STEP INTO THE WORLD OF SLOW DIALYSIS

Nanodialysis is bringing innovative products into the market of blood purification and dialysis based on nanostructured materials. The miniature portable and wearable artificial kidney is an ideal solution for end stage renal disease patients allowing patients to dialyze anywhere, anytime while being mobile, restoring their participation in the society.

Nearly 4 million dialysis patients in 2020
Estimates suggest an increase to nearly 4 million patients on hemodialysis and peritoneal dialysis in 2020. The average patient number growth is 5-6% per year mainly caused by effects from obese and overall aging of population. Overall healthcare costs of dialysis patients in the western world currently reaches to 90 k€/patient/year (dialysis treatment plus medical and hospitalization costs). This would imply an health cost expenditure of over 300 billion € in 2020.

Intermittent hemodialysis in a central clinic
The majority of End Stage Renal Disease (ESRD) patients is dependent on hemodialysis treatment in a central clinic three times a week. Although lifesaving, this treatment is far from ideal. The blood clearance is relatively poor (10%) and the intermittent treatment causes significant variations of concentration levels in the blood. This adversely affects the condition of other organs. The overall life expectancy is poor: 1 out of 6 patients dies within one year. Current dialysis machines are bulky in size and require special equipment for the preparation of dialysate fluid. Each hemodialysis treatment consumes 60-120 liters of dialysate. This large volume of dialysate hampers a mobile, portable or wearable system for use at home.

Slow dialysis while being mobile
For practical and economical reasons dialysis treatment in a central clinic is limited to a 4 hour session. However a longer dialysis duration with a slower rate of toxin removal and water extraction favors the hemodynamic stability and would lower the mortality (see figure, RR relative risk of mortality vs treatment time and Kt/V dialysis dose). Nocturnal home dialysis with 6-8 hours dialysis sessions reveals improved salt and water control, increased solute removal and a marked improvement in quality of life. Slow dialysis is therefore regarded as very beneficial. Up to now slow dialysis was difficult to realize in practice. But with the advent of portable and wearable dialysis 24/7 (semi) continuous dialysis has now become possible.
OUR MINIATURE DIALYSIS SYSTEMS

Current hemodialysis machines need 60-120 liter of fresh dialysate for blood cleansing. This is a major showstopper for miniaturization and mobility. Our miniature artificial kidney uses sorbents for continuous regeneration of dialysate. Herewith only 100 ml of dialysate is needed. Thanks to the efficiency of the nanosorbents, the sorbent system can be very small allowing a handy portable or wearable system.

Wearable system for continuous flow peritoneal dialysis
A wearable dialysis system enables a slow and continuous 24/7 dialysis treatment resembling the functioning of healthy kidneys. Hereby variations of concentration levels in the blood can be kept to a minimum. Thanks to the prolonged duration, the clearance can be improved.
Wearability requires a small and lightweight system but also a (safe) continuous access to the body. The technique of peritoneal dialysis seems best suited for this purpose. With our wearable device, peritoneal dialysate is continuously purified and circulated in the abdomen. This has a big impact on the clearance that is raised to the same level as for frequent home hemodialysis, outperforming in-center hemodialysis. This is quite exceptional for peritoneal dialysis. Glucose is infused continuously at low concentration levels in order to prolong the condition of the peritoneal membrane.

Portable system for home hemodialysis
The miniaturized dialysis system can also be used as an easy to use small home hemodialysis system. The elimination of 60-120 liters of dialysate per session is a big advantage for home use. The system is connected via a standard fistula or shunt blood access. The dialysis process is controlled by an operating system using sensors to ensure safety (pressure, temperature, dialysate conductivity and pH, air bubble detection, fluid leakage). The system is able to run fully automatic as stand-a-lone machine. However, the patient has the ability to interfere and to control the device manually as well. This can be done via an in-built control panel or by a smartphone.
REMOTE SURVEILLANCE FOR EXTRA SAFETY

The miniature portable and wearable dialysis systems are enabled with state-of-the-art ICT-tools for automated control and data sharing, developed in the EU/FP7 Nephron+ project. This offers the patient a user-friendly and easy operation in combination with the possibility to access all data recorded by the system. It also allows online data sharing with a medical center for remote surveillance and rapid assistance in case of an emergency.

Webportal for remote surveillance
The miniaturized dialysis system is remotely monitored by a medical center. Messages and alarms generated by the operating system and sensor data from the portable/wearable artificial kidney are being sent and logged to a webportal. Both doctor and patient have access to the history and actual status of the device and the current treatment. It includes sensor readings, battery status and operation mode. Patient parameters as blood pressure and weight are also recorded daily. Together with feedback from the patient about his health condition (activity level, sleep, feeling well or sick) a database is generated that can be analyzed by the doctor. Based hereon the treatment and the settings of the device can be adapted and fine-tuned to the personal needs of the patient.

Smartphone with patient app as ICT hub
A smartphone is used to control and to read the device, but it also serves as ICT hub to the webportal. Messages, alarms and sensor data are sent via Bluetooth (Continua HDP) to the smartphone and directed further to the webportal via wifi or GS3/4. The smartphone and webportal allow the patient to read all data (device status, measurements, alarms) from the device and to change the operation mode if wanted. The app on the smartphone has a menu for giving feedback about health condition (questionnaires) and retrieval of weight and blood pressure.

Patient monitoring and sensors
Sensors are used to monitor and to control the dialysis operation and to safeguard the patient from malfunctioning. This includes sensors for temperature, pressure, fluid leakage, conductivity, pH and redox state of the dialysate. Patient weight and blood pressure are measured daily and based hereon the volume of excess fluid extraction is being adjusted automatically.
STATUS AND OUTLOOK

Prototype versions have become available in 2013 and 2014. These prototypes have been extensively tested on efficacy and biocompatibility both invitro and invivo (animal trials). Next steps involve satisfying the requirements for manufacturing medical devices and getting approval for conducting clinical trials.

Performance
The clearance achieved by the miniature dialysis system is proportional to the size of the sorbent unit. The invivo hemodialysis experiments have shown that a 200 g unit provides a urea clearance of around 10 ml/min while a 400 g unit achieves 20 ml/min. For creatinine these values are 25 and 50 ml/min respectively. In case of the peritoneal application, the urea clearance is improved from 7 ml/min (standard peritoneal) to 20 ml/min for 10 hrs use/day or >30 ml/min for continuous use. The improvement is possible thanks to continuous purification and circulation of the peritoneal dialysate in the abdomen, hereby maintaining a high concentration gradient over the peritoneal membrane.

Size and weight
The prototype used for the animal trials has a weight of 3.2 kg. It has a display for manual control but the device can also be controlled via the smartphone. After the animal trials a redesign will be performed in view of further weight reduction, ergonomics and medical device manufacturing requirements. A weight reduction of the wearable peritoneal system down to 1.3 kg (1.5 L), including battery, is feasible. The weight of the portable system will be 2.5 kg (4 L).

Benefits for patients and healthcare system
The miniature dialysis system with in-built sensors, control and safety measures offers the patient freedom to dialyze anytime, anywhere. The handy device makes dialysis easy at home/work, for longer periods or continuously, providing higher and more uniform removal of toxins. Resulting in a better health condition at lower costs. The Dutch Kidney Foundation estimated in 2012 the overall healthcare costs for in-center hemodialysis to 85 k€/patient/yr, while home hemodialysis and wearable dialysis are at 45 k€/patient/yr. This is due to reduction in personnel costs, overhead, medication and transportation costs.