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Endovascular temporary vessel occlusion with a reverse thermo-sensitive polymer for bloodless minimal invasive renal surgery

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Abstract

Purpose—To demonstrate the feasibility of reversible vessel embolization using angiographic guidance for delivery of a rapid reverse thermo-sensitive polymer (RTP) to provide hemostasis as an aid for minimally invasive renal surgery in a porcine model.

Materials and Methods—After isolation of the left kidney of 7 anesthetized pigs (50–70 kg) using a surgical robot, a renal angiogram of both kidney was obtained. A 5F angiographic catheter was used to selectively embolize a lower pole segmental artery of the right and left kidney with a thermo-sensitive polymer (LeGoo-XL™, Pluromed). Distal and proximal embolization of the target vessel was compared. Degree and duration of hemostasis and reversibility was determined. After complete hemostasis was obtained angiographically, a partial robotic lower pole nephrectomy was performed on the left kidney only.

Results—Only proximal embolization provided controllable hemostasis. A 20% polymer concentration in a buffer solution of 40% saline and 40% iodine contrast by weight injected at room temperature resulted in a reproducible embolus for more than 30 minutes, the time needed to perform a partial nephrectomy. The radiographic appearance of the embolus was used to determine the total amount of polymer needed. Cold saline completely dissolved any residual polymer at the end of surgery.

Conclusions—Proximal arterial occlusion with a thermo-sensitive polymer can be rapidly reversed with selective intra-arterial infusion of chilled saline. Preceding nephron sparing surgery with transcatheter embolization of the relevant branch of the renal artery with the polymer can facilitate the procedure and ought to be investigated further.

INTRODUCTION

To date, an increasing number of renal malignancies are discovered partly due to improved imaging capabilities. Percutaneous ablative methods have gained acceptance in smaller

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lesions but surgery is still preferred in more complex and larger renal tumors. Nephron sparing surgery is the surgical method of choice if contralateral renal function is impaired. It has also gained greater acceptance for small, single, well localized tumors in patient with a normal contralateral kidney and has proven long term oncologic success (1,2). However, nephron sparing surgery is often still performed as open surgery due to its technical complexity and the difficulties related to clamping of the renal artery and prolonged warm ischemia (3–7). Transcatheter particle embolization of a renal mass prior to surgery is one of the proposed interventional methods to improve hemostasis facilitating minimal invasive surgery (8). Other surgical approaches to warrant blood free minimal invasive surgery have been propagated but these approaches usually increase the complexity of the surgery itself (9–11).

The rapid transition polymer (LeGoo-XL™ Pluromed, Woburn, MA, USA) is a fractionated version of a block copolymer commonly known as poloxamer, a nontoxic (12), non-ionic, biocompatible copolymer with a 70%/30% ratio of polyoxyethylene and polyoxypropylene. There is a well-established history of safe use of poloxamers. The unfractionated poloxamer is used as an emulsifying and solubilizing agents for drug delivery; examples of drugs that include poloxamer as an excipient include: Oraqix (a periodontal anesthetic gel), Zovirax (a topical cream active against herpes virus), Glyquin (decreases the formation of melanin), Methadose (narcotic pain reliever), and Neurontin (anti-epileptic medication) (13,14).

Fractionation of the poloxamer results in a polymer that exhibits rapid reverse thermo-sensitive properties, which make it functional as a temporary vascular occlusion device. LeGoo-XL transitions from liquid at low temperature to viscous gel at higher temperature; the rapid transformation occurs over a range of approximately 1° C starting at approximately 14° C and the viscosity of the gel at 37° C is approximately 1500 Pa s. The expansion coefficient upon gelling is 1.0, however there is a very slight increase in volume when gelling because the water in the product has a small expansion coefficient. The polymer mass reverts back to a liquid with cooling as the heat induced miscellation of the copolymer is reversed allowing the monomer to disperse in flowing blood. Once the monomer are dispersed and diluted they cannot return to a gel. The dissolution speed is dependant upon the surface to volume ratio of the micellated polymer mass. The monomer is excreted in urine with a half life of 25 hours (13,15). Preparations of this polymer injected directly into a target vessel through a larger bore cannula are also used to temporarily interrupt blood flow. Successful use of this approach has been reported during cardiothoracic surgery (15–19). The promising results using direct injection of the polymer into a target vessel led to the idea of a pre-surgical transcatheter embolization, which is the focus of this work.

Based on in vitro experiments, we identified two different embolization techniques using the reverse thermo-sensitive polymer (RTP). In the first method, the polymer can be prepared to obtain a liquid embolic agent targeting the peripheral arterial vasculature and capillary bed forming longer columns of gel in the periphery which propagate back towards the injection site. This type of embolization requires the injection of the polymer chilled to 2–3°C. We have termed this type of embolization “peripheral embolization”. In the second method, the polymer can be prepared as a viscous fluid that forms a plug at the tip of the angiographic catheter occluding the proximal portion of the target vessel. For this type of embolization the polymer is injected at room temperature. This type of embolization was termed “proximal embolization”.

The purpose of the present study was twofold: a) to determine whether blood flow after transcatheter embolization with LeGoo-XL can be promptly reestablished with transcatheter injection of chilled saline, and b) to establish whether transcatheter embolization with the polymer warrants further investigation as an aid to minimally invasive nephron sparing

surgery. Both proximal and peripheral occlusion of the renal vasculature were studied in a porcine model.

MATERIALS and METHODS

Animals

The study was approved by Lahey Clinic Institutional Animal Care and Use Committee.

Seven farm pigs (50–70 kg) were anesthetized with telazol, a combination of tiletamine hydrochloride and zolazepam hydrochloride (4.4mg/kg i.m.) and xylazine (2.2mg/kg i.m.). The animals were intubated with a cuffed endotracheal tube and mechanically ventilated. Anesthesia was maintained using isoflurane gas throughout the procedure. A central venous and arterial line was inserted after direct exposure of the left jugular vein and left common carotid artery. Heart rate, blood pressure, central venous pressure, body temperature, and oxygen saturation were recorded throughout the experiment. Blood pressure was titrated to a mean pressure of 90 mmHg using epinephrine (1:1000) as needed. 5000 units of heparine were injected intravenously prior to angiography.

The right femoral artery was exposed surgically and an 8 F vascular sheath (Terumo, Somerset, NJ, USA) was introduced and secured. The pigs were then placed in a left decubitus position and 5 intraperitoneal ports for the surgical robotic system (da Vinci® S HD robotic system, Intuitive Surgical, Sunnyvale, CA, USA) were created. The peritoneal reflection over the left kidney was removed to allow for better visual inspection and future robotic lower pole partial nephrectomy. The right kidney remained untouched. After isolation of the left kidney the surgical robot was undocked leaving the camera in place and a C-arm with angiographic capabilities was positioned.

Angiography was accomplished under C-arm fluoroscopy. The main right and left renal artery were catheterized with a 7F guiding catheter (Veripath, Abbott, Abbott Park, IL, USA). Heparinized saline was continually infused through the side arm of the introducer and a Tuohy-Borst type adapter (Rotating hemostatic valve 0.096", Abbott Vascular, CA) attached to the guiding catheter. Selective angiography of the renal artery was performed. A 5F angiography catheter (C2 Cobra Catheter, Cook, Bloomington, IN, USA) was coaxially introduced through the guiding catheter. The upper and lower polar arteries were catheterized in sequence and superselective angiograms obtained. The upper pole angiogram was used to identify any additional feeder to the lower pole. The superselective angiogram of the lower was performed to visualize the extent of the target area for embolization and the anticipated demarcation line.

LeGoo-XL was carefully injected under fluoroscopy through the angiographic catheter to avoid reflux into the main renal artery (Figure 1). The catheter was subsequently removed and a repeat angiogram through the guiding catheter was obtained to document its effect. In all animals, the right kidney was embolized first. Embolization was judged successful if the targeted portion of the kidney did not opacify on the selective renal angiogram. If the embolization was unsuccessful or an existing occlusion was recanalized, a repeat injection of the embolic agent was attempted. Reperfusion was defined as re-establishment of flow beyond arcuate arteries.

Embolization of the right kidney was documented by repeat angiograms in intervals of 1–5 minutes and time of occlusion and reperfusion were recorded. Shorter intervals were used in order to assess partial recanalization if fluoroscopy identified the beginning of dissolution of the polymer mass. Embolization of the left kidney was documented by fluoroscopy and direct visualization through the robot camera.

After visual (laparoscopic) and angiographic confirmation of satisfactory arterial occlusion of the left lower pole segmental artery for 5 minutes, the surgical robot was re-docked in order to perform a lower pole partial nephrectomy. The distal portion of the lower pole was resected (Figure 2). Upon completion of resection, the renal tissue was approximated over a hemostatic bolster versus primary capsular closure dependent on the size of the resected renal tissue. Intraoperative blood loss was estimated visually. If flow returned prematurely during resection the experiment was terminated and the animal sacrificed.

At the end of the successful surgical resection, the C-arm was repositioned and a control angiogram was performed. Dissolution of residual embolus was performed with documented injection of physiologic saline chilled to 2–3°C through the guiding catheter. After reperfusion of the targeted portion of the kidney was documented by a selective renal arteriogram the resection plane was observed through the robot camera for an additional 15 minutes to assess rebleeding before the animal was sacrificed. The remnant kidney was analyzed with H&E staining and histopathologic analysis.

Total amount of polymer injected, duration of occlusion and reversibility of embolization with cold saline injection were recorded for each kidney. The amount of injected polymer was determined as the total amount injected minus the priming volume of the 5 French angiographic catheter. The duration of occlusion was determined as the interval between angiographic demonstration of complete occlusion and either angiographic (right kidney) or angiographic and visual demonstration of complete reperfusion. Partial reperfusion was defined as a slow reappearance of the normal color and incomplete angiographic reperfusion of the targeted area with residual polymer mass in subsegmental arteries. Reversibility of embolization was achieved by injection of physiological saline chilled to 2–3°C after completion of the surgical procedure until complete dissolution of the polymer was documented with angiography. The chilled saline was used to cool the residual polymer mass in order to induce dissolution. The amount of saline injected was recorded.

Animal preparation, surgical approach and angiographic technique were identical in all animals.

Preparation of the polymer

The LeGoo-XL™ solution is formed by dissolving the purified polymer in physiologic saline and either contrast or tantalum. Exact concentrations of the polymer for each experiment are given in table 1.

Pilot experiments—For the initial experiment (fig 1) the polymer was mixed with physiologic saline as buffer and 1 g tantalum (Cordis, Bridgewater, NJ, USA) to provide fluoroscopic visualization. In all other experiments the polymer was mixed with buffer solution of physiologic saline and iodine contrast (Omnipaque 300, GE Healthcare). Different preparations of the mixture were tested. Iodine contrast was added in 10% increments of the total mass of the mixture from 20–50%, until adequate opacification was achieved while still maintaining the desired viscosity. Visualization of these different preparations was then assessed in fig 2 and 3.

In the first three animals all injections of the polymer were performed slowly (approximately 1cc/sec for 3 seconds) with the polymer chilled to 2–3°C. The cold polymer solution has a low viscosity similar to a liquid embolic agent allowing further penetration of polymer into the more distal and smaller arteries resulting in a peripheral embolization. To prevent heating of the polymer during the injection, the guiding catheter and the angiographic catheter were flushed with physiological saline chilled to 2–3°C prior to the injection of the polymer. The concentration of the polymer was varied between 15–20%.

In the next pig (pig 4) a more concentrated solution (17% LeGoo-XL™) was delivered at room temperature in order to create a proximal embolus. A rapid hand injection was used to inject the polymer. The rapid increase in viscosity of the polymer during the injection through the catheter limits the total amount of polymer that can be injected before pressure within the catheter prevents further injection.

Final experiments—Proximal embolization was employed in the remaining three animals (pigs 5–7). To allow sufficient volume to be injected in order to achieve the desired duration of occlusion, the rapid hand injection was followed by a subsequent injection using a custom manually powered screw driven injector resembling a balloon inflation device. This two-step injection system was employed in pigs 5–7. The concentration of the polymer was increased to 20%, still allowing rapid hand injection of a small volume of the embolic agent to form an initial embolus, with additional volume delivered via the screw driven injector. In these experiments, the rapid transition polymer was dissolved in a 40% Omnipaque 300, 40% physiologic saline solution (by weight) to enable adequate opacification of the polymer while maintaining appropriate solution viscosity.

Statistical analysis

Duration of embolization between peripheral (pig 1–3) and proximal embolization (pig 4–7) were compared using a Student t-test. Significance level was set at $p < .05$. All analysis were performed using the software SPSS 14.0 (SPSS inc, Chicago, IL, USA)

RESULTS

Anesthesia and surgical preparation of the seven male farm pigs (mean body weight 60.3 kg) was uneventful. Direct visualization of the left kidney showed excellent agreement with angiographic findings. If successful segmental artery embolization was achieved, the lower pole blanched immediately showing a clear demarcation line. The embolus either dissolved spontaneously or was completely dissolved via infusion of chilled saline. Reperfusion was seen as a reappearance of the normal color, and the corresponding angiogram showed complete reperfusion of the targeted area. Partial reperfusion which usually preceded complete reperfusion was seen as a slow reappearance of the normal color. The corresponding angiogram showed partial but incomplete reperfusion of the targeted area with residual polymer in subsegmental arteries.

Mixing the polymer with tantalum (pig 1) did not result in sufficient opacification for direct fluoroscopic visualization; increasing the concentration of tantalum resulted in a solution of excessive viscosity. The embolic effect of the injected polymer in pig 1 was assessed with repeat angiograms through the guiding catheter.

Adding iodine contrast to 20% by weight of the solution allowed direct visualization of the polymer if DSA techniques were used. Adding Omnipaque to 40% by weight in the final polymer preparation yielded sufficient contrast to fluoroscopically monitor the injection of the polymer (Figure 1). A higher concentration did not provide substantially better visualization as determined during experiment 2 and 3, but would further increase the viscosity of the polymer. The preparation of the polymer by weight used in the final experiments (pigs 5–7) was: 20% purified poloxamer, 40% iodine contrast, 40% physiologic saline.

Duration of hemostasis, temperature, concentration and total amount of polymer injected with the two different embolization techniques are given in table 1. Peripheral embolization, employed in pigs 1–3, required a higher volume of polymer compared to proximal embolization (2.1 ± 1.1 ml vs. 0.55 ± 0.17 , $p = 0.005$) to create arterial occlusion. Peripheral

embolization resulted in inconsistent ability to occlude, duration of occlusion and return of flow with the injection of iced saline. This is evidenced in pig 2, where embolization was highly variable and unsuccessful in 1 kidney, resulting in the need for a second injection. Early flow return within less than five minutes after injection of the embolic agent was observed in 4 kidneys, and resolution of the opacified polymer was incomplete despite the injection of iced saline in 2 kidneys (table 1). None of the experiments with peripheral embolization resulted in a stable embolization of the targeted area to allow surgical resection of the lower pole.

Proximal embolization was employed in pigs 4–7, using higher concentrations of the polymer at room temperature. In pig 4, the volume of polymer that could be injected with a single hand injection was limited by the fact that the angiography catheter occluded. This caused insufficient volume of polymer to be injected into the vessel (0.2–0.5 ml) and resulted in premature flow return in pig 4 after 17, 23 and 30 minutes for the respective injections.

In pigs 5–7, the combination of a rapid hand injection with a second screw driven injection using a handheld injector allowed delivery of 0.6ml (pig 5) or 0.7 ml (pig 6 and 7) of LeGoo-XL™, and yielded a robust embolus formation. After the formation of an initial small plug with a rapid hand injection, the embolus could be further expanded distally and proximally to the initial plug with the screw driven injection (Figure 1). Fluoroscopy was used to visualize the slow expansion of the plug and to prevent proximal expansion of the plug into a non-target area. This sufficient volume and robust embolus created a significantly longer duration of arterial occlusion (pig 5–7, 32 ± 2.5 minutes) compared to peripheral embolization (pig 1–3) (15 ± 10.8 , $p < .01$), consistent with the time estimated and needed to perform a lower pole partial nephrectomy (pig 6 and 7). After formation of the proximal embolus which usually surrounded the catheter tip, the angiographic catheter could be removed without any difficulties and did not dislodge the polymer mass. In the final two experiments (pig 6 and 7), robotic partial nephrectomy of the lower pole was performed with minimal blood loss of estimated less than 50 ml (Figure 2). In these cases, upon completion of the resection, an infusion of 20 ml of chilled saline through the angiographic catheter assured rapid and complete plug dissolution with return of flow (Figure 3).

Angiography showed capillary reperfusion, which was mildly delayed compared to the pre-embolization angiogram in some areas of the targeted lower pole. Histological examination using HE stains showed no signs of ischemic damage or embolus fragments in the non-resected portion of the lower pole which was not perfused during the experiment and the non-treated upper pole.

DISCUSSION

Nephron sparing surgery has gained a widespread acceptance for treatment of renal masses. Whereas laparoscopic or percutaneous probe ablative therapies find greatest use in smaller and exophytic lesions, partial nephrectomy is the method of choice for more complex solitary renal masses (20–22). Ideally, this surgery would remove the tumor bearing portion of the kidney leaving the remainder of the kidney untouched. Many open and minimally invasive techniques for partial nephrectomy depend upon clamping the main renal artery (5) thereby producing global warm ischemia of the entire kidney associated with increased acute and chronic renal failure (7). The alternative, not clamping the renal artery, risks a significant increase in blood loss imposing additional challenges especially if minimal invasive techniques are used (4). Minimizing the clamp time is a widely accepted goal of partial nephrectomy (23).

Raymond and coworkers investigated the possibility of transcatheter embolization using a preparation of 22% rapid reverse thermo-sensitive polymer injected at low temperatures into the main renal artery creating a polymer cast of the renal vascular tree (24). They observed variable times of occlusion ranging from 10–80 minutes with spontaneous reperfusion thereafter. In principle this approach is similar to our approach of peripheral embolization. As we targeted the lower pole, our catheter placement was more selective and total volume of polymer needed to occlude the vascular tree of the lower pole was smaller. This may explain to some extent why we observe earlier dissolution of the injected polymer. In 2 animals where we injected a larger volume (> 3ml) of polymer, dissolution was incomplete after 60 minutes which is in keeping with the observation reported by Raymond et al. Similar to their observation we found that parenchyma and vessels of the embolized kidney showed no histopathologic abnormalities.

This feasibility study demonstrates that a transcatheter embolization with a rapid reverse thermo-sensitive polymer can provide targeted hemostasis facilitating minimally invasive partial nephrectomy. The proposed method has several inherent benefits which are likely to outweigh any additional risks related to the angiography and the use of iodine contrast (25):

- Renal vascular dissection is not necessary thereby minimizing the risk of inadvertent renal vascular injury.
- Avoiding renal artery clamping in patients with renal atherosclerosis will reduce the risks of plaque rupture and a consequent shower of emboli.
- The angiographic proximal embolization allowed for very consistent and reversible targeted segmental occlusion in all three final experiments.
- Selective and temporary occlusion to a portion of kidney allowed resection in a relatively bloodless field.
- The uninvolved portion of the kidney remains perfused during the entire surgical procedure, reducing the risk of injury due to warm ischemia.

Vascular occlusion using a thermo-sensitive polymer has previously been evaluated for temporary coronary artery occlusion in the porcine model during coronary artery bypass grafting and excellent preliminary clinical results have been reported in a small series of patients undergoing coronary artery bypass grafting (n=10) and peripheral vascular bypasses (n=3) using LeGoo, a similar composition but tailored for coronary artery and peripheral artery temporary occlusion (16,17,19). In these applications the polymer was injected under direct visualization through a large bore needle to form a plug in the vessel. Similar to our observations there were no signs of ischemia in the targeted area after dissolution of the plug.

The injection of the polymer through a catheter mandated the addition of iodine contrast allowing visualization of the polymer under fluoroscopy. Adding 40% of iodine contrast provided sufficient contrast while maintaining the desired viscosity of the polymer. Using a catheter for the injection of the polymer has the potential to reach areas which are not accessible to direct needle access. However, as a certain length of the catheter is exposed to body temperature the polymer transforms from its liquid state at low temperatures to gel state while still in the catheter. A rapid hand injection followed by a screw driven second injection was needed to inject sufficient polymer to occlude the artery at the tip of the catheter. The rapid increase of viscosity precluded the use of higher concentration of the polymer as pressures needed to inject the polymer would exceed the catheter's specifications. The use of the polymer as a liquid embolic agent targeting peripheral arteries and the capillary bed did not result in stable and reversible hemostasis for two possible reasons. Injected at ice cold temperatures the polymer leaves the catheter in liquid state and

will be dissolved immediately, unable to polymerize if there is sufficient flow in the renal artery. The amount of dissolved and diluted polymer cannot be readily visualized and may be variable from kidney to kidney. Complete dissolution of the polymer is observed if a smaller amount is injected. Large amounts of polymer injected may create a complete obliteration of the peripheral and central arteries in the target area resulting in good hemostasis, but this complete occlusion was more challenging to reverse.

A coaxial technique is needed for a transcatheter application of the polymer as the angiography catheter which is used for injection will be occluded with polymer and needs to be withdrawn to be flushed outside the animal. The guiding catheter allows selective imaging of the renal artery and can potentially be used to occlude the main renal artery if necessary.

Our feasibility study has several shortcomings which will be addressed in further studies. Without a chronic survival model, long-term pathologic data related to the polymer's tissue effect is uncertain. A more refined histopathological examination may be required to rule out acute and chronic effects of ischemia. Possible effect of chilled saline on the endothelium may also have to be assessed; however perfusion of the kidney with chilled saline is a standard procedure during transplant and resective surgery.

The complex blood supply of larger tumors may require a more refined angiographic technique for embolization using smaller 3 and 4 French catheters. Plug formation using these catheters may need further adjustment of the polymer and the injection technique.

The hand injection requires some experience and may be a reason of possible failure to occlude the artery. A fully automated injection would help to standardize this procedure.

Our observations are based on a small number of animals and the final experimental set-up needs further confirmation in larger cohorts and different species.

Conclusion

Proximal arterial occlusion with a rapid reverse thermo-sensitive polymer can be rapidly reversed with selective intraarterial infusion of chilled saline. Preceding nephron sparing surgery with transcatheter embolization of the relevant branch of the renal artery with the polymer can facilitate the procedure and ought to be investigated further.

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References

1. Fergany AF, Hafez KS, Novick AC. Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year followup. *J Urol* 2000;163:442–5. [PubMed: 10647650]
2. Turna B, Kaouk JH, Frota R, et al. Minimally invasive nephron sparing management for renal tumors in solitary kidneys. *J Urol* 2009;182:2150–7. [PubMed: 19758655]

3. Gratzke C, Seitz M, Bayrle F, et al. Quality of life and perioperative outcomes after retroperitoneoscopic radical nephrectomy (RN), open RN and nephron-sparing surgery in patients with renal cell carcinoma. *BJU Int* 2009;104:470–5. [PubMed: 19239445]
4. Guillonnet B, Bermudez H, Gholami S, et al. Laparoscopic partial nephrectomy for renal tumor: single center experience comparing clamping and no clamping techniques of the renal vasculature. *J Urol* 2003;169:483–6. [PubMed: 12544293]
5. Haber GP, Gill IS. Laparoscopic partial nephrectomy: contemporary technique and outcomes. *Eur Urol* 2006;49:660–5. [PubMed: 16504373]
6. Thompson RH, Blute ML. At what point does warm ischemia cause permanent renal damage during partial nephrectomy? *Eur Urol* 2007;52:961–3. [PubMed: 17499424]
7. Thompson RH, Frank I, Lohse CM, et al. The impact of ischemia time during open nephron sparing surgery on solitary kidneys: a multi-institutional study. *J Urol* 2007;177:471–6. [PubMed: 17222613]
8. Vallati, GPG.; Carpanese, L.; Kajal, R.; Crecco, M. ECR: European Radiology. 2009. Role of supraseductive renal tumor transcatheter embolization before laparoscopic partial nephrectomy: Methods, safety and efficacy; p. P205
9. Crain DS, Spencer CR, Favata MA, Amling CL. Transureteral saline perfusion to obtain renal hypothermia: potential application in laparoscopic partial nephrectomy. *JSLs* 2004;8:217–22. [PubMed: 15347107]
10. Janetschek G, Abdelmaksoud A, Bagheri F, Al-Zahrani H, Leeb K, Gschwendtner M. Laparoscopic partial nephrectomy in cold ischemia: renal artery perfusion. *J Urol* 2004;171:68–71. [PubMed: 14665846]
11. Moizadeh A, Hasan W, Spaliviero M, et al. Water jet assisted laparoscopic partial nephrectomy without hilar clamping in the calf model. *J Urol* 2005;174:317–21. [PubMed: 15947682]
12. Singh-Joy SD, McLain VC. Safety assessment of poloxamers 101, 105, 108, 122, 123, 124, 181, 182, 183, 184, 185, 188, 212, 215, 217, 231, 234, 235, 237, 238, 282, 284, 288, 331, 333, 334, 335, 338, 401, 402, 403, and 407, poloxamer 105 benzoate, and poloxamer 182 dibenzoate as used in cosmetics. *Int J Toxicol* 2008;27 (Suppl 2):93–128. [PubMed: 18830866]
13. Boodhwani M, Cohn WE, Feng J, et al. Safety and efficacy of a novel gel for vascular occlusion in off-pump surgery. *Ann Thorac Surg* 2005;80:2333–7. [PubMed: 16305901]
14. Dumortier G, Grossiord JL, Agnely F, Chaumeil JC. A review of poloxamer 407 pharmaceutical and pharmacological characteristics. *Pharm Res* 2006;23:2709–28. [PubMed: 17096184]
15. Goddeeris C, Van den Mooter G. Free flowing solid dispersions of the anti-HIV drug UC 781 with Poloxamer 407 and a maximum amount of TPGS 1000: investigating the relationship between physicochemical characteristics and dissolution behaviour. *Eur J Pharm Sci* 2008;35:104–13. [PubMed: 18644442]
16. Aubin MC, Bouchot O, Carrier M, Cohn WE, Perrault LP. Temporary internal thoracic artery occlusion during off-pump coronary artery bypass grafting with the new poloxamer P407 does not cause endothelial dysfunction. *J Thorac Cardiovasc Surg* 2006;132:685–6. [PubMed: 16935129]
17. Bouchot, O.; Steinmetz, E.; Berne, J. Novel Use of a Gel for Temporary Vascular Occlusion during Surgery of Small Vessels in Human: Preliminary Results. International Society of Minimally Invasive Cardiothoracic Surgery; Boston, MA. 2008;
18. Bouchot O, Aubin MC, Carrier M, Cohn WE, Perrault LP. Temporary coronary artery occlusion during off-pump coronary artery bypass grafting with the new poloxamer P407 does not cause endothelial dysfunction in epicardial coronary arteries. *J Thorac Cardiovasc Surg* 2006;132:1144–9. [PubMed: 17059936]
19. Boodhwani M, Feng J, Mieno S, et al. Effects of purified poloxamer 407 gel on vascular occlusion and the coronary endothelium. *Eur J Cardiothorac Surg* 2006;29:736–41. [PubMed: 16626965]
20. Lane BR, Novick AC. Nephron-sparing surgery. *BJU Int* 2007;99:1245–50. [PubMed: 17441918]
21. Martorana G, Lupo S, Brunocilla E, Concetti S, Malizia M, Vece E. Role of nephron sparing surgery in the treatment of centrally located renal tumors. *Arch Ital Urol Androl* 2004;76:51–5. [PubMed: 15270413]
22. Peycelon M, Hupertan V, Comperat E, et al. Long-term outcomes after nephron sparing surgery for renal cell carcinoma larger than 4 cm. *J Urol* 2009;181:35–41. [PubMed: 19012929]

23. Nguyen MM, Gill IS. Halving ischemia time during laparoscopic partial nephrectomy. *J Urol* 2008;179:627–32. [PubMed: 18082215]
24. Raymond J, Metcalfe A, Salazkin I, Schwarz A. Temporary vascular occlusion with poloxamer 407. *Biomaterials* 2004;25:3983–9. [PubMed: 15046888]
25. Kaufmann TJ, Huston J 3rd, Mandrekar JN, Schleck CD, Thielen KR, Kallmes DF. Complications of diagnostic cerebral angiography: evaluation of 19,826 consecutive patients. *Radiology* 2007;243:812–9. [PubMed: 17517935]

Figure 1.

Images are showing the right kidney of pig 6. The 5F catheter is advanced into the lower pole artery through the guiding catheter in the main renal artery (a). The radiopaque polymer is injected with a forceful manual injection creating an initial plug (b, arrow head) which is further expanded using a screw driven injection with a handheld injector (c, arrow head). An angiogram post embolization demonstrates complete occlusion of the lower pole renal artery with unimpaired perfusion of the upper pole of the kidney. A small amount of contrast is seen around the proximal portion of the plug (d, arrow head).

Figure 2.

The peritoneal reflection over the left kidney was removed to allow for better visual inspection and future robotic lower pole partial nephrectomy (a). After complete occlusion of the segmental artery the lower pole blanched. The distal portion of the lower pole is resected and the cutting plane is free of blood (b).

Figure 3.

Initial (a) and selective angiograms (b) show catheter positioning and the extent of the target area. After injection of the polymer, which can be seen as a small plug in the lower pole renal artery (c, arrow head), the upper pole perfusion remains unimpaired. At the end of the surgical resection complete organ perfusion is restored with the injection of cold saline. The surgical defect after resection of a portion of the lower pole is seen. (d, arrow heads).

Table 1

Summary of data.

Pig/Side	RTP (%/ml)	(°C)	Occlusion	Comment
1R	15%/3.2ml	0	>20 min peripheral	Mono phase injection. Segmental occlusion but flow slow to return despite cold saline infusion (50 ml), 70% reperused at 20 min.
1L	15%/1ml	0	7 min peripheral	Mono phase injection. Segmental occlusion but premature flow return during re-docking of surgical robot. No resection performed
2R	15%/0.7ml	0	0 min peripheral	Mono phase injection. No occlusion.
2R	15%/1.7ml	0	27 min peripheral	Second injection re-occluded lower pole for 27 min.
2L	15%/1.7ml	0	6 min peripheral	Mono phase injection. Segmental occlusion but premature flow return after short duration during re-docking of surgical robot. No resection performed.
3R	15%/2.7ml	0	10 min peripheral	Mono phase injection. Segmental occlusion but premature flow return.
3R	15%/4.2ml	0	30 min peripheral	Mono phase injection. Segmental occlusion for 10 min. Incomplete polymer dissolution despite cold saline infusion (50ml) after 60 min.
3L	20%/2.2ml	2	20 min peripheral	Mono phase injection. Segmental occlusion. Premature flow return during resection.
4R	17%/0.4ml	20	17 min proximal	Mono phase injection. Segmental occlusion but premature flow return after 20 min.
4R	17%/0.2ml	20	30 min proximal	Mono phase injection. Segmental occlusion for 30 minutes. Natural return of flow at 30 minutes.
4L	17%/0.5ml	20	23 min proximal	Mono phase injection. Segmental occlusion. Premature return of flow during resection after 23 minutes.
5R	20%/0.6ml	20	33 min proximal	<u>Two phase injection.</u> Segmental occlusion. Return of flow upon infusion of cold saline at 33 minutes (20 ml).
5L	20%/0.6ml	20	30 min proximal	Two phase injection. Segmental occlusion. Natural return of flow at 30 minutes. Pig died before repeat occlusion and resection was attempted.
6R	20%/0.7ml	20	35 min proximal	<u>Two phase injection.</u> Segmental occlusion. Natural return of flow at 35 minutes.
6L	20%/0.7ml	20	30 min proximal	<u>Two phase injection.</u> Segmental occlusion and partial nephrectomy (estimated blood loss < 50ml). Return of flow with chilled saline(20 ml).
7R	20%/0.7ml	20	30 min proximal	<u>Two phase injection.</u> Segmental occlusion. Return of flow with infusion of cold saline (20 ml).
7L	20%/0.7ml	20	35 min proximal	<u>Two phase injection.</u> Segmental occlusion and partial nephrectomy (estimated blood loss < 50ml). Return of flow with infusion of cold saline (20 ml).

Concentration and amount of injected reverse thermo-sensitive polymer (RTP), the temperature of the polymer before the injection and the duration and location (peripheral vs. proximal) of occlusion are listed for each kidney separately. Embolization was repeated if flow was prematurely reestablished.