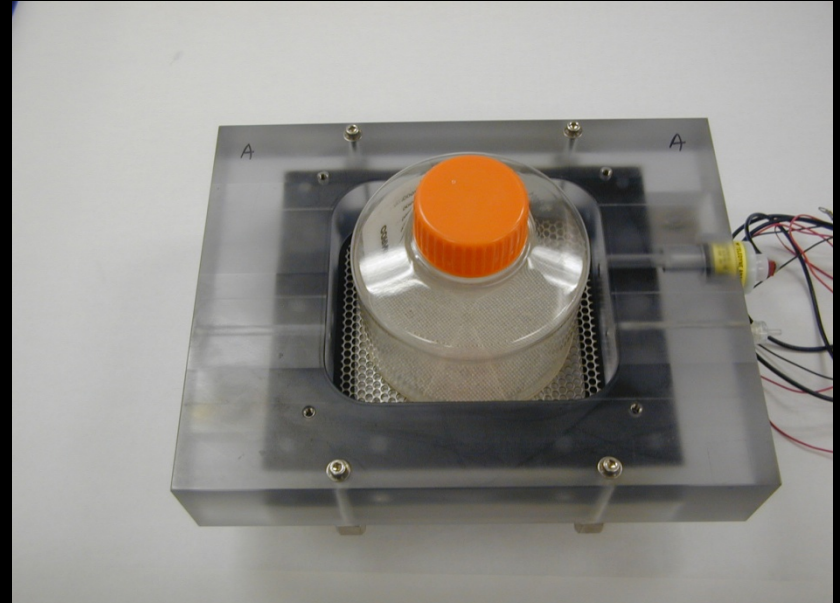
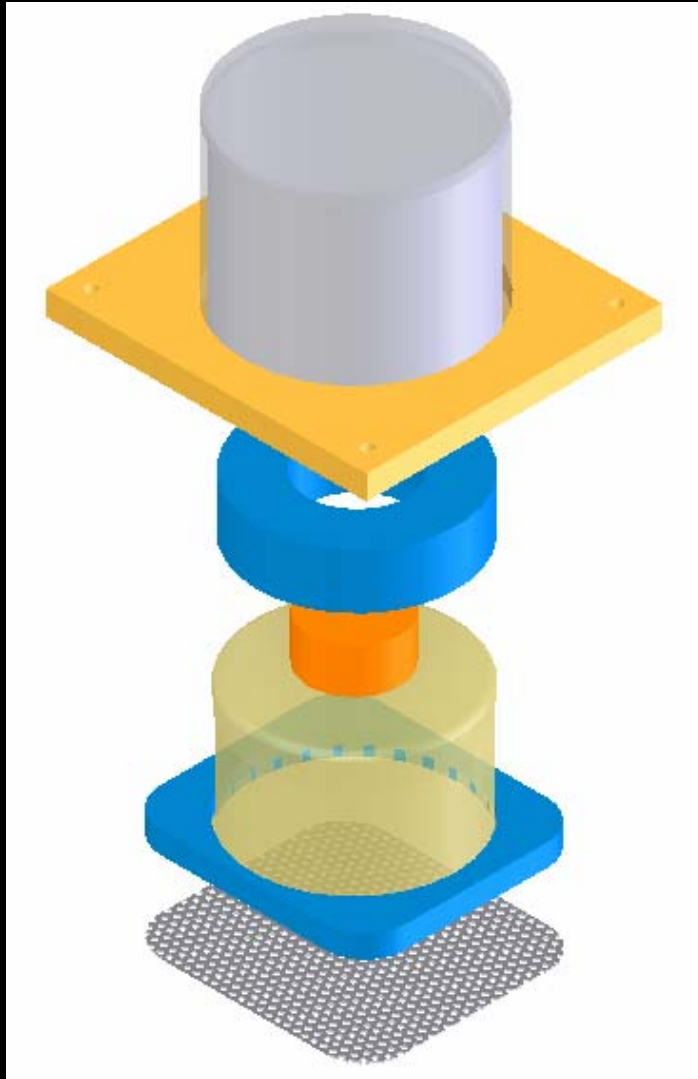


- Experimental Container 1 w/ 21 PCM Units
- ▲— External Temperature
- Experimental Container 2 w/ 2 TS Units

Results with Pressure regulated Shipping container



Combination of Approaches: Silicone Rubber with Enhanced Ambient pO_2



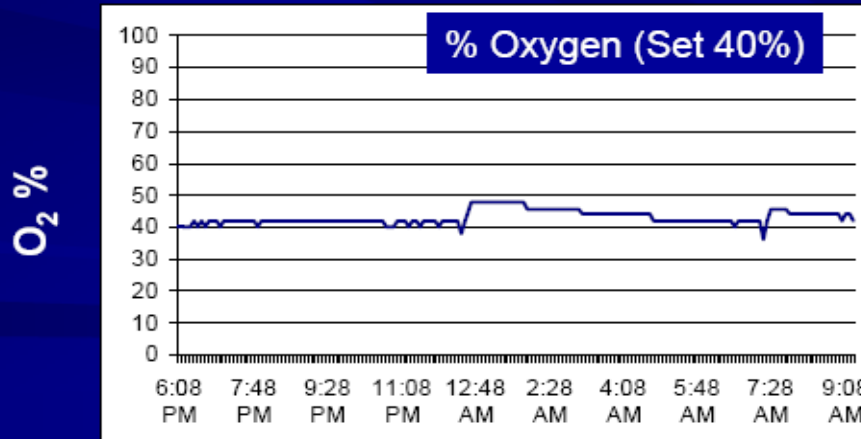
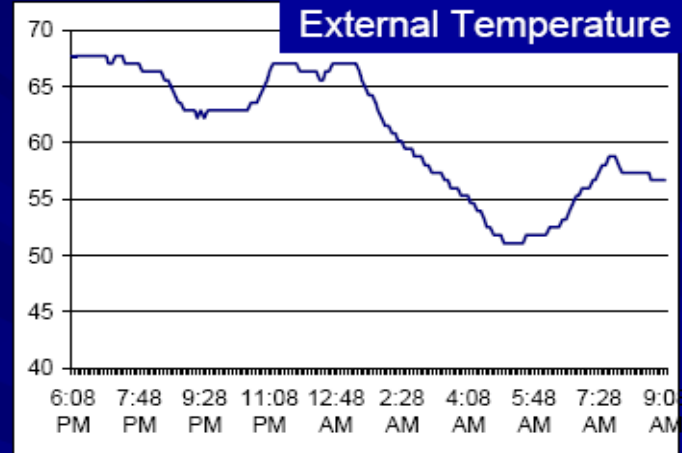
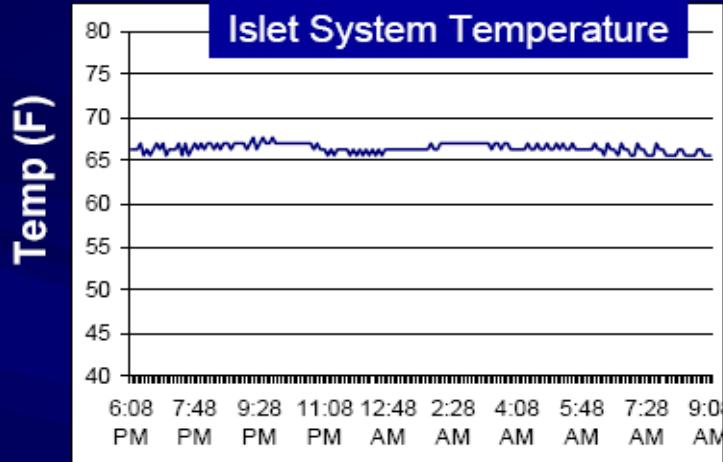
In collaboration with Giner Inc., NIH SBIR Phase II Project, and WW

Giner Portable Islet Culture System with temperature control using a modified thermoelectric chest (Vector 210®)



Test Shipment GINER-UMN

No Islets



Conclusions

- Successful implementation of simple cost-effective approaches can lead to substantial improvements in islet quality for research and clinical transplantation post-shipment
- More sophisticated approaches (Giner EOG) can provide finer level of control as needed

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