Kidney Transplantation at UC Davis
Current Status
What does the future look like?
Rationale for Kidney Transplantation

- Survival benefit vs dialysis
- Improvement in quality of life
- Economic benefit to health care system
Improving the Prognosis

Across all age ranges, but especially for the young, kidney patients on dialysis tend to have far fewer remaining years to live than those who receive transplants.
Patients waiting for kidney transplantation on September 12, 2014

101,244
A Long Wait for a Kidney

Since 1990, the number of people on the waiting list for a kidney transplant has grown sharply, while the number of transplants has increased only slightly.
Waiting time is increasing

• Average waiting time nationally is approaching 5 years

• The last decade over 60,000 patients have died on the list or been de-listed because they were too sick to transplant
Goal

To make transplantation an option for as many patients as possible
Kidney Transplants, Last Ten Years

Source: Organ Procurement and Transplantation Network
Clinical Focus

Pre-transplant

- Optimizing organ preservation
- Non-conventional deceased donors
  - Pediatric donors
  - Donors with acute kid injury
  - ECD, DCD
- Maximizing living donation

Transplantation

- Surgical management
- Reno-protective strategies

Post-transplantation

- Multidisciplinary care
- Optimizing immunosuppression

Recipient morbidity/mortality
Allograft function
Allograft survival
Clinical Research Focus

Pre-transplant
• Utilization of high risk organs
• Managing high risk recipients
  • Elderly
  • Cardiovascular risk
  • Obese
• Addressing ethnic disparities in organ donation

Transplantation

Post-transplantation
• Clinical Trials
  • Reno-protective agents
  • Immunosuppression trials
• Biomarker profiling
• Point of care monitoring

Recipient morbidity/mortality
Allograft function
Allograft survival
Basic/Translational Research Focus

Pre-transplant

• Renal ischemia-reperfusion studies
  • Age response to injury

• Small animal models of organ preservation and transplantation
  • Non-human primate studies

Transplantation

• Interventions
  • Reno-protective agents
  • Stem cell therapy

Post-transplantation

• Biomarker profiling
  “Personalized Medicine for the Kidney”

Recipient morbidity/mortality
Allograft function
Allograft survival
Options for expanding the deceased donor organ pool

- Expanded Criteria Donors (ECD)
- Donation after Circulatory Death (DCD)
- Small pediatric en-bloc kidneys
- Dual Adult Kidneys
- Donors with Acute Kidney Injury (AKI)
- HCV positive donors
- Hepatitis B core Ab positive donors
UC Davis Deceased Donor Transplantation: Small pediatric donors
The Neonatal Intensive Care Unit as a Source of Deceased Donor Kidneys for Transplantation: Initial Experience with 23 Cases

R Perez, C Santhanakrishnan, A Demattos, J McVicar, M Gandhi, D Adey, M Alnimri, B Gallay, C Troppmann

Univ of California Davis Med Center

World Transplant Congress 2014
Rationale for use of kidneys from infant donors

- Excellent quality of kidneys
- High capacity to recover from acute stress/injury
- Kidney allografts will grow with time
Standard pediatric en bloc kidney transplanation
Patient Cohort

Study period January 2011 – April 2014

811 total deceased donor transplants

177 (22%) Small pediatric donors

23 (3%) NICU donors
NICU donor kidney sources
# Neonatal Donor Characteristics

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<tr>
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<th>Median</th>
<th>Range</th>
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<tbody>
<tr>
<td>Donor Age (days)</td>
<td>7</td>
<td>1 - 150</td>
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<tr>
<td>Donor weight (kg)</td>
<td>3.3</td>
<td>1.9 – 5.0</td>
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<tr>
<td>Male : Female</td>
<td>16 : 7</td>
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<tr>
<td>Term creatinine (mg/dl)</td>
<td>0.45</td>
<td>0.1 – 0.9</td>
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<tr>
<td>Donation after circulatory death</td>
<td>65.2%</td>
<td></td>
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<tr>
<td>Imports</td>
<td>100%</td>
<td></td>
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<tr>
<td>Cold ischemia (hrs)</td>
<td>23.1</td>
<td>13.6 – 30.5</td>
</tr>
<tr>
<td>Pulsatile Machine Perfusion</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Final Pump Flow (ml/min)</td>
<td>27</td>
<td>11 - 44</td>
</tr>
<tr>
<td>Final pump resistance (mmHg/ml/min)</td>
<td>0.88</td>
<td>0.39 – 3.0</td>
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### Short term outcomes of kidneys from neonatal donors

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<table>
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<tr>
<td><strong>Patient Survival</strong></td>
<td>100%</td>
</tr>
<tr>
<td><strong>Graft Survival</strong></td>
<td>19/23 (83%)</td>
</tr>
<tr>
<td><strong>Delayed Graft function</strong></td>
<td>9/23 (39%)</td>
</tr>
<tr>
<td><strong>Causes of graft failure</strong></td>
<td>2 Thrombosis, 2 Primary non-function</td>
</tr>
<tr>
<td><strong>Surgical complications within 90 days</strong></td>
<td>14/23 (61%)</td>
</tr>
</tbody>
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Short Term Allograft Function

Serum Creatinine (mg/dL)

Months

1 3 6 12
Addressing the crisis of the current organ shortage

- Kidney wait list at 101,000 and growing
- Neonatal donors an underutilized source of organs
- Multidisciplinary approach to optimize and increase NICU organ donation
Ongoing Studies Utilizing Pediatric Donor Kidneys

- Long term function of pediatric kidneys
- What factors regulate growth of pediatric kidneys
- Pediatric kidney response to ischemia-reperfusion injury
- Optimal use of pulsatile perfusion preservation
- NICU donation
  - What is the effect of donation on the family?
  - What is the effect of donation on NICU staff?
Basic/Translational Research Focus

Pre-transplant
- Renal ischemia-reperfusion injury
- Optimizing organ preservation of high risk organs
- Development of animal models of IR injury and organ preservation

Transplantation
- Interventions
  - Reno-protective agents
  - Stem cell therapy

Post-transplantation
- Biomarker profiling
- “Personalized Medicine for the Kidney”

Recipient morbidity/mortality
Allograft function
Allograft survival
Ex Vivo Normothermic Perfusion: “ECMO for the kidney”
Potential benefits of ex vivo normothermic machine perfusion

- Aerobic metabolism
- Replenishment of energy stores
- Initiates repair/regenerative processes
- Opportunity to assess viability/function
- Provides means to intervene pre-transplant:
  - Drug therapy
  - Biologics
  - Stem cells
Ex vivo normothermic perfusion improves renal arterial blood flow
Ex vivo normothermic perfusion increases urine production

Submitted Academic Surgical Congress 2015
Ex vivo normothermic perfusion results in significant decrease in urine biomarkers of acute injury

Submitted Academic Surg Congress 2015
Ex vivo normothermic perfusion: Present and future applications

• Current Study
  – Assessment of discarded high risk organs

• Clinical Pilot Project planned

• Development of animal models
  – Pharmacologic
  – Gene therapy
  – Stem cells

• “Personalized medicine for the kidney”
The Future of Transplantation: Organ Assessment at Regional Repair Centers

- Donor Hospitals
- Organ Repair Center
The Future of Transplantation: Organ Reconditioning at Regional Repair Centers

- Transplant Center
- Organ Repair Center

[Map showing regional repair centers across the United States]
Opportunities for Intervention

Pre-transplant period

- Expansion of donor pool
- Donor pre-treatment
- Organ preservation
- Organ conditioning

Recipient selection
- Identification of high-risk cohorts
- Recipient pre-treatment

Transplantation

- New operative approaches
- Reno-protective protocols

Post-transplantation

- Immunosuppression trials
- Tolerance protocols

Recipient morbidity/mortality
- Allograft function
- Allograft survival