Wearable Artificial Kidney (WAK)

Raj Munshi, MD
Annual Dialysis Conference 2016

I have no conflicts to report
Extended Hemodialysis

Chertow GM. *NEJM* 2010; 363:2287
Culleton BF. *JAMA* 2007; 298: 1291
Chan CT. *Kidney Int* 2002; 61:2233
Nesrallah GE. *JASN* 2012; 23:894

Enter wearable devices
Not a novel concept…

Dharnidharka SG, Kirkham R, Kolff WJ.

Toward a wearable artificial kidney using ultrafiltrate as dialysate.


Advancements in…

• Miniaturization
• Nanotechnology
• Micromechanics
• Microfluidics

Keys to success

• Access
  • Easy connectology
  • Reduction of infection and clotting
• Miniaturization
  • Filter
  • Pumps
  • Circuit
• Dialysate regeneration
• Reduced priming volume
  • Tolerate going on and off
• Safety
  • Pressure sensors
  • Air detectors
  • Blood leak detector
  • Visible and audible alarms
• Power source
• Ergonomic

Ronco C. Nefrologia 2011; 31(1):9-16
Wearable Artificial Kidney: Dr. Victor Gura

- 1st tested in vitro
- Then animal studies in pigs

Clinical studies
- 1st to test safety & efficacy of ultrafiltration
- 2nd to test the full capability – including hemodialysis

Blood circuit: 65 ml
Dialysate circuit: 375 ml
Activated Carbon Urease Zirconium Sorbent Cartridges

• Activated carbon
  • Absorbs heavy metals, salts, organic substances
  • Nothing is released or exchanged

• Urease
  • urea → ammonia and CO2

• Zirconium
  • Ions (including ammonia) exchanged for Na⁺, H⁺, HCO₃⁻ and small amount of acetate

Clinical studies
A wearable hemofilter for continuous ambulatory ultrafiltration

V Gura, C Ronco, F Nalesso, A Brendolan, M Baies, C Ezon, A Davenport and E Rambod

- 6 patients
  - Mean age 59 years
- 6 hours of ultrafiltration
- Avg. blood flow rate
  - 116 ml/min
- Avg. UF rate
  - 120-288 ml/min
- One patient had therapy discontinued due to clotted catheter


A wearable haemodialysis device for patients with end-stage renal failure: a pilot study

Andrew Davenport, Victor Gura, Claudia Ronco, Miroslav Baies, Carlo Ezon, Edward Rambod

- 8 patients
  - Mean age 51.7 (SD 13.8) years
- 4-8 hours of therapy time
- Avg. flow rates
  - Blood: 58.6 ± 11.7 ml/min
  - Dialysate: 47.1 ± 7.8 ml/min
- Mean urea clearance
  - 22.7 ± 5.2 ml/min
- 2 patients had clotted catheters
- 1 patient with fistula had needle dislodgement

A Wearable Artificial Kidney for Patients with End-Stage Renal Disease

Victor Gura, MD,* Matthew B. Rivara, MD,* Scott Bieber, DO, Raj Munshi, MD, Nancy Colobong Smith, MN, ARNP, CNN, Lori Linke, BA, John Kundzins, BS, Masoud Beizai, PhD, Carlos Ezon, MD, Larry Kessler, ScD, and Jonathan Himmelfarb, MD

Submitted for publication

Objective & Design

- **Objective**
  - To test the safety and efficacy of the WAK device in achieving solute clearance, electrolyte homeostasis and volume removal over a continuous 24-hour period

- **Design**
  - Prospective, non-randomized, exploratory clinical trial in which up to 10 subjects could receive therapy with the WAK for 24 hours while monitored in a hospital setting

Selection criteria

**Inclusion**

- Age > 21 years
- Weight 45 -100 kg
- Double lumen catheter as the access
- Expected survival of no less than 6 months
- Hemoglobin level ≥ 9.0 g/dL prior to WAK treatment

**Exclusion**

- Anticipated transplantation within 2 months
- Recent cardiovascular event or hemodynamic instability
- Active infection
Day of study

- Regular hemodialysis run in the hospital
- 2 hour break
- WAK for 24 hours
  - Eat the great American diet

Achieved flow rates

- blood flow: 42 ± 24
- dialysate flow: 43 ± 20
Solute clearance

Clearance: blood flow dependent

Device performance & technical complications

- One subject – treatment discontinued after 4 hours due to clotting of blood circuit following ambulation
- One subject – WAK treatment discontinued after 10 hours due to observed pink discoloration of the dialysate
- Elevated ammonia noted in one therapy at hour 11
  - Sorbent cartridges replaced
Trial stopped after 7th subject due to:

- Device related technical problems
  - Excessive CO₂ bubbles in the dialysate circuit
    - Exceeded degassing capacity
  - Tubing kinks
  - Variable pump function resulting in fluctuating flow rates

### Subject rating of treatment

<table>
<thead>
<tr>
<th>RTSQ Item</th>
<th>Item Content</th>
<th>Conventional hemodialysis</th>
<th>WAV</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Satisfaction with treatment</td>
<td>4.1</td>
<td>5.1</td>
<td>0.02</td>
</tr>
<tr>
<td>2</td>
<td>Satisfaction with control over kidney disease</td>
<td>5.0</td>
<td>5.1</td>
<td>0.74</td>
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<tr>
<td>3</td>
<td>Satisfaction with treatment side effects</td>
<td>3.4</td>
<td>5.7</td>
<td>0.003</td>
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<tr>
<td>4</td>
<td>Satisfaction with treatment-related demands</td>
<td>3.9</td>
<td>4.7</td>
<td>0.22</td>
</tr>
<tr>
<td>5</td>
<td>Convenience of treatment</td>
<td>4.0</td>
<td>4.9</td>
<td>0.04</td>
</tr>
<tr>
<td>6</td>
<td>Flexibility of treatment</td>
<td>3.3</td>
<td>5.3</td>
<td>0.04</td>
</tr>
<tr>
<td>7</td>
<td>Satisfaction with freedom afforded by treatment</td>
<td>2.6</td>
<td>5.9</td>
<td>0.007</td>
</tr>
<tr>
<td>8</td>
<td>Satisfaction with understanding of treatment</td>
<td>5.1</td>
<td>5.7</td>
<td>0.03</td>
</tr>
<tr>
<td>9</td>
<td>Satisfaction with time taken by treatment</td>
<td>2.7</td>
<td>5.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>10</td>
<td>Discomfort or pain involved with treatment</td>
<td>3.9</td>
<td>5.0</td>
<td>0.04</td>
</tr>
<tr>
<td>11</td>
<td>How well treatment fits in with lifestyle</td>
<td>3.1</td>
<td>5.7</td>
<td>0.002</td>
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<tr>
<td>12</td>
<td>Would you recommend this treatment to others</td>
<td>3.9</td>
<td>5.9</td>
<td>0.06</td>
</tr>
</tbody>
</table>

### Total treatment satisfaction score

| Total | 46 | 70 | <0.001 |

Abbreviations: RTSQ, Renal Treatment Satisfaction Questionnaire

### Need for children

- Reduction in extracorporeal blood volume space
- Improved volumetric control systems
- Reduced blood flow demand
  - Smaller catheter
- Novel catheter and filter technology
**Impact to children**

- Miniaturization
- Nanotechnology
- Micromechanics
- Microfluidics

**Location**

<table>
<thead>
<tr>
<th>Location</th>
<th>Avg. BFR</th>
<th>Avg. DFR</th>
<th>Urea Cl</th>
<th>Creatinine Cl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td>116</td>
<td>-----</td>
<td>3.1</td>
<td>3.2</td>
</tr>
<tr>
<td>London</td>
<td>58.6</td>
<td>47.1</td>
<td>22.7</td>
<td>20.7</td>
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<tr>
<td>Seattle</td>
<td>42</td>
<td>43</td>
<td>17</td>
<td>16</td>
</tr>
</tbody>
</table>
286 Patients were screened for eligibility

Excluded (n=296)
- 224 Were ineligible
- 12 Declined to participate

192 Consented to study participation

Excluded (n=12)
- 1 Was excluded due to scheduling conflict
- 1 Developed an infection prior to WAK treatment and was deemed ineligible
- 1 Had symptomatic hypotension prior to initiation of WAK treatment and was deemed ineligible

7 Were enrolled and underwent treatment with the WAK

7 Were analyzed
- 5 Completed 24-hour WAK treatment
- 2 Were excluded from analysis

### A

<table>
<thead>
<tr>
<th>Study Timepoint</th>
<th>Mean Blood Urea Nitrogen (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-WAK</td>
<td></td>
</tr>
<tr>
<td>Conventional HD session</td>
<td></td>
</tr>
<tr>
<td>WAK treatment</td>
<td></td>
</tr>
<tr>
<td>Post-WAK</td>
<td></td>
</tr>
</tbody>
</table>

### B

<table>
<thead>
<tr>
<th>Study Timepoint</th>
<th>Mean β-microglobulin (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-WAK</td>
<td></td>
</tr>
<tr>
<td>Conventional HD session</td>
<td></td>
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<tr>
<td>WAK treatment</td>
<td></td>
</tr>
<tr>
<td>Post-WAK</td>
<td></td>
</tr>
</tbody>
</table>
Sorbents in dialysis

- 1960s NASA seeking to purify waste H₂O, and human waste effluent to minimize H₂O carriage used sorbents
- 1st used in purification of blood when zirconium phosphate used to remove ammonium from a test solution
  - Reynolds
- Sorbent technology soon applied to effluent dialysate from an artificial kidney to test dialysate reuse potential
- REDY system (REcirculation of DialYsate) soon emerged

REDY: REcirculation of DialYsate

- Used a disposable one use sorbent cartridge that contained
  - Activated charcoal
  - Urease
  - Zirconium phosphate
- All used in series
  - Only 6L of tap water was required
  - Water quality reached near ultrapure
- No drain was needed
- Widely used in Australia in 70s-80s for in-hospital acute kidney injury and home hemodialysis
Issues Addressed

<table>
<thead>
<tr>
<th>Previous</th>
<th>Now</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Aluminum toxicity</td>
<td>• Aluminum sorbent vehicle removed</td>
</tr>
<tr>
<td>• Spill over acidosis</td>
<td>• Avoided if appropriate cartridge size is selected</td>
</tr>
<tr>
<td>• Zirconium escape</td>
<td>• Not been reported in modern constructs</td>
</tr>
<tr>
<td>• Increase in dialysate Na</td>
<td>• Changes in dialysate Na can be mathematically modelled thus</td>
</tr>
<tr>
<td>• Cost non competitiveness</td>
<td>would need to be compensated for within the dialysis prescription</td>
</tr>
</tbody>
</table>