

<b>Project Title:</b>	Remote ischaemic preconditioning in renal transplantation
<b>Project Ref:</b>	08-52-02
<b>Cost:</b>	£811,528
<b>Lead Applicant &amp; Institution:</b>	Professor Raymond MacAllister Clinical Pharmacology University College London
<b>Start Date:</b>	1 July 2009
<b>Plain English Summary:</b>	<p>Kidney transplantation transforms the lives of patients with kidney failure who would otherwise require dialysis treatment. However, there is a growing shortage of kidneys for transplantation, and the number of patients on the transplant list is steadily increasing. This is despite an increase in the number of living donors who are prepared to gift a kidney for transplantation. Moreover, approximately one third of transplants fail within the first 10 years, and these patients need to restart dialysis and rejoin the transplant list. Therefore, maximising the life-span of the transplanted kidney will benefit recipients, and by optimising the use of this scarce resource, increase the number of patients who will receive a transplant.</p> <p>The injury to the kidney that occurs during the transplant surgery is an important factor in the short- and long-term success of the transplant. When the kidney is removed from the donor, it is isolated from its usual blood supply, resulting in damage known as ischaemic injury. After the kidney is transplanted and the blood supply reconnected from the recipient, there is a further injury, known as reperfusion injury. Together, this inevitable consequence of transient interruption of the kidney's blood supply, is termed ischaemia-reperfusion injury. It can prevent the kidney from working normally immediately after the transplant, or in the longer term accelerate the reduction in kidney function that eventually leads to the kidney failing.</p> <p>The kidney, like many organs, has innate mechanisms that make it resistant to interruption of its blood supply. One of these is called remote ischaemic preconditioning (RIPC), a whole-body reflex stimulated by brief periods of interruption of the blood supply to one part of the body. Importantly, this reflex is activated by reducing the blood supply to parts of the body that are resistant to low blood flow conditions (e.g the limbs), yet can protect other parts of the body that are more sensitive to reduced blood flow (e.g the heart and kidney). In a small study of living donor kidney transplantation, we have shown that short-lived periods of low blood flow to the arm (to activate remote ischaemic preconditioning) improved kidney function in the first 2 years of transplantation. In this research proposal we plan to extend this study so that we can establish with certainty the size of the benefit of RIPC in living donor transplantation.</p> <p>Patients recruited to this trial will undergo standard transplantation</p>

	<p>procedures. The only additional procedure is the stimulation of RIPC, achieved by inflating a blood pressure cuff on the arm. The cuff is inflated for 5 minutes to completely interrupt blood flow to the arm, after which it is deflated. This procedure does not pose a risk to the patient's health even when it is carried out several times. The simplicity of the procedure, together with its safety and low cost, mean that should it be proven to be of benefit in this trial, it will be easy to implement it as part of transplantation. This trial brings together a team of investigators are from 7 renal transplant centres (in the UK and in Holland) that perform 300 living donor transplants annually. An advantage of this study is that it is embedded in the usual practice of the different transplant centres which makes it good value for money. The costs of the study are mainly to pay for research nurses (to recruit patients and collect results). The other main expense is the co-ordination of the trial using an experienced Clinical Trial Unit.</p>
<p><b>Abstract:</b></p>	<p><u>Design:</u> Multicentre double-blind randomised controlled trial  <u>Setting:</u> Kidney transplant units in the UK and Holland  <u>Target population:</u> Patients undergoing living donor kidney transplantation  <u>Intervention being evaluated:</u> Intermittent limb ischaemia to induce remote ischaemic preconditioning prior to kidney transplantation  <u>Measurement of outcomes and duration of follow up</u>  <u>Primary outcome:</u> glomerular filtration rate (GFR) 12 months after transplantation  <u>Secondary outcomes</u></p> <ol style="list-style-type: none"> <li>1. Time for serum creatinine to fall by 50%</li> <li>2. eGFR 6 months after transplantation</li> <li>3. Kidney graft cortical tubulointerstitial fibrosis at 6 months (digital analysis of Sirius red staining in biopsy material)</li> <li>4. RIPC-induced protein expressional changes in kidney tissue</li> <li>5. Incidence of delayed graft function (serum creatinine levels increase, remain unchanged, or decrease less than 10% per day in three consecutive days in the first week after transplantation)</li> <li>6. Incidence of acute rejection during the first 12 months after transplantation</li> <li>7. Long-term outcomes using renal registry data 2-5 years after transplantation (serum creatinine/eGFR, graft survival, patient survival)</li> </ol> <p><u>Duration of follow-up:</u> 1 year within the trial, 5 year follow-up using renal registry data</p>
<p><b>ISRCTN: (if applicable)</b></p>	<p>30083294</p>
<p><b>Project Protocol:</b></p>	<p><a href="http://www.eme.ac.uk/projectfiles/085202protocol.pdf">www.eme.ac.uk/projectfiles/085202protocol.pdf</a></p>
<p><b>Project website: (if applicable)</b></p>	<p><a href="http://repair.lshtm.ac.uk/">http://repair.lshtm.ac.uk/</a></p>
<p><b>URL of this Page:</b></p>	<p><a href="http://www.eme.ac.uk/projectfiles/085202info.pdf">www.eme.ac.uk/projectfiles/085202info.pdf</a></p>