Heart, Lung and Circulation (2019) **28**, 1292–1300
1443-9506/04/$36.00
https://doi.org/10.1016/j.hlc.2018.06.1050

ORIGINAL ARTICLE

Development of a Porcine Model of Coronary Stenosis Using Fully Percutaneous Techniques Suitable For Performing Cardiac Computed Tomography, CT-Perfusion Imaging and Fractional Flow Reserve

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Received 9 January 2018; received in revised form 18 June 2018; accepted 26 June 2018; online published-ahead-of-print 11 July 2018

Background The aim of this study was to develop and describe percutaneous coronary angiographic techniques to create a porcine model of acute coronary stenosis with methacrylate plugs that can by assessed using fractional flow reserve (FFR), invasive coronary angiography and coronary computed tomographic (CT) perfusion imaging without introducing artefacts associated with surgical models.

Methods Following animal care and institutional approval and using percutaneous coronary catheterisation techniques within an animal laboratory we introduced precision drilled methacrylate plugs into one of the three main coronary arteries of 10 experimental female pigs. Coronary pressure wire measurements were performed across the experimental stenosis for the calculation of FFR. Invasive coronary angiograms were obtained in stenosed arteries. Animals were transported to a dual source CT scanner (Siemens Healthcare, Forcheim, Germany) and CT perfusion imaging was performed.

Results Ten (10) pigs were investigated with seven data sets obtained. Three (3) pigs expired prior to CT imaging secondary to pneumothorax, high grade coronary stenosis with induced cardiac arrhythmia and iatrogenic air embolism. Graded coronary stenosis was produced in six pigs in the LAD (2), LCX (2) and RCA (2) territories and one animal served as a control. Fractional flow reserve ranged from 0.21 to 0.91. Myocardial blood flow derived from dynamic CT perfusion imaging ranged from 3.5 to 136.7 ml/100 ml of tissue/minute. No artefacts from the deployment of the methacrylate plug, nor the plug itself, were identified.

Conclusions Fully percutaneous preparation of a pig model of acute coronary stenosis is feasible and provides subjects for imaging that are free of surgically induced artefact. This technique is substantially less expensive than

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surgically induced coronary stenosis and can be performed using standard catheterisation techniques with mobile imaging equipment. The technique is extendable to produce multivessel acute coronary stenosis and can be used for multimodality imaging.

Keywords Animal model • Methacrylate • Fractional flow reserve • CT angiography

Introduction

Similarities between the cardiovascular anatomy and physiology of humans and swine have made swine a commonly used experimental model for the study of human cardiovascular diseases [1]. Investigation of computed tomographic (CT) perfusion imaging techniques would benefit from an animal model that does not introduce artefact that may influence evaluation of the myocardium. Previous experimental studies of coronary stenoses have used either long-term endothelial trauma plus an atherogenic diet to produce coronary lesions [2], or short-term surgical techniques to introduce balloon catheters or external narrowing agents (hydraulic compression devices, ligatures) to simulate coronary stenosis/blockage [3–5]. These techniques often do not produce the desired anatomical lesion and may introduce substantial artefacts (surgical clips, mediastinal air, haemorrhage, abnormal fluid collections) that degrade subsequent cardiac imaging studies.

In a collaborative investigation at our institution we developed a technique for producing methacrylate plugs with precision drilled holes which are introduced into target coronary arteries of live subject animals to simulate coronary stenoses. The procedure is performed with full percutaneous access and does not require surgical intervention. In this report, we outline the methodology of the technique and describe our initial success in implementing it in a study of coronary CT perfusion.

Methods

Preparation of Methacrylate Plug

Methyl methacrylate is an organic compound which, prior to polymerisation, is a colourless liquid formed by the methyl ester of methacrylic acid. Since 1955 [6] it has been used extensively for the production of vascular corrosion casts, most commonly in the form of Batson's No. 17 Plastic Replica and Corrosion Kit (Polysciences Inc., Warrington, PA, USA) [7]. Since methacrylate has a density essentially identical to non-contrast enhanced blood it is not detectable on non-contrast enhanced CT images [8]. Thus, plugs with holes drilled through them are useful for modelling non calcified coronary stenoses in cardiac CT experimental animal studies.

Methacrylate plugs are formed by placing the mixed monomer, catalyst and promoter within a form to produce a cast [9]. There is 30 minutes of working time before the polymer hardens. It is fully cured in 2–3 hours.

Methacrylate plugs were moulded for pig coronary arteries in this experiment by injecting the liquid polymer into 13 cm long 10 Fr, 12 Fr and 14 Fr Check-Flo® femoral access sheaths (Cook Medical, Bloomington, IN, USA). The sheaths have internal diameters of 3.40 mm, 4.11 mm and 4.78 mm respectively. When cured, the resulting methacrylate rods were removed and sliced into 7 mm and 4 mm lengths. Precision 1 mm holes were drilled to create a central lumen. Holes were enlarged using 1.58 mm and 1.98 mm drills to produce a selection of stenoses of varying severity (Figures 1 and 2). The cut leading edges of the drilled plugs were rounded using fine grade sandpaper to reduce vascular endothelial trauma as they were advanced into the target coronary artery.

Preparation of the Animal and Procedural Suite

The study was approved by the University of British Columbia Animal Experimentation Committee (UBC Animal Care Certificate A12-0048) and was carried out according to the

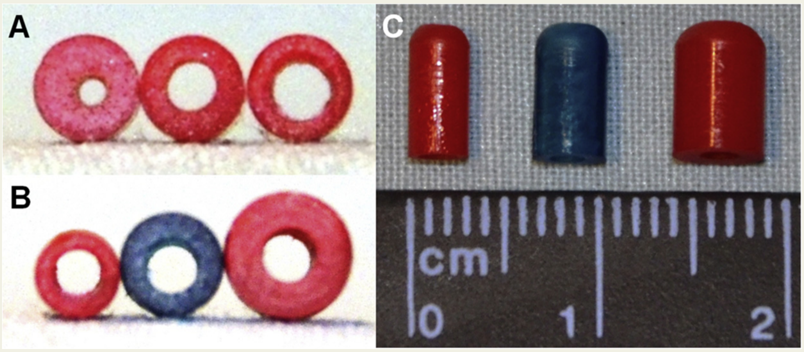

Figure 1 The methacrylate plugs were first cast in sheaths producing 3.3 mm, 4.0 mm and 5.0 mm diameter rods (Panel A). Each size rod was precision bored with a 1 mm, 1.5 mm or 1.98 mm drill (Panel B) creating anatomical stenoses ranging from 40–96%. The plugs were cut into 7 mm lengths and bevelled on the leading edge (Panel C) to facilitate entry into the access sheath and deployment into the coronary artery.

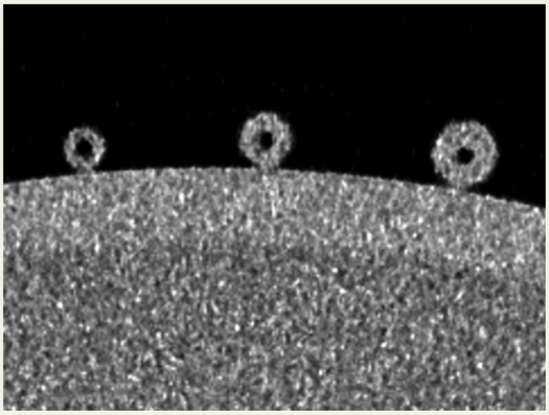

Figure 2 The methacrylate plugs of 3.3 mm, 4.0 mm and 5.0 mm diameter (each with a 1 mm lumen) imaged taped to the side of a standard body phantom.

Canadian guidelines for use and care of animals. Following assessment by animal care staff, 40–60 kg female Yorkshire pigs were brought to the animal laboratory attached to our facility. All animals were pre-treated with oral clopidogrel 600 mg 24 hours prior to the experiment. In the holding area, the animals were initially anaesthetised using an IM injection of ketamine (20 mg/kg). They were then intubated and ventilated with anaesthesia maintained using halothane. The subjects received maintenance IV fluid support (rate 10 mL/kg/hr) via a cannula in an ear vein. Buprenorphine SQ at 0.01 mg/kg was given as required for analgesia as assessed by the animal care technician. Anaesthesia was maintained using both the gas anaesthetic and intravenous propofol (diprivan, 3–4 mg/kg/hr). Once stabilised and instrumented the subjects were secured in a supine position to an operating room (OR) table and imaged using a mobile C arm fluoroscopy unit (GE Medical Systems, Milwaukee, WI, USA). The fluoroscopy C arm was positioned on the left side of the subject with imaging monitors at the foot of the OR table. An invasive pressure monitor was positioned above the C-arm and connected to the pressure manifold for continuous BP monitoring during the procedure. A hand held SonoSite® ultrasound unit (SonoSite, Inc. Washington, DC, USA) was available at the foot of the bed to assist in locating femoral vessels. This set-up allowed the primary operator to perform the invasive procedure from the subject's right side with an assistant positioned on the left (Figure 3).

Cannulation of the Femoral Vessels

The general orientation of the pig femoral artery and vein mimics human anatomy. However, due to differences in pelvic anatomy and the depth of pelvic vessels, we found that human vascular landmarks and vessel palpation could not be successfully used for localisation. Hand-held vascular ultrasound guidance targeted to the inguinal crease was used to assist in location and cannulation of the femoral artery and vein using a modified Seldinger technique.

The femoral vein was cannulated using 10 cm long 7 Fr sheath (Terumo Corporation, Tokyo, Japan). In the first two studies, due to the depth of the femoral vein and the acute angle of insertion, the sheath backed out of the femoral vein during contrast injections. Therefore, for the succeeding eight subjects a 5 Fr Beacon® Tip Royal Flush® Plus High-Flow multi side hole straight catheter (Cook Medical) was passed up the inferior vena cava with the tip positioned in the supra renal IVC and contrast media delivered.

The femoral artery was initially cannulated using a 10 cm long 7 Fr sheath (Terumo Corporation). This sheath was too small for the introduction of the methacrylate plugs and was up-sized over a stiff guidewire (Amplatz Extra-stiff wire, Cook Medical). Over the stiff guidewire a 13 cm long 12 Fr or 14 Fr Check-Flo® femoral sheath (Cook Medical) (Figure 4) was placed. The size of sheath was chosen to be matched to the size of the sheath used to produce the methacrylate plug. We

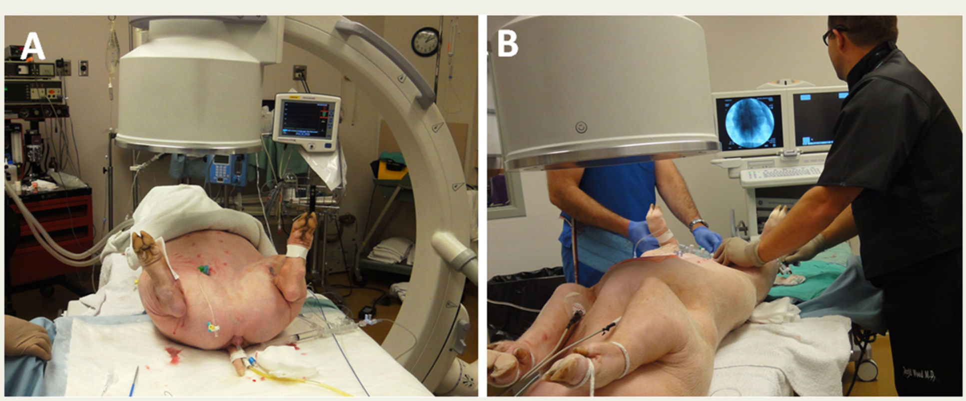

Figure 3 The set-up of equipment in the fluoroscopy procedural suite. (A) A blood pressure monitor and intravenous (IV) pole with burettes containing heparinised saline and contrast was placed on the left above the C-arm and connected to a manifold for invasive pressure monitoring and contrast injections by the operator's assistant also standing at the subject's left. (B) The primary operator worked from the right side through right femoral access. Fluoroscopy monitors at the foot of the bed ensure both the primary operator working on the subject's right and assistant working on the left can easily view live fluoroscopy images during the procedure.

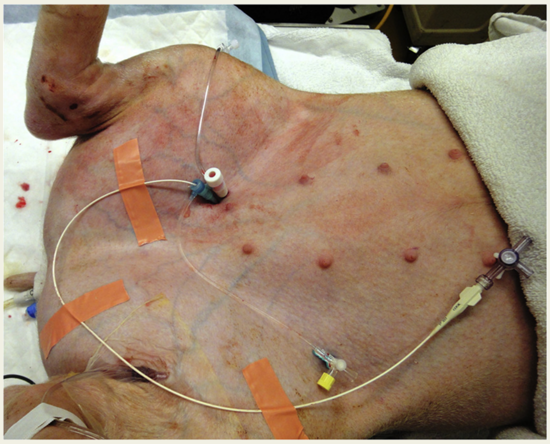

Figure 4 Final placement of access sheaths. In the right inguinal crease a 12 Fr sheath (white cap) is in the femoral artery for placing the methacrylate plug. An 8 Fr sheath (blue cap) in the femoral vein contains a 5 Fr straight tip catheter for administering contrast. Adenosine can be administered through the side port (yellow cap) of the venous sheath.

found that plugs produced using a 12 Fr forming sheath would still pass though 12 Fr access as there is some retraction of the methacrylate as it hardens. If the plug diameter was to be chosen following sheath placement, a 14 Fr sheath was placed. We noted that the depth of the femoral artery often introduced a sharp bend in the access sheath which did not affect small sheaths but caused difficulty in the passage of larger sheaths when standard 0.038″ J-wires were used for the sheath exchange. Careful predilatation with an introducer over the Amplatz extra-stiff wire and the use of fluoroscopy to ensure there is no kinking of the wire that could cause tearing of the iliac artery (Figure 5) led to no issues with sheath placement. Once placed, the sheaths were sutured into position for safety during transport.

Once the access sheaths were deployed, intravenous heparin was administered. Whilst coagulation is similar between humans and pigs [10,11] we found the dose required to prevent thrombosis of the catheter equipment was increased compared to humans. After early thrombotic events with our second and third subjects at standard dosing we subsequently administered 8,000 units at femoral cannulation, 8,000 units at the time the methacrylate plug was deployed and a further 8,000 unit bolus if the procedure was prolonged or if there was evidence of clot in the catheter equipment.

Cannulation of the Coronary Arteries

The technique for engaging the coronary arteries is analogous to the procedure in humans. A guide catheter with an attached Tohey access device (COPILOT Bleedback Control Valve, Abbott Vascular, CA, USA) was used to allow contrast injection through the Tohey sideport and wire manipulation. The relatively shallow aortic arch and the orientation of the coronary ostia in the pig make cannulation with traditional Judkins coronary catheters extremely difficult. Prior experience had found the optimal catheter to be the Hockey Stick (HS) guide (Figure 6). This allowed for selective engagement of either left or right coronary artery origins.

Once engaged in the coronary ostia, hand injected contrast angiograms were performed to provide a roadmap to determine which vessel would be most easily cannulated and to determine methacrylate plug diameter. Although this decision was influenced by individual pig coronary anatomy, within our study cohort all three coronary territories (left anterior descending, left circumflex and right coronary artery) were successfully cannulated.

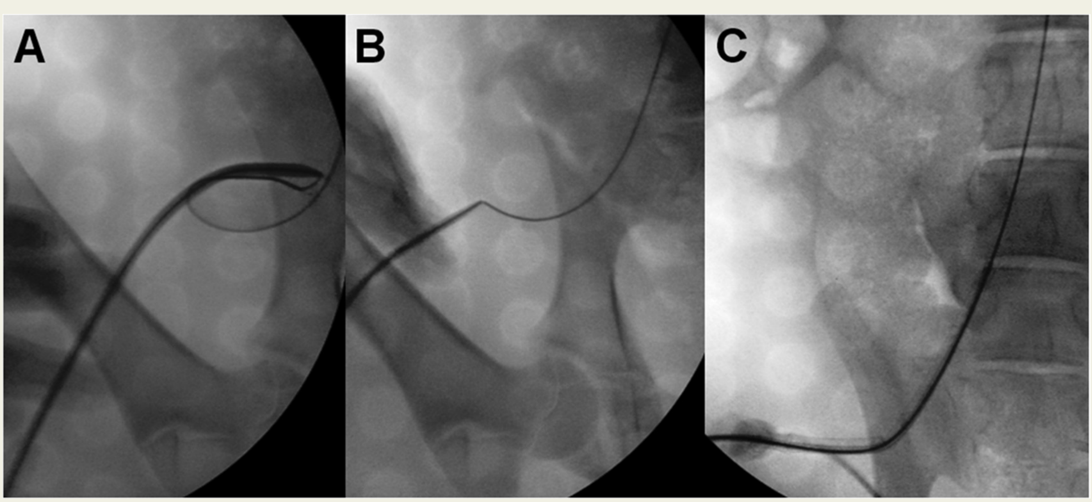

Figure 5 Fluoroscopy of the sheath exchange. While attempting an exchange with a standard J-wire the angle of insertion into the artery has caused a kink in the wire that produced resistance to passage of the 12 Fr introducer. Fluoroscopy showed the wire looped in the artery (A). The wire was withdrawn and straightened but the kink remained (B). A 6 Fr introducer was carefully passed into the vessel and with traction the kinked wire was removed and replaced with an extra stiff wire. The 12 Fr sheath was passed easily over this wire (C).

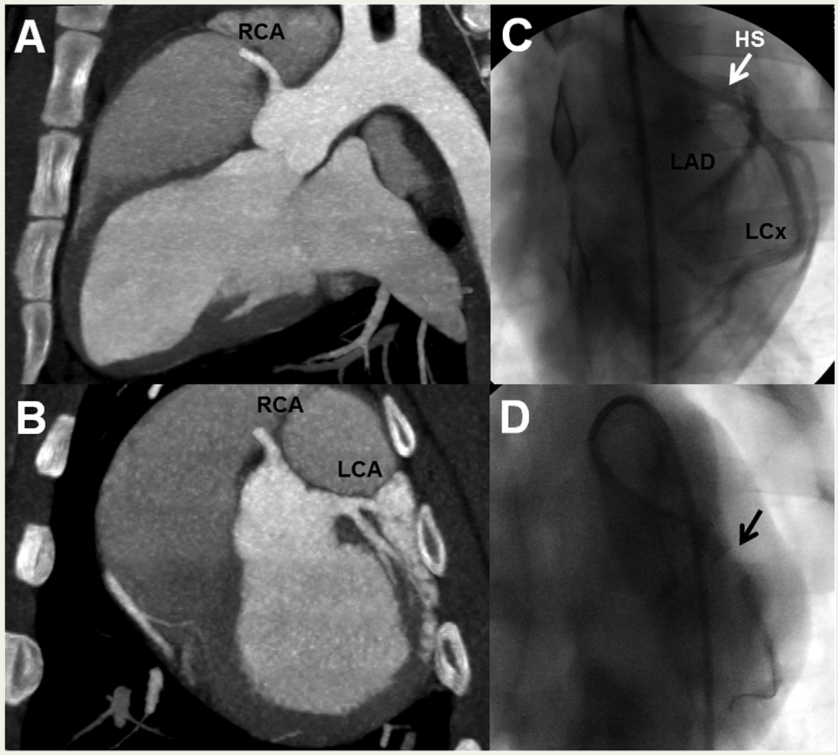

Figure 6 The porcine aortic arch requires a Hockey Stick guide to selectively engage the coronary arteries. The arch is shallow in sagittal plane (panel A) compared to human anatomy. In coronal plane (panel B) the right coronary artery (RCA) arises superiorly while the left coronary artery arises from a horizontal lateral position. The Hockey Stick (HS) guide (in coronal plane in panel C) engages the left coronary artery and allows placement of a methacrylate plug (panel D – arrow) into the circumflex artery.
Abbreviations: LAD, left anterior descending artery; LCx, left circumflex artery.

Introducing the Methacrylate Plug

Since we were interested in measuring fractional flow reserve (FFR) following plug placement, the target vessel was initially wired using a Certus™ PressureWire™ (St Jude Medical, Uppsala, Sweden). In the first subject, we found this wire alone did not give sufficient support during catheter exchange so a second Balance Middle-Weight (BMW) (Abbott Vascular) wire was also passed. Using fluoroscopic guidance to ensure the two guidewires remained deep in the distal target coronary artery, the HS guide was disengaged and removed. If the distal wire position was lost and could not be re-established the HS guide was re-introduced and the wires repositioned in the distal coronary vessel. With the HS guide removed, the methacrylate plug was threaded over the two guidewires. The HS guide was then rethreaded on the guidewires and used to push the plug into the target coronary artery (Figure 7). The plug was successfully advanced past acute bends or kinks using a combination of firm advancing pressure on the HS guide, gentle traction on the access sheath and fluoroscopic guidance. While the methacrylate plug was not visible using fluoroscopy, the radio-opaque tip of the HS guide was used as a marker. Using fluoroscopy, the stable distal coronary position of the two guidewires was confirmed during delivery of the plug through the vascular system. Migration of the guidewires out of the distal coronary artery into the proximal coronary artery or aorta occasionally occurred as the HS guide traversed the sheath, pelvis or aortic arch. Alternately, guidewire loops were occasionally formed in the aortic arch or left ventricle as the HS guide was pushed forward. When the HS guide encountered these loops it caused rapid loss of distal wire position in the coronary artery. Loss of guidewire position during delivery of the plug was a major problem as the plug could not be retrieved and uncontrollably embolised into the distal systemic circulation. Gentle traction to maintain guidewire position during plug delivery combined with removal of the Tohey attached to the HS guide minimised these guidewire position problems. Subtle manipulation and torqueing of the HS guide facilitated smooth transition from the aorta into the coronary ostia. Once the plug engaged the coronary artery it was usually pushed distally until it was wedged by antegrade coronary blood flow. Hand injections of contrast media were useful to show the position of the plug relative to the HS guide and coronary artery. If the plug did not migrate spontaneously to the wedged position, it was pushed distally by the HS guide. Coronary angiograms

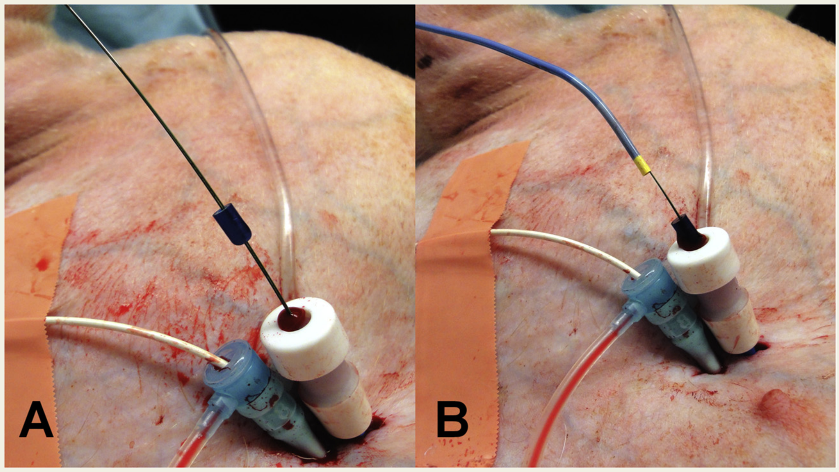

Figure 7 Sequence for introducing the methacrylate plug. The guide catheter is withdrawn with the guidewires still in-situ in the target coronary vessel. The methacrylate plug is threaded over the wires (A) and the guide catheter re-introduced behind it to act as a pusher (B). The plug has a bevelled leading edge to facilitate its passage through the haemostatic valve on the sheath and minimise trauma to the endothelium as it passes around the aortic arch and into the ostium of the target vessel.

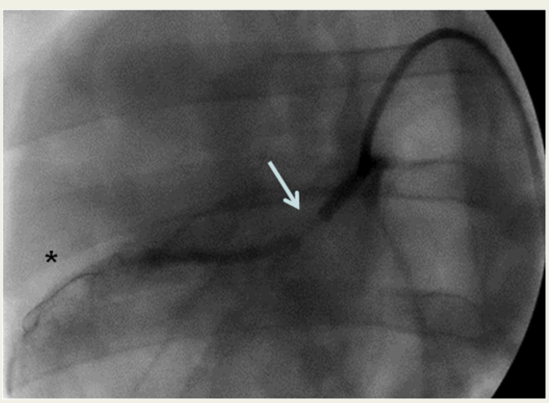

Figure 8 The methacrylate plug (arrow) is deployed in the left anterior descending artery. The guidewires (asterisk) are still in the distal vessel.

were obtained using hand injections through the HS guide to confirm the final position of the plug (Figure 8). Once the wedged plug position was confirmed 8,000 IU of heparin was administered and the BMW support wire was removed. For this study, coronary artery FFR pressure measurements were made distal and proximal to the plug during an intravenous adenosine infusion (Adenoscan, Sanofi-Aventis, France) at 180 μg/kg/min using a Radi Analyzer® console (St. Jude Medical Inc., St. Paul, MN, USA).

Once the FFR measurements had been obtained, a mobile monitoring unit was attached to the femoral artery sheath for continuous monitoring of haemodynamics during transport and in the CT scanner. Gas anaesthesia was discontinued and anaesthesia was maintained using bolus injections of IV propofol administered by the animal care technician. The animal was transferred to a transport trolley, ventilated by hand using an Ambu® bag (Ambu Australia, Warriewood, NSW, Australia) and draped in a fashion to allow visual monitoring.

Procedure at the CT Scanner

The animal was transferred from the trolley and placed head first in the left lateral decubitus position on the CT scanner table (Siemens Definition Flash, Siemens Medical Solutions, Forcheim, Germany) (Figure 9). Computed tomographic scanner electrocardiogram (ECG) input wires were connected to four ECG pads and the tracings automatically interrogated for the largest signal. Continuous IV propofol anaesthesia was introduced using an infusion pump. The animal was hand ventilated using an Ambu® bag and anaesthesia continuously monitored by the animal care technician. An intravenous (IV) pole was positioned next to the CT gantry with an IV pump for administering adenosine via the side port of the femoral venous sheath. All CT scans were obtained in suspended respiration to simulate clinical breath holds. Intravenous contrast media (Optivue 370, Bracco Diagnostics, Ontario Canada) was delivered into the IVC below the right atrium using a 5 Fr Beacon® Tip Royal Flush® Plus High-Flow multi side hole straight catheter. Contrast enhanced CT acquisitions were performed to assess myocardial perfusion (Figure 10). For dynamic CT perfusion the CT scanner rapidly alternated between two table positions to produce repeated imaging of the myocardium over time (anatomic coverage of 73 mm z-axis with detector width of 38 mm, and a 10% overlap between both acquisition ranges). Gantry rotation time was 285 msec, slice collimation 32 × 1.2 mm and tube voltage 100 kV. Contrast was injected in a monophasic bolus of 60 ml @ 6.5 ml/s via the catheter in the supra-renal inferior vena cava (IVC). Data acquisition began with the contrast injection and lasted 30 seconds. On

Figure 9 Set-up for performing cardiac computed tomographic (CT) perfusion studies on an animal subject. The animal is positioned on the gantry in the left lateral decubitus position to allow access at the head end for staff to perform ventilation via Ambu bag (not shown). The intravenous anaesthesia pump is on the floor. An intravenous (IV) pump is positioned next to the gantry to deliver an adenosine infusion via the femoral vein sheath side-port. The pressure manifold and monitor from the operating suite are brought to the CT suite and positioned next to the IV pump for continuous monitoring via the femoral arterial sheath. A heart rate and oxygen saturation monitor is sitting on the scanner table. The pressure injector is connected to the multi-side hole catheter positioned in the supra-renal inferior vena cava. All monitors face the CT control room.

completion of the CT imaging protocol the animal was euthanised in the CT suite and returned to the animal laboratory.

The CT perfusion data was evaluated on a dedicated Siemens multi-modality workplace workstation. Dynamic CT perfusion data was analysed using the Volume Perfusion CT Myocardium package. Regions of interest were drawn within the myocardium in areas representing stenosed coronary territories to produce myocardial blood flow data.

Results

The procedural results for our study are listed in Table 1. All subjects had successful femoral access cannulation and insertion of the methacrylate plug into the arterial vasculature. One subject did not have final placement of the plug in the coronary artery due to fluoroscopy imaging equipment failure. Three (3) of the first four subjects expired prior to completing the CT imaging protocol secondary to respiratory and coagulation problems. All subjects completing the protocol received either 16,000 or 24,000 units of heparin. The invasive FFR ranged from 0.21 to 0.91. The myocardial blood flow derived from dynamic CT perfusion imaging ranged from 3.5 to 136.7 ml/100 ml of tissue/minute. No artefacts from the deployment of the methacrylate plug, nor the plug itself, were identified.

Discussion

Animal models are highly desirable for investigation of CT techniques as multiple comparative studies can be performed in a single subject without the limitation of intravenous contrast media volume or radiation exposure. Previous animal studies of coronary disease have required an open surgical technique for producing coronary stenoses. However, these techniques require dedicated surgical expertise, have the potential to introduce artefact into the subsequent CT images (especially air in the mediastinum) and are expensive.

Developing a fully percutaneous technique that is analogous to conventional human coronary angiography significantly reduces the complexity of this procedure, allows it to be performed in sites without surgical support and potentially broadens the scope of studies that can be performed using the animal model. In addition to CT this technique could be applied in studies of magnetic resonance imaging where access to the animal in the MR scanner is limited or be

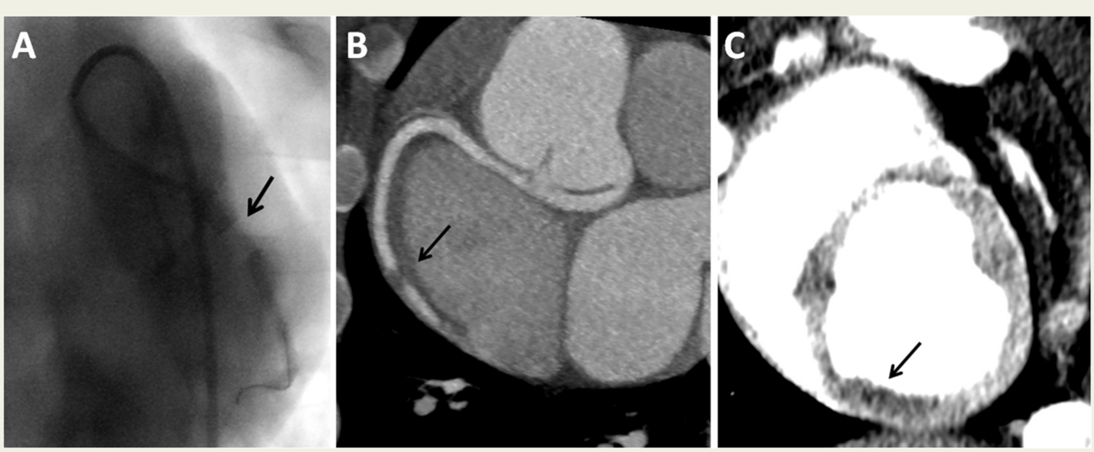

Figure 10 Cardiac computed tomographic (CT) perfusion imaging of a coronary stenosis in the right coronary artery. The methacrylate plug is shown on invasive angiogram (panel A – arrow) and confirmed on CT coronary angiogram (panel B – arrow). After CT perfusion imaging a perfusion defect is visible in short axis in the inferior segments.

Table 1 Procedural Outcomes.

ID	Weight (kg)	Heparin (IU)	Artery cannulated	PLUG Length (mm)	PLUG Diameter (mm)	PLUG Lumen diameter (mm)	TIMI Flow grade	ECG changes	FFR	Average myocardial blood flow (ml/100 ml of tissue/min)	CT protocol completed
1	56	4000	RCA	7.00	3.30	1.98	1	ST dep	0.37	–	No[a]
2	47	4000	LCX	7.00	3.30	1.98	1	ST elev	0.40	–	No[b]
3	52	16,000	RCA	7.00	3.30	1.98	3	None	0.91	96.6	Yes
4	52	16,000	RCA	7.00	3.30	1.58	2	ST dep	0.79	–	No[c]
5	50	16,000	RCA	7.00	4.00	1.58	2	ST elev	0.61	50.3	Yes
6	51	16,000	RCA	na	na	na	3	None	1.00	87.8	Yes[d]
7	48	16,000	LCX	7.00	4.00	1.58	2	ST elev	0.68	18.8	Yes
8	45	24,000	LCX	7.00	3.30	1.58	3	ST dep	0.89	115.1	Yes
9	58	24,000	LAD	7.00	3.30	1.58	3	ST dep	0.91	94.6	Yes
10	54	24,000	LAD	7.00	3.30	1.00	1	ST elev	0.21	14.4	Yes

Abbreviations: FFR, fractional flow reserve; ST dep, ST depression; ST elev, ST elevation; VF, ventricular fibrillation; CT, computed tomography.
[a]Ventilator induced bilateral pneumothoraxes.
[b]Thrombosis of coronary artery precipitating myocardial infarction and VF arrest.
[c]Iatrogenic air embolism of coronary artery precipitating VF arrest.
[d]Equipment failure of fluoroscopy C-arm during case – animal imaged as control subject with FFR of normal vessel.

useful for cross-modality imaging as the animal can be transferred between suites with only vascular access sheaths in-situ.

This study is the first to document the use of methacrylate plugs for simulating coronary stenoses. Once deployed, the plugs produced the required lesions with a range of both ischaemic and non-ischaemic severity assessed by FFR. As the technique was developed for studies evaluating CT perfusion it was equally important for the model to produce graded ischaemia but also avoid introducing imaging artefacts. This technique is therefore noteworthy as no evidence of the instrumentation or the methacrylate plug was noted in the CT imaging.

A learning effect was demonstrated by the higher success rate in the last six cases and marked shortening of the total procedural time between early and later subjects (Figure 11). The most significant factor in improving procedural time was the use of the BMW intracoronary wire to support the placement of the methacrylate plug.

The higher dose of heparin used after the second subject reduced the risk of thrombotic events. Access to coagulation monitoring using activated clotting time measurement was not available in the animal laboratory but the protocol of bolus doses heparin at the time of femoral cannulation and plug deployment, with a discretionary extra dose, caused no major bleeding or thrombotic events. Since there are no pre-existing collateral vessels in the myocardium in this acute stenosis experimental model [12] these animals are susceptible to ventricular fibrillation from acute coronary ischaemia. Whilst this did not occur in our study subjects it can be successfully treated using defibrillation.

The myocardial blood flow results are similar to that reported from other animal studies and the FFR values are analogous to those found in clinical practice. The CT analysis was performed on clinically available vendor software and it would be expected that findings from this model could be easily applied to clinical evaluation as well.

It is important to recognise that these projects require multiple skills sets. It is a limitation that the technique we describe utilises a combination of interventional coronary and vascular skills and was successful due to the collaboration between the cardiology and radiology departments at our institution. The CT scanner we used is located in our Emergency Department and, therefore, the project required extensive planning with multiple services to ensure there was no interruption to clinical service. Standard operating procedures were developed to prescribe study and transfer protocols and clearly outline procedures if the CT scanner was required for urgent clinical imaging. Significantly, the ischaemia time (reflecting the time from measurement of the FFR in the animal laboratory, the transfer to the CT suite and completion of the CT imaging protocol) was consistently low (Figure 11) reflecting the success in co-ordinating the transfer and completing the CT imaging in the clinical environment.

Conclusion

The procedure described above represents a fully percutaneous technique for introducing a coronary stenosis with graded ischaemia in a swine model that is suitable for CT imaging studies without introducing artefacts. The closed

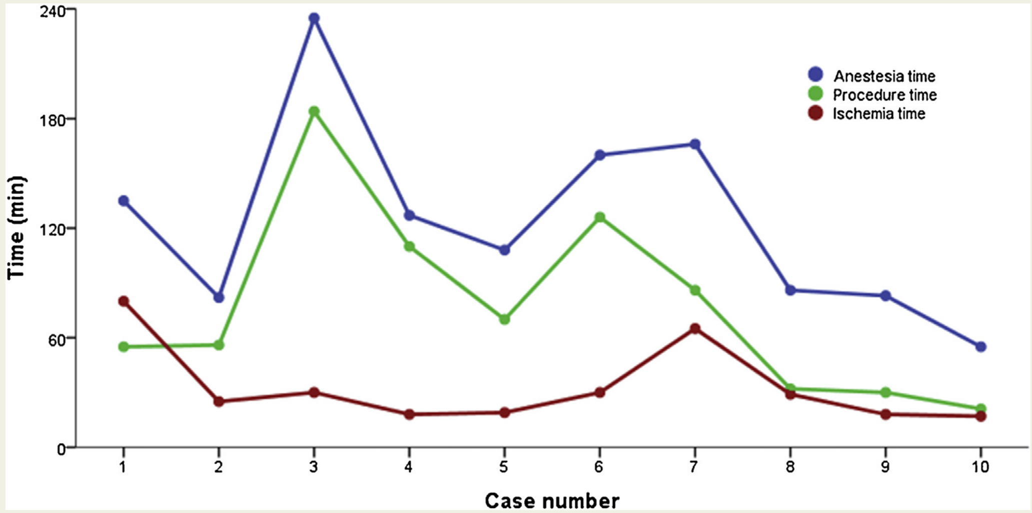

Figure 11 The effect of experience and procedural refinement on successive cases. Cases 1 and 2 were performed with no attempt to target a specific coronary artery. Subsequent cases took longer as specific arteries were targeted increasing the complexity of vessel targeting and plug deployment. However, with experience and improved technique, the final cases were performed consistently quickly. In most cases the transfer of the animal from procedure suite to the CT scanner in the clinical area was uncomplicated, reflected by consistently short ischaemia time.
Glossary: Anaesthesia time = time from induction of anaesthesia to completion of study protocol; Procedure time = time from femoral puncture to completion of study protocol; Ischaemia time = time from placement of methacrylate plug in the coronary artery to completion of study protocol.

chest, limited vascular access and intravenous anaesthetic protocol allow this technique to potentially be used for multiple imaging modalities and allow animal imaging to be performed if needed in a clinical environment.

Acknowledgements

The study received Funding Support from the Canadian Radiological Foundation, Ottawa, Canada, the Cardiology Research Fund, Vancouver General Hospital, Vancouver, Canada, and the Department of Radiology Research Fund, Vancouver General Hospital, Vancouver, Canada.

References

[1] Swindle MM, Makin A, Herron AJ, Clubb Jr FJ, Frazier KS. Swine as models in biomedical research and toxicology testing. Vet Pathol 2018;49 (2):344–56.

[2] Arthur DG, Thompson KG, James KAC, Maccoll AJ. Development of an arterial thrombosis model in pigs for investigating the thrombogenicity of different dietary fats (abstract). N Z Vet J 1993;41(1):46.

[3] George RT, Silva C, Cordeiro MA, DiPaula A, Thompson DR, McCarthy WF, et al. Multidetector computed tomography myocardial perfusion imaging during adenosine stress. J Am Coll Cardiol 2006;48(1):153–60.

[4] Mahnken AH, Klotz E, Pietsch H, Schmidt B, Allmendinger T, Haberland U, et al. Quantitative whole heart stress perfusion CT imaging as noninvasive assessment of hemodynamics in coronary artery stenosis: preliminary animal experience. Invest Radiol 2018;45(6):298–305.

[5] Perez de Prado A, Cuellas-Ramon C, Regueiro-Purrinos M, Gonzalo-Orden JM, Perez-Martinez C, Altonaga JR, et al. Closed-chest experimental porcine model of acute myocardial infarction-reperfusion. J Pharmacol Toxicol Methods 2009;60(3):301–6.

[6] Batson OV. Mtg Amer Assoc Anatomists (68th Session); 1955, Philadelphia, PA.

[7] Baile EM, King GG, Muller NL, D'Yachkova Y, Coche EE, Pare PD, et al. Spiral computed tomography is comparable to angiography for the diagnosis of pulmonary embolism. Am J Respir Crit Care Med 2000;161(3 Pt 1):1010–5.

[8] Coxson HO, Baile EM, King GG, Mayo JR. Diagnosis of subsegmental pulmonary emboli: a multi-center study using a porcine model. J Thorac Imaging 2005;20(1):24–31.

[9] Palmerini T, Serruys P, Kappetein AP, Genereux P, Riva DD, Reggiani LB, et al. Clinical outcomes with percutaneous coronary revascularization vs coronary artery bypass grafting surgery in patients with unprotected left main coronary artery disease: a meta-analysis of 6 randomized trials and 4,686 patients. Am Heart J 2017;190:54–63.

[10] Karnicki K, Owen WG, Miller RS, McBane 2nd RD. Factors contributing to individual propensity for arterial thrombosis. Arterioscler Thromb Vasc Biol 2002;22(9):1495–9.

[11] Osterman FA, Bell WR, Montali RJ, Novak GR, White RI. Natural history of autologous blood clot embolization in swine. Invest Radiol 1976;11 (4):267–76.

[12] Verdouw PD, van den Doel MA, de Zeeuw S, Duncker DJ. Animal models in the study of myocardial ischaemia and ischaemic syndromes. Cardiovasc Res 1998;39(1):121–35.