

## US researchers test pig-to-human transplant in donated body

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In this photo provided by the University of Alabama at Birmingham, surgeons prepare to transplant kidneys from a genetically modified pig into the body of a deceased recipient in September 2021. The experimental procedure was a step-by-step rehearsal for operations they hope to try in living patients possibly later in 2022, part of a quest to use animal organs to save human lives. Credit: UAB via AP



Researchers on Thursday reported the latest in a surprising string of experiments in the quest to save human lives with organs from genetically modified pigs.

This time around, surgeons in Alabama transplanted a pig's kidneys into a brain-dead man—a step-by-step rehearsal for an operation they hope to try in living patients possibly later this year.

"The organ shortage is in fact an unmitigated crisis and we've never had a real solution to it," said Dr. Jayme Locke of the University of Alabama at Birmingham, who led the newest study and aims to begin a clinical trial of pig kidney transplants.

Similar experiments have made headlines in recent months as research into animal-to-human transplants heats up.

Twice this fall, surgeons at New York University temporarily attached a pig's <u>kidney</u> to blood vessels outside the body of a deceased recipient to watch them work. And earlier this month, surgeons at the University of Maryland Medical Center gave a dying man a <u>heart</u> from a gene-edited pig that so far is keeping him alive.

But scientists still needed to learn more about how to test such transplants without risking a patient's life. With the help of a family who donated a loved one's body for science, Locke mimicked the way human organ transplants are done—from removing the pig "donor" kidneys to sewing them inside the deceased man's abdomen.

For a little over three days, until the man's body was removed from life support, the pair of pig kidneys survived with no sign of immediate rejection, her team reported Thursday in the *American Journal of Transplantation*.



That was only one of several key findings. Locke said it wasn't clear if delicate pig kidney blood vessels could withstand the pounding force of human blood pressure—but they did. One kidney was damaged during removal from the pig and didn't work properly but the other rapidly started producing urine as a kidney should. No pig viruses were transmitted to the recipient, and no pig cells were found in his bloodstream.



This August 2021 photo provided by Julie O'Hara shows Jim Parsons, a 57-year-old Alabama man who was declared brain-dead from a September 2021 dirt bike racing accident. Parsons' family donated his body for research at the University of Alabama at Birmingham, where scientists hope one day to use animal organs to save human lives. "After we heard about what the study was about, that it had the potential to save hundreds of thousands of lives, we knew without a doubt that that was something that Jim would have definitely put his seal of approval



on," said O'Hara, Parsons' ex-wife. Credit: Courtesy Julie O'Hara via AP

But Locke said the kidney experiment could have more far-reaching impact—because it shows that a brain-dead body can be a much-needed human model to test potential new medical treatments.

The research was conducted in September after Jim Parsons, a 57-yearold Alabama man, was declared brain-dead from a dirt bike racing accident.

After hearing this kind of research "had the potential to save hundreds of thousands of lives, we knew without a doubt that that was something that Jim would have definitely put his seal of approval on," said Julie O'Hara, Parsons' ex-wife.

The need for another source of organs is huge: While more than 41,000 transplants were performed in the U.S. last year, a record, more than 100,000 people remain on the national waiting list. Thousands die every year before getting an organ and thousands more never even get added to the list, considered too much of a long shot.

Animal-to-<u>human transplants</u>, what's called xenotransplantation, have been attempted without success for decades. People's immune systems almost instantly attack the foreign tissue. But scientists now have new techniques to edit pig genes so their organs are more human-like—and some are anxious to try again.

The recent string of pig experiments "is a big step forward," said Dr. David Kaczorowski of the University of Pittsburgh Medical Center. Moving on to first-stage trials in potentially dozens of people is "becoming more and more feasible."



A heart <u>transplant</u> surgeon, Kaczorowski has done experiments testing pig organs in non-human primates that helped pave the way but "there are only things we can learn by transplanting them into humans."

Hurdles remain before formal testing in people begins, including deciding who would qualify to test a pig organ, said Karen Maschke, a research scholar at the Hastings Center who will help develop ethics and policy recommendations for the first clinical trials under a grant from the National Institutes of Health.



In this photo provided by the University of Alabama at Birmingham, surgeons check whether kidneys from a genetically modified pig are working in the body of a deceased recipient in September 2021. The experimental procedure was a step-by-step rehearsal for operations they hope to try in living patients possibly later in 2022, part of a quest to use animal organs to save human lives. Credit:



UAB via AP

Scientists also still have much to learn about how long pig organs survive and how best to genetically alter them, cautioned Dr. Robert Montgomery of NYU Langone Health, who led that center's kidney experiments in the fall.

"I think different organs will require different genetic modifications," he said in an email.

For the newest kidney experiment, UAB teamed with Revivicor, the subsidiary of United Therapeutics that also provided organs for the recent heart transplant in Maryland and the kidney experiment in New York. Company scientists made 10 genetic changes to these pigs, knocking out some genes that trigger a human immune attack and make the animals' organs grow too large—and adding some human genes so the organs look less foreign to people's immune systems.

Then there are practical questions such as how to minimize time spent getting pig organs to their destination. UAB housed the altered pigs in a germ-free facility in Birmingham complete with an operating room-like space to remove the organs and ready them for transplant.

Revivicor chief scientific officer David Ayares said future plans include building more such facilities near transplant centers.

**More information:** First clinical-grade porcine kidney xenotransplant using a human decedent model, *American Journal of Transplantation* (2022). DOI: 10.1111/ajt.16930



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