

# Increasing the post-transplant viability of kidney by means of ex-vivo normothermic perfusion in a porcine model

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## INTRODUCTION:

A short period of isolated normothermic perfusion (NP) can be used to improve the condition of the kidney after periods of warm and cold ischemic injury [1]. We have assessed the capability of NP to increase the viability of kidney after a long cold ischemia storage period using the ARK system developed by EBERS.

## METHODS:

Female pigs were selected for both control and NP groups. Left kidneys were extracted and flushed with Ringer's lactate at 4°C. Kidneys were stored in ice for 20 hours with Custodiol HTK.

- Control group: In the control group, preserved kidneys were reimplanted and right kidney nephrectomies were performed.
- NP group: kidneys were connected to the ARK system for 3-hour NP before reimplantation. Right kidney nephrectomies were performed.

The ARK system is formed by a portable preservation unit, which features peristaltic and infusion pumps, heating and oxygenation systems, sensors and a control unit; and a disposable closed circuit, where the organ and the perfusate are contained in sterile conditions (Figure 1).

Normothermic perfusion conditions were the following:

- Kidneys were perfused with a perfusion solution composed by Ringer lactate, 20% human albumin, red blood cells as oxygen carriers, creatinine and sodium bicarbonate. The perfusate was supplemented continuously with a nutrients solution, insulin and a vasodilator.
- Secreted urine was collected for analysis and the corresponding lost volume of perfusate was replaced in the circuit.
- Renal flow rate, mean arterial pressure, urine output, temperature, glucose concentration, hematocrit and oxygen saturation were recorded continuously.
- A blood gas analyzer was used to record parameters for acid-base homeostasis.
- Serum and urine samples were obtained hourly for offline biochemical analysis.

All pigs' evolution was monitored for 7 days after reimplantation.

Group	Group size	Mean CS time (hours)	Normothermic Perfusion
Control	n=5	21:54	No
NP	n=5	19:39	Yes

Table 1. Summary of the analysis groups and test conditions. NP: Normothermic Perfusion, CS: Cold Storage



Figure 1. Normothermic Perfusion Machine prepared for the perfusate preparation prior to the perfusion process

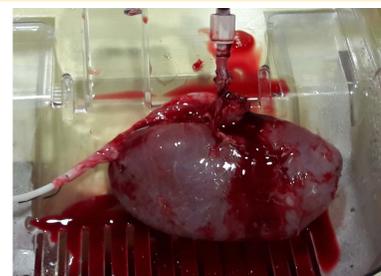


Figure 2. Picture of the kidney taken at the start of the perfusion process.

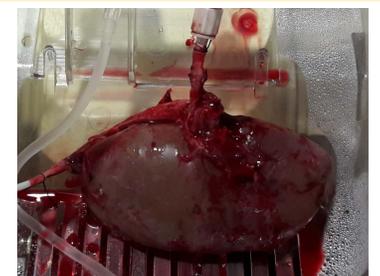


Figure 3. Picture of the kidney taken after 3 hours of perfusion.

## RESULTS:

ARK NP system was able to maintain physiological levels of temperature, mean arterial pressure and arterial oxygen saturation in all cases throughout the 3-hour NP. Biochemical analyses in the transplanted animals show clear differences between groups:

- Control group: biochemical analyses show that urea increases to values >500 mg/dl, creatinine exceeds 17 mg/dl and potassium remains over 6-7 meq/l. Overall, the trend for these variables shows a continuous increase in the values until humane endpoints were reached.
- NP group: these variables follow a different trend, reaching a maximum in post-surgery days 3 and 4 (120-330 mg/dl for urea, 10-18 mg/dl for creatinine and 5-7 meq/l for potassium), decreasing in the subsequent days to healthy levels. End of the studies was scheduled after 7 days of monitoring the animals proceeding to their sacrifice and corresponding analysis.

Survival rate after 7 days was 0% in the control group and 100% in the NP group.

## Biochemical results:

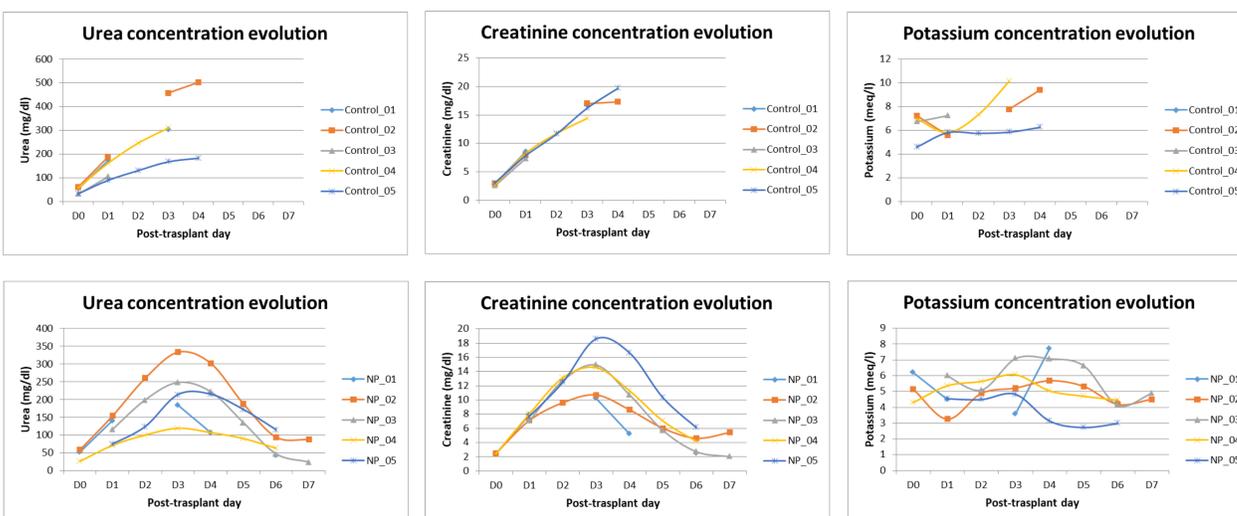


Figure 4. Biochemical analyses (urea, creatinine and potassium). Summary of the results obtained for control and NP groups in the 7 days following the kidney reimplantation.

Group	Biochemical analyses		
	Urea (mg/dl)	Creatinine (mg/dl)	Potassium (meq/l)
Control	182 - 593	14,4 - 23,5	6,25 - 10,14
NP	119 - 333	10,2 - 18,6	4,82 - 7,72

Table 2. Peak range values in biochemical results for urea, creatinine and potassium concentration in both Control and Normothermic Perfusion groups. NP: Normothermic Perfusion.

	Control Group	NP Group
Survival ratio	0%	100%

Table 3. Survival ratio after 7 monitoring days for both control and Normothermic Perfusion groups.

## DISCUSSION AND CONCLUSIONS:

Collectively, data illustrate the capacity of NP applied with the ARK system to increase the viability of kidneys that had been previously subjected to long periods of cold ischemia.

[1] Hosgood SA et al. J Sur Res. 2013; 182:153-160

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