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# Early results of a non-heartbeating donor (NHBD) programme with machine perfusion

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**Abstract** Freeman Hospital, Newcastle upon Tyne restarted their non-heartbeating donor (NHBD) programme in September 1998 using machine perfusion, due to early poor results with conventional cold storage (45% graft survival, phase II). Since then, 15 NHBD kidneys have been transplanted. The retrieval protocol consisted of in situ perfusion with a double balloon triple lumen cannula in Maastricht category II male donors age range 13–59 years. Mean primary warm ischaemic time was 24.8 min (range 10–44). All kidneys were machine perfused through a locally developed perfusion system. The viability was assessed by serial measurements of total GST (maximum acceptable limit of 200 units/l) and intrarenal vascular resistance (IRVR) was recorded. Fifteen of the 22 kidneys (68.62%) were transplanted. Delayed graft function (DGF) was seen in ten recipients (66.6%), two kidneys had immediate function (IF), one organ was exported, two recipients died of unrelated causes and a further seven kidneys were discarded (two had high tGST, two were infected and three had poor flow characteristics). In phase III, a success rate of 91.7% was thus achieved, which was better than the phase II period ($P = 0.027$, Fisher 2-tail test). Machine perfusion has been successfully introduced in phase III to the Newcastle NHBD programme and facilitates viability assessment of NHBD kidneys.

**Key words** Renal transplantation · Non-heartbeating donor · Machine perfusion

## Introduction

Over the past 10 years, there has been a decrease in the supply of donor organs leading to increasing waiting times for potential recipients. Non-heartbeating donors (NHBD) can provide an alternative supply of organs, which should substantially increase the donor pool. In Newcastle, NHBD kidneys have been used for transplantation for a period of 10 years. In the early period (1988–1993) excellent results were obtained (90.5% success); however, these donors were controlled NHBD, Maastricht category III. In the second phase (1994–1998), increasing numbers of donors were obtained from the Accident and Emergency Department unit. These patients were failed resuscitation for cardiac arrest (category II). The rates of success in this period were poor (45.5% success) and the programme, was halted. In the third phase of the programme, we utilised machine perfusion of the kidneys and GST enzyme analysis to assess viability.

## Material and methods

In phase III (September 1999 to present) we developed a machine perfusion and viability assessment protocol for NHB kidneys.

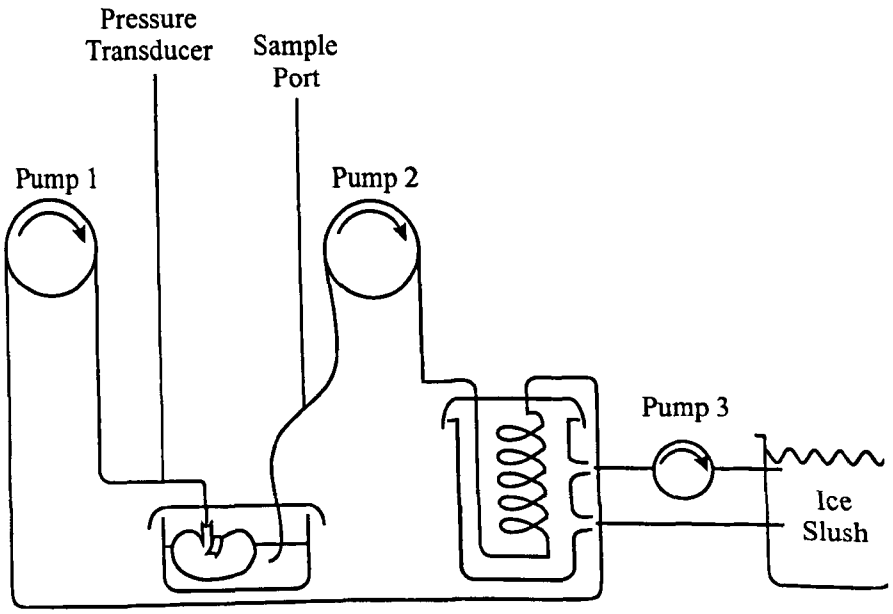


**Fig. 1** Schematic diagram of Newcastle perfusion system

### Retrieval

In situ organ perfusion was performed by our on-site transplant team by cannulating the femoral artery using a double balloon triple lumen (DBTL) cannula. The preservative solution was cold (4–8 °C) Marshall's solution. The venous venting was through placement of a cannula into the femoral vein. No radiological confirmation of placement was done. After retrieval, the kidneys were cold stored and transported to the Freeman Hospital, where machine perfusion and viability assessment were carried out.

### Pump perfusion system

The technique has been described elsewhere [2]. However, in summary a Bellco BL 760 blood pump module was used for perfusion. One pump in the system provided fluid to the renal artery and the other retrieved it through a heat exchanger. The temperature of the system was maintained between 4 and 9 °C (Fig. 1). The pump was capable of delivering a flow rate of 28–480 ml/min and pressures were maintained at 45–60 mmHg. Thus, a closed system of perfusion was achieved.

### Organ chamber

An anaesthetic humidifier chamber was found to be suitable for the purpose and could also be sterilized for re-usage.

### Flow rates

These were calculated by measuring the amount of perfusate pumped by the "arterial" pump per minute at various dial settings on the Bellco machine. After calibrating the machine and producing a graph of rotor speed against volume, the flow rates could be determined from the graph at a given rotor speed.

### Perfusate

The Newcastle modification of University of Wisconsin solution [11] was used. A 500 ml aliquot of this solution was placed in the organ chamber, the lines being primed from this point.

### Monitoring

#### *Pressure*

A standard arterial pressure transducer was connected to a three-way tap on the arterial tubing. The pressure changes were monitored on an oscilloscope, which was a standard patient monitor (Datascope 2000 I). The systolic and diastolic pressures were shown on the monitor. The resistance was calculated by dividing the mean pressure by the flow rate.

#### *Total glutathione S transferase (tGST)*

After connecting the kidney to the perfusion circuit, samples were taken of the perfusate at 0, 1, 2, 4, 6 and 8 h from the venous port. These were analysed by the Biochemistry Department for total GST. After correction for 100 g weight, the cut-off for viability was kept at 200 U/l (personal communication, J. K. Kievit).

## Results

### Phase I (1988–1993)

Organ harvesting was performed from 11 controlled NHBD (Maastricht category III) in this time. From these, 21 kidneys were subsequently transplanted. Nineteen transplants (90.5 %) were successful in that the recipients were alive and free of dialysis. This is comparable to the graft success seen in our successful pro-

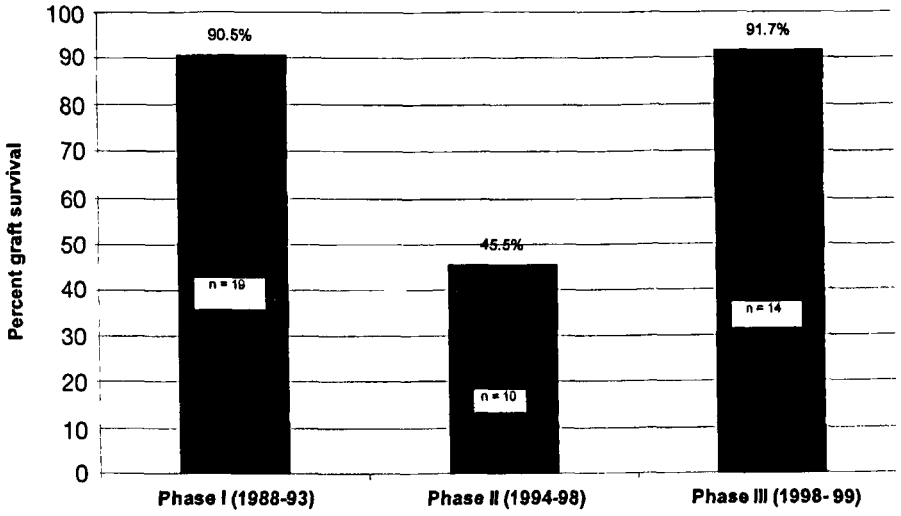


**Fig. 2** NHBD programme – Newcastle upon Tyne

gramme using standard brain dead donors (BTS guidelines).

Phase II (1994–1998)

Six donors were harvested, from which 11 transplants were performed. Out of the 11 kidneys transplanted, only five were successful (45.5%). In this phase, uncontrolled (category II) donors were used. No machine perfusion or viability assessment was undertaken during these years. Primary non-function was the major source of failure. This phase was terminated on ethical grounds. In planning phase III, ethical permission was granted. The aim of phase III was to boost the success to the levels obtained in the phase I NHBD programme but using the same donor source as phase II.

Phase III ( September 1998–April 1999)

There were 15 potential NHB donors. In two cases the next of kin refused retrieval after cannulation and failure of cannulation occurred in one case. The mean age of donors was 41.9 years (13–59 years) and the mean primary warm ischaemic time (first WIT) was 24.8 min (10–44 min). Eleven of our NHBD were Maastricht category II from the Accident and Emergency Department of the Royal Victoria Infirmary, while the remaining four belonged to category III from the regional hospitals.

Thus we retrieved 22 kidneys from 11 donors; one NHB kidney was imported while one was exported. Out of these, seven kidneys were not utilised for the following reasons: two kidneys did not perfuse at retrieval and one had poor flow rates on machine. Two kidneys had high tGST (above 200 U/l) and one donor was positive for VDRL (two kidneys). Thus 15 NHB kidneys were transplanted locally (one organ imported and machine perfused).

Ten (66.6%) recipients had delayed graft function (DGF). DGF was defined as the need for dialysis within 1 week of transplantation. Two kidneys had immediate function (IF) and one had primary non-function (PNF). There were two deaths, one in the first post-operative day due to myocardial infarction and the other at 34 days in the post-operative period due to cerebral ischaemia following repeated respiratory arrests with a functioning graft. If the two recipients who died are not considered, then the graft success rate is 91.7%. This success rate is significantly better than the 45.5% seen in phase II using the same donor source ($P = 0.027$, Fisher 2-tail test) (Fig. 2).

## Discussion

There is a debate as to the utility of machine perfusion of donor kidneys. In 1981, Opelz and Terasaki concluded no added advantage of machine perfusion in HB donors [15]. Machine perfusion fell into disrepute due to its complex logistics needs [3, 8, 16]. It was also reported in some cases that machine perfusion was damaging to the graft [14].

Renewed interest in this method of preservation came about through the use of marginal organs and improved preservative solutions (University of Wisconsin). With the improved solutions, the incidence of delayed graft function could be reduced using kidneys from heart beating donors or those with prolonged cold ischaemia [4, 12]. Increased demand for viable organs has led to a recent upsurge in retrieval from the NHB donors. The difficulty experienced here was the viability of such kidneys. As the primary warm ischaemic times are prolonged with

such donors, viability assessment and organ modulation have been done by machine perfusing the NHBD kidneys before implantation [1, 5, 7, 9].

The measurement of intrarenal vascular resistance and alpha GST is practised by the Maastricht group, who have increased their donor pool by 20% [10]. Most of the studies have demonstrated a beneficial effect of pulsatile perfusion in NHBD kidneys [13, 17]. Machine perfusion has been shown to improve the graft function in cases of marginal kidneys as well as those with prolonged cold ischaemic times [17].

Pulsatile perfusion has enabled us to evaluate the serial rise in tGST over time, which is one of the parameters used in assessment of NHBD kidney [6].

In conclusion, we have demonstrated the need for assessment of NHB kidneys prior to implantation using known enzymatic parameters along with evaluation of intrarenal resistance and flow characteristics of the kidney on the pulsatile perfusion system. When instituted in phase III of the Newcastle NHBD programme, it provided excellent graft survival.

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