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A Dual Chamber Stent Prevents Organ Malperfusion in a Model of Donation after Cardiac Death

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Abstract

Background—The paradigm for Donation after Cardiac Death (DCD) subjects donor organs to significant ischemic injury. A dual-chamber Organ Perfusion Stent (OPS) would maintain organ perfusion without impacting natural cardiac death. A center lumen allows uninterrupted cardiac blood flow, while an external chamber delivers oxygenated blood to the visceral vessels.

Methods—A prototype OPS was constructed from commercial stents. In a porcine model, the OPS was deployed, followed by a simulated agonal period. Oxygenated blood perfused the external stent chamber. Organ perfusion was compared between controls (n=3) and OPS (n=6). Finally, a custom nitinol dual chamber OPS was fabricated using a retrievable “petal and stem” design.

Results—Endovascular OPS deployment achieved visceral isolation without adverse impact on cardiac parameters. Visceral oxygen delivery was 4.8 fold higher as compared to controls. During the agonal period, organs in OPS treated animals appeared well perfused, contrasting to

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malperfused controls. A custom nitinol and polyurethane OPS was easily recaptured with simple sheath advancement.

Conclusions—An OPS maintained organ perfusion during the agonal phase in a model of DCD organ donation without adversely impacting cardiac function. Ultimately, the custom retrievable design of this study may help resolve the critical shortage of donor organs for transplant.

INTRODUCTION

The single most significant obstacle facing solid organ transplantation remains overcoming the critical shortage of healthy donor organs. In the United States, of the over 120,000 patients awaiting a solid organ transplant, only 1 of 4 will actually receive one. Among consented organ donors, periods of insufficient blood flow lead to organ injury and represent the greatest hurdle to the availability of healthy donor organs¹. Rapid cooling of the organ is the best way to avoid injury to the donor organ and provide the best long term outcome. The ideal organs are recovered from Donation after Brain Death (DBD) or living donors (LD), wherein blood flow remains normal until the exact moment when the organs are cooled. As the combined number of DBD and LD has plateaued, donors from these groups are unlikely to resolve the current shortage of organs for transplant. In the last decade, growth has been demonstrated in another donor group, Donation after Cardiac Death (DCD), which includes patients with severe non-recoverable injuries²⁻⁴. An example of a potential DCD donor would be a patient with a severe head injury who would never recover but does not meet the stringent criteria for brain death. After family consent for organ donation, the patient has cardiopulmonary life support discontinued and during the “agonal period”, as the heart begins to fail, perfusion of organs becomes inadequate. The malperfusion leads to irreversible ischemic organ damage and the longer the agonal period, the more damage to the organs. Current standards dictate that organs be discarded for agonal periods over 30 minutes for the liver and over 40 minutes for the kidneys. In addition to fewer organs being recovered from each consented DCD donor, organ function and patient outcomes are inferior among DCD organs^{2, 5-8} including failure of the transplanted organ. For these reasons, minimizing ischemic time is instrumental towards improving the availability and outcomes of DCD donor organs.

The ethics of DCD organ recovery pose several important obstacles towards reducing ischemic injury and these include: 1) surgical exposure of organs must not occur prior to cardiac death and 2) cardiac death must not be expedited. Approaches such as dual occlusive balloon catheters have been described to isolate organ perfusion^{9, 10}, but the resulting complete aortic occlusion would expedite cardiac death and therefore, cannot be used before a natural cardiac arrest. Moreover, as significant ischemic injury has already occurred by the time of cardiac arrest, post-mortem approaches have failed to offer any benefit to the outcome of DCD organs.

To meet these challenges, we developed a novel stent approach with the goal of isolating the visceral arteries for oxygenated perfusion separate from the systemic circulation. For vascular isolation in a critically ill prospective donor, a stent design offers several clear advantages. As the stent is placed percutaneously, it requires no incisions and is similar to

the catheters a donor would already have in place. The inherent radial force of a stent mediates apposition to the vessel wall to create a vascular seal. The designs of traditional stents, however, do not meet the simultaneous objectives for visceral (abdominal organ) perfusion while maintaining uninterrupted cardiac flow. A cornerstone of our approach is a dual-chambered Organ Perfusion Stent (OPS). A central stent lumen provides uninterrupted flow from the heart to the rest of the body, while an external chamber consolidates perfusion of the four visceral vessels. With this approach, the stent isolates the aorta into two zones for separate “cardiac” and “organ” perfusion (Figure 1). The flow of blood in each chamber would circulate as follows: *Cardiac perfusion*: Blood from the heart would continue to flow through the center lumen of the stent to the lower body and extremities. The blood would return to the heart through normal venous pathways from the lower body, thus avoiding strain on the dying heart. This would allow for uninterrupted, albeit agonal, blood flow to the heart, brain and extremities. *Abdominal perfusion*: A standard venous cannula would deliver blood to a pump/oxygenator and a perfusion sheath carries oxygenated blood to the external stent chamber thereby perfusing only the arteries of the isolated abdominal organs.

Conceptually, one of the biggest obstacles to an OPS approach are concerns over whether stent placement would expedite cardiac death in the prospective donor. Any significant decrease in the preload (pressure of blood into the heart) or increase in the afterload (pressure out of the heart) would expedite cardiac death, against ethical tenets for a prospective DCD organ donor. Our proposed approach effectively addresses this issue. The OPS reduces the aorta size by less than 50% of normal which is unlikely to significantly impact blood flow by vascular hemodynamic principles¹¹. As a result, we did not expect that this approach would increase cardiac work or expedite cardiac death. In fact, modern experience with endovascular aortic repair suggests that these stent grafts can rapidly remodel aortic hemodynamics without significant risk, even among patients with substantial cardiopulmonary disease¹².

In summary, we have designed a novel dual chamber stent to isolate the abdominal organs from the unpredictable function of the dying heart to preserve organ function during the agonal phase of DCD organ donation. This contrasts to any other previous approaches in that the heart would continue to function, failing on its own terms. This feature would allow visceral perfusion to be initiated prior to withdrawal of life support and to provide optimal outcome for donor organs, without expediting death of the prospective donor. The objectives of this study are to examine whether the stent deployment increases cardiac stress, if the stent can successfully consolidate visceral arteries and whether the dual chamber approach can improve delivery of oxygen as compared to control agonal simulation. Finally, our study will examine a custom retrievable stent design such that this approach would not commit the patient to organ donation until the time of cardiac death.

METHODS

Dual chamber OPS from modification of commercially available stents

A commercial hybrid OPS prototype fabricated by end to end sutured anastomosis between two 12 mm iliac limb seal zones (Cook, Bloomington, IN) and an intervening 6 mm Viabahn stent (Gore, Flagstaff, AZ) for a total length of 25 cm (Figure 2). Polytetrafluoroethylene

(PTFE) sealant tape (3M, St. Paul, MN) and medical grade cyanoacrylate (MG30, ASI, Frankfort, IL) were used for added hemostasis. A long 10 French sheath (Cook, Bloomington, IN) was placed through a small pilot hole in the flare of one end of the OPS, and suture fixed. The OPS stent was delivered through an 18 French vascular sheath (Gore, Flagstaff, AZ).

DCD organ recovery model

Nine Yorkshire pigs (80-90 kg) were placed under general anesthesia and administered amiodarone to prevent ventricular fibrillation. A pulmonary artery catheter was placed by a jugular approach (Cat#777F8, CCombo V, Edwards Lifesciences, Irvine, CA) among OPS treated animals. Cardiac measures were recorded before, during and after deployment of the OPS (n=6). An arterial line was placed for hemodynamic monitoring and for aortography. Following abdominal exposure for documentation of organ perfusion, the OPS was placed into the lumen of the iliac artery in the heparinized animal. A standard venous cannula (Edwards Lifesciences) was placed into the iliac vein. Controls (n=3) underwent sheath placement without OPS deployment. The OPS was deployed by sheath withdrawal to include the celiac, SMA and renal arteries in the external stent compartment. Isolation of all four visceral vessels was demonstrated angiographically. Perfusion was initiated (Figure 1C) and the agonal state was simulated by reduced ventilation to under 4 breaths per minute as well as induced hypotension with esmolol and propofol titrated for a target Mean Arterial Pressure (MAP) of 60 mm Hg for 30 minutes followed by 40 mm Hg for another 30 minutes. Arterial blood gases were drawn systemically and from the external stent chamber. Abdominal organs were inspected at 60 minutes during the agonal period.

Perfusion

The venous cannula was connected in series to a Centrimag centrifugal pump (Thoratec, Pleasanton, CA), pediatric oxygenator (Minimax, Medtronic, Minneapolis, MN), arterial filter (Affinity Pixie, Medtronic, Minneapolis, MN) and back to the arterial cannula of the external chamber. The pump was set at 5000-5500 rpm to achieve maximal flow rates. The sweep rate was set between 2.5 and 4.0 liters per minute (3.0 on average) for removal of CO₂ as guided by arterial blood gases.

Custom retrievable and dual-chambered stent

The nitinol backbone was fashioned into a dual chambered design (OPS) by first thermal shape setting (Lindberg/Blue M Moldatherm Box Furnace, Fisher Scientific, Pittsburgh, PA) of 0.014 inch nitinol wire (WSE001400000SG, NDC, Fremont, CA) onto an aluminum mandrel (Figure 5). Contacting wires were joined by precision-pulsed, micro laser welding (LZR-100, Sunstone Engineering, Payson, UT). Thermal shape setting at 500°C allowed for distribution of stress points caused during welding. Rapid cooling of the stent to 20°C in 10 seconds (quenching) restored superelastic properties (self-expanding and radial force) to the nitinol backbone.

Electrospun polyurethane stent wraps

Nitinol stent scaffolds were covered with a custom polymer wrap (Figure 5). Poly (ester urethane) urea (PEUU) was electrospun onto an aluminum mandrel with a narrow central cylindrical section with bellbottom flares at both ends (12 mm ends tapered to 6 mm in the middle). PEUU was synthesized from polycaprolactone diol ($M_n = 2000$), 1,4-diisocyanatobutane and putrescine, as described previously¹³. The electrospinning protocol has been reported previously¹⁴. Briefly, PEUU was dissolved in 1,1,1,3,3,3-hexafluoroisopropanol at a concentration of 12% (w/v), and electrospun onto a rotating and translating stainless steel mandrel at a rate of 3 ml/h, voltage of 19 kV and at a distance of 17 cm. Two polymer wraps were sutured end to end using 6-0 PTFE suture (Gore).

Statistics

Measurements of cardiac parameters during OPS placement ($n=6$) and pH measurements between OPS and controls were compared using a T-test analysis.

RESULTS

A commercial hybrid OPS can maintain uninterrupted aortic flow while maximizing perfusion of abdominal organs

The key objectives in DCD organ recovery are to maintain organ perfusion without open surgery and without impacting the natural cardiac death of the prospective donor. A prototype dual chamber OPS was modeled to achieve separation of visceral blood flow from the unstable hemodynamics of the agonal donor. Commercial stent components were used to create a hybrid prototype stent with proximal and distal seal zones and a smaller diameter central aortic perfusion lumen with an external visceral perfusion chamber (Figures 1 and 2). A venous cannula was connected to an external pump/oxygenator and then back to the external chamber of the OPS to provide visceral perfusion.

An OPS does not adversely impact cardiac physiology

A theoretical concern of a dual chamber OPS approach is the concern that stent deployment would expedite cardiac death in the prospective donor. As the OPS reduces the diameter of the aorta size by less than 50% of baseline, it is unlikely the stent would significantly reduce flow¹¹ or increase cardiac strain. In order to objectively examine the impact of an OPS on cardiac stress, we monitored cardiac physiology both before and after deployment of an OPS in a porcine model. Comparing the averages before and after OPS deployment, no significant change was observed in the Heart Rate (HR), Mean Arterial Pressure (MAP), Mixed Venous Oxygen (SvO_2), or Central Venous Pressure (CVP). Small but significant decreases were observed in the Cardiac Output (CO) ($P=0.01$) and Right Ventricular End Diastolic Volume (RVEDV) ($P=0.05$) which is not entirely unexpected given the offloading of visceral perfusion from the heart by the stent. We concluded that cardiac function is not adversely impacted by deployment of the OPS (Table 1).

An OPS increases perfusion to consolidated visceral vessels

Following device deployment, angiography confirmed continuous cardiac perfusion of the center lumen of the stent and isolated visceral perfusion by the external compartment (Figure 3). Initial experience with a 10 french sheath for both venous inflow and arterial outflow revealed inadequate average flow volumes under 180 ml/min. Replacement of the initial narrow 10 French venous sheath with a larger 20 Fr venous standard bypass cannula immediately improved flow volumes to over 700 mL/minute. The perfusion circuit consisted of perfusion pump, oxygenator and arterial filter. Oxygen partial pressures of visceral blood flow among OPS treated animals were an average of 4.8 fold higher than control animals. Despite improved visceral perfusion, changes in systemic pH were not significantly different as compared to controls ($P = 0.51$). In addition, after a 60 minute agonal period, abdominal organs among OPS animals were visually better perfused as compared to controls (Figure 4).

Second generation custom OPS with recapture ability

A permanent stent would obligate a potential consented DCD patient to organ donation against ethical principles. As a result, the feature of retrievability would be essential for clinical application of dual chambered stents to organ recovery. Towards this goal, we developed a retrievable stent based upon a novel “stem and petal” design (Figure 5A). The “petals” provide radial force for vessel apposition while the wires converge distally to form a single “stem”. The fabric of the stent terminates prior to the stem and this allows for distal flow beyond the stent. As the stem remains permanently attached to the petals, the transition allows recovery of the stent by simple advancement of the vascular sheath. The nickel-titanium alloy, nitinol, is widely used in many modern self-expanding stents and has properties that are also ideal for a retrievable stent design^{15, 16}. For this study, a petal and stem nitinol scaffold was fashioned into the dual chamber stent design. While our analysis revealed that our custom nitinol stent achieves only 57% of the radial force of a commercial aortic stent, the stem provides longitudinal resistance to migration. A PEUU wrap was electrospun onto a mandrel and affixed to the scaffold to create the final custom OPS (Figure 5B). The OPS was retrieved successfully by simple sheath advancement in less than 30 seconds (Figure 5C).

Another notable limitation of the commercial hybrid OPS prototype was the integrated perfusion lumen which significantly limited the diameter of the arterial perfusion lumen and hence volume flow. Given the elastic properties of electrospun PEUU, we next examined a “modular” approach for the perfusion lumen (Figure 6). In this approach, the main body of the stent is delivered first, followed by passage of the perfusion lumen over a pre-positioned wire to dock with the main stent through a small pilot hole in the stent fabric. In delivering the perfusion lumen separately, the device delivery size was significantly reduced and the arterial perfusion lumen was increased from 10 to 12 French. This modification led to further improvements in flow rate exceeding 1.2 L/minute, almost double the volume flow of the integrated 10 French sheath of the commercial hybrid OPS.

DISCUSSION

Despite a growing potential pool of potential DCD donors ²⁻⁴, ischemic injury during the agonal phase frequently leads to discard of donor organs and perpetuates the critical shortage of donor organs for transplant ¹. Donation after Cardiac Death (DCD) represents an important alternative to limited DBD or LD donors and yet malperfusion during the agonal period results in irreversible ischemic organ damage and discard. As a result, minimizing organ ischemic time during recovery would profoundly improve the availability of donor organs for transplantation.

Vascular stents have offered an alternative to open surgical procedures including patients with comorbid issues that would have been prohibitive to open surgery. In the context of donor organ recovery, open surgical exposure during the agonal phase commits a patient to organ donation prior to cardiac death and as a result has been ethically incompatible with DCD organ recovery. Alternately, a retrievable stent approach to prevent ischemic organ injury would offer minimally invasive protection from ischemia and, in the event of spontaneous patient recovery, could be removed with conventional vascular closure techniques. A cornerstone of the OPS is a novel dual chamber stent, which contrasts to conventional linear or even branched stents used in aortic repair. The dual chamber stent allows the visceral vessels to be rapidly isolated and perfused with oxygenated blood. This, in turn, protects the organs from malperfusion and hypoxia of the systemic agonal circulation.

A second difference in the OPS as compared to traditional stent technology is the management of vascular branches. The treatment of traditional vascular pathology such as aneurysms and traumatic vascular injury mandate stenting into individual branch vessels in order to prevent aneurysm rupture or ongoing bleeding, respectively. For the purpose of perfusing potential donor organs, the individual access of the four vessels to the abdominal organs is unnecessary and would require significant X-ray imaging, lengthy procedural time, potentially toxic contrast to the donor organs, as well transport of critically ill patients outside of the intensive care unit. By consolidating all of the visceral vessels into a single compartment (Figure 1), our strategy simplifies the process to a bedside procedure that could be deployed within minutes. It has been shown that there is significant consistency in the anatomy and visceral branches relative to bone landmarks. In fact, the vessels of the abdominal organs originate in the area confined by vertebrae T12-L2 in 100% of cases ¹⁸. As a result, bone landmarks can be used to predict visceral anatomy characteristic of the young DCD donor population and bedside OPS delivery may be achievable with X-ray or portable fluoroscopy. The third departure from conventional aortic stents is a fully retrievable design. Although some stents allow partial recapture, this study reports the first aortic stent that can be recaptured after complete functional device deployment. Although the likelihood of spontaneous recovery of a DCD donor during the agonal period is extremely rare, this retrievable design would ensure that the device could be removed without surgery in the unlikely event that the prospective donor did not progress to cardiac arrest.

The ethics of DCD mandate that surgery to expose the organs should not occur until after cardiac death and that cardiac death must not be expedited²¹⁻²³. As a result of their impact on cardiac death, other nonsurgical approaches⁹²⁴, cannot be used until after cardiac death and as a result cannot reverse the ischemic injury of the preceding agonal period. A dual-chamber OPS directly addresses these key ethical concerns. Our data confirms that the OPS can be deployed without increasing cardiac strain and improves delivery of oxygen to the organs. As a result, the OPS may achieve the goal of preventing ischemic injury while respecting key ethical principles. Although as part of this study full abdominal exposure was performed to inspect organ perfusion, we expect that in clinical use, this would be an entirely percutaneous. Although our study has addressed several potential ethical concerns related to this technology, other issues such as informed consent must be defined prior to clinical implementation.

Early in the inception of this device, a second venous OPS was conceived to provide complete venous and arterial isolation. This was abandoned when it was observed that effluent blood was not different from agonal blood in terms of oxygenation. As an added advantage of the arterial-only stent approach, the venous cannula allows for ongoing filtration of systemic metabolic wastes by the liver and kidneys during the agonal period. Adequate visceral flow is critical towards preventing ischemic organ injury. Our initial use of a 10 french perfusion lumen to the external stent compartment maintained a reasonable overall delivery size, but at 700 mL/min was inadequate for normal visceral blood flow estimated at 2.5 L per minute^{19, 20}. The development of a custom OPS and adoption of a modular perfusion lumen further increased flow significantly without increasing device size.

One theoretical concern is the development of limb ischemia as a result of a device placed in the through the femoral artery. While this is possible, it is notable that our custom stent was placed through a 14 french sheath, which is smaller than percutaneous arterial cannulas used currently for extracorporeal membrane oxygenation. In addition, limb ischemia is well tolerated for up to 6 hours, and with anticipated removal of this device within an hour among rare patients that do not expire, the risk of limb injury would be unlikely. Another potential limitation of our study was the use of systemic heparin, which is required in the thrombogenic porcine model. Most organ recovery centers in the United States do, in fact, use therapeutic heparin during organ recovery. In those regions that do not use heparin, there may be a role for heparin bonded stent materials, if needed. Experience with modern stent grafts suggests that anticoagulation is not required despite the fact that these grafts are left permanently in the vasculature.

Donor ethics imply that a prospective DCD donor should be offered the same end of life care as non-donors. Under the current paradigm for DCD donors, all life support is simultaneously discontinued for all prospective donors. During this agonal period the abdominal organs are without adequate blood flow. By contrast, for non-donors, end of life care is actually at the discretion of the consenting patient or their family. For instance, families of non-donors may elect for end of life care by requesting any combination of the following: 1) withholding cardiopulmonary resuscitation (CPR) in the event of an arrest 2) withholding medications to support blood pressure 3) discontinuation of a ventilator 4) withholding dialysis or 5) withholding feeding. We are proposing a new paradigm for donor

end of life care that is more consistent with the benchmark of non-donors. Instead of a global withdrawal of life support, we propose an approach that would ensure: 1) organ perfusion without the need for surgical incisions 2) cardiac death would not be expedited 3) the device would be removable, so as not to commit a prospective donor until the time of cardiac death.

In summary, this novel stent design will insulate the abdominal organs from the unpredictable function of the dying heart to preserve organ function during the agonal phase of DCD organ recovery. This approach should allow visceral perfusion to be initiated prior to withdrawal of life support and to provide optimal outcome for donor organs, without expediting death of the prospective donor. Most importantly, the custom retrievable dual chambered stent described would not commit the patient to organ donation until the time of cardiac death. The dual chamber stent approach may have additional utility when rapid isolation of visceral perfusion is required, such as delivery of visceral thrombolytics, vasoactive agents or even chemotherapy. Future studies will more rigorously quantify longterm outcomes in terms of histologic organ ischemia, stent impact of the vessel intima and serum markers of organ injury of post-agonal organs. We expect that further development of a retrievable, dual chambered stent will allow for rescue of a significant pool of otherwise unused organs, addressing the critical shortage of organs for transplantation.

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References

1. Scalea JR, Redfield RR, Rizzari MD, Bennett R, Anderson ME, Anderson JE, et al. When Do DCD Donors Die? Outcomes and Implications of DCD at a High-volume, Single-center OPO in the United States. *Ann Surg*. 2015
2. Reid AW, Harper S, Jackson CH, Wells AC, Summers DM, Gjorgjimajkoska O, et al. Expansion of the kidney donor pool by using cardiac death donors with prolonged time to cardiorespiratory arrest. *Am J Transplant*. 2011; 11:995–1005. [PubMed: 21449941]
3. Garcia-Valdecasas JC. DCD donors: a unique source to significantly increase organ donation. *J Hepatol*. 2011; 55:745–6. [PubMed: 21704004]
4. Klein AS, Messersmith EE, Ratner LE, Kochik R, Baliga PK, Ojo AO. Organ donation and utilization in the United States, 1999–2008. *Am J Transplant*. 2010; 10:973–86. [PubMed: 20420647]
5. Grewal HP, Willingham DL, Nguyen J, Hewitt WR, Taner BC, Cornell D, et al. Liver transplantation using controlled donation after cardiac death donors: an analysis of a large single-center experience. *Liver Transpl*. 2009; 15:1028–35. [PubMed: 19718636]
6. Skaro AI, Jay CL, Baker TB, Wang E, Pasricha S, Lyuksemburg V, et al. The impact of ischemic cholangiopathy in liver transplantation using donors after cardiac death: the untold story. *Surgery*. 2009; 146:543–52. discussion 52-3. [PubMed: 19789011]
7. Reich DJ, Hong JC. Current status of donation after cardiac death liver transplantation. *Curr Opin Organ Transplant*. 2010; 15:316–21. [PubMed: 20414112]

8. Snyder RA, Moore DR, Moore DE. More donors or more delayed graft function? A cost-effectiveness analysis of DCD kidney transplantation. *Clin Transplant*. 2013; 27:289–96. [PubMed: 23350938]
9. Kootstra G, van Heurn E. Non-heartbeating donation of kidneys for transplantation. *Nat Clin Pract Nephrol*. 2007; 3:154–63. [PubMed: 17322927]
10. Garcia-Rinaldi R, Lefrak EA, Defore WW, Feldman L, Noon GP, Jachimczyk JA, et al. In situ preservation of cadaver kidneys for transplantation: laboratory observations and clinical application. *Ann Surg*. 1975; 182:576–84. [PubMed: 1103757]
11. Kohler TR, Nance DR, Cramer MM, Vandenburghe N, Strandness DE Jr. Duplex scanning for diagnosis of aortoiliac and femoropopliteal disease: a prospective study. *Circulation*. 1987; 76:1074–80. [PubMed: 3311451]
12. Lim S, Halandras PM, Park T, Lee Y, Crisostomo P, Hershberger R, et al. Outcomes of endovascular abdominal aortic aneurysm repair in high-risk patients. *Journal of vascular surgery*. 2015; 61:862–8. [PubMed: 25704411]
13. Guan J, Sacks MS, Beckman EJ, Wagner WR. Synthesis, characterization, and cytocompatibility of elastomeric, biodegradable poly(ester-urethane)ureas based on poly(caprolactone) and putrescine. *J Biomed Mater Res*. 2002; 61:493–503. [PubMed: 12115475]
14. Stankus JJ, Guan J, Wagner WR. Fabrication of biodegradable elastomeric scaffolds with sub-micron morphologies. *J Biomed Mater Res A*. 2004; 70:603–14. [PubMed: 15307165]
15. Szold A. Nitinol: shape-memory and super-elastic materials in surgery. *Surg Endosc*. 2006; 20:1493–6. [PubMed: 16858524]
16. Shabalovskaya SA. Surface, corrosion and biocompatibility aspects of Nitinol as an implant material. *Biomed Mater Eng*. 2002; 12:69–109. [PubMed: 11847410]
17. Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR). OPTN / SRTR 2012 Annual Data Report. Rockville, MD: Department of Health and Human Services, Health Resources and Services Administration; 2014.
18. Prakash, Mokhasi V, Rajini T, Shashirekha M. The abdominal aorta and its branches: anatomical variations and clinical implications. *Folia Morphol (Warsz)*. 2011; 70:282–6. [PubMed: 22117246]
19. Lote, C. Principles of Renal Physiology. 5. New York: Springer-Verlag; 2012.
20. Perko MJ, Nielsen HB, Skak C, Clemmesen JO, Schroeder TV, Secher NH. Mesenteric, coeliac and splanchnic blood flow in humans during exercise. *J Physiol*. 1998; 513(Pt 3):907–13. [PubMed: 9824727]
21. Algahim MF, Love RB. Donation after circulatory death: the current state and technical approaches to organ procurement. *Curr Opin Organ Transplant*. 2015; 20:127–32. [PubMed: 25719900]
22. Rady MY, Verheijde JL, McGregor J. Organ procurement after cardiocirculatory death: a critical analysis. *J Intensive Care Med*. 2008; 23:303–12. [PubMed: 18647817]
23. UNOS. Model Elements for Controlled DCD Recovery Protocols. editor: United Network for Organ Sharing; 2007. www.unos.org/wpcontent/uploads/unos/Appendix_B_AttachIII.pdf. In: https://www.unos.org/wpcontent/uploads/unos/Appendix_B_AttachIII.pdf
24. Gravel MT, Arenas JD, Chenault R 2nd, Magee JC, Rudich S, Maraschio M, et al. Kidney transplantation from organ donors following cardiopulmonary death using extracorporeal membrane oxygenation support. *Ann Transplant*. 2004; 9:57–8. [PubMed: 15478893]

Figure 1. An Organ Perfusion Stent compartmentalizes blood flow

(A) An OPS consolidates multiple branches into a single isolated organ compartment (Zone 2) that is separate from the systemic circulation (Zone 1). (B) **Cardiac Perfusion:** Blood from the heart passes through the large central lumen of the organ perfusion stent to perfuse the lower body and then returns through veins to the heart. (C) **Abdominal Perfusion:** Blood from a percutaneous venous cannula is oxygenated and pumped back to the external stent compartment where isolated visceral arterial branches are perfused.

Figure 2. A Commercial Hybrid OPS

An OPS was fashioned from commercial iliac limb seal zones, a covered stent and a perfusion lumen (the blue catheter is a placekeeper for a guidewire). The center lumen carries agonal bloodflow from the heart while the perfusion lumen delivers oxygenated blood to the external compartment. The stent is delivered through a standard endovascular sheath.

Figure 3. Angiography of an OPS *in vivo* illustrates the separate stent chambers
(A) Cardiac Perfusion: including the center lumen (dotted parallel lines), and top end of the stent (arrow). **(B) Abdominal Organ Perfusion:** The external chamber isolates perfusion of the four visceral vessels.

Figure 4. An OPS maintains perfusion in the agonal period

A dusky appearance consistent with malperfusion of the kidney (**A**) and liver (**C**) in a control animal after a 60 minute agonal period. By contrast, an animal treated with an OPS reveals normal color of the kidney (**B**) and liver (**D**) suggesting preserved perfusion.

Figure 5. A custom retrievable Organ Perfusion Stent (OPS)

(A) A “petal and stem” stent design includes “petals” that remain attached to a long “stem” to facilitate retrieval. The nitinol scaffold includes a narrower center section to create an external perfusion compartment (B) The stent covered with an electrospun PEUU. (C) Rapid retrieval of the OPS by advancement of the vascular sheath is demonstrated within a clear plastic conduit.

Figure 6. Demonstration of a modular perfusion lumen

(A) The stent shown alongside the 12 Fr perfusion lumen, which is guided over a wire (B) for modular docking with the main OPS for a fluid tight seal (C). The complete OPS after docking of the perfusion lumen.

Table 1

Cardiac function is not adversely impacted by OPS deployment

Comparing the values before and after OPS deployment in six animals, no significant change was observed in the HR, MAP, SvO2, or CVP. Small but significant decreases were observed in the CO (P=0.01) and RVEDV (P=0.05) which are not entirely unexpected given the offloading of visceral perfusion work.

	#1		#2		#3		#4		#5		#6		p-Value
	before	after	before	after	before	after	before	after	before	after	before	after	
HR	67	78	70	72	85	84	78	84	80	69	55	59	0.278
MAP	87	74	85	122	62	82	68	75	68	109	68	79	0.095
SvO2	84	78	70	88	97	97	90	88	83	95	88	79	0.629
CVP	15	8	9	8	12	12	6	6	9	8	20	18	0.179
CO	5.25	4.75	4.38	4.07	3.90	2.86	4.70	4.30	4.47	4.20	3.45	3.17	0.012
RVEDV	258	205	353	307	131	126	165	163	219	182	84	81	0.053