

# Innovations In Transplantation

## Xenotransplantation

A pig's kidney has been transplanted into a human and was not immediately rejected for the first time. The medical advancement, called a "transformative moment" by researchers, could pave the way to help the thousands of people in need of organ transplants every year.

On September 25, researchers at New York University performed the transplant, called xenotransplantation, in a two-hour procedure. The kidney, which was obtained from a genetically engineered pig, was placed in a brain dead human who had been placed on a ventilator with the consent of her family. The kidney was attached to the blood vessels in the donor's upper leg and kept outside the abdomen, where it was covered with a protective shield, for the duration of the 54-hour study.

Researchers observed that the body was producing levels of urine and creatinine that were "normal and equivalent to what is seen from a human kidney transplant," NYU said, and there were no signs of the body rejecting the organ.

Dr. Robert Montgomery, who led the surgical team, said in a statement that the procedure was a "transformative moment in organ transplantation." He told Dr. Jon LaPook in a CBS Evening News exclusive interview that the procedure "was even better than I expected."

"The kidney turned a beautiful pink color and immediately urine started pouring out of the ureter," he said. "...There was complete silence for a few minutes while we were sort of taking in what we were looking at, which was incredible. It was a kidney that was immediately functioning."

Chad Ezzell, chief clinical officer of LiveOnNY, a non-profit organization that facilitates organ and tissue donation in New York City, said in a statement that the research is "an incredible scientific achievement."

"We are entering a new era for our field and this will give new hope to those on our wait list as this important research moves forward," Ezzell said.

The idea of using animal organs for transplants is not new, Montgomery told LaPook, but historically, animal-to-human transplants have not been compatible.

"When you cross species with a transplant and it happens immediately, humans have preformed antibodies circulating in their blood that are directed towards most of them towards a single molecule that was lost during evolution from pig to man," he said. "And so when you put an organ from a pig into a human, it's immediately rejected."

What allowed this transplant to work, Montgomery said, was genetically engineering the donor pig so that it didn't have the enzyme that the human body is designed to immediately attack.

"I think it will be something that, you know, eventually will be perfected to the point where it'll be an alternative to a human organ," Montgomery said. "...I have hope."

Adapted from: [https://www.cbsnews.com/news/pig-kidney-transplant-human-patient/?fbclid=IwAR0UV\\_YIVBZQdsRNuSoTJgQAvCpfGVrmoKPi8cFp3lkPh4RXOBaFdADqRTE](https://www.cbsnews.com/news/pig-kidney-transplant-human-patient/?fbclid=IwAR0UV_YIVBZQdsRNuSoTJgQAvCpfGVrmoKPi8cFp3lkPh4RXOBaFdADqRTE)

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## Artificial organs

A cut above 3D printing is what scientists refer to as creating artificial organs via a process called bioprinting. What this means is the exciting potential for scientists to create replicas of individuals' organs. With the ability to create synthetic ovaries, blood vessels and even a pancreas, artificial organs can be implanted into the patient's body. And they gradually begin to grow in the patient taking over the place of the original organ that was not working correctly.

Needless to say, bio-printing promises a revolutionary shift in the medical field that could dramatically alter success rates in theatre. This, of course, is dependant on the potential of the replicated organs to settle within the human body with ease. If this is the case, it could mean that the life-saving transplants' success rate would increase each and every year.

Adapted from: <https://www.newspronto.com/health/63766-6-advancements-in-medical-technology-in-2019>

## Hypothermic ex-vivo perfusion

Cardiac specialists at The Alfred have already performed five human heart transplants after using a novel method known as 'hypothermic ex-vivo perfusion' to preserve the donor heart during transit.

A recent successful transplant performed on a Melbourne man saw the donor heart record an 'ischemic' time - which refers to the time the heart does not have blood supply - of more than seven hours, the longest period of time recorded worldwide to date.

The trial could potentially double the amount of time donor hearts remain viable for transplantation – increasing the current four hour standard to eight hours. This would mean donor hearts could travel greater distances, ultimately saving more lives.

Cardiothoracic surgeon at The Alfred, and co-principal investigator, Professor David McGiffin, said the process involves putting donor hearts on an "ex-vivo perfusion machine", which pumps a liquid called perfusate through the heart muscle, cooling it to 8°C and keeping it supplied with oxygen.

"If the trial demonstrates that the donor heart is better protected with ex-vivo perfusion as opposed to ice slush in a cooler, it could mean all donor hearts are transported using ex-vivo perfusion, no matter what distance," Professor McGiffin said.

The Alfred's director of cardiology and co-principal investigator, Professor David Kaye, said the patients involved in the trial had recovered well, which could be in part attributed to the nutrition and oxygen provided to the donor heart by the perfusion system.

"The best chance that a patient has of surviving heart transplantation is if they come out of the operating room with a well-functioning heart despite a very, very long ischemic time, and that's what we think this system will deliver."

Adapted from: <https://www.alfredhealth.org.au/news/keeping-hearts-alive-outside-the-body/>

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## Using lower-quality organs

Transplantation of a “lower-quality” kidney to a person in end-stage renal failure is more cost-effective and has greater quality-of-life benefit than remaining on dialysis waiting for a better kidney, a health economics study has found.

Health economist at Australian Centre for Health Services Innovation (AusHSI), Dr Sameera Senanayake said health systems around the world had been unable to meet growing demand for kidney transplants.

“Deceased donor kidneys are graded for quality according to criteria which include age, history of hypertension or diabetes and cause of death.”

Dr Senanayake said the shortage of donor kidneys and the high demand for them had led to the suitability criteria for deceased donor kidneys being expanded and more marginal-quality kidneys being used.

“However, low and marginal-quality kidneys have tended to be discarded due to the greater likelihood of higher risk of graft failure, delayed graft function and increased medication costs for the health service,” he said.

“Patients and doctors are faced with a dilemma ‘do I accept a kidney that may not be the best or do I wait for a better kidney?’”.

Dr Senanayake’s study is the first economic evaluation to assess the cost-effectiveness of transplanting deceased donor kidneys of different qualities. “It is the first to assist patients and clinicians in making decisions on accepting a marginal quality kidney or remaining on dialysis while waiting for a better-quality kidney,” he said.

“The average age of kidney transplant in Australia is 51 years. This study analysed three age groups – 40, 50 and 60 years - from the Australia and New Zealand Dialysis and Transplant Registry which reports outcomes of dialysis treatment and kidney transplantation for end-stage kidney disease patients.

“We modelled different treatment scenarios and outcomes, including quality of life improvements, and four grades of donor kidneys against each age group.

“We found that transplanting a kidney of any quality is cost-effective and more beneficial in terms of quality of life for patients compared to remaining on dialysis.

“We found it is not a cost-effective strategy for any age group to depend on dialysis in hope of receiving a higher quality kidney.”

Dr Senanayake said the study could nudge health providers to reduce the discard rates of low-quality kidneys in favour of more kidney transplants and seek funding to remove the short-term financial disincentives inherent in transplanting low-quality kidneys.

Adapted from: <https://www.qut.edu.au/study/health/news?id=175169>

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## Organ transport devices

Queensland saw a record 199 kidneys transplanted in 2016 – 60 more than in 2015, thanks to two transport devices affectionately called Mork and Mindy.

The Princess Alexandra Hospital (PAH) is the only transplantation centre in Australia and New Zealand with the Life Port kidney transport devices, which safely extend the 'usable life' of donor kidneys from 12 to 23 hours.

Visiting the PAH today on World Kidney Day, Minister for Health and Ambulance Services Cameron Dick said it was exciting to see PAH leading the country in organ preservation, which is giving more patients access to life-saving transplants.

"As soon as a donor's family makes that decision to donate a life-saving organ, time becomes crucial for our transplant specialists," he said.

"The Mork and Mindy boxes extend that window of time, giving medical teams increased flexibility and the opportunity to preserve the kidneys for longer before they are transplanted.

"In a decentralised state like Queensland, this is critical to giving patients access to a life-saving transplant no matter where they live in our sparse state.

The boxes provide a sealed, sterile environment where a specially formulated solution is gently pumped through the kidney at cold temperatures to minimise tissue damage while the organ is being preserved outside the body. During this time, the device frequently captures and records data on temperature, flow rate, vascular resistance and pressure, offering clinicians important additional data.

Dr Aimee Cunningham, PAH Manager Transplant Services, said the Mork and Mindy boxes were essential during busy periods and to ensure distance wasn't a barrier for patients.

"Kidneys are different from other donor organs. They are matched on tissue typing, physiology and immunology. For some of these patients, getting a match is like winning the lottery," Dr Cunningham said.

"Not giving those patients that opportunity because they live too far away is simply not an option. The Life Port boxes mean we can continue to provide excellent care regardless of where people are in Queensland."

Adapted from: <https://metrosouth.health.qld.gov.au/news/%E2%80%98mork-and-mindy%E2%80%99-make-record-number-of-organ-transplants-possible>

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## Organ incubation systems

New technology which creates a “mini intensive care unit for livers” has safely expanded the number of donor livers transplanted in Queensland by more than 10%, giving life and hope back to people who urgently need a new liver to survive.

This organ incubation system is making use of precious donated livers which previously would not have been used, often due to the distance between donor and recipient.

Queensland’s liver transplant team at Brisbane’s Princess Alexandra Hospital was the first Australian transplant hospital to trial this novel preservation technology, with patients first consenting to participate in research from mid-2018.

Qld Liver Transplant Service surgeon Dr Peter Hodgkinson said it had tripled the time donor livers could be safely preserved outside the body, from around 8 hours right up to 24 hours.

“So far, 24 of the 26 marginal livers revived on the OrganOx machine have been successfully transplanted to grateful Queensland patients from the organ transplant waitlist,” he said.

For perspective, there were 49 liver transplants in Queensland last year and 10 of these proceeded because of the OrganOx.

Unlike conventional storage on ice, the OrganOx Metra machine gently perfuses donated livers with fluids, nutrients, and oxygenated blood at room temperature to help restore function. Revived livers quickly blush pink and can even produce bile and metabolise glucose while being perfused.

Dr Hodgkinson said the preservation technology was currently applied only to “orphan” donor livers, that were previously considered ‘marginal’, ie. livers which previously might not have been suitable for transplantation.

“With this technology, those livers can now be stabilised and carefully observed to determine their actual suitability to transplant.

“Previously we had to be very conservative in our choices. This new machine takes a lot of risk out of that equation.”

This technology has proven particularly effective in Queensland, given the logistical challenges posed by longer distances and organ retrieval times, as well as the increasing number of organs donated after cardiac death (rather than only after brain death).

“Previously, when you had a small donor pool and a very large state to cover, it would be a huge risk to take, particularly if that transplant failed and another was needed urgently.”

“Historically, liver transplants have had a 90% survival rate after five years, but now our five-year survival rate has improved to 96%.”

Adapted from: <https://metrosouth.health.qld.gov.au/news/australian-first-transplant-tech>

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## Drone transportation

Game changing technology for a critical mission in healthcare: drones for organ transplants are proving their worth. "MissionGO, a leader in unmanned aircraft solutions that is transforming logistics; LifeSource, the organ procurement organization (OPO) serving the upper Midwest; and Mercy Hospital, part of the Allina Health system, today announced the first-ever test flight carrying a human pancreas via an Unmanned Aircraft System (UAS) conducted on May 5," says a press release.

Following a moment of silence led by Lead Pilot Ryan Henderson to honor the donor hero, this historic flight transported a research pancreas from Mercy Hospital in Coon Rapids, flew a 10-mile circuit over the Mississippi River, then returned to Mercy Hospital. This flight successfully demonstrated the viability, value, efficiency gains and delivery speed of lifesaving organs via UAS within the Twin Cities metro area.

Organ transportation is both critical and complex, requiring multiple partners to cover all aspects of the mission. For this operation, the pancreas was monitored for the duration of the flight "using MediGO's hardware and software platform to provide the real-time location status of the organ to all critical stakeholders," says the press release. In addition, LifeSource performed a biopsy on the pancreas before and after the flight "to study the impact of UAS transportation on a human organ, revealing no changes in pre and post flight biopsies." Beyond the complexities involved in transporting organs, operators require flight telemetry: "MissionGO's aircraft was monitored with AlarisPro's new flight data recorder known as the AlarisAIR (Automated Independent Recorder) which provides flight telemetry data through both cellular and Bluetooth networks."

"LifeSource has set an audacious goal of transplanting 1,000 organs in one year by 2027; last year, we facilitated 603 transplants," said Susan Gunderson, LifeSource Founder & CEO. "Organ transplant is a race against time; this is one of many transformative solutions to help us save more lives."

MissionGO tested drones for organ transplants in 2019 and 2020, transporting a research corneas and a research kidney. MissionGO has also made progress in certifying their MG Velos 100 UAS: and they hope to integrate drones into the LifeSource and Allina Health programs.

"The future is here – there's a demand in the market for innovative and sustainable solutions in the commercial and medical industry. MissionGO is here to prove that unmanned aircraft are a reliable mode of transportation for precious cargo," said Frank Paskiewicz, MissionGO Executive Vice President for UAS Cargo Operations. "LifeSource and Allina Health have been incredible partners that are pioneering new solutions for the organ transplant industry."

"Organ transport by an unmanned aircraft is an incredible innovation for health care," said Robert Quickel, MD, vice president clinical service line, surgical procedural administration for Allina Health. "These test flights are an inspiring step in overcoming obstacles and increasing the number of viable, life-saving organs that our transplant patients so desperately need."

Adapted from: <https://dronelife.com/2021/06/14/drones-for-organ-transplants-missiongo-and-alarispro-transport-first-human-pancreas-via-uav/>



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## 10p statins

Thousands of lives could be saved globally by giving patients a 10p statin before transplants, doctors have said, as the NHS launches the world's largest clinical trial in organ donors.

The medical breakthrough is predicted to dramatically increase the supply of organs for transplant. Currently, demand for organs vastly exceeds the number available. Every year thousands of people die waiting for a transplant, including hundreds in Britain.

Many potential organs for donation, particularly the heart and lungs, are damaged. Removing the organ and reattaching it in the recipient can exacerbate the damage. As a result, thousands of organs offered can never be used. Three-quarters of hearts offered cannot be used because they are damaged or do not function well.

Now leading doctors, surgeons and researchers say giving all donors a statin before their organs are removed could reduce inflammation and minimise or even reverse that damage. The pioneering act could be of real clinical benefit to organ recipients, significantly boosting their chances of survival.

In a world first, organ donors in the UK involved in a groundbreaking trial are being prescribed a single dose of simvastatin hours before their organs are removed. The intervention costs just 10p and takes only 30 seconds but is set to revolutionise organ donation.

Prof John Dark, a leading organ donation expert and a lead investigator of the trial, said he was hopeful that giving statins to organ donors would become standard.

The cholesterol-lowering drugs are already one of the world's most popular medications. "What we hope is that this study will affect practice throughout the world and result in every organ donor being given a statin ... with potentially thousands of lives saved," said Dark.

Dark, a professor of cardiothoracic surgery at Newcastle University and a former heart and lung surgeon who has performed more than 500 transplants, said his team would look to confirm the benefits that statins could have on organs including the heart, lungs, pancreas, liver and kidneys.

"We expect better-quality organs to come from donors who have been treated with simvastatin. A previous, smaller study in Finland has shown that this was clearly the case for the heart and hinted at improvements in quality for lungs and liver also.

"Interestingly, in lung donation the recipients who got organs from donors treated with simvastatin showed half the level of primary graft dysfunction, which measures organ damage," Dark said. "What we hope to do in the future is to make statins part of the standard treatment for organ donors and then explore other drugs that may continue to improve the condition of donated organs."

Prof Paul Dark, the NIHR national specialty lead for critical care, said the trial was vital. "Previous studies have shown statins can reduce inflammation and improve organ quality," he said. "This new study is critical research which we hope will show major benefits to the recipient donor."

Adapted from: [https://www.theguardian.com/society/2021/sep/19/use-of-10p-statin-in-organ-donation-could-save-thousands-of-lives?fbclid=IwAR3XWlriihBGcte7SU\\_Q9TyBPB\\_fj3aswoS2wFqE7CkDPpykoCUTbfGEVMg](https://www.theguardian.com/society/2021/sep/19/use-of-10p-statin-in-organ-donation-could-save-thousands-of-lives?fbclid=IwAR3XWlriihBGcte7SU_Q9TyBPB_fj3aswoS2wFqE7CkDPpykoCUTbfGEVMg)