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Development Prospects for Dialysis: New Technologies and Their Impact on the Treatment of Chronic Renal Failure

Olishova Risolat, Odiljonova Ruzixon, Xoshimov O'tkirjon, Muhammadjonov Azizbek, Baxromjonova Dilnoza
Students of Andijan State Technical Institute

Azimov Sarvarbek
Assistant teacher of Andijan State Technical Institute

Abstract: *The current standard of care for patients with end-stage renal disease (ERSD) is a kidney transplant or dialysis when a donor organ is not available. The goal of this review is to assess the potential of two of the most recent innovations in kidney transplant technology—the implantable bioartificial kidney (BAK) and kidney regeneration technology—in addressing the aforementioned problems related to kidney replacement for patients with ERSDA major limitation of the current technology is that both implantable BAK and kidney regeneration technology are still in preclinical stages, and thus their potential effects cannot be comprehensively generalized to human patients.*

Keywords: *Chronic kidney failure, Dialysis, Kidney regeneration, Kidney technology, Kidney transplant.*

INTRODUCTION: Currently, over two million people around the world suffer from end-stage renal disease (ESRD). The best treatment for current patients with ESRD is a kidney transplant [1]. This method of treatment is severely limited by donor organ availability. In 2018 alone, over 100,000 people in the United States were on the kidney transplant waiting list, while only 21,000 organs were available for transplant [1]. The need for donor organs in the United States is predicted to rise by 8% each year [2]. The current standards of care for patients with kidney failure or ESRD include full kidney transplant with a donor organ, in-center hemodialysis (HD) or peritoneal dialysis (PD), or at-home HD via an external machine. The severe lack of donor kidneys leads to extended dialysis treatments as the norm to treat patients with ESRD. Long-term dialysis is associated with several comorbidities, including an increased risk for kidney cancer. Additionally, patients who receive a kidney transplant have been found to be at higher risk for cancer in general due to the immunosuppressant drugs required after transplant surgery [3]. The field of kidney replacement technology has evolved greatly over the last two decades, with improvements in nanotechnology, cell growth techniques, and bioreactors. Two of the most recent technological advancements in this field are the implantable bioartificial kidney (BAK) and kidney regeneration technology. Both techniques are in preclinical stages and aim to fully replace normal kidney functionality. Both technologies address donor organ shortages as well as complications from dialysis and immunosuppressants. The purpose of this review is to analyze recent progress in kidney replacement technology and assess its potential impact on reducing risks associated with dialysis and donor organ kidney transplants, specifically donor shortages, renal failure, and risk of cancer.

History of renal replacement technology

The major limitation in both current devices is that they still do achieve full kidney functionality; they are focused on ultrafiltration and remain lifestyle limiting, albeit less so than traditional dialysis. They require external machinery and systems, which limit mobility for the patient using it. Additionally, the lack of endocrine and metabolic functionality causes poorer outcomes for dialysis patients over time compared with patients who received a full transplant. The two newest iterations in renal replacement technology, the implantable BAK and kidney regeneration technology, address the limitations of the AWAK and WAK devices

Figure 1. Prototype of the wearable artificial kidney. Filtration components are attached to a belt for the patient to wear.

The implantable BAK will provide another alternative for ESRD patients. This device not only reduces time on dialysis, but also replaces total kidney functionality. The filtration component of kidney function occurs at the glomerulus. Ultrafiltration of the blood is performed to remove toxic waste from circulation and retain important materials within systemic circulation, such as albumin. The regulatory component of the kidney occurs at tubular segments attached to the glomerulus. Ultrafiltrate from the glomerulus moves along the kidney tubule, which reabsorbs fluid and solutes to finely regulate the excretion of various amounts of solutes and water in urine. Both of these functionalities are necessary in a fully functional kidney unit. The implantable BAK combines a high efficiency filter connected in series with a bioreactor of cultured renal tubule epithelial cells to achieve classification as a fully functioning kidney unit (Fig. 4, 5) [5,6].

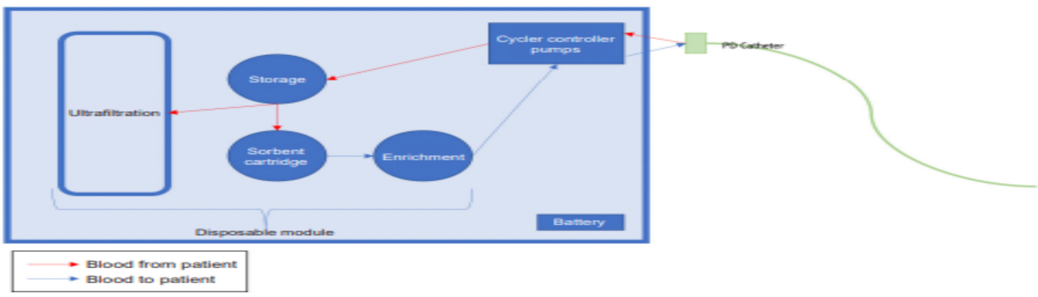
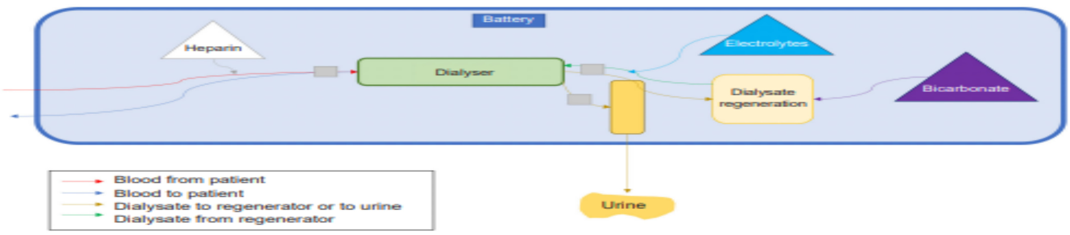


Figure 2. Schematic of the automated wearable artificial kidney.



The implantable BAK achieves solute transfer with convective transport, which is independent of concentration gradient and instead depends on a hydraulic pressure gradient across a membrane. This method of transport for toxin removal is advantageous because it mimics the natural glomerular process of toxin clearance of solutes with a higher molecular weight and solutes of the same diffusion rate. Convective transport in an implantable device can be achieved with polysulfone hollow fibers, which can be lined with renal endothelial cells and placed into the arteriovenous circuit using the common iliac artery and vein [6]. This arteriovenous connection allows the device to operaA major limitation in creating the implantable BAK is the miniaturization aspect. An avenue that has been explored to create the device prototype is microelectromechanical systems (MEMS) (Fig. 6). MEMS is an industrial toolkit that applies mature manufacturing techniques from the semiconductor industry to miniature electromechanical devices, such as pumps, valves, and sensors. This technology can be used to produce silicon membranes containing ‘slit-shaped’ pores that are necessary for producing an implantable BAK [10]. Another engineering challenge for the implantable BAK is to design it such that the membrane maximizes water permeability while minimizing leakage of albumin and other important macromolecules. This challenge is overcome using silicon nanotechnology slit pores. A challenge in using silicon is the oxide coating that can form when exposed to oxygen. The coating can be prevented by modifying the silicone surface with a highly hydrated polymer by grafting an organic polymer to the silicon nanopore surface [10,11]. A long-term challenge for the implantable device is combating coagulation; a sustainable anticoagulation solution will be essential for a fully implantable BAK device. Further limitations of the implantable device are the size and pump requirements of modern dialyzers, and the water volume required for dialytic therapy [11]. te on blood pressure rather than an externally- or battery-powered pump.

Conclusion The two newest innovations in renal replacement technology—implantable BAK and cellular kidney regeneration— create a fully functioning alternative to long-term dialysis or a donor organ. They improve on previous iterations of renal replacement technology by accomplishing all aspects of normal kidney functionality, while also being fully implantable and autologous to allow patients maximum mobility. Additionally, these technologies may have the potential to address many associated risks of dialysis and kidney transplants, such as potential infections, effects of immunosuppression, and the risk of cancer - specifically renal cancer. As these technologies move out of preclinical testing stages into clinical testing and eventual clinical practice, they must be further studied to analyze their impact on instances of renal cancer in kidney transplant patients.

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