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Review Study about Portable and Wearable Artificial Kidney Systems

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Abstract

Kidney renal failure is a life-threatening disease in which one or both kidneys are not functioning normally. The only available treatment other than a kidney transplant is to start on dialysis sessions, whether it is peritoneal or Hemo-dialysis[1].

For some patients, the dialysis procedure is an exhausting and sometimes expensive trip to the specialized dialysis centers since it must be done about three times a week, depending on the physician's decision depending on the glomerular filtration rate of the kidneys[2-4].

Different researchers have made many attempts over the years to replace conventional dialysis machines with more accessible at-home dialysis systems to provide patients with comfortable treatment sessions at the time they want without the need to change their lifestyle to fit the dialysis center's schedule.

A review of the critical methods utilized in the creation and application of a portable dialysis machine that resembles the traditional dialysis center devices was conducted using a number of prior studies (research conducted between 2009 and 2024); the goal of all studies was to create a device that consists of filtering system, detection system to ensure there is no blood leakage and all parameters are within the acceptable limits, alarm system, and dialysate regeneration system, and each method will be described precisely in this review.

As a result, the discussed studies found that using peristaltic pump pumps with a phase difference by half cycle between blood and dialysate will cause a higher urea clearance rate; multiple studies focused on the modification of the dialyzing filter to find that using Polyethene glycol surface-modified silicon nanopore membranes, dual-layer hollow fiber membranes, the use of BRECS cell therapy, carbon activated blocks, all contributed highly in enhancing the dialyzing process providing the patients with highly efficient blood purification session.

Keywords: Home hemodialysis, Cener-based hemodialysis, Portable dialysis machine, Wearable artificial kidney.

دراسة مراجعة حول أجهزة الكلية الصناعية المحمولة والقابلة للإرتداء

حسنين علي لفته ، فنار صفاء حسين

الخلاصة:

الفشل الكلوي هو مرض يهدد الحياة حيث تكون فيه احدى الكليتين او كلتاهما لاتعمل بشكل طبيعي, والعلاج الوحيد المتاح بخلاف زراعة الكلى هو البدء في جلسات الغسيل الكلوي, سواء كان غسيل الكلى البريتوني او غسيل الكلى الدموي. بالنسبه لبعض المرضى تعتبر عملية غسيل الكلى رحلة مرهقة ومكلفة في بعض الأحيان الى مراكز غسيل الكلى المتخصصه حيث يجب ان تتم حوالي ثلاث مرات في الاسبوع, وذلك حسب قرار الطبيب وكفاءة الكليتين في تنقية الدم.

قام باحثون مختلفون بالعديد من المحاولات على مر السنين لاستبدال أجهزة غسيل الكلى التقليدية بأنظمة غسيل الكلى المنزلية التي يسهل الوصول إليها لتزويد المرضى بجلسات علاج مريحة في الوقت الذي يريدونه دون الحاجة إلى تغيير نمط حياتهم لتناسب جدول مركز غسيل الكلى.

تم إجراء مراجعة للطرق الهامة المستخدمة في إنشاء وتطبيق جهاز غسيل الكلى المحمول الذي يشبه أجهزة مراكز الغسيل الكلوي التقليدية باستخدام عدد من الدراسات السابقة (الأبحاث التي أجريت بين عامي ٢٠٠٩ و٢٠٢٤)؛ وكان الهدف من جميع الدراسات هو إنشاء جهاز يتكون من نظام ترشيح ونظام كشف لضمان عدم وجود تسرب للدم وجميع المعلمات ضمن الحدود المقبولة ونظام إنذار ونظام تجديد الديال الكلوي، وسيتم وصف كل طريقة بدقة في هذه المراجعة.

وكنتيجة لذلك، وجدت الدراسات التي تمت مناقشتها أن استخدام مضخات المضخة التمعجية مع اختلاف الطور بمقدار نصف دورة بين الدم وسائل الدياليزات سيؤدي إلى ارتفاع معدل تصفية اليوريا؛ وركزت دراسات متعددة على تعديل مرشح الدياليزات لتجد أن استخدام أغشية السيليكون النانوية المعدلة السطح من البولي إيثيلين جلايكول وأغشية الألياف المجوفة ثنائية الطبقات واستخدام العلاج بالخلايا البولي إيثيلين جلايكول والكتل الكربونية المنشطة، كلها ساهمت بشكل كبير في تعزيز عملية الدياليزات مما يوفر للمرضى جلسة تنقية دم عالية الكفاءة.

1. Introduction

Chronic kidney disease (CKD) denotes a state or situation in which the kidneys have sustained damage, resulting in impaired blood filtration capabilities. The medical disorder is labeled as "chronic" because a slow decline in kidney function characterizes it. The preceding harm has the potential to lead to the buildup of toxic chemicals in the human body. CKD can trigger many supplementary health concerns. End-stage kidney disease (ESKD) is a highly critical and potentially fatal condition that impacts around 3 million individuals globally[5]. treatment, according to the National Kidney Foundation[6]. Chronic renal disease is the 18th most significant cause of death worldwide. Over 2 million people globally use dialysis or kidney transplants for survival, whereas just 10% may require therapy to survive. Most renal failure patients are treated only in the United States, Japan, Germany, Brazil, and Italy. Just 12% of people on Earth reside in these five nations. More than 50% of the Global population lives in 100 developing countries, but only 20% receive treatment[7].

The best course of treatment is thought to involve kidney transplantation. Nevertheless, the average kidney transplant in the US takes 3.6 years, and graft failure is a severe risk[8]. Furthermore, not every patient is a good candidate for a kidney transplant Many treatment methods have been used through the years, and many trials to achieve the ultimate cure for (CKD) have been made. Regarding the engineering side, there were many attempts to construct suitable machines that meet the function of both kidneys in addition to the regular dialyzing machines that are already available at the hospitals.

The traditional hospital dialysis method is thought to be very restrictive to the patient's life because it requires the patient to attend the facility at set times regardless of his daily obligations. It is also thought to be somewhat expensive, and occasionally, the patient is so sick that he is unable to leave his home but still needs to go for his dialysis session. For example, in Iraq, the mortality rate among renal failure patients is very high due to low renal care given to the patients, and the number of dialysis machines number is low regarding the number of (ESKD) patients since the dialysis centers are mainly located in the center, not in the most needed regions[9].

Thus, the development of wearable or portable dialyzing devices was required to improve patient lives and enable them to go about their daily activities without having to visit the hospital when they could receive treatment in the comfort of their own homes, offering them greater privacy and relief.

Creating such a system will undoubtedly face many challenges, such as the weight, which sometimes requires the patients to stay connected to the machine for a long time[10], ensuring safe vascular access, and, most importantly, monitoring the patient distantly in case of the need to medical staff intervention[11]. which might be solved using intelligent wearable systems that are dedicated to monitoring older adults from a distance[12], water consumption which can be replaced using dialysate regeneration circuit[13], and the most important is that infections are very likely related to home-dialysis care[14], there for some patients with their family members have many concerns in taking responsibility providing at home medical care despite the flexibility and low cost of the home dialysis units[15], for that the patients need to be educated and well trained[16, 17]. Also, they need to be highly trained to do appropriate needle insertions (cannulations) in order to have more confidence in their selves[18, 19] and may use one of the telemedicine means that helps to keep the patient under continuous observation[20, 21].

2. Literature Review

Many studies have been done over the years to discuss the ability and possibility of designing portable and wearable dialyzing units. There were many attempts to achieve the exact clearance of the blood waste in a conventional dialyzing unit.

The research presented in this review paper will review a wide range of literature focusing on the creation of suitable circuits that mimic the functional and metabolic nature of the kidneys, as well as the creation of a machine that is lightweight and compact-shaped.

In 2009, Gura V. al. illustrated that WAKs have been used to treat renal insufficiency for decades. Their study explained the importance of using double channel pulsatile counter phase flow in the machine, high-flux membrane, and an optimum pH level of the dialysate. After comparing the clearance and flow of this modified WAK pump in Fig.1 with the conventional pumps, the results were very satisfactory, as the ammonia adsorption had higher levels when the dialysate pH was raised to 7.4. Also, it was noticed that the clearance had higher levels when using pulsatile flow rather than a steady flow. The most important finding is that complex molecules such as Beta2 microglobulin were removed, and high creatinine clearance was delivered; therefore, WAK could be a highly effective method for delivering daily dialysis to patients[22].

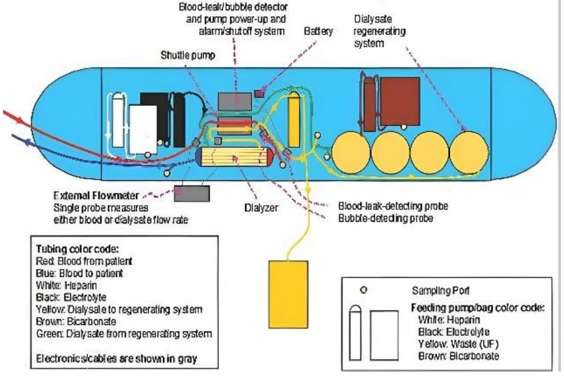


Figure (1): Schematic of WAK system [22]

In 2012, Deborah A B. et al. reported that dialysis improves small solute removal but not metabolic, endocrine, or immunomodulatory kidney function in ill patients. Organ malfunction causes most acute renal failure (ARF) deaths, not dialysis dosages. They developed, manufactured, and tested a culture vessel, cryo-storage device, cell treatment delivery system, and Bioartificial Renal Epithelial Cell System (BRECS) as in Fig.2. The current BRECS uses renal epithelial cells, but it could be expanded to provide cell-based medicines. Therapeutic extracorporeal circuit cells must be sticky, culturable in isolation or coculture, low-shear perfusion culture-maintainable, and anabolic, catabolic, regulatory, or secretory[23].

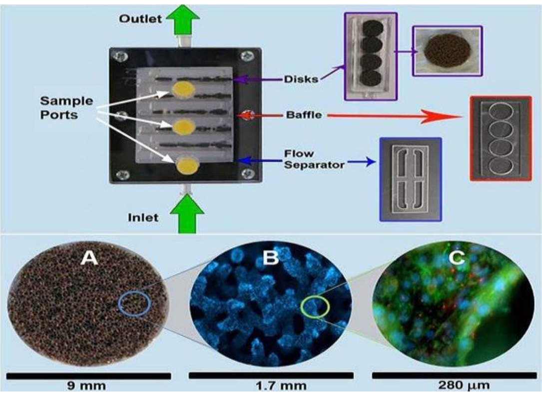


Figure (2): Bioartificial Renal Epithelial Cell System (BRECS) design [23].

In 2013, Fissell W. et al. stated that two approaches are being developed to provide patients with better outcomes regarding their health and comfort. While the first involves making dialysis-based wearable gadgets, the second method consists of designing implantable devices based on the biological nephron Fig.3. The success of these devices depends on solute removal, electrolytes, acid-base, volume homeostasis, patient acceptance, and affordability. These therapies can enhance patients' quality of life by offering greater frequency and prolonged dialysis than in-center programs. New paradigms for treating CKD patients using wearable and implantable devices may improve survival and quality of life[24].

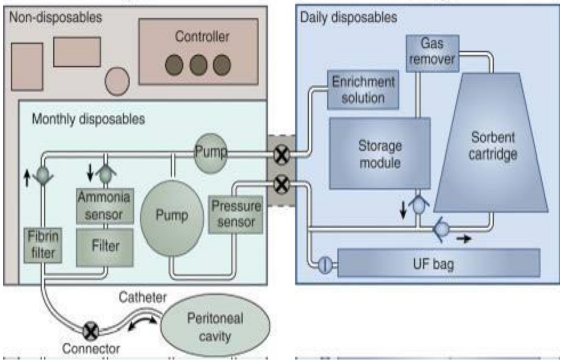


Figure (3): Schematic the artificial wearable ambulatory kidney [24]

According to Tijink M. (2013), waste solutes build up in the body's fluid as end-stage renal disease develops from renal failure. Protein-bound solutes accumulate and have an adverse effect on end-stage renal disease, but they are not eliminated by conventional renal replacement treatment. They employ a hollow fiber mixed matrix membrane (MMM) Fig.4 in their inquiry to get rid of these dangerous substances. This MMM removes protein-bound materials and hard-to-remove creatinine from human plasma solutions[25].

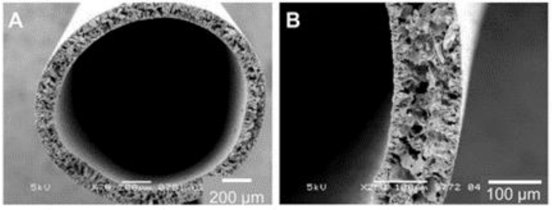


Figure (4): electron microscopy images of single layer hollow fiber MMM SL[25].

In 2015, Davenport A. explained that home hemodialysis (HD) has numerous benefits compared to dialysis conducted in a center-based setting. Dialysis device design improvements have reduced preparation and cleaning time. Nevertheless, without night dialysis, patients will continue to face the possible risk of fluid loss. Consequently, Wearable or implantable devices may allow dialysis patients to work and perform everyday duties, increasing dietary flexibility[26], Fig.5 illustrates the flow of peritoneal dialysate through AWAK.

In 2015, Salhab H. et al. referred to the fact that hemodialysis saves renal insufficiency patients. Hemodialysis patients often have cardiac and circulation issues and fatigue. To address these issues, the study proposes a wearable artificial kidney (WAK) as in Fig.6 to reduce the size of dialysis apparatuses. WAK has blood and dialysate circuits. Dialyzer purifies the patient's blood before reintroducing it. This study uses an advanced microcontroller and multiple sensors to measure many parameters such as, fluid flow sensor, pressure sensor, conductivity sensor and blood leak sensor. WAK alarms are visual and audible. This method warns patients of probable difficulties. The dialyzer's semipermeable membrane, which mimics renal function, removes hazardous compounds, trash, and excess fluids[27].

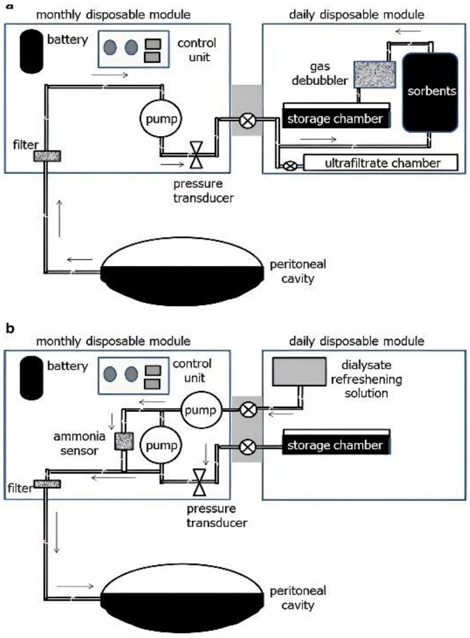
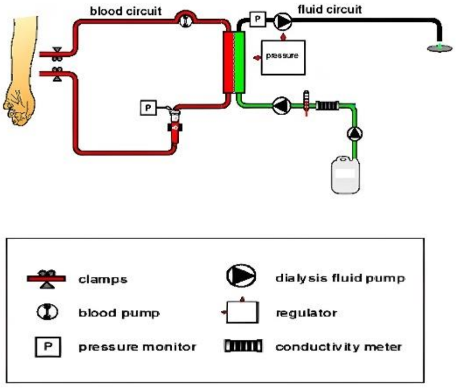


Figure (5): Peritoneal dialysate flows through automated wearable artificial kidney (AWAK)[26].



Figure(6): Hemodialysis flow diagram[27].

In 2016, Chevtchik N. et al. showed that in dialyzed renal patients, there is limited elimination of metabolic waste products, which increases morbidity and death. Applying the bioartificial kidney equipment (BAK) incorporates a combination of A "living membrane" consisting of functioning proximal tubule epithelial cells (PTEC), which could be a potent way to remove such metabolites more thoroughly. This upgraded system incorporates active organic cationic transport, which is essential for eliminating uremic metabolites as in Fig.7[28].

The need for innovative hemodialysis technology to improve patient autonomy and quality of life was addressed by Gura V. in 2016. Human trials were conducted on a wearable artificial kidney, often known as a portable hemodialysis system shown in Fig.8. Dialysate-regenerating sorbent technology is used in this FDA-approved device. Testing was done on up to ten individuals to determine whether the wearable artificial kidney could sustain the balance of solutes, electrolytes, and volumes for a full day. Every participant in the study maintained hemodynamic stability, and no significant adverse events were recorded [29].

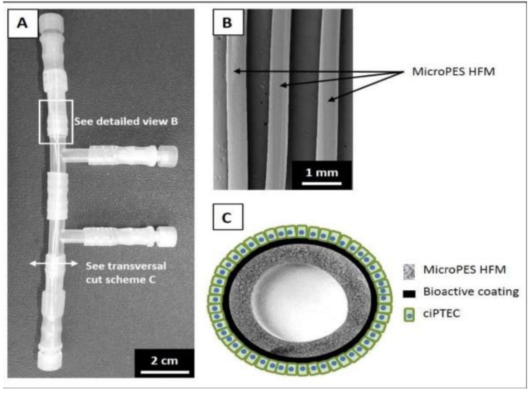


Figure (7): (A)Three MicroPES hollow fiber membranes (HFM) (B) SEM image of three MicroPES HFM. (C) Scheme of a transversal cut of one "living membrane"[28].

Figure (8): An artificial kidney prototype that can be worn[29].

In order to lower nursing requirements and medical expenses, Rajhans N. et al. (2017) set out to build home hemodialysis equipment as in Fig.9 that increases mobility and employability. The main objective of the wearable dialysis unit is to reduce pump size for wearability by building portable dialysis equipment. Through adsorption filtration, sorbent materials and catalytic mechanisms can enhance blood purification. The device can deliver round-the-clock dialysis, enabling patients to manage their treatment at home[30].

A workable strategy to improve the duration, effectiveness, and cost of dialysis was highlighted by Lee C. et al. in 2017. They discussed and addressed the several kinds of portable machines that are on the market or being explored, like the Vincenza WAK, the AWAK, and wearable hemodialysis devices. Several devices that meet these parameters are being researched. Despite concerns about safety, functionality, and efficacy, nanotechnology may make peritoneal dialysis such as in Fig.10 and hemodialysis systems wearable and portable[31].

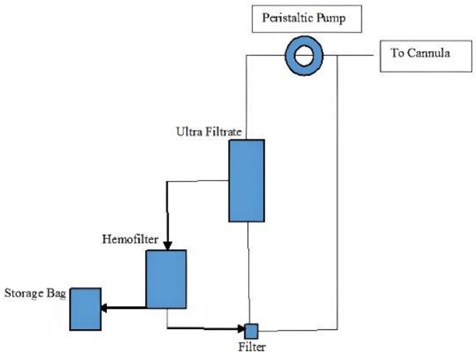


Figure (9): Schematic Diagram of Wearable Dialysis Unit[30].

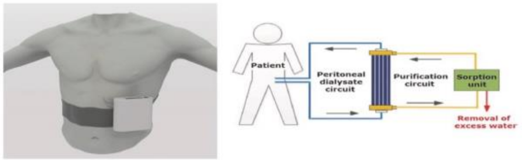


Figure (10): Conceptualized wearable peritoneal dialysis system[31].

Innovation has been impeded by the challenges posed by the conventional approach to eliminating solutes and maintaining biological components in an anticoagulated blood circuit, as demonstrated by Kimberly A J. et al. in 2017. In order to function like renal cells without blood, a bioartificial renal epithelial cell system, or BRECS, was developed as in Fig11. The effectiveness of this device in treating end-stage renal disease was investigated in an extensive animal trial. This approach preserved the use of cell therapy and a biological device to treat uremic diseases using peritoneal dialysis fluid[32].

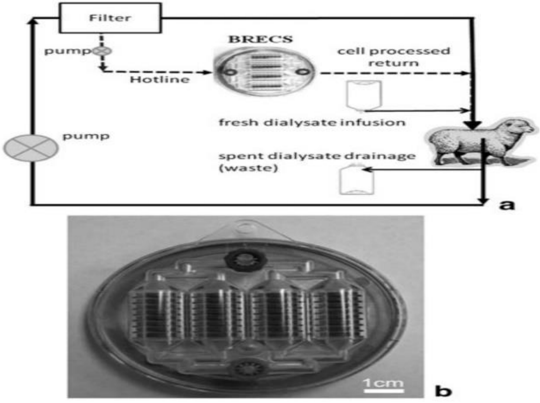


Figure (11): A wearable Kidney Using a BRECS[32].

In 2017, Wester M. et al. examined the significant variations in potassium and phosphate plasma levels in patients receiving standard intermittent hemodialysis. Goats in good health underwent dialysis using a central vein catheter as in Fig.12. The infusion of potassium and phosphate resulted in plasma concentrations similar to those achieved during dialysis[33].

The (BRECS), which treats acute kidney injury by delivering renal cell therapy via an external circuit, was presented by Pino C. et al. in 2017. In order to support cell therapy, the BRECS was made to be frozen, delivered frozen, recovered frozen and used in a therapeutic loop for extracorporeal hemofiltration. This approach resolves the distribution and storage problems that limited cell treatment[34].

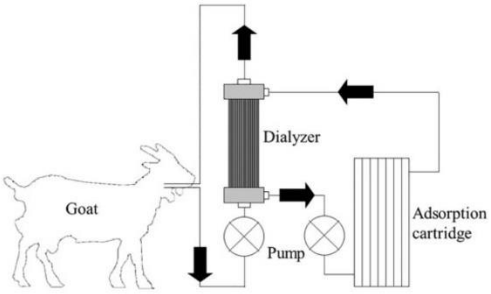


Figure (12): Experimental setup[33].

Yi-Chun D. et al. in 2017 focused on a vital subject regarding the dialysis procedure, which is the need for continuous insertion of needles into patients' vessels that may cause a severe side effect such as infection or hematoma that may lead to death. Therefore, they invented a small wearable device that works on the detection of any blood leakage using a sensing patch consisting of 10 sensors arranged to surround the site of puncture and can detect up to 0.1 mL of blood, and the wireless module will continuously transmit the risk levels as shown in Fig.13 [35].

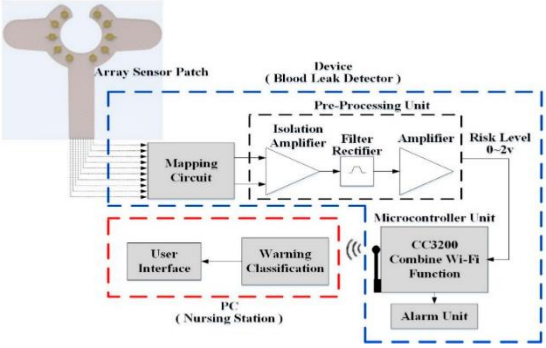


Figure (13): System Architecture[35].

In 2018, Bazaev N. et al. carried out in vitro trials on a 15 Kg dog with a healthy condition to test the clearance efficiency of a wearable artificial kidney device that works on the principle of Peritoneal Dialysis (PD) as in Fig.14 to make sure that the machine has an acceptable blood indicators clearance such as urea, creatinine, and uric acid[36].

In 2018, Salani M. et al. presented three inventions that would reduce the necessity for conventional machines. The three technologies mentioned in this article aim to reduce the enormous amount of water used during each dialysis session and also minimize the electrical consumption used in the conventional dialysis machines; by achieving this, it was possible to have a self-care dialysis treatment with more comfort and lower costs to the patients, Fig.15 demonstrates the suggested system[37].

According to van Gelder M. et al. (2018), HD equipment may improve patient mobility and independence by increasing the frequency and duration of outpatient dialysis. Dialysis via peritoneum (PD) enhances blood survival and purification as in Fig.16. The clinical application of bioartificial kidneys using renal cells still needs to be revised. When used in conjunction with extracorporeal therapy, the bioartificial kidney can partially replace endocrine, metabolic, immunoregulatory, and secretory renal tubular functions[38].

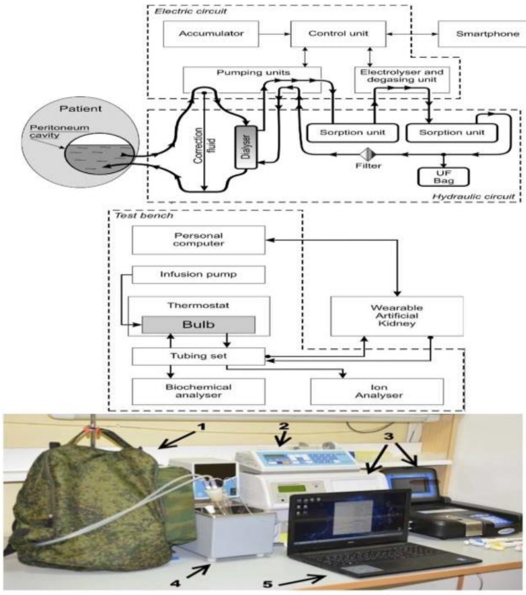


Figure (14): Device functional diagram (top)and test bench functional diagram[36].

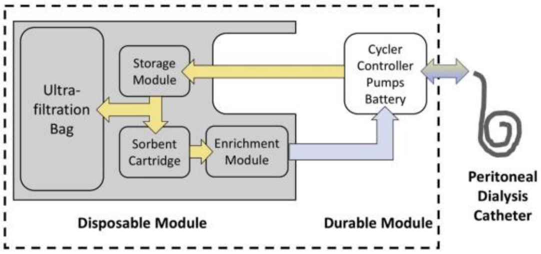


Figure (15): The automated wearable artificial kidney (AWAK) system[37].

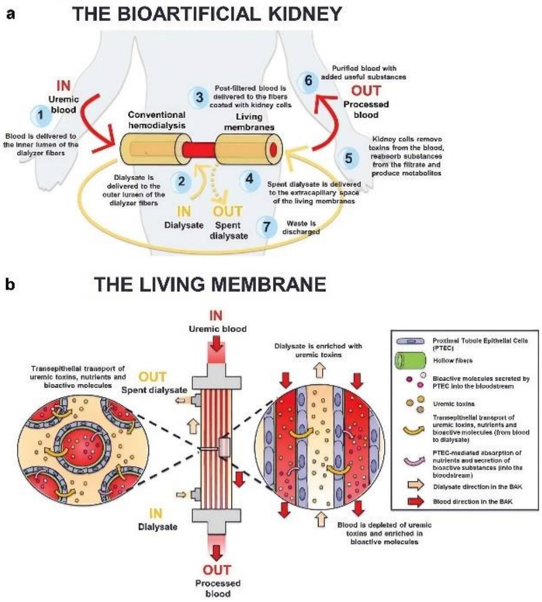


Figure (16): The automated wearable artificial kidney (AWAK) system[37].

In 2018, Gerritsen K. developed WEAKID (Wearable Artificial Kidney), which is a small dialysis machine shown if Fig.17 that can be used during the day or night as a portable device. The technique employed is continuous peritoneal dialysis (PD), which effectively addresses the limitations of existing PD methods. It enables the ongoing renewal of the dialysate, enhances the elimination of waste products, and leads to improved overall health results. The method is expected to enhance the popularity of peritoneal dialysis (PD) among individuals with (ESKD). It may lead to a transition from hemodialysis (HD) to PD in the field of dialysis[39].

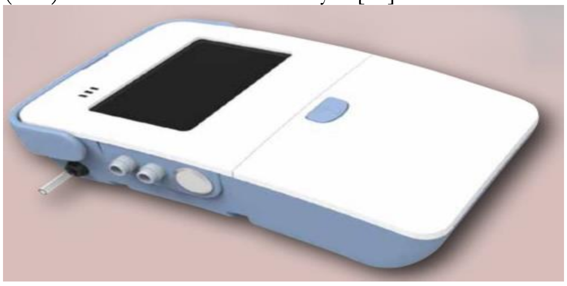


Figure (17): Prototype of the wearable WEAKID system[39].

In 2019, Castro A. et al. contemplated formulating the initial conceptual proposal for appropriate vascular access (VA) as in Fig.18 regarding the Wearable Artificial Kidney (WAK) and the Wearable Ultrafiltration (WUF) equipment. Employing a device like a chronic CVC is the most practical choice. Subcutaneous systems offer a potential solution for enabling the continuous operation of WAK or WUF devices as patients engage in their everyday activities[40].

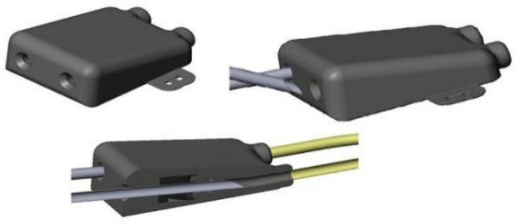


Figure (18): The miniaturized port concept, with biocompatible-material needle-free system[40].

In 2019, Sankaran S. et al. explained that the most significant drawbacks of the conventional dialysis machines are dialysis's time, expense, and patient challenges. A portable technology model for aiding kidney diseases patients has been designed to conquer these constraints as shown in Fig.19 and Fig.20. To help with daily life, "miniaturized portable hemodialysis" equipment has been developed, making it easier to carry than traditional ones. The portable dialysis system aims to improve patient life and allows people with renal failure to manage their medication at their accessibility, relieving them while enhancing their well-being[41].

The innovative wearable and portable Rene Artificial Portable (RAP) for extracorporeal blood ultrafiltration was described by Boscariol P. et al. in 2019. RAP can remotely control patients with congenital heart failure and renal failure who have an excessive fluid buildup. The research team used mechatronic design in the disciplines of electronics, mechanical, electrical, and medicine as shown in Fig.21. The interdependencies and relationships between these areas were taken into account in the design process. The device must function independently for a considerable amount of time in order to satisfy the patient's therapeutic movement patterns[42].

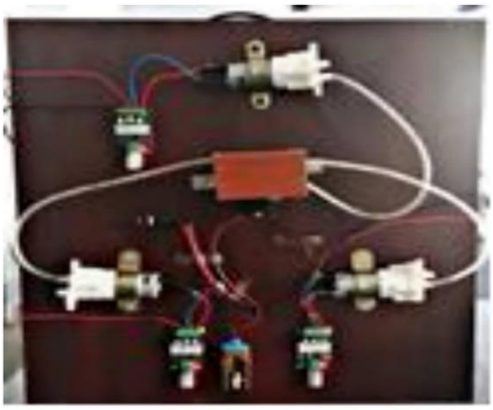


Figure (19): Front side of Dialysis Machine Prototype[41].

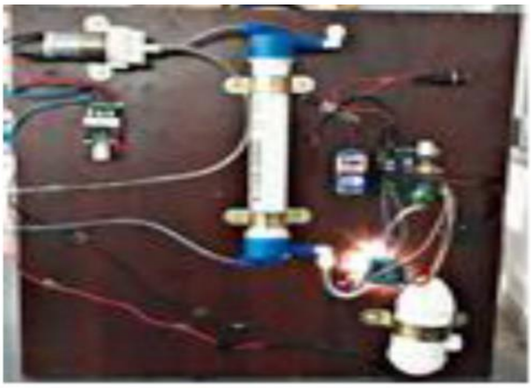


Figure (20): Back side of Dialysis Machine Prototype[41].

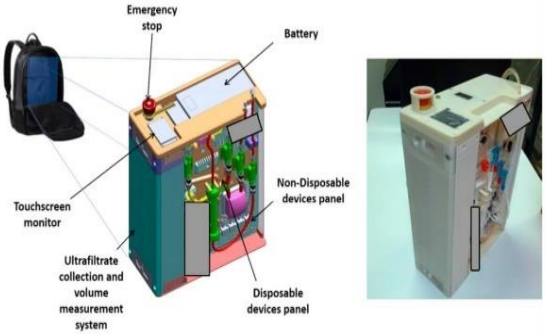


Figure (21): Rene Artificial Portatile (RAP) 3D sketch and prototype[42].

In 2019, Di Liberato L. et al. developed a device for home dialysis (DMI) to cater to a diverse array of therapies, encompassing HD (hemodialysis), HF (hemofiltration), HDF (hemodiafiltration), isolated ultrafiltration, and PD (peritoneal dialysis). The developers of the system have considered user-friendliness. This is evident in utilizing a small cartridge resembling a PD (peritoneal dialysis) device for all therapies; by integrating a warming sack into the disposable part and utilizing many pictograms, the user interaction is streamlined and made more user-friendly[43].

In 2020, Van Gelder M. et al. examined various methods for eliminating urea in a portable dialysis system, considering both chemical and medical viewpoints. A wearable artificial kidney (WAK) that could eliminate high toxin levels more often (up to permanently) outside the hospital would provide advantages to those with Huntington's disease (HD) and Parkinson's disease (PD). When attached to the patient's body, the ideal dialysis machine would be small and light, weighing less than 2.0 kg, which will significantly enhance patients' freedom, mobility, and engagement in social and economic activities[44].

In the same year, Christa N. H. et al., instead of thinking of replacing or developing the conventional hemodialysis and peritoneal dialysis, which both depend on the diffusion principle between the blood and the appropriate dialysis solution, in addition to the available research to mimic the glomerular function of the kidney, they thought of simulating the ion transportation of the nephron using activated wafer electrode ionization (AWEDI). The primary role of the nephron is to facilitate the movement of different positively charged ions, negatively charged ions, organic substances, and water between the glomerular ultrafiltrate and the peritubular blood[45].

The results showed that (AWEDI) in Fig.22 has the same features, and the selectivity for a single ion can vary between 3% and 30% from one test to another, depending on the concentrations used in each run[46].

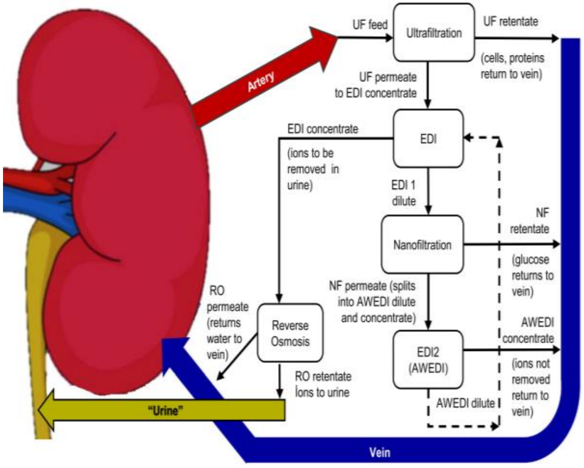


Figure (22): Configuration of the artificial kidney device[46].

Moustapha F. et al., in 2020, studied the relationship between the blood flow rate and the dialysis flow rate and its impact on the clearing rate. This was done by performing three different dialysis flow rates while maintaining constant dialysis parameters. It was found that when the dialysis flow is 1.5 than blood flow, it gives an adequate dialysis dose, which also contributes significantly to water preservation[47].

Yasamen R. et al., in 2020, studied the quality of the dialysis water in dialysis centers in Iraq. The study was conducted in four dialysis centers in Baghdad, and samples were taken from three different places: the dialysis water tanks, the dialysis unit outlet, and the distribution network. The samples were later analyzed, which were not satisfactory and did not comply with the national standards[48]; the samples from the distribution network had about 75% aluminum and high chloride concentrations[49].

In 2021, Jha C. compared home hemodialysis (HHD) utilizing a portable machine to center-based hemodialysis for end-stage renal failure (ESRF) patients in the UAE to determine cost-effectiveness. The research strategy was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method, which is an advanced analysis method that provides reporting guidance to achieve a high-quality systematic review[50].The analysis results showed that home Hemodialysis is more affordable and provides increased survival rates than the in-center-based method[51].

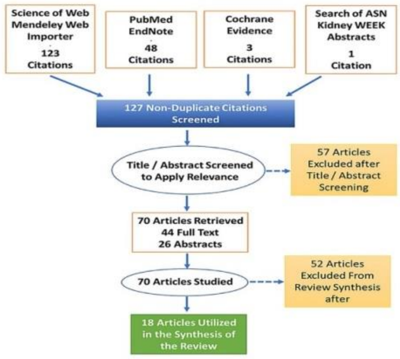


Figure (23): Prisma research flow diagram**[51].**

To give ESRD patients more flexibility when traveling, Anna Jónsdóttir A. et al. planned to modify the engineering of portable dialysis equipment in 2021. Researchers gathered travel goals and issues from patients and caregivers while organizing an overnight trip. They conducted a quantitative analysis of questions that permit multiple-choice answers and are grouped according to their frequency. Demonstrate that visiting family makes up the majority of participants' travel motivations. However, because of modern dialysis machines' designs or therapy scheduling problems, people either feel ultimately constrained or encounter significant challenges when organizing overnight trips. The study results showed that a device weighing about 20 Ib was an acceptable option for about one-third of the participants as in Fig.24. By minimizing the weight to about 5 Ib, more participants, about 80%, would be satisfied[52].

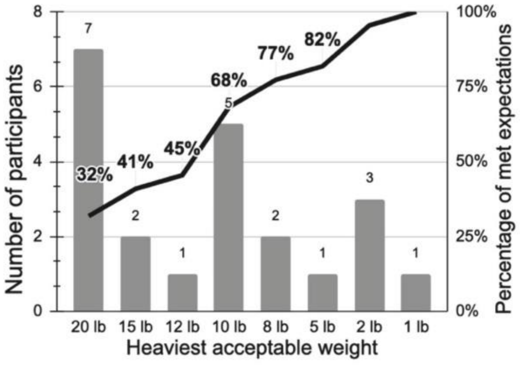


Figure (24): Heaviest acceptable weight of a portable dialysis device[52].

In 2022, Htay H. et al. evaluated the effectiveness and safety of the (AWAK) device shown in Fig.25 in patients with Parkinson's disease. By Encompassing Parkinson's disease patients from a solitary center in Singapore for the period of 2016 to 2018, subjects underwent a maximum of nine AWAK therapies for 72 hours and were monitored for one month. The study revealed no significant adverse events (SAEs) associated with the AWAK-PD device. However, it was observed that 60% of the patients experienced abdominal pain[53].

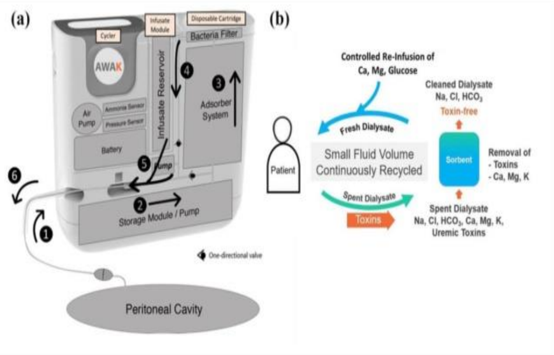


Figure (25): AWAK-PD device and its mechanism[53].

In 2022, Tang Y. et al. reported that current artificial kidney development focuses on miniaturization, biocompatibility, and metabolic activity. Recent research focuses on:

- Silicon nanopore membranes.
- Utilizing tissue engineering techniques to develop bioreactors specifically designed for renal cell cultivation.
- Methods for regenerating dialysate These initiatives address artificial kidney technology limitations. Due to rapid technical advancement, mobile or in-body artificial kidneys may become available. A mobile dialysis kidney may consist of a battery, safety parts, a dialyzer, and a unique system for the regeneration of dialysate. At the same time, a peritoneal device is connected to the peritoneal cavity of the patient and has a disposable part that can be changed after dialysis as in Fig.26[54].

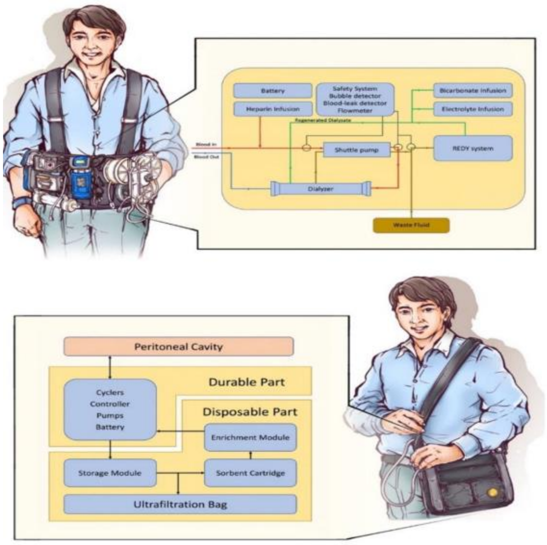
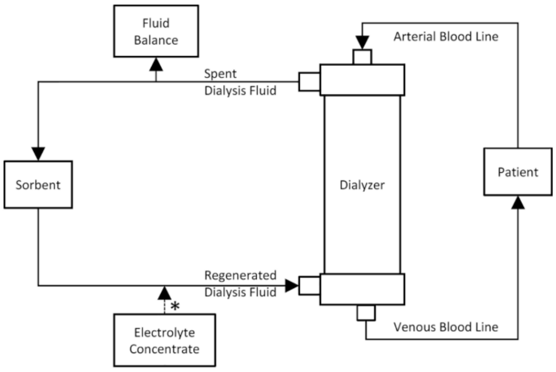


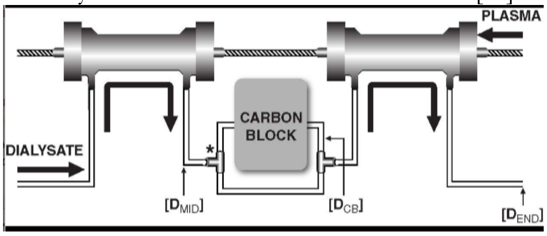
Figure (26): Basic concepts of a wearable hemodialyzer and a peritoneal-based wearable artificial kidney[54].

In 2022, Groth T. et al. considered wearable and implantable prosthetic kidneys that eliminate uremic poisons and maintain electrolytes. By providing accessible (Kidney Replacement Therapy) KRT solutions that are inexpensive and secure and can improve lives. Thus, transplantation and home dialysis must be evaluated for downsides. Recognizing and overcoming the hurdles of inventing wearable and renal prosthesis technologies may improve the quality of life of chronic renal disease patients[55].



Figure(27): Regenerating Dialysis System[55].

Seolhyun L. et al., in 2022, investigated new methods to reduce the amounts of dialysate used in the new portable dialysis machines, and this may be done using activated carbon blocks as in Fig.28. This is done by passing the waste dialysate through the activated carbon blocks and analyzing the solution before and after passing through the blocks. As a result, it was found that the blocks can increase the clearance rate of many uremic solutes rather than the others[56].



Figure(28): Dialysate Location to Bypass the carbon block or pass through it[56].

Lucena R. et al. in 2023, discussed the importance of dialysis water used in convection treatment such as Hemodiafiltration (HDF). It emphasized the importance of improving the disinfection and filtering methods used in the reverse osmosis stations to ensure higher-quality dialysis treatment. Also, suggested reusing the rejected dialysis water as a means to reduce water consumption since the patients' number is increasing, which will lead to more water consumption. Continuous monitoring of the dialysis machine's water consumption and the use of a sound water treatment system will contribute significantly to water preservation[57].

Table (1) below summarized the literature review.

3. Methodology

In Gura V. et al. research, a comparison between three flow systems was done (WAK, conventional pumps, and continuous steady flow pumps); this comparison between systems was based on the weight, dimensions, and performance of both blood and dialysate fluid. After reaching stabilized flow parameters such as cycles per minute, flow and pressure were recorded using pressure sensors and flow meters and then analyzed with respect to time. While the BRECS discussed by Buffington D. et al., which is a cell bioreactor represented by a porous niobium-coated carbon disk that allows for cell growth, porcine and human epithelial cells were isolated, expanded, and cultured for future clinical application to mimic the function of the epithelial cell. Three central systems were later discussed by Fissell W. et al. and later by Davenport A. using new methods that minimizes the overall weight and shape of the machines, in the artificial wearable ambulatory kidney system for PD dialysis a battery-powered pump was used along with an everyday disposable fluids cartridge that contains essential fluids for dialysis to be continuously regenerated and also uses a monthly changeable assembly that comprises filters and ammonia detector, the second system for Hemodialysis uses three mini pumps that ensure a steady and opposite flow between the blood and dialysate and have a safety system to protect the patient in the case of emboli presence in the returning blood to patient and detects if there was a blood leakage in the system and the most important is the dialysate regenerating system, the last system is an implantable artificial kidney that uses iliac vessel for arterial blood inflow and blood return for vein with ultrafiltrate system that uses silicon nanopore membrane or hollow fiber tubes that contains cultured renal cells which filters the wastes to the bladder.

Rajhans N. et al. aimed to minimize the dialysate water using chemical sorbents that absorb other chemicals, which will reduce the water consumption from 120 Liter per session to about 6 Liters; the sorbents regeneration method along with the restricted blood pump is very effective when removing excessive urea and replacing it with beneficial compounds. Bazaev N. et al. performed in vitro and vivo trials on a 15 Kg dog by connecting two abdominal catheters in the extracorporeal contour of the abdominal cavity; this was done by the collection of blood samples and analysis of laboratory markers (creatinine, electrolytes, total protein with fractions) using a blood analyzer; sampling of the used peritoneal dialysis solution and determination of the primary components. The concentrations of dialysis indicators (urea, creatinine, uric acid) are measured using a biochemical analyzer, whereas the concentrations of ions ($Na+$, $K+$, $Cl–$, $Ca2+$) are measured using an electrolyte analyzer.

Castro A. et al. discussed the importance of choosing the proper vascular access when choosing to use wearable or portable dialysis machines; it is known that arteriovenous fistula (AVF) has the best results since it is safer and has a low mortality percentage[58], while central venous catheter (CVC) is mainly used in end-stage patients. It requires a high sterilization level and constant cleaning and washing of hands[59]. Each one has advantages and disadvantages, especially the risk of causing hematoma there. A new method was suggested, which is a small device of a titanium connector in junction with a polytetrafluoroethylene graft[60]; the study was made by implanting 13 devices with blood flow (100-450 ml/min) to check for different body reactions.

An innovation by Boscariol P. et al. used a creative method of minimizing the ultrafiltration system by arranging three layers: the first layer for disposable parts, the second for non-disposable, and the third for electronics parts, which contributes significantly to reducing the overall shape and weight of the device.

The new device suggested by Di Liberato L. et al. depends mainly on the idea to be used easily by implementing a small cartridge that can be used for a lot of treatments that is similar to PD, with an internal warming bag and user interface system. It also replaced the reverse osmosis water with a 5-liter bag of dialysis fluids, and the machine was tested in the center for nine patients.

A vital survey was made by Anna Jónsdóttir A. et al. to provide the possible suitable options regarding the weight and shape of the portable or wearable dialyzing machine when traveling or moving from one place to another, this survey was done by contacting the patients by telephone or email and asking them multiple questions regarding their need from traveling, the maximum accepted weight for them, all these questions were on a form, and it all was gathered for later analysis.

Htay H. et al. evaluated the effectiveness of the AWAK device by performing dialyzing sessions on patients with different pathology histories. All patients received three awake sessions. Each session was for 7 hours, and the serum samples were taken before and after each session, as well as before and after the overall sessions for evaluation.

As for the study made by Seolhyun L. et al., the collected dialysate was obtained from individuals undergoing hemodialysis. Dialysate samples were collected on nine occasions from two or three patients. Nine tests were conducted, with each one involving the passage of wasted dialysate from a distinct subject through a carbon block containing around 200 g of activated carbon over four intervals. Chemical analysis was conducted on the spent dialysate at the start of each trial and after it passed through the block at the end of each period. Metabolon conducted the metabolomic study.

Table (1): Summary of the relevant studies

Author/Year	**Type**	**Weight**	**Number of Subjects**	**Employed Technology**
Gura V. et al./2009	Wearable Device	Light	12 animals	Pumps with batteries offer double-channel pulsatile counter-phase flow.
Deborah A B. et al. /2012	Portable Device	Acceptable	In vitro trial	A Bioartificial Renal Epithelial Cell System (BRECS) consists of a culture vessel and a cryostorage unit.
Fissell W. et al. /2013	Wearable, Implantable Device	Light	Pigs models and two patients for short duration	Design of implantable devices that draw inspiration from the structure and function of the biological nephron
Tijink M. et al. /2013	Portable Device	Acceptable	Uremic plasma from 6 patients Blood plasma from 6 healthy donor	Utilizes a hollow fiber mixed matrix membrane (MMM) for the purpose of eliminating these dangerous substances.
Salhab H. et al /2015	Wearable Device	Light	In vitro trial	This investigation measures many factors using an advanced microcontroller and many sensors.
Chevtchik N. et al. /2016	Implantable Device	Light	In vitro trial	Implementation of a hybrid "living membrane" that contains functional proximal tubule epithelial cells (PTEC).
Gura V. et al. /2016	Wearable Device	Acceptable	10 patients	Uses dialysate-regenerating sorbent technology.
Rajhans N. et al. /2017	Portable Device	Acceptable	In vitro	Minimizing the unit requires shrinking the peristaltic pump and absorption filter. The dialysate-free design uses convection to transfer solutes. Nano sorbents diminish ultrafiltrate size.
Kimberly A J. et al. /2017	Like Filter	Light	Female sheep with (35-45 kg)	Bioartificial Renal Epithelial Cell System (BRECS) that can operate like renal cells without blood.
Wester M. et al. /2017	Cartridge	Light	Pigs models	A cartridge containing 80 g of sodium poly(styrene-divinylbenzene) sulphonate and 40 g of iron oxide hydroxide is used to eliminate potassium and phosphate through adsorption.

Pino C. et al. /2017	Device Like Filter	Light	Computer aided design prototype	The Bioartificial Renal Epithelial Cell System (BRECS) which is an instrument that utilizes cells to provide renal cell therapy for the treatment of acute kidney injury.
Yi-Chun D. et al. / 2017	Wearable blood leakage detector	Light	Simulated hand and blood	10 sensors surrounding puncture site with mapping circuit and wireless module.
Bazaev N. et al. /2018	Wearable	Acceptable	A 15 kg dog	It carries out peritoneal dialysis with regeneration of spent dialysate in its extracorporeal circuit.
Salani M. et al. /2018	Suggestion to reduce the conventional machines.	WAK<5 kg AWAK<2kg IAKw500	20 male patients	For WAK and AWAK, water and electrical consumption are reduced. For IAK, it combines artificial filters and living cells.
Boscariol P. et al. /2019	Wearable	Light	In vitro trail on a test bench	Breakthrough of wearable and portable Rene Artificial Portatile (RAP) for extracorporeal blood ultrafiltration.
Di Liberato L. et al./2019	Portable	Acceptable	9 patients	A small cartridge resembling a PD (peritoneal dialysis) device for all therapies, including a heated bag within the disposable component, and simplifying the user interface by incorporating numerous pictograms.
Christa N. H. et al. /2020	Implantable	Acceptable	No in vivo trials.	Activated wafer electrode ionization (AWEDI).
Groth T. et al. /2022	Considered wear able and implantable prosthetic kidneys	_____	In vitro trials	KRT solutions.
Seolhyun L. et al. / 2022	Sorbent	_____	Three Patients.	Activated Carbon Blocks.

4. Results and discussions:

The pump's nature was assessed by Gura V. et al. WAK pumps pump the blood and dialysate concurrently, with a phase difference of half a cycle, using larger amplitudes and pulse frequencies compared to roller pumps; this phase difference ensures a more effective clearance rate as the case with urea clearing it was found that in has increased by 20%. The blood flow rate (Qb) was 95 ml/min, and the dialysate flow (Qd) was 90 ml/min, resulting in peak flows of 349.5 and 342.5 ml/min, respectively. Therefore, they concluded that urea clearance is a linear function with flow speed and pulsation frequency as shown in Fig (29).

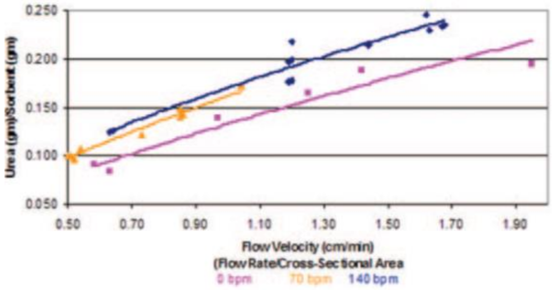


Figure (29): Linear Removal of Urea by WAK System[29].

HREC viability was lost by 10% as a consequence of cryopreservation at -140°C for long-term storage, transfer to -80°C for short-term storage, thawing, and maintenance at 37°C for clinical use, according to the BRECS design published by Buffington D. et al. Based on these findings, the BRECS can be credited as the pioneering device capable of maintaining cells, achieving overall cryopreservation temperatures, and being reconstituted for cell therapy. Making, storing, distributing, and using cell-based devices for treatment is more accessible than using conventional devices with an all-in-one design. High HREC density BRECS units can be mass-produced in bulk using human renal progenitor cells. Therapeutically relevant device supply will be made possible by cryopreserving and maintaining BRECS at temperatures of liquid nitrogen. Most clinics use ultralow -80°C freezers for short-term storage and on-demand therapy. The storage capacity is sufficient for acute and emergencies.

A cost-effective method for producing miniaturized electromechanical devices, silicon micromachining, has been suggested by Fissell W. et al. to be used in filtration to achieve nearly complete control. This would result in flat-sheet membranes with incredibly regular elongated slit-shaped pores of 5–10 nm, which are produced by controlling pore diameter and form throughout a few centimeters of a silicon wafer. These prototype membranes outperformed round-pore polymer membranes in vitro and in vivo[61]. and similar projected hydraulic permeability and steric and electrostatic hindrances[62]. Blood–material interactions were studied in vitro and in vivo. Polyethylene glycol surface-modified silicon nanopore membranes did not alter hydraulic permeability or sieving curves from the first to the 96th hour in an ultrafiltration cell using citrated bovine blood.

The glomerular and tubule membranes, which reabsorb ultrafiltrate, must be connected for an implanted artificial kidney to function correctly. Therefore, patients still manage to eliminate enough waste with just 2% or more of urine flow daily. Reverse osmosis water systems may inspire a "tubule" membrane that reabsorbs water and solutes. Developing one that can differentiate between solutes for reabsorption and excretion is a work in progress. Some technical challenges may be intractable, but a bioreactor could help. Before being deployed in clinical settings, renal tubule cell bioreactors are cultured in tissue culture for extended periods.

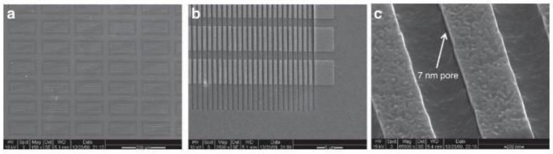


Figure (30): Scanning electron microscope images showing silicon nanopore membranes. (a) Low magnification; (b) higher magnification and (c) tilted, high magnification[24].

As Tijink M. et al. demonstrated in their prior research [63], dual-layer mixed matrix membranes (MMMs) can simultaneously incorporate both diffusion and adsorption processes within a single phase. After one hour, DL3 (dual-layer hollow fiber MMM) reaches a state of near saturation, but the diffusion of creatinine persists throughout the whole duration of the experiment. Following a typical 4-hour hemodialysis session, both diffusion and adsorption had an equal role in the overall elimination of creatinine. A total of approximately 40 milligrams of creatinine per gram of membrane was eliminated within 4 hours. While it is not possible to directly apply this data to real-life situations, a rough calculation based on similar removal rates suggests that around 45 grams (or 0.6 square meters) of a particular substance, MM, would be needed to eliminate the daily production of creatinine (roughly 1800 milligrams), which appears to be within a reasonable range.

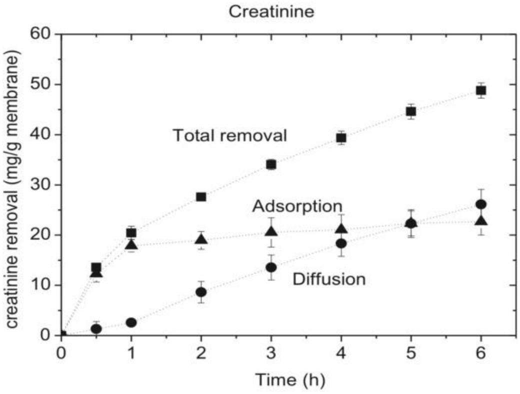


Figure (31): Average creatinine total removal plotted vs. time. Total removal is the amount of creatinine removed from the feed solution[63].

Later, in 2016, Gura V. et al. proved that the WAK is a dialysis invention that can fundamentally transform the manner in which dialysis therapy is administered. This FDA-approved exploratory clinical research demonstrates that treating persons with end-stage renal disease (ESRD) using a little sorbent-based hemodialysis device that can be worn device for 24 hours is well-tolerated and leads to successful regulation of electrolyte levels, removal of waste substances, and elimination of excess fluid. Although this study faced several technical issues related to the device, it successfully demonstrates the feasibility of the WAK as a groundbreaking dialysis technology. The WAK has the potential to revolutionize the treatment of end-stage renal disease (ESRD) by offering patients more options and improving their overall quality of life.

Maaike K. V. et al. discussed the primary obstacle in the creation of a WAK, which lies in the establishment of a highly effective urea elimination technique. Enzymatic hydrolysis, electrochemical breakdown, physisorption, and chemisorption have been investigated; however, all of these approaches have inherent drawbacks. Table 2 provides a concise overview of the options for eliminating urea and their respective benefits and disadvantages.

Table(2): Summary of methods for eliminating urea.[44], add some explanations to the caption like what +++ in the table mean.

Technique	Selectivity	Toxic by-product	Competence in removing urea	Urea removal rate	Notes
Enzymatic hydrolysis	+++	Ammonium	+++	+++	Specific storage conditions, a plan to prevent salt leak, and a large quantity of cation-exchanger are required.
Electrochemical decomposition	–	Oxidation products	–	+	In order to eliminate oxidation products, AC was necessary due to biocompatibility concerns.
Physisorption	–	None	+	++	Competition with water.
Chemisorption	–	None	+	–	Complex syntheses of sorbent

Rajhans N. et al. found per their research that this design emphasizes blood flow through a peristaltic pump and two filtrates. Peristaltic pumps deliver blood to the filter. The first filter will be parallel to the dialyzer (ultrafiltrate). The second filtrate (hemofilter with high-flux membranes) will only adsorb. A filtration unit can be added to the device to prevent the addition of purified water and it will also recirculate the water into the machine. The machine reproduces ultrafiltrate without dialysate due to convection. This device achieves its goal of making the pump wearable by reducing its size. This arrangement allows overnight dialysis with fewer difficulties. With this machine, the patient can receive dialysis at home.

Johnston K. et al. proposed that CFPD therapy managed a nephric sheep's uremia and maintained Oxygen consumption and glutathione metabolism are indicators of BRECS cellular viability and functionality. With viability staining, RECs can survive for up to seven days after treatment. The results showed that a WeBAK without a cellular therapy for chronic renal failure can be enhanced with the use of an anticoagulated blood circuit. BRECS cell treatment improves immunological homeostasis in uremia, and 1,25 vitamin D3 may help. A wearable bioartificial kidney for ESRD can be developed by enhancing CFPD with a sorbent-based dialysate regeneration system that clears uremic toxins and perfuses a cell therapy device like the BRECS.

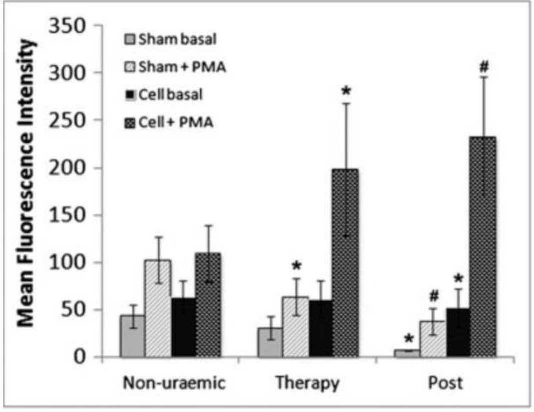


Figure (32): Oxidative activity of systemic neutrophils was retained by uremic sheep that received renal cell therapy[32].

A small dialysis device has demonstrated clinically significant, plasma concentration-dependent potassium and phosphate removal in awake, non-uremic goats, according to Wester M. et al. A cartridge with ion exchangers (poly(styrene-divinylbenzene)), sulphonate, and FeOOH) adsorbs potassium and phosphate from a dialysate circuit. By pre-rinsing with a calcium- and magnesium-containing solution, the ion exchangers did not absorb calcium and magnesium. No significant side effects were detected throughout the experiments.

Another method was proposed by Pino C. et al. with devices mentioned in their article that were recently employed in the preclinical evaluation of the BRECs for treating AKI resulting from septic shock in a well-established pig model[64]. The findings from this study using a pig model indicate that the use of BRECS cell therapy administered through an external circuit showed that SLA-BRECs with 24 disks, each disk 2 mm thick, showed positive results because of its ability to plant more significant cell numbers, providing better cell growth. All this has led to enhanced therapeutic effects, including improved cardiovascular function and increased survival time, compared to pigs who did not receive the treatment. [65].

The results of the newly invented wearable device for blood leakage by Yi-Chun D. et al. showed that under normal HD flow, it had a time response of fewer than 2 seconds, for 500 ml/m flow, it had a time response of less than 1 second, and the device's battery could operate for up to 8 hours, while the wireless module could send the results to a distance of 60 m.

While Boscariol P. et al. have unveiled RAP's initial pre-clinical model, a portable and wearable blood ultrafiltration apparatus. The design consists of standard, off-the-shelf components (such as pumps, actuators, membranes, and sensors) and additive manufacturing, as well as custom elements like a sensorized ultrafiltrate tank and an innovative electromechanical clamp. The final design for the box's shape, which allowed for a backpack or trolley case, achieved the best compromise between ergonomics and miniaturization. A 5-hour study was made to test the machine by comparing the UF volume set point (5 mL/min) to estimated and measured quantities. With the exception of a short initial interval, when the UF tank design prevented counting the extracted volume, the liquid removal rate was calculated accurately and followed the planned one with minimal error. Thus, this test verified the ultrafiltrate removal rate reading and regulation.

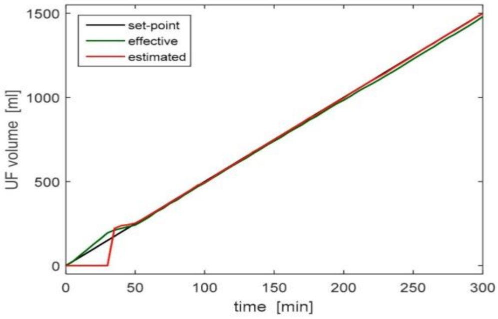


Figure (33): Ultrafiltrate volumes set in the device (black), estimated by RAP (red) and effectively measured by external scale (green)[42].

The new novel approach of activated wafer electrode ionization (AWEDI) suggested by Christa N. H. et al. implies the usage of ion exchange wafers had high selectivity for different cations (sodium, potassium, calcium, and magnesium), which provides a high selection range of transportation across the nephron, and this is controlled simply by current not by the flow.

The results of the carbon activated blocks showed that it absorbed most, but not all, of the 264 uremic solutes tested, especially those that binds to plasma proteins. When the dialysate flow through the block was 300 ml/min the blocks cleared about 216 solutes out of 264, The block affected 93%±6% of 35 out of 36 solutes with a plasma-free fraction of less than 0.3. It did not have a substantial impact on only one solute. The most important result is that reducing the dialysate volume was successful.

It was found that saving the dialysis rejection water will have a good impact as a mean for preserving water and it could be used again for other purposes such as for gardening if it was within the accepted limits [66], or can be used in the aquaponics and horticulture field[67] This can be done by many different means that aims to filter the waste water such as using nanocellulose functionalized–hybrid membranes[68, 69].A very important factor that insures a healthy and contamination free dialysis treatment, is the TDS level.

The total dissolved solids must be within the acceptable limits according to the national standards [70], if TDS was out of the normal range, it would lead to many different health issues such as bone disease, hemolysis, dementia or even bacterial contamination that leads to chronic liver disease[71-73].

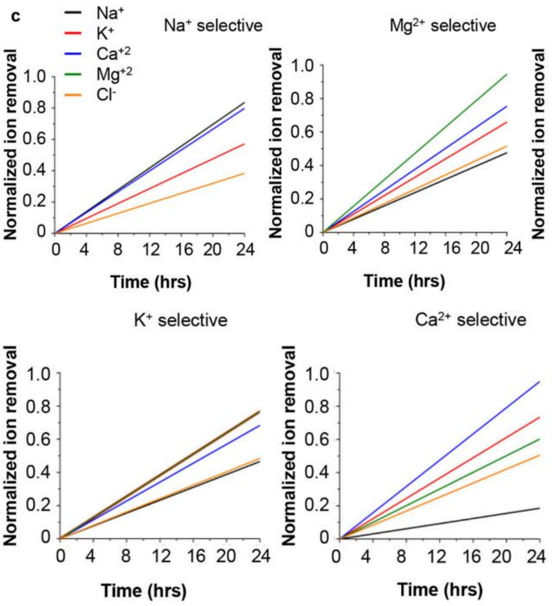


Figure (34): Selectivity for Different Cations[46].

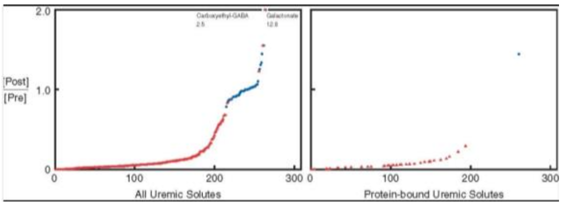


Figure (35): Adsorption Capability of Carbon Block to Dialysate uremic solutes[56].

5.Conclusion.

Although hemodialysis is considered a life support procedure, it provides costly partial removal of waste products from metabolism with associated low quality of life for patients[74, 75] , and in some cases it might cause depression to the patients undergoing treatment[76]. Innovative dialysis technologies are being developed to overcome these problems and enhance patient care, such as portable and wearable artificial kidney systems. Over the past decade, a number of research projects have developed technologies intended to replace or even reach a near result to the conventional dialysis machines. This review paper aims to make a comprehensive study of the essential techniques that researchers used to evaluate and mimic center-based dialysis machines. The review also includes a summarized description of the researchers' results and the overall conclusion they have reached, which will help future researchers develop further inventions in this field. This study concluded that it is feasible to create miniature devices with clearance rates that are comparable to those of regular machinery based on more recent research and that home based dialysis units provides low recovery time compared to the conventional machines[77]. It is essential to take into consideration that over the years, the Hemo-dialysis sessions have become not as effective as it was at the beginning, and that is due to the progressive accumulation of protein-bound molecules and toxins in the bloodstream that the dialyzer fails to filter out of the patients' system due to the continuous deterioration in the kidneys functions causing in lower filtration rate. [78]. These patients are switched to either hemodiafiltration (HDF) or CRRT treatment depending on their condition[79] since a lot of researches are suggesting that (HDF) should be the conventional dialysis method since it has lower cardiovascular side effects and lower mortality rates[13, 80, 81].

There is now an ongoing study at Al-Nahrain University that observes the TDS levels in the waste solution for each patient, which results in waste for blood filtration and relates it to the duration of the renal failure history for the patients, and we plan to create a portable dialysis system that can be attached to a wheelchair to help the patients do their dialysis session at any place they want.

This study concluded that it is quite feasible to create miniature devices with clearance rates that are comparable to those of regular machinery based on more recent research. With today's advanced technology and ongoing research, it is quite feasible that dialysis patients may be able to complete their treatments at home in settings that they find more secure and comfortable.

5. References

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