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Much progress has been made since the first successful organ transplant was conducted in 1954 by Dr. Joseph Murray when he transplanted a kidney between identical twins. Transplantation has revolutionized the treatment of formerly fatal diseases such as congestive heart failure, end-stage chronic liver disease, and severe interstitial lung disease. Timely transplantation of harvested organs into recipients is critical. As time lapses with a transplanted organ outside of a body, the risk of tissue degradation increases. Is that why organs are placed in coolers during transport? Are there any novel solutions to expand the time allowable between organ harvesting and organ transplantation?

To learn more about why we use coolers, the current challenges in the field, and what the future looks like, I asked two transplant specialists, Dr. Ivana Milojevic from George Washington University School of Medicine and Dr. Shambu Aryal, the director of INOVA's Lung Transplant Program. Dr. Milojevic explained that harvested lungs could only remain outside the body for 6 hours, after which they are no longer viable for transplantation. This means physicians must work in the middle of the night with utmost urgency or risk losing a precious donor-matched lung. Organs are kept in coolers before being transplanted to prevent tissue necrosis and ischemic degradation of viable tissue. Even donors that are a good match will not be transplanted to recipients more than 1200 miles away due to the risk of degradation.

Ex-vivo organ perfusion (EVOP) seeks to solve the issues related to tissue degradation while the organ is outside of the body. EVOP is a method through which explanted organs are perfused with a warm solution designed to recreate the in-vivo environment in which an organ normally functions. EVOP enhances the amount of viable tissue within an explanted organ, allows physicians to monitor the physiologic parameters of the organ, and even creates a way for antibiotics, anticoagulants, and other medications to be "given" to the organ to improve its state before it is transplanted into a patient. The first instance of ex-vivo lung perfusion was carried out in 2001 in Sweden.

There are currently three main models for ex-vivo organ perfusion. The first model involves transporting an organ from the site of ex-plantation to a third party site at which the organ is perfused. The organ is then transported again to its final site for transplantation. This method still involves putting the organ on "ice" during transport, thereby creating time for tissue to die. This "cold" transport time creates a distance restriction for sourcing organs.

Another method involves less ischemic time and relies on an institution having an in-house organ perfusion system. However, this method still involves putting the organ into freezing conditions during transportation. This method limits organ transplantation as both the donor and the patient must be located in the same institution.

Transmedics, the company I am writing about today, is seeking to enhance the viability of donor organs through the creation of the first fully-portable EVOP. This new method being pioneered by Transmedics involves no ischemic time as the organ is explanted and immediately put into their OCS™ machine. This machine is fully portable, and the organ is perfused the entire time from ex-plantation to just before its implantation into a donor. Not only does this

involve zero ischemic time, but it also allows organs to be sourced from greater than 1200 miles, which could increase the amount of available organ donors.

Dr. Aryal estimated that EVOP has enhanced the availability of donor lungs by 20-30% and that the Transmedics system might increase that number as ischemic time would drop and the viable distance from which lungs can be sourced could increase drastically. Further increase in availability might be possible by expanding donation to those who become donors after cardiac death. Donors after cardiac death are less common, and organs are often in worse condition, but EVOP, and especially, the Transmedics OCS™ machine can help enhance the viability of these organs. One of the stated goals of Transmedics is to utilize organs after cardiac death. In 2019, the Transmedics system facilitated the first successful heart transplantation after Death from Cardiac Arrest.

Few novel and revolutionary technologies were affordable at their outset. Drawbacks to Transmedics include a hefty price tag that can exceed $120,000 per organ transplantation. One of the major clinical trials examining the Transmedics method is the INSPIRE Trial. The trial showed that using Transmedics' OCS™ machine led to less severe primary graft dysfunction relative to cold storage of ex-planted organs. While Transmedics are in the initial innings of rolling out their OCS™ technology nationally, they are the current frontrunner in terms of shaping the future standard of care for organ transplantation.

The author has no conflicts to report.