

# An Implantable Bioartificial Kidney for Treating Kidney Failure

An innovative device that aims to provide the benefits of kidney transplantation while addressing the limited number of donor organs.

BY SHUVO ROY, PhD, AND WILLIAM FISSELL, MD

End-stage renal disease (ESRD) currently affects over 600,000 people in the United States, with fewer than 20,000 donor organs available for transplant. This is a growing problem as the number of patients on the transplant wait list is hovering at 100,000, and the prevalent ESRD population is increasing at 4% to 5% annually.<sup>1,2</sup> At present, the only alternative to kidney transplant for the vast majority of patients with ESRD is hemodialysis, a procedure fraught with morbidity and eventual mortality. After vascular access is established in the form of an arteriovenous fistula, arteriovenous graft, or venous catheter, a typical in-center hemodialysis schedule is three sessions per week for 3 to 5 hours per session, in which blood is pumped through an extracorporeal circuit to filter uremic toxins. The procedure is exhausting, and many patients experience pervasive complications, such as infection and metabolic deficiencies. The mortality for dialysis patients is high, with only 35% of patients still living after 5 years of treatment.<sup>1</sup> In contrast, the 5-year survival rate for transplant recipients ranges from 73.5% to 85%, depending on whether the recipient received a deceased or living donor transplant.<sup>2</sup> Consequently, a key question arises—how can the effective results of a kidney transplant be offered to patients with ESRD without more organ supply?

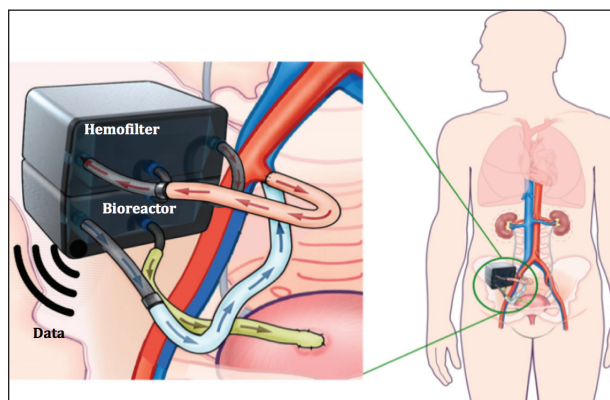
## IMPLANTABLE BIOARTIFICIAL KIDNEY

### How It Works

The implantable bioartificial kidney aims to provide the many health benefits of a kidney transplant while addressing the limited number of donors. The device filters uremic toxins from the blood, while also mimicking tubular functions, such as selective water and salt reabsorption (Figure 1). After a single surgery to establish a permanent blood con-

nection, the bioartificial kidney processes blood continuously, which mitigates the inconveniences and morbidities associated with intermittent hemodialysis.

The bioartificial kidney is a two-stage system that consists of (1) a hemofiltration unit to remove toxins and (2) a renal cell bioreactor to provide other biological functions of a healthy kidney.<sup>3</sup> For the hemofilter, silicon nanotechnology is used to produce a highly efficient and compact membrane, which relies on the body's blood pressure to perform ultrafiltration without the need for pumps or power supply. For the cell bioreactor, recent advances in the field of regenerative medicine are applied to grow renal tubule cells to perform metabolic functions. By better mimicking healthy kidney function, the bioartificial kidney alleviates the necessity of constant physician oversight and a heavy regimen of immunosuppressive medication.



Courtesy of Shuvo Roy, PhD

**Figure 1.** The bioartificial kidney will be located in the iliac fossa and provide continuous therapy and maximum mobility to the patient. It will not require pumps or a power supply for operation.

### Progress to Date

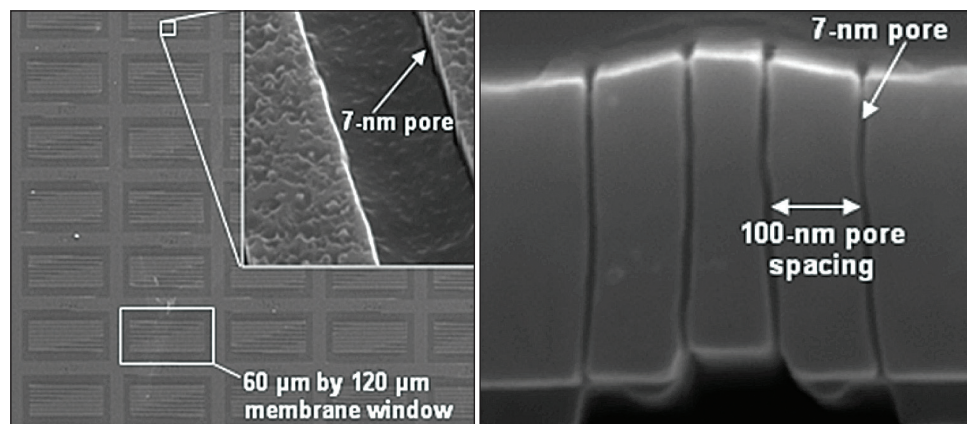
Robust silicon membranes have been fabricated and tested to confirm toxin clearance at pressures comparable to blood (Figure 2). The membrane materials were also assessed for safety and blood compatibility, and there was no coagulation during 1-month testing in large animals. For the cell bioreactor, a reliable supply of human-derived cells and suitable methods of storage via cryopreservation techniques have been established. Moreover, experiments have shown that the renal cells in a miniature bioreactor provide biological activity, including the ability to selectively reabsorb water, while maintaining a barrier to urea and creatinine, for up to 2 months.

The feasibility of the discrete device components has been individually demonstrated, and the next steps are design optimization and integrating the components into scaled-up prototypes for long-term preclinical studies and eventual testing in patients with ESRD.

### Project Plan

A project plan has been developed with the goal of first-in-human testing of the implantable bioartificial kidney, in which a multidisciplinary team of engineers, doctors, and scientists will build and test increasingly complex prototypes in stages. The work will involve a combination of engineering improvements to the silicon membranes, benchtop experiments with the combined hemofilter and cell bioreactor, and packaging of the device for preclinical testing. After laboratory experiments show successful device performance, the bioartificial kidney will be implanted in human subjects.

The bioartificial kidney was selected by the US Food and Drug Administration (FDA) to participate in its Innovation Pathway 2.0 (IP 2.0) pilot program. The Center for Devices and Radiological Health launched IP 2.0 to help safe, breakthrough medical products for ESRD reach patients in a timely manner. Through IP 2.0, FDA scientists, reviewers, and leadership worked with our team to shorten the overall time (and cost) to complete the regulatory assessment and review of technology for approval of the first-in-human testing plan and also establish a collaborative framework for subsequent clinical trials for the premarket approval studies.



**Figure 2.** Semiconductor fabrication techniques are used to produce arrays of robust silicon membranes with nanoscale pores (left). The precise control over pore size and spacing allows for the development of a compact device suitable for implantation and pumpless operation (right).

Courtesy of Shuvo Roy, PhD.

A key recommendation from IP 2.0 discussions was that the hemofilter should be evaluated in patients with ESRD under an investigational device exemption pilot study. For the investigational device exemption approval, preclinical testing of the hemofilter will be performed using canine or porcine models over a 30-day period. In order to demonstrate feasibility of the cell bioreactor, a short-term extracorporeal study in a porcine model was suggested as the prerequisite preclinical study.

### SUMMARY

Although the implantable bioartificial kidney is in its early stages of development, this innovation has the potential to affect how ESRD is managed in the future. For more information on the implantable bioartificial kidney, visit <http://kidney.ucsf.edu>. There is also a Facebook page for outreach to patients and their friends and family members interested in the latest updates on preclinical studies and progress toward clinical trials. ■

1. United States Renal Data System (USRDS). USRDS 2013 annual data report: atlas of end-stage renal disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2014.
2. Hart A, Smith JM, Skeans MA, et al. OPTN/SRTR 2014 annual data report: kidney. *Am J Transplant*. 2016;16(suppl 2):11–46.
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