LETTER TO THE EDITORS

A novel, customized 3D-printed perfusion chamber for normothermic machine perfusion of the kidney

Ahmer Hameed[1,2,3], Suat Dervish[1], Natasha Rogers[1,3,4], Henry Pleass[2,3] & Wayne Hawthorne[1,2,3]

1 Westmead Institute for Medical Research, Westmead, NSW, Australia
2 Department of Surgery, Westmead Hospital, Westmead, NSW, Australia
3 Sydney Medical School, University of Sydney, Sydney, NSW, Australia
4 Department of Renal Medicine, Westmead Hospital, Westmead, NSW, Australia
E-mail: Wayne.Hawthorne@sydney.edu.au

Dear Editors,

Normothermic machine perfusion (NMP) prior to transplantation has gained significant prominence in the recent past, and has been clinically utilized in the setting of liver, heart, lung, and kidney transplantation [1]. Nicholson and Hosgood were the first to report a series of kidney transplants following a brief period of pre-implantation NMP in 18 marginal donors; the success of this initial study and further investigations has led to a multi-center randomized control trial that is currently underway in the UK [2–4].

One consideration that may impact the subsequent widespread uptake of clinical NMP systems is cost. In particular, the costs of consumables for each individual organ need to be sufficiently low to stimulate further uptake by transplant centers. Consumables must also be sterilizable and provide ease of use for the clinical team.

Our NMP set-up has been described previously [5]. We initially used a custom-designed metal chamber, however this was difficult to clean/re-sterilize, and did not adequately collect and funnel all residual blood into the reservoir. This prompted the design and development of the 3D-printed perfusion chamber (Fig. 1).

The 3D-printed chamber employs gravity drainage of renal venous outflow and any other blood leak (e.g. biopsy site) into a funnel-shaped cavity; only the renal artery is cannulated, allowing open drainage from the renal vein. The chamber is placed above the blood/perfusion fluid reservoir, and therefore blood can drain into the reservoir without necessitating an additional pump mechanism. The need for a separate reservoir may be completely obviated depending on the prime and packed red cell volume used in the circuit.

The kidney itself is placed on a fenestrated 'mesh' that can be incorporated into the print; this requires the additional printing of polyvinyl alcohol supports that need to be dissolved in water post-printing. A separate, reusable, and sterilizable stainless steel mesh can alternatively be used (Fig. 1d–e), significantly reducing print times.

Use of such a chamber affords the following advantages:

1. Low cost – the chamber is printed using copolyester (CPE+) or polypropylene (Ultimaker B.V., Geldermalsen, The Netherlands) on an Ultimaker 3 extended 3D printer (Ultimaker B.V., Geldermalsen, The Netherlands). Costs per print are estimated at approximately 15–20 USD.
2. Printable at the transplant center on-demand, and readily sterilizable. An ever increasing range of printable materials allows for specific print properties. Advanced printers can print polypropylene, which if used, can be safely autoclaved. If CPE is employed, sterilization can be achieved using ethylene oxide gas or gamma irradiation; in this situation, it is prudent that a relevant number of chambers are preprinted and made available for use 1–2 weeks prior to any anticipated need. We have successfully printed and used both CPE and polypropylene for the purposes of NMP.
3. Its components and dimensions can be readily and easily modified by altering print settings.
4. The chamber obviates the need to (i) cannulate the renal vein (and therefore avoids the need to shorten the vein prior to transplantation), and (ii) ensure a blood-tight circulation with little to no leak.
5. The chamber is compatible with perfusion constituents. Albumin, which is an important constituent of the perfusate in some normothermic perfusion setups [6], is not significantly adsorbed by CPE and therefore remains in the perfusate. An isolated perfusion test was

doi:10.1111/tri.13361

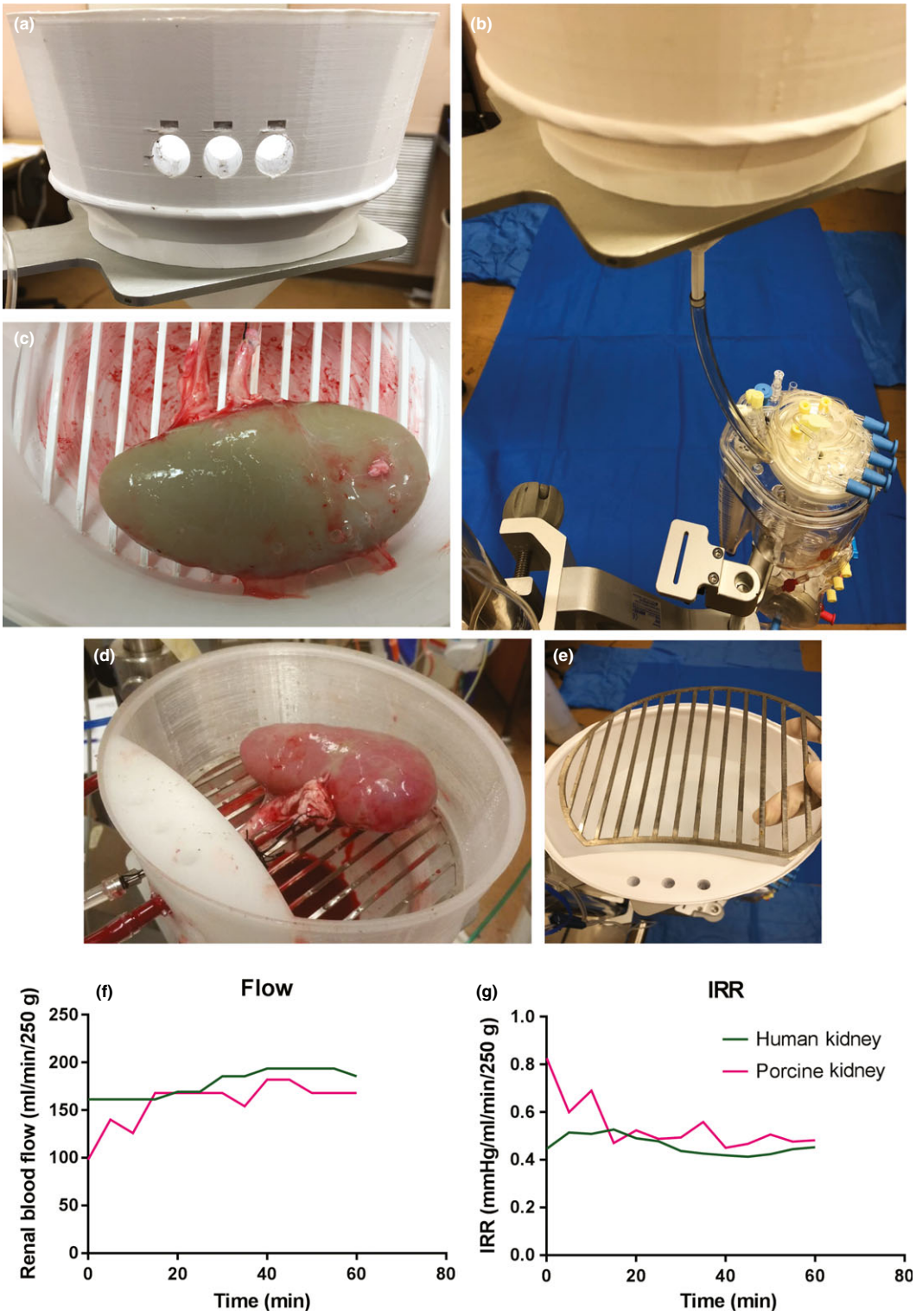

Figure 1 Customized, 3D-printed kidney perfusion chamber. (a) Front aspect, with holes for arterial and ureteric cannulae; (b) Side aspect, showing 1/4 inch PVC tubing draining the chamber directly into the venous inflow port of the reservoir; (c) Perfusion chamber with 'mesh' (upon which kidney sits) incorporated into print; (d–e) Perfusion chamber with mesh in this case provided by a reusable, custom-cut stainless steel metal sheet. The perfusion chamber in (d) was printed using polypropylene (autoclavable), whilst the perfusion chamber in the other images was printed using copolyester. (f–g) Renal blood flow and intra-renal resistance (IRR) in one porcine kidney and one discarded human kidney placed on the 3D-printed perfusion chamber during 1 h of NMP. The human and porcine kidneys produced 43 and 180 ml of urine, respectively.

Transplant International 2019; 32: 107–109

performed using 20% human albumin diluted in 100 ml of 0.9% sodium chloride; this was circulated into and out of the 3D-printed perfusion chamber via 1/4 inch PVC tubing using a pump generating a flow rate of 0.5 l/min. There was no albumin adsorption over 1 h (albumin concentrations at 0, 30, and 60 min of perfusion were 99, 97, and 102 g/l, respectively).

We have successfully perfused 12 discarded human kidneys and 17 porcine kidneys using this set-up [7,8]. Each kidney had declining intra-renal resistance (IRR) and increasing flow, in addition to evidence of urine output. Examples of flow and intra-renal resistance parameters in one porcine and human kidney respectively are presented in Fig. 1f–g.

Overall, it is hoped that the innovative use of 3D-printing technology can further help facilitate the uptake of normothermic machine perfusion of different organs, including the kidney, by lowering costs and promoting ease of perfusion.

Funding

John Loewenthal Project Grant (Royal Australasian College of Surgeons).

Conflicts of interest

The authors have declared no conflicts of interest.

Acknowledgements

3D printing was performed in the Flow Cytometry Core Facility that is supported by Westmead Institute and the Westmead Research Hub.

REFERENCES

1. Hameed AM, Hawthorne WJ, Pleass HC. Advances in organ preservation for transplantation. *ANZ J Surg* 2017; **87**: 976–980.
2. Nicholson ML, Hosgood SA. Renal transplantation after ex vivo normothermic perfusion: the first clinical study. *Am J Transplant* 2013; **13**: 1246–1252.
3. Hosgood SA, Saeb-Parsy K, Wilson C, Callaghan C, Collett D, Nicholson ML. Protocol of a randomised controlled, open-label trial of ex vivo normothermic perfusion versus static cold storage in donation after circulatory death renal transplantation. *BMJ Open* 2017; **7**: e012237.
4. Hosgood SA, Nicholson ML. Ex vivo normothermic perfusion of declined human kidneys after inadequate in situ perfusion. *Am J Transplant* 2014; **14**: 490–491.
5. Hameed AM, Miraziz R, Lu DB, *et al.* Extra-corporeal normothermic machine perfusion of the porcine kidney: working towards future utilization in Australasia. *ANZ J Surg* 2018; **88**: E429–E434.
6. Selzner M, Goldaracena N, Echeverri J, *et al.* Normothermic ex vivo liver perfusion using steen solution as perfusate for human liver transplantation: First North American results. *Liver Transpl* 2016; **22**: 1501–1508.
7. Hameed AM, Lu B, Miraziz R, *et al.* Intra-renal delivery of drugs targeting ischemia-reperfusion injury of the kidney in a rodent model and porcine model of normothermic machine perfusion. The Transplantation Society of Australia and New Zealand Annual Scientific Meeting, Melbourne Convention Centre, 29th April-1st May, 2018. *Transplant Direct* 2018; **4**: S1.
8. Hameed AM, Rogers N, De Roo R, *et al.* Normothermic machine perfusion of non-utilized human kidneys – our first two cases. The Transplantation Society of Australia and New Zealand Annual Scientific Meeting, Melbourne Convention Centre, 29th April-1st May, 2018. *Transplant Direct* 2018; **4**: S21.