Wearable Artificial Kidney
Back to the future?
Presentation Outline

- RRT: needs and wants
- The challenge of a WAK
- History of WAK
- Current market situation
- Actual perspective and future direction
- Wearable to implantable?
- Conclusions
The epidemic of CKD

Costs: more than $30 billion/year in the US

Mortality rate of CKD patients = metastatic carcinoma of breast, colon or prostate


Better patient tolerance, but stagnant outcomes despite improvement in techniques

Current RRT: high-flux HD

HEMO study, 2002

Renal Replacement Treatment: needs and wants

Better patient tolerance, but stagnant outcomes despite improvement in techniques

Current RRT: high efficiency PD

ADEMEX study, 2002

R. Paniagua et al, “Effects of Increased Peritoneal Clearances on Mortality Rates in Peritoneal Dialysis: ADEMEX, a Prospective, Randomized, Controlled Trial”, J Am Soc Nephrol 2002 May; 13(5)1307-20
“Modern” treatments eventually not superior to traditional ones?

A move towards convection  

Current RRT: HDF

Canaud B et al, Mortality risk for patients receiving hemodiafiltration versus hemodialysis: European results from the DOPPS Kidney Int 69:2087–2093, 2006
Authors' conclusions

“We were unable to demonstrate whether convective modalities have significant advantages over HD with regard to clinically important outcomes of mortality, dialysis-related hypotension and hospitalization. More adequately-powered good quality RCTs assessing clinically important outcomes (mortality, hospitalization, quality of life) are needed.”

Rabindranath KS et al: Cochrane Database of Systematic Reviews 2008, Issue 1
### Renal Replacement Treatment: needs and wants

Haemodiafiltration and mortality in end-stage kidney disease patients: a pooled individual participant data analysis from four randomized controlled trials

**HDF Pooling Project**

Sanne A.E. Peters,1,2 Michiel L. Bots3, Bernard Canaud,4, Andrew Davenport,5 Muriel P.C. Grooteman,5 Fatih Kircilli,6 Francesco Locatelli,7, Francisco Maduell,8 Marion Morena,9,10,11, Menso J. Nube,9 Erkan Ok,9 Ferran Torres,12,13, Mark Woodward,14,15,16 and Peter J. Blankestijn16 on behalf of the HDF Pooling Project Investigators

#### Current RRT: HDF

**Advance Access**  
**October 22, 2015**

<table>
<thead>
<tr>
<th>Causes of mortality</th>
<th>HD Events/100 PY</th>
<th>HDF Events/100 PY</th>
<th>HR (95% CI) for HDF versus HD</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-causes</td>
<td>1369</td>
<td>1367</td>
<td><strong>0.86</strong> (0.75; 0.99)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>1302</td>
<td>1289</td>
<td><strong>0.77</strong> (0.61; 0.97)</td>
</tr>
<tr>
<td>Infections</td>
<td>1302</td>
<td>1289</td>
<td>0.94 (0.68; 1.30)</td>
</tr>
<tr>
<td>Sudden death</td>
<td>1302</td>
<td>1289</td>
<td>0.99 (0.68; 1.43)</td>
</tr>
</tbody>
</table>

#### Follow-up 2.5 years (1.9-3)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Online HDF: BSA-adjusted convection volume (L/session)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;19</td>
</tr>
<tr>
<td>All-causes</td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>0.91 (0.74; 1.13)</td>
</tr>
<tr>
<td>Adjusted</td>
<td>0.83 (0.66; 1.03)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>1.00 (0.71; 1.40)</td>
</tr>
<tr>
<td>Adjusted</td>
<td>0.92 (0.65; 1.30)</td>
</tr>
</tbody>
</table>

Dysomogeneous sample, different study design and inclusion criteria → “Observational” data
Optimal convection volume for improving patient outcomes in an international incident dialysis cohort treated with online hemodiafiltration

Bernard Canaud1,2, Carlo Barbieri2, Daniele Marcelli2,3, Francesco Bellocchio2, Sudhir Bowry2, Flavio Mari2, Claudia Amato2 and Emanuele Gatti2,3

Higher convective volumes improve survival

Wouldn’t it be only a matter of dialysis time?

Canaud B et al, Optimal convection volume for improving patient outcomes in an international incident dialysis cohort treated with online hemodiafiltration, KIDNEY INT. 2015 NOV;88(5):110-16
- Continuous, **round-the-clock** metabolic and fluid regulation
- Excretion of water soluble, middle molecular weight and protein-bound toxins, in addition to small molecular weight toxins
- **Function automatically, imposing no restriction** to the individual’s life

Current RRT: daily dialysis

Frequent Hemodialysis Network Daily Trial

Frequent Hemodialysis Network Daily Trial

Frequent Hemodialysis Network Daily Trial

Current RRT: daily dialysis

Long-Term Effects of Frequent In–Center Hemodialysis

Glenn M. Chertow,* Nathan W. Levin,† Gerald J. Beck,‡ John T. Daugirdas,§ Paul W. Eggers,‖ Alan S. Kliger,‖ Brett Larive,‡ Michael V. Rocco,** and Tom Greene,+++ for the Frequent Hemodialysis Network (FHN) Trials Group


Comparing PD modalities

Dialysis: the longer the treatment, the better?

Longer and more frequent dialysis is infeasible for most patients:
- Nowhere to do it
- Nobody to do it
- Who pays?
- Patients want freedom
3 reasons for developing a WAK:

- **Clinical**: better outcomes and quality of life for daily dialysis
- **Technical**: take advantage of technological progress
- **Socio-economics**: costs of current RRT modalities, unacceptable mortality rates for CKD patients

The challenge for a WAK

“It seems like one factor the nephrology community was never able to fully identify and modify is dialysis time…”

The WAK is intended to be used for CRRT 24h a day 7 days a week

Must be able to deliver proposed CrCl of 30 ml/min and UF 30 ml/min

Light weight, ergonomic, energy independent, safe; no risk of clotting, infection, toxicity

C Ronco et al, Critical Care Nephrology, 2º edition, Elsevier
Technical requirements for a WAK

Dialysate regeneration
Power sources
Vascular Access
Dialysis membranes
Pumping system
Monitoring system

“whoever wishes to foresee the future must consult the past; for human events ever resemble those of preceding times”

N. Machiavelli
Discourses on the First Ten Books of Titus Livius,
Chapter XLIII
1513 b.c.

**Portable/wearable artificial kidney (WAK) - initial evaluation.**

**Stephens RL, Jacobsen SC, Atkin-thor E, Kolff W.**

**Abstract**

This report discusses the modus operandi and results achieved using this new mode of haemodialysis. An insulated 20 L dialysate bath acts as a carrying case for the system. When empty the case is large enough to hold the wearable module and complete supplies for one week's operation. The total weight is 17 kg. The wearable unit consists of a combined blood and dialysate pump (1.2 kg), rechargeable batteries, tubing, Dow dialyser and charcoal regeneration module with a **total weight of 3.5kg**. Ideally the patient dialyses using a single needle some 3 hours/day, 6 days/week. **It is necessary for the wearable module to be connected to the 20 L dialysate bath for an average of 90 minutes** to achieve adequate urea and 5+ removal. One patient was dialysed on 35 consecutive days and 4 others were dialysed intermittently. Routine laboratory tests and mass balance studies were performed on all patients. Ultrafiltration rates reached 700 ml/hour, routine serum chemistries remained stable and mass balance studies demonstrated a daily removal of urea 14-20 G, creatinine 1500-2000 mg, uric acid 500-900 mg and K+ 30-55 mEq. It is concluded that dialy dialysis with WAK is biochemically adequate and also permits the patient a much less restricted existence.
WAK: hypothesis (1977)

Landè, “In search of a 24 hours per day artificial kidney”, Journal of dialysis 1977
Adsorption
separation of a solute from its solvent by a solid agent

REDY System (Recirculating DialYsis)

Sorbent dialysis, suitable for HD and PD

Blumenkrantz, Application of the Redy sorbent system to HD and PD, Artificial Organs, 1979
History of Wearable Artificial Kidney

REDY or not? (1979)

Blumenkrantz, Application of the Redy sorbent system to HD and PD, Artificial Organs, 1979
WAK: REDY or not? (1979)

Drawbacks:

- Cartridge weight, cost, and unregenerability
- Na\(^+\) and H\(^+\) load (in exchange for NH\(_4^+\) produced by urea breakdown by urease)
- Aluminium release

Standard REDY cartridge: 3,3 kg of active compounds, suitable for 3 HD sessions (removal of 50 g urea)

Blumenkrantz, Application of the Redy sorbent system to HD and PD, Artificial Organs, 1979
11 patients, thrice/weekly dialysis 6-7 hours, 3 REDY cartridge per week, independent for water supply and drainage

Slight elevation of creatinine and urea

**REDY: first clinical application**

**TABLE II. Comparison of Pre-dialysis Biochemistry and pH in Single-pass System (SPS) Patients and Sorbent Regeneration Dialysate (SRD) Patients**

<table>
<thead>
<tr>
<th></th>
<th>Single-pass system (SPS)</th>
<th>Sorbent Regeneration of Dialysate (SRD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Blood Urea (mmol/L) + SEM</td>
<td>SRD (1) 31 mmol/L</td>
</tr>
<tr>
<td></td>
<td>22 ± 0.8</td>
<td>26 ± 1.2</td>
</tr>
<tr>
<td></td>
<td>Plasma Creatinine (mmol/L)+ SEM</td>
<td>25 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>970 ± 40</td>
<td>1083 ± 27</td>
</tr>
<tr>
<td></td>
<td>Plasma Sodium (mmol/L) + SEM</td>
<td>1100 ± 30</td>
</tr>
<tr>
<td></td>
<td>139 ± 0.9</td>
<td>141 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>Plasma Potassium (mmol/L) + SEM</td>
<td>140 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>4.9 ± 0.1</td>
<td>4.3 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>Plasma Bicarbonate (mmol/L) + SEM</td>
<td>141 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>24 ± 0.5</td>
<td>17.4 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>pH + SEM</td>
<td>7.33 ± 0.05</td>
</tr>
<tr>
<td></td>
<td>7.40 ± 0.03</td>
<td>7.37 ± 0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.38 ± 0.06</td>
</tr>
<tr>
<td>Leucocyte Potassium</td>
<td>(mmol/kg cells dry weight) + SEM</td>
<td>424 ± 19</td>
</tr>
<tr>
<td></td>
<td>400 ± 24</td>
<td>-</td>
</tr>
<tr>
<td>Plasma Calcium (mmol/L) + SEM</td>
<td>2.52 ± 0.02</td>
<td>2.60 ± 0.03</td>
</tr>
<tr>
<td></td>
<td>2.37 ± 0.02</td>
<td>2.49 ± 0.03</td>
</tr>
<tr>
<td>Plasma Phosphate (mmol/L) + SEM</td>
<td>1.75 ± 0.05</td>
<td>1.80 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>1.95 ± 0.1</td>
<td>2.06 ± 0.1</td>
</tr>
</tbody>
</table>
2 ESRD patients in HD
inter-dialytic UF through a polysulphone
minifilter (femoral AV shunt)
0.6 ml/min UF (average 800 ml/day)
Anticoagulation through injected salycilate
Continuous wearable hemofiltration (1986)

Continuous Arterio-venous Hemofiltration in a Wearable Device to Treat End-stage Renal Disease

A. Murisasco, J. P. Reynier, A. Ragon, Y. Boobes, M. Baz, C. Durand, P. Bertocchio, C. Agenet, and M. El Mehid

A-V Schribner shunt
2 patients treated daily for 1 and 3 months
3-4 minicartridges per day

Problems:
- Maintaining access patency
- Risk of long term Al toxicity

Murisasco et al, Continuous arterio-venous hemofiltration in a wearable device to treat end-stage renal disease, Trans Am Soc Artif Intern Organs, 1986
**WAK: modern times (2005)**

Continuous renal replacement therapy for end-stage renal disease. The wearable artificial kidney (WAK).

**Contrib Nephrol** 2005;149:325-333.

**Gura V**, **Beizai M**, **Ezon C**, **Polaschegg HD**.

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**TABLE 260-1**

<table>
<thead>
<tr>
<th>BIOCHEMICAL INDEX</th>
<th>GROUP I</th>
<th>GROUP II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective urea clearance (mL/min)</td>
<td>24.3 ± 1.4</td>
<td>23.9 ± 3.5</td>
</tr>
<tr>
<td>Effective creatinine clearance (mL/min)</td>
<td>25.5 ± 1.4</td>
<td>24.7 ± 3.2</td>
</tr>
<tr>
<td>Total urea removal (g)</td>
<td>12.7 ± 2.8</td>
<td>12.0 ± 2.9</td>
</tr>
<tr>
<td>Total creatinine removal (g)</td>
<td>0.9 ± 0.2</td>
<td>1.0 ± 0.1</td>
</tr>
<tr>
<td>Total phosphorus removal (g)</td>
<td>0.8 ± 0.2</td>
<td>0.84 ± 0.4</td>
</tr>
<tr>
<td>Total potassium removal (mmol)</td>
<td>71.9 ± 13.3</td>
<td>89.1 ± 25.7</td>
</tr>
<tr>
<td>Extrapolated standard Kt/V (urea)</td>
<td>5.4 ± 2.4</td>
<td>8.4 ± 1.5</td>
</tr>
</tbody>
</table>

*In uremic pigs. In Group I, a blood flow rate of 44 mL/minute was used; in Group II, blood flow rate was 75 mL/minute. Values are means ± SD. Data from Gura V, Beizai M, Ezon C, Polaschegg HD: Continuous renal replacement therapy for end-stage renal disease: The wearable artificial kidney (WAK). In Ronco C, Brendolan A, Levin NW (eds): Cardiovascular Disorders in Hemodialysis. Basel, Karger, Contrib Nephrol 2005;149:325-333.

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**History of Wearable Artificial Kidney**

Dialysate continuously regenerated through a sorbent unit (tot dialysate 375 ml)
A wearable haemodialysis device for patients with end-stage renal failure: a pilot study

Andrew Davenport, Victor Gura, Claudio Ronco, Masoud Beizai, Carlos Ezon, Edmond Rambod

### WAK: modern times (2007)

Mean treatment time 6.4 h  
Mean blood flow 58.6 ml/min  
Mean dialysate flow 47.1 ml/min

<table>
<thead>
<tr>
<th>Treatment time (h)</th>
<th>Weight (kg)</th>
<th>Extracellular fluid/total body fluid</th>
<th>Urea removed (mmol)</th>
<th>Creatinine removed (mmol)</th>
<th>Plasma urea clearance (mL/min)</th>
<th>Plasma creatinine clearance (mL/min)</th>
<th>Standard hourly urea clearance (Kt/V)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td>Before treatment</td>
<td>After treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 1</td>
<td>4</td>
<td>81.6</td>
<td>80.7</td>
<td>0.342</td>
<td>0.339</td>
<td>6.2</td>
<td>5.4</td>
</tr>
<tr>
<td>Patient 2</td>
<td>4</td>
<td>59.7</td>
<td>59.3</td>
<td>0.343</td>
<td>0.337</td>
<td>9.1</td>
<td>5.4</td>
</tr>
<tr>
<td>Patient 3</td>
<td>4</td>
<td>56.4</td>
<td>55.5</td>
<td>0.345</td>
<td>0.342</td>
<td>5.7</td>
<td>3.6</td>
</tr>
<tr>
<td>Patient 4</td>
<td>7</td>
<td>62.6</td>
<td>62.3</td>
<td>0.324</td>
<td>0.319</td>
<td>7.0</td>
<td>5.4</td>
</tr>
<tr>
<td>Patient 5</td>
<td>8</td>
<td>56.5</td>
<td>56.9</td>
<td>0.344</td>
<td>0.343</td>
<td>14.0</td>
<td>15.2</td>
</tr>
<tr>
<td>Patient 6</td>
<td>8</td>
<td>88.5</td>
<td>86.7</td>
<td>0.327</td>
<td>0.320</td>
<td>15.5</td>
<td>8.9</td>
</tr>
<tr>
<td>Patient 7</td>
<td>8</td>
<td>117.3</td>
<td>115.8</td>
<td>0.352</td>
<td>0.350</td>
<td>18.0</td>
<td>13.4</td>
</tr>
<tr>
<td>Patient 8</td>
<td>8</td>
<td>48.0</td>
<td>46.6</td>
<td>0.337</td>
<td>0.335</td>
<td>6.7</td>
<td>4.5</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>6.4 (2.0)</td>
<td>71.3 (23)</td>
<td>70.5 (22.6)</td>
<td>0.339 (0.009)</td>
<td>0.335 (0.010)</td>
<td>10.3 (4.8)</td>
<td>7.7 (4.4)</td>
</tr>
</tbody>
</table>

No hemolysis, stable electrolytes and pH, no alteration in BP or HR

Problems:

Release of bubbles of carbon dioxide (decomposition of urea by urease)

- One patient had clotting of the CVC
- One patient had clotting of the circuit
- One patient suffered fistula needle dislodgement and temporary disconnection

Fluids are propelled in a pulsating fashion but on opposing cycles, so that pressures peak in one compartment when the other compartment pressures are at trough pressures, and vice versa (Fig. 260-2). The device also features reservoirs with heparin to be infused into the blood circuit as well as magnesium and calcium to be infused into the dialysate. These infusions are accomplished by auxiliary small pumps at prescribed rates. An additional auxiliary pump, volumetrically controlled, removes ultrafiltrate.

The governing principles of this design are reflected in six specific considerations:

1. The optimal design would incorporate light, small, and energy-efficient parts requiring minimal amounts of energy from commonly available batteries but delivering efficient mass transfer across a dialyzer membrane to satisfy the highest dialysis adequacy. To meet this objective, hemodiafiltration was the most suitable modality. The double-pulsation mechanism for both blood and dialysate, oscillating at half-cycle differences, generates intermittent pressure changes across the dialyzer membrane, providing flow characteristics completely different from those of conventional dialysis machines. The transmembrane pressure (TMP) gradient changes direction with each pulsation at different magnitudes along the hollow fiber: High increased convection forces higher mass transfer from the blood to the dialysate compartment in the proximal aspect of the fiber, while at certain parts of the pulsating cycle, fresh sterile fluid is propelled from the dialysate into the blood compartment, generating "post dilution," thus accomplishing hemodiafiltration.

2. The amount of dialysate necessary for a conventional dialysis treatment usually exceeds 100 L. With such a burdensome load, designing a wearable device would be impossible. The only way to overcome this problem is to use a sorbent regeneration system that constantly removes undesirable substances and excess electrolytes from the fluid so that a constant supply of fresh dialysate is provided. The WAK uses only 375 mL of fluid that is recirculated through several canisters containing urease, zirconium, and activated charcoal. These sorbents have been used successfully for several decades in the regeneration of dialysate with the REDY system, and more recently a new conventional dialysis machine has been brought to market using this time-honored system. This solves the weight burden problem created by the need for a large volume of dialysate.

Reverse flow is not permitted by the pump valves → push-pull flow

Fresh dialysate back filters into the blood compartment in the distal portion of the hollow fiber → sort of post-dilution → “pulsatile push-pull HDF”

HEMO study: increasing pre-dialysis serum β₂-microglobulin was a primary risk factor for mortality.

Average β₂-microglobulin and phosphate clearances were about respectively 50% and 95% of creatinine clearance.

Will longer treatment time saturate sorbents? Is β₂-microglobulin representative of the clearance with WAK of potential middle-sized uremic toxins?

9 pigs with urethral ligation; UF for 8 hours

A wearable hemofilter for continuous ambulatory ultrafiltration

V Gura\textsuperscript{1}, C Ronco\textsuperscript{2}, F Nalesso\textsuperscript{2}, A Brendolan\textsuperscript{2}, M Beizai\textsuperscript{3}, C Ezon\textsuperscript{3}, A Davenport\textsuperscript{4} and E Rambod\textsuperscript{5}

6 volume overloaded patients (in HD)
UF for 6 hours

Table 3 | Patient parameters during treatment with the wearable hemofiltration device

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Mean ± s.d.</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP mm Hg pre-UF</td>
<td>119.0</td>
<td>111.0</td>
<td>90.3</td>
<td>88.3</td>
<td>138.0</td>
<td>109.7</td>
<td>109.4 ± 18.5</td>
<td>0.03</td>
</tr>
<tr>
<td>MAP mm Hg post-UF</td>
<td>87.3</td>
<td>111.0</td>
<td>98.7</td>
<td>76.7</td>
<td>120.0</td>
<td>117.0</td>
<td>101.8 ± 17.3</td>
<td></td>
</tr>
<tr>
<td>Total UF (ml)</td>
<td>770</td>
<td>984</td>
<td>708</td>
<td>1610</td>
<td>1233</td>
<td>1201</td>
<td>1084.3 ± 335.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Na\textsubscript{UF} (mmol)</td>
<td>107.8</td>
<td>132.8</td>
<td>97.0</td>
<td>223.8</td>
<td>172.6</td>
<td>171.7</td>
<td>150.0 ± 47.6</td>
<td></td>
</tr>
</tbody>
</table>

Shows mean arterial pressure (MAP), volume ultrafiltered (UF), and sodium removed in ultrafiltrate (Na\textsubscript{UF}). Data expressed as mean ± s.d.
Evolution of the concept: **WAKMAN**

WAK: the problem of extracorporeal circulation

- Continuous anticoagulation and a complex monitoring system → risk of clotting despite aggressive heparinization (Neff, Murisasco, and lastly Davenport)
- Risk of occult bleeding or disruption of the blood circuit or disconnection
- Will continuous extracorporeal circulation affect the longevity of the vascular access?

Is peritoneal dialysis the solution for a WAK?

→ continuous flow peritoneal dialysis → potentially more efficient than the conventional inflow/outflow PD


Spent dialysate filtered through a small polysulphone filter (to remove fibrin) and then circulated through 4 cartridges containing activated charcoal (removes creatinine) and polystyrenic resins (remove middle-molecules).
Proposed treatment schedule: peritoneum filled in the morning with 2 l of fresh PD solution, after 2 h (50% plasma/dialysate equilibration) recirculation is activated for 10 h at 20 ml/min. Glucose may be added to achieve UF if needed through a line connected to a small reservoir. Icodextrin exchange overnight for further UF.

Considering an in vitro net clearance of 11.2 l/day for creatinine (and adding 4-5 l clearance for overnight exchange and equilibration) → weekly clearance > 100 l
Double catheter or single-catheter tidal PD

Fibrin-debris trap

Regeneration of proteins in spent dialysate
→ autologous protein containing dialysate, reducing risk of protein loss and enhancing protein-bound toxins (aluminium, drugs as salicylate) clearance, and glucose sparing effect for UF

Expected flow rate 96 l/day (8-12 fold increase over the current dialysate use of 8-12 l per 24h)

The sorbent cartridge needs to be replaced every 4-8 hours!!

Current Market Situation

The smallest “portable” HD device

The System One

Chronic therapy at home or on the road
The NxStage System One helps make home therapy more accessible. It is the only truly portable hemodialysis system cleared for home use during the day or overnight. The System One was designed to provide simplicity, flexibility and portability to make home hemodialysis a practical reality, without compromising safety.

Due to NxStage's continuous innovation, patients now have the opportunity to enjoy the clinical and lifestyle benefits of more frequent home hemodialysis.

The System One Difference

Making Dialysis Accessible
The simple interface is easy to learn and use.

Our 24/7 technical support gives you peace of mind while dialyzing, no matter when or where.

Designed for the Home
Simple plumbing connections and standard electrical plug minimize the impact on your home.

Integrated dialysate mixing conserves water usage and fits your lifestyle.
Renal Solutions, Inc. Announces Acquisition by Fresenius Medical Care

Nov 29, 2007, 00:00 ET from Renal Solutions, Inc.

Xcorporeal Announces Signing Agreement for the Sale of Substantially All of Its Assets

December 18, 2009 04:30 PM Eastern Standard Time

LOS ANGELES--(BUSINESS WIRE)--Xcorporeal, Inc. (Pink Sheets: XCRP) (the "Company" or "Xcorporeal") announced today that on December 14, 2009 it signed an asset purchase agreement (the "Purchase Agreement") with National Quality Care, Inc. ("NQC"), and together with the Company, the "Sellers"), and Fresenius USA Inc. (the "Purchaser"), a Massachusetts corporation and a wholly owned subsidiary of Fresenius Medical Care Holdings Inc., to sell substantially all of the assets of the Sellers to the Purchaser for an aggregate cash purchase price of $8,000,000 (the "Purchase Price") and certain additional royalty payment rights. The Purchase Price will be payable to the Sellers in three installments. The Company's board of directors has unanimously approved the Purchase Agreement. The sale represents the conclusion of a process to sell substantially all of the Company's assets. The closing is scheduled to occur on or before February 28, 2010.

In addition, the Purchaser will pay royalties to the Sellers during the life of the patents included in the HD WAK Technology being transferred to the Purchaser, as well as royalties to the Sellers during the life of the patents included in the superorbital technology being transferred to the Purchaser.

AWAK TECHNOLOGIES ENTERS INTO AN EXCLUSIVE AGREEMENT WITH BAXTER INTERNATIONAL FOR THE DEVELOPMENT OF WEARABLE DIALYSIS TECHNOLOGY

Singapore — 7 Jan, 2013: AWAK Technologies announced today it has entered into an exclusive agreement with Baxter International, Inc. for the development of innovative wearable dialysis technology. The agreement enables AWAK to continue the development of its investigational peritoneal dialysis-based automated wearable artificial kidney.
Current Market Situation

Solutions under development
A regenerable potassium and phosphate sorbent system to enhance dialysis efficacy and device portability: an in vitro study

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Actual perspectives and future directions

Batch tests and regenerability

Dynamic tests with sorbent beads [RES-A and FeOOH]

in 3h 10 and 5 mEq of K and PO₄ removed

All sorbents adsorbed some Ca and Mg → solvent preloading → no need for post-cartridge supplementation

**Conclusion:**
Adequate potassium and phosphate adsorption from dialysate can be achieved by the use of **modest amounts of RES-A and FeOOH**. RES-A shows excellent and FeOOH acceptable regenerability under mild conditions. Use of ZIR-car and ZIR-hydr may further increase phosphate adsorption but may compromise sorbent regenerability. Use of polymeric amines for phosphate adsorption may enhance sorbent regenerability.

Hydrolysis of urea by urease (REDY) large amount of cation exchange material (Zirconium Phosphate) to remove NH$_4$+. NH$_4$+ is partly exchanged for Na+ with consequent Na+ release.

Removal of Urea in a Wearable Dialysis Device: A Reappraisal of Electro-Oxidation


can be miniaturized, needs no regeneration, is inexpensive.
Graphite electrodes: less chlorine release

Higher current led to higher urea removal, but higher chlorine release

Removal of chlorine with activated carbon downstream

60 ml (30 g) of AC resulted in chlorine levels below recommended limits with inlet urea concentration 20 mM (56 mg/dl)

CO₂ (400 mmol daily) and N₂ generation → degassing system should be included

Potential disadvantage of EO: generation of large quantities of oxidative by-products that could negatively affect REDOX state (however downstream AC oxygen reduction potential was low)

Can EO be safely applied in vivo??

Nanoporous biomaterials for uremic toxin adsorption in artificial kidney systems: A review

Considering scarce urea adsorption with activated charcoal (REDY and others) there is plenty of room for improvement in terms of nanoporous materials for adsorption.

Zeolite → high capacity of removing uremic toxins, but tend dissolve partially in the dialysate fluid (amphoteric nature).
**Cell therapy?**

**RAD**: a combination of living tubular cells supported on polymeric substrata acting as a scaffold for the cells.

**Renal Tubule Assist Device**

**Wearable to implantable**
Initial clinical results of the bioartificial kidney containing human cells in ICU patients with acute renal failure


58 patients receiving CVVH for ARF and multiple organ failure → 40 received RAD therapy

Renal cell therapy improved the 28-day mortality rate from 61% (control group only CVVH) to 34% (RAD + CVVH group)
Bioartificial kidney (BAK) = conventional synthetic hemofilter + RAD

Problems with implantable BAK:
- Pump size must be reduced
- Dialytic water volume
- Biocompatibility of silicon membranes
- Necessity for long-term anticoagulation
- Vascular perfusion of the BAK

HNF: application of atomically precise nanotechnology to RRT

Two membranes operating in series simulating glomerular and tubular function

NO dialysate, operates all by CONVECTION

Could provide 30 ml/min of GFR operating 12 hours per day (computer modeling)

Nissenson et al, Continuously functioning artificial nephron system: the promise of nanotechnology, Hemodialysis international 2005; 9:210-217
**Wearable to implantable**

**Human Nephron Filter**

**G membrane**: mimics glomerulus using convective transport to generate a plasma UF

**T membrane**: mimics renal tubule selectively reclaiming solutes by convection

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Conclusions

Vascular access is a big issue

Urgent need for **LONG-TERM information**:  
- Assess long-term biocompatibility of devices  
- Human clinical trials to evaluate efficacy in comparison to standard treatments

Will the WAK improve outcomes in ESRD?

Can the WAK be worn by humans over prolonged and continuous periods of time?