# Scientists engineer vascularized kidney tissue

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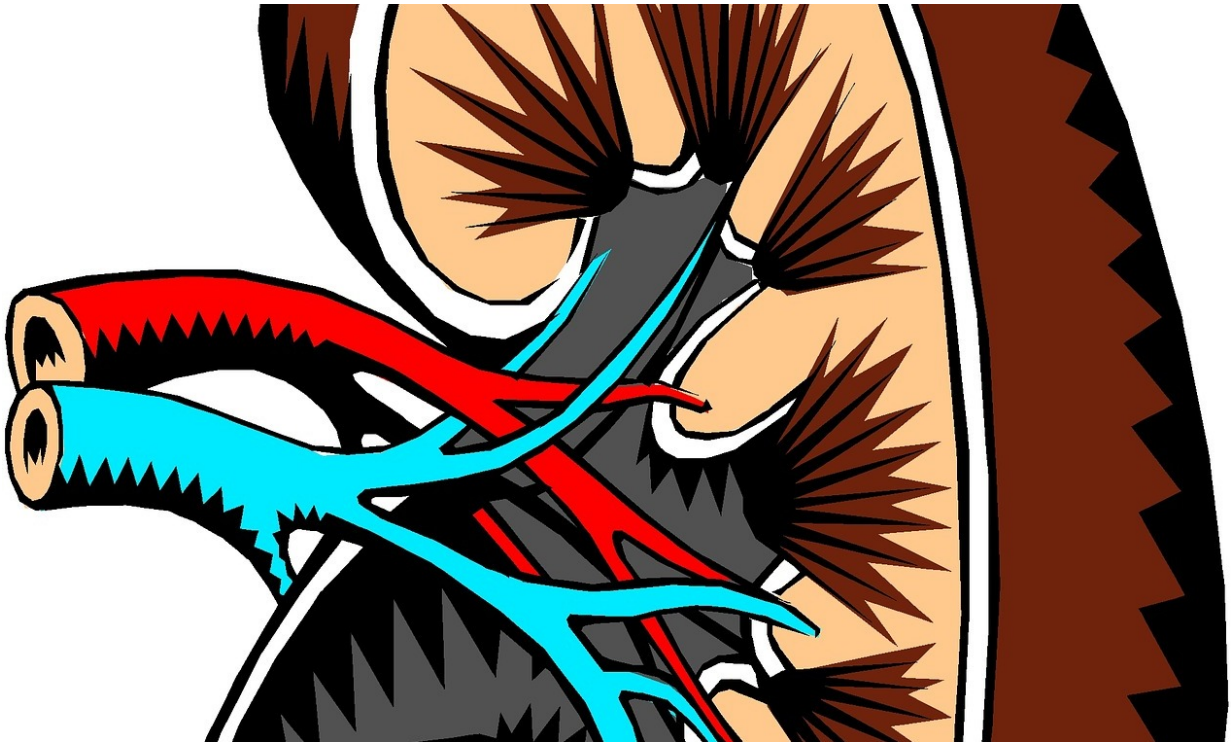

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Wake Forest Institute for Regenerative Medicine (WFIRM) researchers have shown the feasibility of bioengineering vascularized functional renal tissues for kidney regeneration, developing a partial augmentation strategy that may be a more feasible and practical approach than creating whole organs.

In the proof-of-concept study published online this month in *Acta Biomaterialia* journal, the scientists created a novel biomimetic, collagen-based vascular scaffold—a mold—that is structurally identical to native kidney tissue that was able to develop vascularized tissue.

"The use of this scaffold system could address the challenges associated with vascularization and may be an ideal treatment strategy for augmentation of renal function in patients with chronic kidney disease," said James Yoo, M.D., Ph.D., lead author and professor of regenerative medicine at WFIRM. "Vascularization continues to be one of the major hurdles affecting the survival and integration of implanted 3-D tissue constructs."

In the United States, chronic kidney disease is prevalent, affecting more than 700,000 patients living with end stage renal disease. Although dialysis has supported the survival of patients with end stage renal disease, kidney transplantation remains the only definitive treatment. However, there are currently nearly 100,000 people on the waiting list, with nearly 9,000 patients being removed yearly due to deteriorating medical condition or death, which reflects the current state of ongoing organ shortage.

The limitations of current therapies for end stage renal disease led WFIRM researchers to explore the development of renal 3-D constructs with the goal of improving, restoring, or replacing partial or total renal function.

"A universal challenge in engineering large solid organs is the need for vascularization," said Anthony Atala, M.D., a co-author of the paper and director of WFIRM. "Kidneys depend on complex 3-D vascular networks for tissue survival and renal function, but the intricate nature of the renal vasculature makes replication difficult."

In order to treat chronic kidney disease, the WFIRM researchers knew they needed to address the feasibility of applying their vascular scaffold in the context of partial renal implantation. They have shown that the vascular scaffolds can be perfused and endothelialized in the lab, but the question of integration and functionality in a clinical model remained.

Various materials and combinations of collagen hydrogel, endothelial cells and renal cells were tested. Using polycaprolactone (PCL) solution and collagen as the casting and scaffold materials, respectively, the scientists essentially made molds using donor kidneys as templates, creating hollow scaffolds that were cultured in renal growth medium before implantation into the preclinical model. The level of neovascularization, survival of implanted human renal cells, and renal structure formation was evaluated.

The renal vascular scaffold showed a 3-D branching architecture with visible hollow channels that were interconnected and continuous. These branching structures were able to allow perfusion similar to native blood vessels. The researchers showed that the vascular scaffolds integrated with the host vessels and supported renal cell viability.

"The biomimetic vascular scaffold coated with endothelial cells showed significantly enhanced vascularization, as compared to the uncoated scaffold and hydrogel only groups," Yoo said. "Along with the improved vascularization effects, the endothelial cell-coated scaffolds showed a significant renal cell infiltration from the neighboring host tissue, as compared to the other groups."

The results are promising and support continued exploration of this method to further evaluate renal function of the implanted constructs and address limitations such as improving systemic renal function.

"Overall, we are very pleased with the outcomes thus far," Atala said.

"Further work is necessary to establish a reliable and reproducible system for clinical translation."

**More information:** Jennifer Huling et al, Kidney regeneration with biomimetic vascular scaffolds based on vascular corrosion casts, *Acta Biomaterialia* (2019). DOI: 10.1016/j.actbio.2019.04.001

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