# Innovation in Organ Transplantation Makes Best Use of Short Supply

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Just as we celebrate the 79 people per day on average who receive a solid organ transplant in the United States, we as physicians must be motivated to find new solutions for the 18 who die each day due to the shortage of donated organs.[1]

In 2012, more than 28,000 organ transplants were performed nationally, with 646 taking place in Wisconsin. This means more transplants per capita are performed in Wisconsin than the national per capita average. However, there are more than 2200 people in our state on the waiting list for an organ transplant,[2] and the statistics tell us that not all will receive one.

With the need for organs outpacing supply, it is incumbent upon us to be the best possible stewards for these precious resources. Through innovation in surgical techniques, treatment protocols and research, the Medical College of Wisconsin (MCW), with its clinical partners, is developing new means to optimize the use of donor organs.

Our efforts are built on a strong clinical platform comprising a solid organ transplantation joint program among MCW, Froedtert Health, Children's Hospital of Wisconsin, and BloodCenter of Wisconsin. Led by Johnny C. Hong, MD, the program is skilled in every type of solid organ transplantation. To help meet the needs of those requiring solid organ transplantation in Wisconsin, the partner organizations have made recent investments in growth and sustainability. This, in turn, has led to programmatic enhancements and new opportunities, such as our lung transplantation program receiving certification from the Centers for Medicare & Medicaid Services.

Our MCW-Froedtert-Children's Hospital of Wisconsin transplant center leads eastern Wisconsin in providing expanded access to kidneys donated from live donors through the National Kidney Registry. Last summer, our transplant center participated in the world's second largest kidney chain, which involved 28 donors, 28 recipients, and 19 transplant centers. We transplanted a 55-year-old Racine man with a kidney from an altruistic donor after the man's son-in-law donated a kidney on his behalf to another recipient in the chain. With organs in short supply, kidney chains help increase the chances of finding a donor match.

Saving multiple lives with 1 organ demonstrates using available resources to their fullest potential, an ability that MCW's surgical expertise and collaborative, integrated teams allow. Last year, Dr Hong and his team performed the first in situ split liver transplant in Wisconsin, in which the liver from a single deceased adult donor was divided into 2 functional grafts. One portion was received by a critically ill infant at Children's Hospital and the other by an adult patient at Froedtert. The liver's remarkable ability to regenerate makes such a procedure possible. In December, the team successfully completed a live donor liver transplant, an option available in only a handful of programs in the country.

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For those requiring lung transplantation, the availability of organs is particularly problematic. The physiological changes that occur in the deceased donor upon brain death cause detrimental changes in the lungs, limiting the ability to use them for transplant. Fluid and protein deposition and alveolar damage often cre-

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ate a dysfunctional organ with only about 20% of available lungs being suitable for transplant. However, when Robert B. Love, MD, joined MCW in 2012 he brought with him a research program and technology capable of reversing the damage. He is the data monitor for the Food and Drug Administration (FDA) in a clinical trial investigating the efficacy and safety of ex vivo lung perfusion.

In this tailored rehabilitation process, the lungs are removed from the donor and put on a physiological circuit, ventilated and continuously perfused by a solution providing nutrition, antibiotic, antiviral, and anti-inflammatory medications to enhance the organ viability. Simultaneously, excess fluid is removed and together, these processes rehabilitate lungs to a point that they are healthy enough for transplant.

This ex vivo technology currently is approved for clinical use in Canada and several countries in Europe, and FDA approval for the United States is anticipated this year. Preliminary results suggest that incorporation of this technology could double the lung supply and substantially shorten the waiting list. Organ rehabilitation may someday include gene therapy and has potential applications for other organs as well.

Technological advances also are helping bridge patients to transplant. Mechanical circulatory support has led to extended life for adult and pediatric patients at MCW, Froedtert Hospital, and Children's Hospital as they await heart transplants. Recently, a team led by Ronald Woods, MD, PhD, reported the first long-term successful bridge of a single ventricle patient with the Heartware® ventricular assist device.

Perhaps even more remarkable, the patient was 100% sensitized to human leukocyte antigens (HLA), which can increase wait times and hinder good outcomes for heart transplant patients. The virtual crossmatch, a strategy developed at MCW in collaboration with the Children's Hospital Herma Heart Center transplant program and the BloodCenter, can be used to predict histocompatibility and has become standard practice for sensitized organ transplant candidates. Using this tool, the patient was transplanted with a compatible organ and a negative crossmatch. This further demonstrates a commitment to making optimal use of the precious few organs available.

Reducing the number of transplants that fail due to organ rejection remains a critical area of needed advancement to maximize our limited organ supply. Michael E. Mitchell, MD, and Mats Hidestrand, PhD, are co-principal investigators for a new National Institutes of Health grant to develop a noninvasive method for monitoring rejection in children and adults with heart transplants. Biopsy, which carries high costs and inherent risks, is the current monitoring standard. This research instead uses targeted sequencing to precisely quantify the amount of donor specific cell free DNA in recipient plasma. Donor cell free DNA increases in patients undergoing solid organ rejection, and this technology provides the promise for more sensitive and early detection of rejection so that medical therapy to reverse these processes can be more precisely administered.

The MCW team has assembled a consortium of major adult and pediatric heart transplant centers to participate in a prospective blinded longitudinal study to test this rapid, highly sensitive and cost-effective approach for monitoring rejection. It is worth noting that this technology may similarly benefit other (noncardiac) organ transplant recipients.

In addition to practice and research innovation, we also provide education to our community about life-saving organ transplantation and donation. In October, Froedtert and the Medical College of Wisconsin earned gold level recognition from the US Department of Health and Human Services for outreach for organ donation and registration efforts. As physicians, we continuously strive to develop innovative strategies to improve outcomes for transplant recipients. It is our obligation to ensure the gift of life reaches its intended destination.

## References

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