
Editorial

The Bio-Artificial Implantable Kidney

Oana Stirbu^{1,2,3}, Iancu Viorel Pitea¹ and Mircea Calin Tandrau^{1,2,3}

¹Clinical Emergency County Hospital Arad, Hemodialysis Centre, ²Vasile Goldis Western University of Arad, ³Avitum Arad Dialysis Centre, Arad, Romania

Abstract

End-stage kidney disease (ESKD) is a debilitating and costly condition, currently affecting more than 4,5 million people around the globe, with an ascending trend. The currently used treatments for ESKD include single-pass hemodialysis, single-pass peritoneal dialysis, and allograft transplantation. A series of alternative therapies is currently under development, either in preclinical or clinical trials, aiming to increase the performance and affordability of the current treatments or to propose completely new approaches. This article summarizes the latest developments of those alternative therapies, with a focus on the bio-artificial implantable kidney.

Key words: End-stage kidney disease, dialysis, kidney transplantation, alternative therapies, bio-artificial implantable kidney

Introduction

Chronic kidney disease (CKD) has been recently acknowledged as one of the most worrisome threats to global public health due to the increasing number of cases and the associated morbidity and mortality, which are predictably going to steadily increase in the coming years [1-3]. Although tremendous progress has been made toward decreasing the rate of progression to end-stage kidney disease (ESKD) with novel medications aimed at improving kidney survival [4], there are still alarming numbers of people reaching the end of kidney life. This situation requires renal replacement therapies, which currently include single pass hemodialysis, single pass peritoneal dialysis, and allograft transplantation, available globally to no more than a third of the population in need [2,5,6]. This is due to the significant economic burden associated with kidney replacement therapies, especially with dialysis, which is, in fact, the second-best option. Kidney transplantation, which associates much better prognosis and health-related quality of life and hence represents the first option, is facing serious issues related to the shortage of available donor organs and the low eligibility

of the ESKD population for receiving a renal graft (no more than 30% of the patients are on the waiting lists) [KDIGO guidelines 2020] [6].

In an effort to increase the availability of therapy and improve the lifespan and quality of life for ESKD patients, new options are the subject of research and have reached preclinical or clinical stages [5,7,8].

Those are: 1) wearable and portable dialysis machines, 2) alternative biological kidneys [xenotransplantation and lab-cultivated human kidney tissue] and 3) a hybrid of the two aforementioned methods, the bio-artificial implantable kidney.

Dialysis improvement and portability

Hemodialysis machines now use at least 120-150 liters of water per dialysis session and also require electricity, making this therapy dependent on water access and purification stations. Peritoneal dialysis uses less water but implies additional patient involvement and required resources and has durability issues. Novel dialysis machines will use sorbent-based techniques [9] for dialysate regeneration and advanced polymeric and inorganic membranes for toxin removal [10] in order to drastically reduce the amount of water required, avoid stationary infrastructure, as well as to improve performance [5,11,12]. This would allow treatments to be performed at home or even provide portability for the dialysis machines. They are currently under clinical trials [3,5].

Alternative biological kidneys:

Xenotransplantation: Attempts to use xenotransplantation as treatment for ESKD in humans started decades ago, with primate organs but failed mainly due to immunological rejection [7].

Clinical trials have been in place since 2024 for xenotransplantation with genetically edited pig kidneys. CRISPR-cas9 technology has been used to remove immunogenic xeno-antigens from the cells of embryonic pigs and to introduce human complement and coagulation regulators [5,13,14].

In 2025, two entities (United Therapeutics and eGenesis) were credited by the FDA in the USA with conducting clinical trials in xenotransplantation, with promising results. A news article published in the journal *Nature* on September 8th, 2025 [15], reports six-month survival in a human recipient after porcine kidney xenotransplantation, marking an important milestone in this field.

However, the actual clinical availability of the organs poses a few serious concerns in terms of durability, ethics, and the risk of xenosis [13,14,16].

Other obstacles that need to be overcome are the physiological differences between human and pig kidneys, leading to the persistence of erythropoietin deficiency, the inability of pig renin to activate the human RAAS, and the urinary loss of uric acid [14-16]. Those concerns will probably delay the implementation of the treatment by several years [13,14].

Regenerative medicine seeks to restore or replace compromised renal function through the in vitro generation of renal tissue, from human induced pluripotent stem cells (iPSC) as the optimal cellular origin [3,5,7,11].

The principle comes into practice by applying stem cell technologies, tissue engineering, 3D bio-printing, and bioengineering approaches to construct human kidney tissue in the lab [7,17,18].

Human iPSC can be stimulated to develop in the direction of nephrogenic (NPC) and ureterogenic progenitor cells (UPC), from which further specialization leads to the over 20 types of kidney cells that compose the nephron and, respectively, the urinary tract [19].

One of the most important achievements is the development of kidney organoids, that are three-dimensional [3D] multicellular structures generated in vitro from human induced pluripotent stem cells [iPSCs] that self-organize to recapitulate nephrogenesis in the human kidney, including nephron-like units, to the stage of embryonic kidney [in mice] [7,8,18].

Microfluidic organ-on-chip platforms have enabled dynamic perfusion and co-culture of the tubular epithelial cells with human endothelial cells, resulting in enhanced vascular network formation within organoids [7,19].

In October 2025, a team of researchers [8] announced obtaining kidney progenitor assemblies (KPA), a more advanced structure in which the nephrons undergo extensive development and fuse to a centrally located collecting system, recapitulating nephrogenesis up to the stage of a newborn mouse kidney [8].

At this point, however, the lab generated kidney tissue is unable to function independently within a host, lacking the structural and functional complexity required [7].

Producing an organ as complex as the kidney requires specific environment and triggers present in the developing embryo, as well as structures derived from mul-

tipule stem cell origins [7,20]. Injecting human iPSC derived cells into developing organs of different animal species in the stage of blastocyst [blastocyst complementation] [21], leads to interspecies chimeric organogenesis and is envisioned as a promising approach to address these challenges in organ production [7,19]. Other promising strategies involve recellularization of decellularized kidney scaffolds [17,22], and cell attachment and differentiation that is improved by chemokines and AKI-CKD cytokine cocktails administered through the ureter and renal artery [21].

Despite all these advances, it appears that developing fully transplantable, functional kidneys remains a formidable and somewhat distant challenge [23]. Critical barriers include precise control over cellular differentiation, tissue organization, and vascularization, as well as translational concerns related to safety, efficacy, ethics and regulatory oversight [19].

The bio-artificial implantable kidney:

The first device using human kidney proximal tubule epithelial cells (PTECs) in an artificial construct was the Renal Assist Device (RAD) [12,24], used in phase I and II clinical studies. For the treatment of a limited number of acute kidney injury patients in an intensive care unit, in the early 2000s [20,24-26], a bioreactor was coupled in series with a conventional hemofilter. The renal cells (PTECs) were layered on the inner surface of the hollow fibers of the bioreactor, in series with a hemofilter and used for continuous renal replacement therapy [24]. Although the experiment was a success, decreasing the mortality of critical patients by more than 30%, the logistical difficulties of manufacturing and maintaining viable cell-based devices, as well as reported thrombocytopenia constituted a redoubtable problem that prevented wider exploring and use of the method [27,28].

The bioartificial implantable kidney (iBAK) is an investigational product under development in both the USA and Europe since 2018. The concept envisions biomimetic membranes that would replicate the glomerular filtration and the presence of live renal epithelial cells to provide tubular functions [29]. As in the real-life kidney, the blood is first filtrated through a semipermeable membrane similar to the one in the glomeruli (the hemofilter component of the iBAK), then the ultrafiltrate will be processed by the PTECs in the bioreactor component. What results is directed to the urinary bladder to be evacuated [27,30]. The iBAK is implanted in the abdominal cavity, in the iliac fossa, connected to the iliac vessels, and it produces urine that is eliminated in the urinary bladder [27]. The purpose of the iBAK is to be used as a long-term substitute for a kidney, in patients with ESKD.

The project requires the application of several advanced technologies: nanotechnology, membrane techno-

logy, stem cell technology, bioengineering, and information technology.

The hemofilter component is created from ultrathin flat sheets of silicone nanopore membranes (SNM) with slit-shaped pores [5-8 nm×2 μm] [10,27,31]. These membranes are assembled in parallel-plate configurations within a hemofilter cartridge, dimensions 11,5/5,7 cm [27], which is then connected to the vascular system for direct blood flow and ultrafiltrate collection. The filtration takes place without the need for a pump other than the heart. The result is an ultrafiltrate that is then processed within the bioreactor [27].

The bioreactor component contains a confluent monolayer of human proximal tubule epithelial cells (PTECs), supported by a synthetic, highly selective silicon nanopore membrane. The bioreactor is engineered for scalability and long-term viability [27,32].

The proof of concept for the bioreactor has been reported by Kim *et al.*, in 2023, after successfully implanting bioreactors in pigs and obtaining 90% cell viability at 7 days without the use of anticoagulation or immunosuppression.

The silicon nanopore membrane, which is found in the structure of both components, has unique characteristics [5,10,27,31]. The precisely controlled pore size (5-10 nm) and geometry (slit-shaped or straight channel), allow the membrane to mimic the glomerular filtration barrier and enable selective permeability for water and small solutes while retaining larger proteins, such as albumin [27]. The SNM allows for effective filtration with low driving pressures, such as blood pressure, suitable for implantable applications [10,27]. The structure of the SNM is ultrathin, <1 μm, which minimizes resistance to solute and water transport and supports a compact device design. The surface of the SNM is modified for hemocompatibility with a polyethylene glycol [PEG] fine layer, which is applied by liquid deposition and doesn't obstruct the pores in order to reduce protein fouling and thrombogenicity, potentially reducing or even eliminating the need for anticoagulant therapy [10,27]. The membrane also expresses immunoisolation capacity due to the small size of the pores, providing immunoprotection for the encapsulated renal cells placed on the other side of the SNM [27]. The mechanical robustness of the membrane is achievable despite its thin structure and is needed to withstand physiological blood flow rates and pressures encountered in implantable devices [33].

Basic functions of the ibak

The iBAK performs in a similar manner to the native kidney in terms of the removal of uremic toxins and excess water through mechanical filtration, similar to glomerular function. It is designed to replicate the active reabsorption and secretion of electrolytes and solutes (e.g., sodium, glucose, bicarbonate) by the tubu-

lar cells located in the bioreactor. However, the number of inserted tubular cells is smaller than that in the normal kidney due to the spatial limitations of the device and the implantability requirements [10,27].

The tubular cells in the structure of the iBAK are capable to perform metabolic activities, such as the hydroxylation of vitamin D to 1,25-dihydroxyvitamin D and ammonia production [20], but they do not have the ability to produce erythropoietin [27].

The iBAK has multiple advantages compared to conventional renal replacement therapies, as it provides restoration of multiple kidney functions [20,27]. In addition, it confers continuity and autonomy in therapy, similar to a transplanted kidney. The clearance of protein-bound uremic toxins and middle molecules is augmented compared to dialysis [34]. The design of the iBAK reduces the need for immunosuppression and anticoagulation [27]. All things considered, the iBAK has the potential to offer a better quality of life and reduced healthcare costs.

In a recent press release (from 4th November 2025), a representative of the Kidney Project in the USA declared that the initial objective of the project will be to restore kidney function to the level of stage 3 or 4 of CKD and, further, to improve to the final goal of a fully functional kidney.

The realistic outlook for novel kidney replacement therapies development:

Expert consensus suggests that while a "revolution" in kidney replacement therapies is likely before 2040 [35], most advances in the next decade will focus on enhanced dialysis and increased dialysis device portability rather than fully functional bioartificial or regenerated kidneys [5,36]. However, the breakthrough achievements in multiple domains of medical science in recent times allow for hope that radical change is possible for the well-being of ESKD patients.

Conflict of interest statement. None declared.

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