Pearls from Procurement

What the Clinician Needs to Know-Devices Machine Perfusion

RODNEY JONES

VICE PRESIDENT STRATEGIC PARTNERSHIPS

NORA

Disclosures

NONE RELATED TO THIS TALK

THE NATIONWIDE ORGAN RECOVERY TRANSPORT ALLIANCE

PREVIOUS XVIVO

Overview of organ transplantation process

- DBD = Donation after Brain Death
  - The Harvard Medical School's ad hoc committee defined brain death in 1968 using the following criteria
- DCD = Donation after Circulatory Death
  - Christiaan Barnard was a South African surgeon who performed the world's first human-to-human heart transplant on December 3, 1967
- NRP = Normothermic Regional Perfusion
  - Procedure that uses a machine to circulate blood through organs after a donor's heart has stopped beating.
- HMP = Hypothermic Machine Perfusion
- NMP = Normothermic Machine Perfusion
- HOPE = Hypothermic Oxygenated Machine Perfusion
- COR = Controlled Oxygenated Rewarming

Traditional Cold Storage vs. Machine HMP & NMP Perfusion

- Cold storage V. machine perfusion

  Gold Standard; 1960 Collins , UW : Low Na+ High K+ / ice 4^{o}c

  Gold Standard

  Safe, Efficacious, Affordable

- Machine perfusion;

  Expensive, complex, resource intensive

Cold Storage v. Machine Perfusion

Method	Temp	Organ	Merits	Challenges
Cold Static Storage	0-8°c	KI,LI,LU,HT	Low Cost, Simple	Metabolic Accumulation, No Assessment
Hypothermic Machine Perfusion	0-8°c	KI,LI,LU,HT	Provides Oxygen and Metabolic Substrates	No Assessment, Perfusion time limited
Normothermic Machine Perfusion	35-38°c	KI,LI,LU,HT	Provides O2, Substrates, Metabolic Viability, Assessment and Repair	Perfusion Time Limited, Complex, Labor Intensive
Controlled Oxygenated Rewarming	8-20°c	KI,LI,LU	Gradual Warming of Perfusate to mitigate Reperfusion Injury	TBD

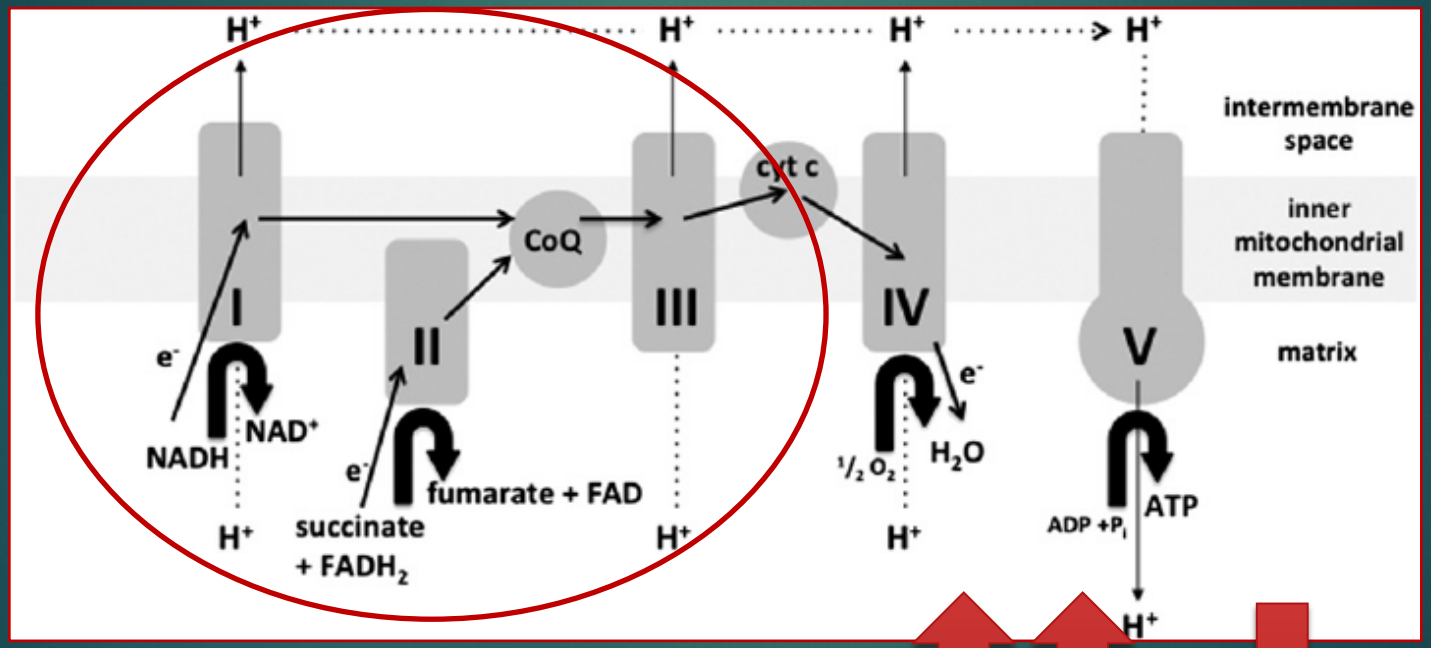
Hypothermic Machine Perfusion

- HMP 0-8^{o}
- 1968 Belzer preformed 1st Kidney concept generating metabolic substrates for the generation of ATP
- 1990 saw an increase in HMP due to increased demand and use of marginal organs. HMP demonstrated improved outcomes and graft function. (Mainly Kidney Driven)

Indications for Hypothermic Machine Perfusion

- Prolonged warm Ischemia
- Uncontrolled DCD
- Poor and/or incomplete flush during organ recovery
- High risk and/or marginal donor
- Prolonged allocation
- Prolonged transport

Mechanisms of Action with the addition of Oxygen in HMP

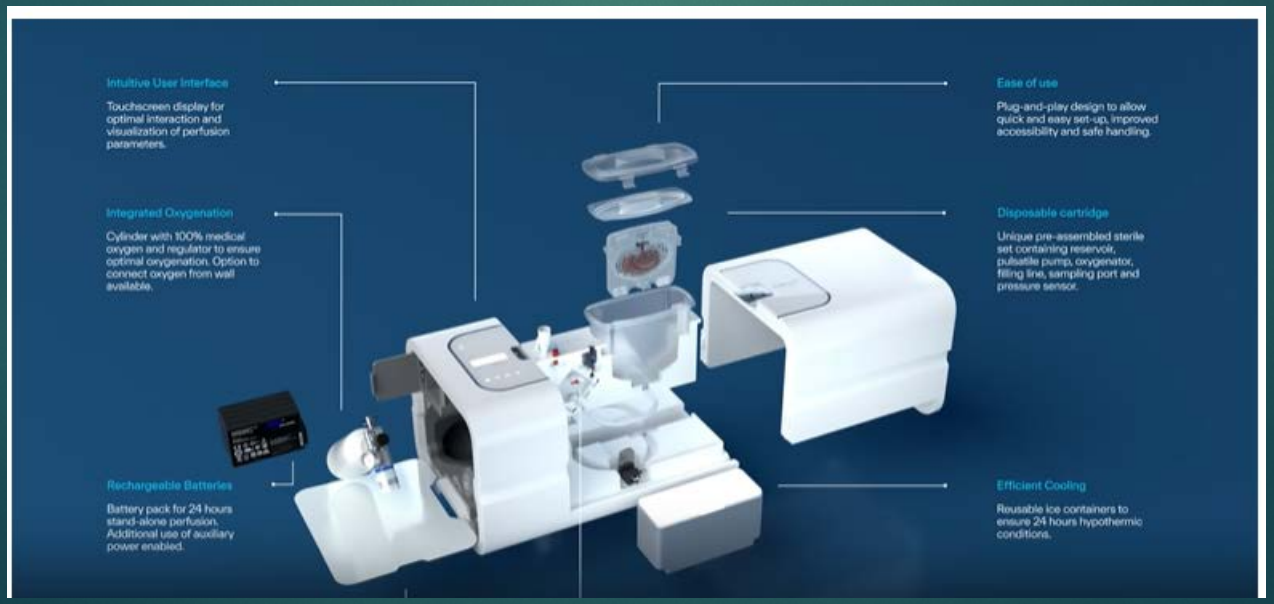


The Mitochondrial Electron Transport Chain = = ATP ROS IRI

Oxygenated versus standard cold perfusion preservation in kidney transplantation (COMPARE): a randomized, double-blind, paired, phase 3 trial
Lancet 2020 Nav 21, 396 (10263) 1653-1662

- 19 European Centers
- 197 Kidney Pairs randomized, double blinded phase 3 trial
- 106 pairs transplanted
- DCD donors >50YO
- 1KI w/ HMPO, 2nd KI/ HMP alone
- 11.% Improved Renal Function
- 73% Fewer graft failures
- 44% Lower Incidence of acute rejection
- 31% Reduced incident of severe post transplant complications

FDA Approved Kidney Devices



Normothermic Machine Perfusion

35-38^{o}c

- Maintains metabolic activity and viability
- Designed primarily as an assessment tool
  - Expanded use
- 2007 Steen et al, first lung after 6 hr EVLP assessment
- 2008 Cypel et al, 12hr w/ change in protocol
- 2016 first NMP in Livers
- 2021 OCS Heart System, indicated for DCD hearts

Challenges for NMP

- Lack of Standardization
  - Various protocols
- Logistical Complexity
  - Not easily transported, Not approved for commercial transport
- High Cost
  - $50,000-$100,000
- Technologically Complex
  - Requires special knowledge , CCP/ECMO/RRT/Other
- Perfusion Related Injuries
  - Mechanical injuries, microvascular damage, shear stress, edema
- Perfusate Challenges
  - Mimics blood, nutrients, oxygen carrying capacity

Benefits of NMP

- Real Time Functional Assessment
- Improved Marginal Organ Utilization
- Reduced Ischemia Reperfusion Injury
- Enhanced Organ Function Post – Transplant
- Improved Graft Survival
- Facilitation of Complex Transplants
- Improved Matching Opportunities

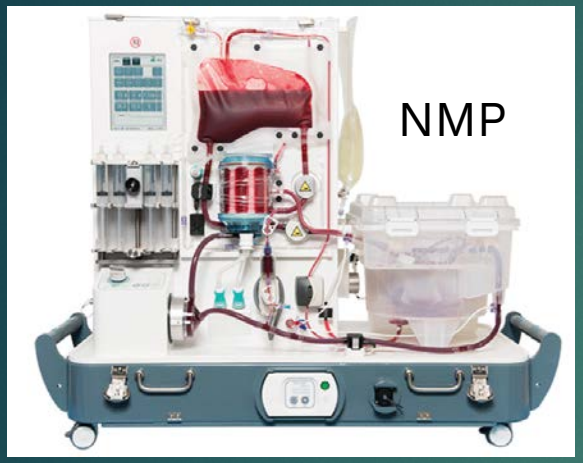
The Goal for NMP

- Organ Assessment
- Organ Repair
- Prevent Ischemia Reperfusion Injury
- Organ Immuno-modulation
- Remove metabolic waste
- Organ regeneration
- Supply Oxygen and Nutrients

Liver Assessment

- FMN
- Transaminase
- Bile Production / Ph , Glucose, BiCarb
- Lactate
- Glucose clarence
- Coagulation

NMP- Liver



NMP-Lung

Non-Transport, Extensive Evaluation

Transportable , limited evaluation

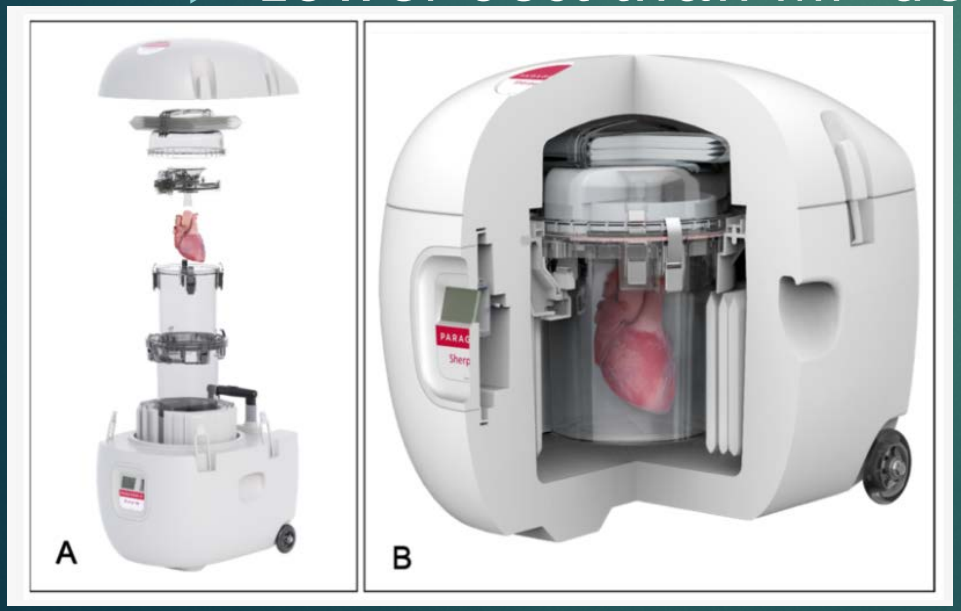
Heart NMP / HOPE

FDA Approved, Transportable

Clinical Trail , Transportable, 8°c

Alternative Devices Not Perfusion, but preservation

- No Assessment
- Maintains constant temperature w/o ice
- Prolonged safe storage
- Lower cost than MP devices



Conclusion

- HMP
  - Safe, Effective, Improved Outcomes, Affordable, easily transportable, Oxygen compatible, No Assessment
- NMP
  - Complex, Effective, Assessment, Improved Outcomes, Expensive, difficult to transport, labor intensive.
- Face changing coolers
  - Promising results, safe, affordable, transportable, No Assessment, No Oxygen

Q&A

- Open floor for questions and discussion