EXECUTIVE SUMMARY

All Academic in Confidence Information has been removed.

BACKGROUND

End-stage renal disease (ESRD) is the terminal stage of chronic kidney disease. It affects one million individuals worldwide with prevalence expected to increase due to the growing elderly population and the rising incidences of diabetes and hypertension.

Current treatment for ESRD involves renal replacement therapy (RRT), ideally by kidney transplantation, or renal dialysis. Due to the increasing prevalence it is estimated that the overall growth in the number of patients being treated with RRT will increase by 6-8% per year in England alone. Of the two RRT treatments available kidney transplantation is regarded as the most clinically and cost effective treatment, providing long term benefits in both patient survival and quality of life.

Unfortunately many eligible patients are prevented from receiving a transplant due to the limited supply of donor organs and have to remain on dialysis with a significant cost to the NHS of £30,800 per patient per year. In terms of total NHS spend, for the period 2005 to 2006, England alone spent £932 million on renal services (1% of its total budget) of which 46% was spent on dialysis and 16% on transplantation.

In 2007, 6480 patients were on the active waiting list for a kidney an 11% increase since 2006. Current transplant waiting times stand at 841 days for adults and 164 days for children with 3% of patients dying while on the waiting list.

Kidney Donors

Most kidneys for transplantation are obtained from donors who have been certified dead by brain stem criteria (donation after brain death, DBD donor, also known as heart-beating donors). The number of available donors from this population is however decreasing as a result of fewer fatal road traffic accidents, improved intensive care facilities and a decrease in the number of deaths from intracranial haemorrhage. Due to this decline and in an attempt to meet demand the cadaveric donor pool has been expanded over recent years to include donors who have died from a cardiac arrest (donation after cardiac death, DCD donor, also known as non-heart beating donors) and extended criteria donors (ECDs). It is likely that the decline in DBD donors will continue and in order to meet demand the use of kidneys from DCD donors and ECDs will continue to increase. Both DCD donors and ECDs have higher rates of primary non-function (PNF) and delayed graft function (DGF) resulting in further dialysis and re-transplantation. This results in additional pressure on the transplant list and can be reduced with optimal preservation. With the expansion in the donor pool and the increased number of people on the waiting list it is essential that the viability of all donated kidneys is maximised.

The Transplantation Process

Within the UK kidney allocation is overseen by UK Transplant who ensures that organs donated for transplant are matched and allocated to patients in a fair and unbiased way. The actual process of organ retrieval and transplantation is however organised and funded at a regional level within the 26 renal transplant centres, 21 of which are in England and Wales.

The current retrieval process is however scheduled to change as a result of the report issued in January 2008 by the Department of Health '*Organs for Transplants: A report from the Organ Donation Taskforce'.* This report made 14 recommendations aimed at increasing organ donation by 50% over the next 5 years to address the severe shortage of organs for transplantation. The Government has accepted all 14 Taskforce recommendations including the establishment of a UK-wide Organ Donation Organisation under the possible auspices of the NHS Blood and Transplantation Authority.

Kidney Preservation

Kidney preservation, from the time of retrieval through the period of tissue typing and matching, is an integral part of kidney transplantation. Maintaining organ viability during transport is also essential. Appropriate organ preservation is a critical prerequisite for a successful clinical outcome following transplantation. With the extension of the donor pool criteria to include kidneys from expanded donors including DCD donors there is an increased need for a preservation technique which adequately maintains all kidneys irrespective of the donor type and/or the length of cold ischaemic time from recovery to transplantation.

Currently two different organ preservation modalities are used for grafts retrieved from deceased donors: cold (static) storage (CS) and machine perfusion (MP).

Two CS solutions are currently available in the England and Wales: Marshall's solution (Soltran) and University of Wisconsin (cold storage) solution (ViaSpan).

The MP systems currently available in England and Wales include: LifePort® Kidney Transporter (Organ Recovery Systems) and Waters' RM3 Renal Preservation System (Waters Medical Systems). While available we are unaware of the Waters' machine being used clinically in any transplant centre in the UK. At present LifePort is the machine of choice for MP both in the UK and Worldwide.

Current Practice

Within England and Wales each transplant unit is responsible for the preservation method used and also for the purchasing the equipment/materials required. Currently CS is the most commonly used preservation method with MP primarily reserved for kidneys from DCD or ECD donors. Of the 21 renal transplant units 8 currently use both MP (LifePort) and CS.

With the anticipated change in the retrieval system and the introduction of a single Organ Donation Organisation it is important that, in providing guidance to the NHS, the appraisal takes this change into account and addresses any consequential changes in the way that organs are preserved between retrieval and transplantation. From the perspective of manufacturers of preservation technologies the establishment of a single Organ Donation Organisation (potentially the NHS Blood and Transfusion Authority) will result in a change to the customer base, with likely or possible provision of technologies to just one central organisation rather than to all the individual transplant units around the UK. The central organisation would then be responsible for directing the preservation technologies utilised by the national retrieval teams.

Machine Perfusion

While benefits of MP are well documented with data spanning over 30 years the majority of these data are for old MP technology and from poor quality trials. With the advent of new MP technology (LifePort) it is important that the evidence base is updated and that the update incorporates the final results from the following two landmark trials:

- The Machine Preservation Trial. A prospective, international, randomised trial conducted comparing MP and CS in matched pairs of donor kidneys
- PPART study. A multicentre randomised controlled study of cold **p**ulsatile **p**erfusion in **a**systolic donor **r**enal **t**ransplantation coordinated by The British Transplantation Society in conjunction with UK Transplant.

Both these trials are due to report later in 2008 and will provide a robust database on which the Appraisal Committee will be able support their decisions on clinical and cost effectiveness. On this basis we would recommend that the first Appraisal Committee meeting is delayed until this dataset is made available to them.

Benefits of Machine Preservation

Published literature on MP supports both the clinical and economic benefits of MP compared with CS for kidneys irrespective of the donor type. Compared with CS, MP significantly improves both DGF and long term graft survival in addition to improving utilisation rates of donated kidneys. MP is the only organ preservation modality that provides surgeons with the opportunity to both objectively evaluate a kidney's performance and safety *ex vivo* while providing a therapeutic benefit that improves outcomes post transplantation. The increased use of MP will, in addition to increasing the number of kidneys viable for transplantation, reduce the requirement for continued dialysis or re-transplantation as a result of improved outcomes. While ensuring that the NHS meet demand and Government targets, MP has, compared with CS, the potential to provide significant cost savings due to an increase in utilisation of donor kidneys and a reduction in dialysis and hospital costs.

LIFEPORT KIDNEY TRANSPORTER

The LifePort Kidney Transporter introduced in 2004 is a new class of machine preservation device optimised for both preservation and transportability from the donor hospital operating theatre to the recipient operating theatre. Separate CS is not required at any point in the process.

LifePort provides a sealed, sterile, protected environment for a single kidney. The kidney is protected by an organ cradle and surrounded by cold perfusion solution. Perfusate is pumped through the vasculature via a connection to the renal artery with a custom LifePort® cannula.

More than 250 LifePorts are deployed worldwide and over 10,000 kidneys have been successfully preserved since 2004. Within England and Wales LifePort is currently used in 8 centres for the preservation of DCD donor kidneys with approximately 160 kidneys perfused in 2007.

Key features and benefits of LifePort include its portability, ease of use, continuous data collection and protection of the kidney. LifePort is designed to travel unattended like an ice box. Safety features include redundant preservation (dynamic perfusion plus back-up cold storage) which eliminates the risks associated with equipment failure. LifePort can be left unattended including during travel and does not require a technician to monitor the perfusion device during preservation. Both batteries and ice last for at least 24hours.

LIFEPORT EFFECTIVENESS

The Machine Preservation Trial

The Machine Preservation Trial is the first prospective, international, randomised study conducted comparing MP and CS. It is an investigator-driven 12-month trial currently ongoing in the Eurotransplant region.

Organ donors were ≥16 years of age and only kidney pairs from either DBD donors or DCD donors were included in the study. Kidneys from each kidney pair were randomly assigned to MP (LifePort Kidney Transporter) or CS. MP parameters (flow and renal resistance) were not used and recipient centre surgeons were blinded for preservation method at the time of organ offer.

The study is currently ongoing with 12-month results anticipated May 2008.

[redacted]

Results for 6-months

[redacted]

Primary Endpoint - DGF

[redacted]

Secondary Endpoints

Functional DGF

[redacted]

Primary Non-Function

[redacted]

Graft survival

[redacted]

Discussion

DGF

[redacted]

PNF

[redacted]

Graft Survival

[redacted]

Conclusion

[redacted]

Future Analysis

[redacted]

COST EFFECTIVENESS

[redacted]

A review of published evidence supports the cost effectiveness of MP over CS. In a systematic review of the data up to 2001 the authors concluded that there was 80% probability that MP will be cost effective over CS for DCD donor kidneys and a 50-60% probability than MP will be cost effective over CS for DBD donor kidneys. It is important to note that while clearly demonstrating the cost effectiveness of MP compared with CS the findings are based on older MP technologies and a less than robust database period. Results for the new MP technology (LifePort) and the landmark LifePort trials would be expected to improve cost effectiveness of MP further.

Budget Impact

In order to address the current availability of MP and ensure uniformity in how kidneys are preserved the provision of LifePort to all renal transplant units needs to be addressed. The provision of LifePort to all units also has the potential to reduce ownership issues opening the exchange of all cadaveric kidneys not just those from the DBDs as currently occurs.

Increasing the use of MP to all 21 renal transplant centres in England and Wales would (without subtracting any cost savings) result in budget impact to the NHS of £819K in Year 1 and £1.09million in Year 5. These costs include the costs of those 13 centres without a LifePort purchasing two machines (at £21,500 per centre in Year 1) and all 21 centres purchasing disposable perfusion kits and MP solution (at £475) for each kidney. Numbers of kidneys preserved range from 1137 in Year 1 to 2283 in Year 5. If the full costs of transplantation required for all transplantations are considered along with the costs for dialysis avoided for those recipients with a functioning graft at 12-months then **MP offers cost savings of approximately £8.2 million in Year 1 and £16.6 million in Year 5.**

In comparison with CS the superior effectiveness of LifePort offers significant savings by:

- increasing immediate function compared with CS. Each successful transplant removes someone from renal dialysis at a cost of £30,800 per patient per year
- reducing the requirement for short term dialysis (at a cost of £84 per day) post transplantation
- reducing the incidence of PNF compared with CS by 50% and avoiding further long term dialysis costs and re-transplantation costs

[redacted]

Conclusion

Organ Recovery Systems supports this appraisal of preservation technology for the storage of donated kidneys.

Since the advent of both CS and the initial MP technologies the cadaveric donor pool has expanded and now includes increasing numbers of DCDs, and older, sicker DBDs. In order to maximise a successful outcome after transplantation of all donor kidneys optimal preservation technologies must be utilised in order to maintain organ viability during preservation and transportation. There is a clinical need for an MP system which effectively preserves all cadaveric kidneys irrespective of the donor type from kidney retrieval to transplantation. Compared with CS, MP improves the success of transplantation outcomes reducing DGF, improving graft survival and increasing utilisation. MP is effective across the whole donor pool including those kidneys which are exposed to long CITs. MP is also associated with significant cost savings compared with CS due to an increase in utilisation rate and a reduction in dialysis and hospital costs. While evidence supports the clinical and cost effectiveness of MP in preserving kidneys from DBD donors (including ECDs) and DCD donors the majority of data is for old MP technology and from poor quality trials and requires updating to include benefits of the newer MP technology (LifePort) and the results from robust clinical trials including the Machine Preservation Trial.

Of the MP systems the LifePort Kidney Transporter offers all the benefits of MP but within an easy to use system which does not require continual monitoring and can be left to travel unattended like the ice box used for CS.

Currently 8 renal transplant units in England and Wales use LifePort MP for the preservation of DCD donor kidneys. The limitation to DCD kidneys is primarily due to the current funding structure in which each centre is responsible for purchasing an MP system with that system becoming the property of that hospital. Due to this ownership there is a reluctance to transfer machines between hospitals. Provision of MPs to all units would resolve this issue.

Six-month results from the landmark Machine Preservation Trial, a prospective RCT, comparing two preservation modalities (within a European transplant organisation) for kidney transplantation from all deceased donors, are available on an academic in confidence basis. These results provide the **most robust evidence to date** on the effectiveness of MP

[redacted] The benefits of MP in preserving all donor kidneys has the potential to maximise utilisation of the donor pool and help the NHS and Government meet both clinical need and targets while ensuring a successful clinical outcome for the clinician and patient