Report OCL-500-PRE-001.2

OCCLUSIN® 505 ARTIFICIAL EMBOLIZATION DEVICE

A PRECLINICAL STUDY OF THE SAFETY AND EFFICACY OF OCCLUSIN® 505 ARTIFICIAL EMBOLIZATION DEVICE IN PIGS

Final Study Report

15 December 2011

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Preclinical Study Report Approval

PRECLINICAL STUDY REPORT
OCL-500-PRE-001.2

Report Title: A Preclinical Study of the Safety and Efficacy of Occlusin® 505 Artificial Embolization Device in Pigs

Report Number: R-OCL-500-PRE-001

Start Date: 16 May 2007

Completion Date: 20 Jun 2007

Study Director: Irwin Griffith

Author: Irwin Griffith

Version: Version 1.2

Date of Report: 18 July 2008

Date of Revision 15 December 2011

Approval Signatures:

Irwin Griffith
(Study Director)
Signature 4 Jan 2011 Date

Irwin Griffith
(Author)
Signature 4 Jan 2011 Date

Adrienne Perry
(Quality Assurance)
Signature 05Jan2011 Date

*IM*Biotechnologies Ltd.
Advanced Technology Centre
#113, 9650 – 20th Avenue, NW
Edmonton, AB T6N 1G1

1. Abbreviations

AED	Artificial Embolization Device
A/G Ratio	Albumin/Globulin Ratio
AST (Sgot)	Aspartate aminotransferase (Serum glutamic oxaloacetic transaminase)
ALT (Sgpt)	Alanine aminotransferase (Serum glutamic-pyruvic transaminase)
CBC	Complete blood cell count
CCAC	Canadian Council on Animal Care
CFR	Code of Federal Regulations
cGMP	Current Good Manufacturing Practices
FDPs	Fibrin degradation products
GLP	Good Laboratory Practice
IACUC	Institutional Animal Care and Use Committee
ISO	International Standards Organization
IU	International Unit
OCL 500	Occlusin® Artificial Embolization Device
OCL 505	OCL 500 with a size range 300 – 425 µm
PBS	Phosphate Buffered Saline
PLGA	Poly(DL lactic-co-glycolic acid)
PTT	Partial thromboplastin time
PVA	Polyvinyl alcohol
RBC	Red blood cell
RDW	Red Cell Distribution Width
PT	Prothrombin time
SD	Standard Deviation
µg	Microgram
µm	Micrometer
mL	Milliliter
vWF	von Willebrand Factor
WBC	White blood cell

®Occlusin is a registered trademark in Canada.

2. Summary

The purpose of this preclinical study was to evaluate the safety, effectiveness, and biocompatibility of Occlusin® 505 Artificial Embolization Device (OCL 505). This study also examined other important device-related issues including the ease of injection, extent of target vessel occlusion, rate of resorption, migration to non-target tissues, recanalization of the target vessel, and local tissue reaction.

The effectiveness of OCL 505 as an artificial embolizing device (AED) was evaluated in pigs by implanting the device in branches of the hepatic and renal arteries to infarct the liver (one or several lobes) and kidney (one pole or the entire organ), respectively. OCL 505 was implanted by transcatheter arterial administration and the target vessels were occluded to effective stasis. Procedural data and follow up clinical and haematological data were recorded. Test animals were sacrificed on either the day of treatment or one month after embolization. The tissue response to OCL 505 was examined histologically.

OCL 505 microspheres were clearly identified in all occluded arteries. The particles were spherical in animals sacrificed immediately after embolization. At one month post procedure there was evidence of particle remodelling consistent with the particles undergoing biodegradation. No evidence of non-target embolization was seen in any animal. Occlusion of the renal artery caused significant chronic ischemia in the occluded kidneys. Contralateral kidneys showed signs of hypertrophy to compensate for the loss of function by the occluded kidney. All occluded livers were viable without evidence of chronic ischemia.

No device related issues or adverse events were recorded. OCL 505 was an effective and safe embolic agent when used as tested.

3. Introduction

3.1 Product Overview

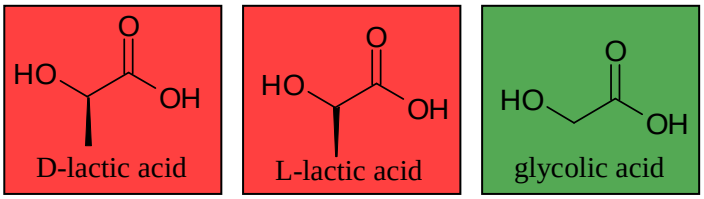
Occlusin® 505 AED is an embolotherapeutic agent consisting of poly(DL lactic-co-glycolic acid) (PLGA) microspheres that are coated with bovine fibrillar collagen type I. The embolotherapeutic agent used in this study, OCL 505, was manufactured with nominal particles sizes of 300-425 μm.

3.2 Intended Use/Indication for Use

OCL 505 is intended to be used as an artificial embolization device in the treatment of hypervascularized tumors. These tumors often arise in the liver, kidneys, and the uterus.

3.3 Materials Characterization

PLGA has long been used as suture material and more recently as a sustained-release drug delivery vehicle. PLGA is synthesized as a copolymer of glycolide and DL-lactide (Schematic 1) with the ratio of the monomers governing the rate of biodegradation.



Schematic 1 shows a representation of D-lactic acid, L-lactic acid and glycolic acid monomers that are polymerized to form PLGA.

Collagen is a family of closely related extracellular proteins that form major constituents of connective tissue of animals, giving the tissues strength and flexibility. At least 14 different types exist, each composed of tropocollagen. Tropocollagens have a common triple-helical structure, but vary in composition between the different collagen types that are localized in different tissues. Type I collagen is the most common type of collagen.

3.4 Mechanism of Action

OCL 505 acts as an embolization agent based on physical blockade of the target blood vessel(s), leading to blood stasis and subsequent clot formation. In addition, OCL 505 can promote vascular occlusion by activating platelets and consolidating clot formation.

OCL 505 can use two distinct pathways to capture and activate platelets *in vivo*. In the first pathway, collagen-specific receptors on platelets can recognize and directly bind to the collagen on the surface of the OCL 505 microspheres. This binding activates the platelets. Platelet activation causes a complex cascade of events, including the release of chemokines, the recruitment of other platelets from the blood and platelet aggregation, that causes the formation of a tight clot. In the second pathway, von Willebrand Factor (vWF) in the blood can bind to the collagen on the surface of the OCL 505 microsphere. Specific receptors on the platelets then bind to the vWF-collagen complex. Binding of the platelets to the vWF-collagen complex leads to platelet activation and clot formation as described above.

3.5 Justification for Species Selection

The organ systems, vascular network, and haemostatic system of the pig closely resemble that of humans (1). Therefore, pigs are often the species of choice for studying safety and efficacy of embolotherapeutic agents (2 - 5).

Durock-Yorkshire-Landrace cross pigs (9 weeks old at study entry) represent a cross of common pig breeds and were selected for use in this study as they were readily available.

3.6 Justification for Number of Animals Tested

Twelve pigs were treated with OCL 505 as detailed in Table 1. Four animals were sacrificed acutely after embolization of their renal (two animals) or hepatic (two animals) arteries. This provided critical information for acute embolization of each organ system. Eight animals were sacrificed one month post-embolization of renal (four animals) or hepatic branch (four animals) arteries. Four animals per organ system provided sufficient experience with the product to evaluate the properties of OCL 505 *in vivo* in each organ system one month post-embolization while minimizing the total number of animals used in the study.

Table 1: Study Design

Study Type	Sacrificed	Test Procedure	Test Article	Number of Animals	Pig Number
Acute	Following Embolization	Renal artery embolization	OCL 505	2	9, 10
		Hepatic artery embolization	OCL 505	2	11, 12
One Month (Chronic)	4 Weeks Post Embolization	Renal artery embolization	OCL 505	4	1 to 4
		Hepatic artery embolization	OCL 505	4	5 to 8

3.7 Justification for Selecting the Sex of Animals Tested

There is no difference in the vasculature of male and female pigs in the liver or kidneys. Castrated males were selected for use in this study as they were readily available.

3.8 Study Compliance

This study was conducted at the Metabolic Unit and Ellerslie Research Facility at the University of Alberta in compliance with the Food and Drug Administration (FDA) Good Laboratory Practice (GLP) Regulations for Nonclinical Laboratory Studies (21 CFR Part 58) and applicable University of Alberta SOPs. The Quality Assurance Unit of ViRexx Medical Corp. (Edmonton, AB) performed quality assurance auditing and inspected activities of procedures and analyses and reporting of findings.

The test article was manufactured in compliance with cGMP regulations.

The University of Alberta is AAALAC accredited, has an Animal Welfare Assurance issued by the American National Institutes of Health's Office of Laboratory Animal Welfare (A5070-01), has an IACUC responsible for compliance with applicable laws and regulations concerning the humane care and use of laboratory animals, and is accredited by the Canadian Council on Animal Care.

4. Study Objectives

The primary objective of this preclinical study was:

(a) To evaluate the efficacy and safety of OCL 505 as an artificial embolization agent in causing infarction/regression of the target organ.

The secondary objectives of this preclinical study were:

(a) To determine the integrity of OCL 505 in the arterial vessel on the day of implantation and one month after implantation.

(b) To detect any systemic toxicity associated with the implantation of OCL 505.

(c) To determine the nature and extent of local tissue reaction to the implantation of OCL 505.

(d) To determine the extent of recanalization of the target blood vessels.

(e) To determine the ease of using OCL 505 as an embolic device.

5. Materials and Methods

5.1 Animals

Twelve castrated male Durock-Yorkshire-Landrace cross pigs were used in the study. All animals were 9 weeks of age when they entered the study and 14-15 weeks old at time of sacrifice. Pigs received ear tags with unique numbers to identify individual animals (Pigs 1 to 12).

5.2 Animal Care

Animals were housed inside the Metabolic Unit at the University of Alberta under conditions consistent with all mandated provincial and national regulations. All animals received water and food *ad libitum* by qualified animal care providers. Animal health was monitored by the Director of Animal Care for the Faculty of Agriculture, Forestry and Home Economics and veterinary care was provided as necessary. Animals were housed in the facility for at least one week prior to the embolization procedure.

All animals were physically examined and their vital signs recorded according to the schedule in Appendix A. Individual animal weights are recorded in Appendix B. All animals were vaccinated with Enterisol Ileitis (Boehringer Ingelheim) and Suvaxyn E (Wyeth) for the prevention of ileitis and erysipelas, respectively. Both vaccines were administered in the drinking water per manufacturer's instructions the day prior to surgery.

Animals were transported from/to the Metabolic Unit and to/from the Ellerslie Research Facility for surgery in an approved animal trailer under the care of qualified animal care providers. Chronic animals (those sacrificed one month following the surgical procedure) were transported to the Ellerslie Research Facility the day before surgery and returned to the Metabolic Unit the day after surgery. Acute animals were transported to the Ellerslie Research Facility on the day of surgery and sacrificed on site immediately after the embolization procedure.

Chronic animals received intramuscular injections of Buprenex Injectable® (buprenorphine hydrochloride; 0.05 mg/kg; Reckitt & Colman Pharmaceuticals, Richmond, VA) as an analgesic. These animals also received Excenel® (ceftiofur hydrochloride; 3 mg/kg; Pharmacia & Upjohn; Orangeville, ON**)** as an antibiotic. Both drugs were administered intramuscularly for two consecutive days, starting on the day of surgery.

5.3 Anesthesia and Euthanasia

5.3.1 Anesthesia of Animals Sacrificed One Month Post Embolization. Four animals were embolized at 10 weeks of age and four animals were embolized at 11 weeks of age. All animals were sacrificed one month after embolization (14 – 15 weeks of age). These animals were anesthetized with 5% isoflurane and maintained on ventilation at approximately 2% (+/- 0.5%) isoflurane as needed for the duration of the embolization procedure. Following the completion of surgery, the isoflurane was reduced to 0% and ventilation continued until the animals recovered from anesthesia

5.3.2 Anesthesia of Animals Sacrificed Acutely Following Embolization. Four animals were embolized at 15 weeks of age and sacrificed immediately following surgery. These acute animals were sedated with 11 mg/kg of Ketaset® (ketamine hydrochloride; 10 mg/kg; Fort Dodge Animal Health, Fort Dodge, IA) and 2.2 mg/kg xylazine hydrochloride (Rompun®, Bayer Animal Health) given intramuscularly. After sedation, the animals were anesthetized with and maintained on isoflurane (1.5% and 1 %, respectively) for the duration of surgery.

5.3.3 Euthanasia. All animals were euthanized with 120 mg/kg sodium pentobarbital (Euthanyl®, Bimeda-MTC Animal Health Inc., Cambridge,

ON) administered intravenously in accordance with manufacturer's instructions.

5.4 OCL 505

OCL 505 microspheres (300 – 425 µm) were manufactured at Brookwood Pharmaceuticals (Birmingham, AL) in compliance with cGMP regulations. All material used in this study was from Lot number FL288. The contents of a vial (400 mg/vial) were suspended in 5 – 10 mL of Sodium Chloride for Injection 0.9% USP. Appendix C lists the volumes of each dose of the reconstituted device. Omnipaque™ 300 (Amersham Health) or Omnipaque™ 240 (Amersham Health) was used as contrast agent. Omnipaque 300 was added to the suspended particles in a 3-to-1 Omnipaque 300 to Sodium Chloride ratio. The volume of Omnipaque 240 required was calculated using the following formula:

Volume of Omnipaque 240 (mL) = Volume of saline (mL) x 3.75.

5.5 Embolization Procedure

Embolization procedures were carried out under general anesthesia by means of femoral (pigs 1 to 10) or brachial (Pigs 11 and 12) artery cannulation. All animals were treated in a similar manner with standard angiographic equipment. A 5F Beacon Tip Torcon NB Advantage Catheter (Cook Incorporate, Bloomington, IN) was directed to the target tissue under fluoroscopic guidance. Once the position of the catheter was confirmed, OCL 505 suspended to neutral buoyancy was injected into the target artery at the discretion of the interventional radiologist who conducted all of the device implantation procedures (see Section 5.9). Small increments of OCL 505 were administered until the radiologist determined that effective stasis had been achieved. Procedural data were recorded.

Target arteries were clearly identified in all 12 animals. Embolization to effective stasis was achieved in all cases. The post procedure course was uneventful and there were no procedural related complications.

5.5.1 One Month Embolization Study of the Renal Artery. A one month study was conducted in four pigs (Pigs 1 – 4) alternatively targeting either the right (Pig 2 and Pig 3) or the left renal artery (Pig 1 and Pig 4). The contralateral kidney served as both histologic and arteriographic control. After embolization of the renal artery the animals were treated with Metacam® (0.2 mg/kg; Boehringer Ingelheim Vetmedica; Burlington, ON), a non-steroidal anti-inflammatory analgesic, for 48 hours and then as needed. Three blood samples of approximately 5 mL each were drawn from each animal according to the schedule in Appendix A. The blood samples were used to evaluate the clinical laboratory parameters outlined in Section 5.6

Animals were euthanized as described in Section 5.3.3. A gross examination of the target and non-target kidney was performed after they had been surgically exposed. The tissues specified in section 5.7 were collected for histologic examination.

5.5.2 One Month Embolization Study of the Hepatic Artery. OCL 505 was implanted into the hepatic artery of four anesthetized pigs (Pigs 5 to 8) by transcatheter arterial injection. Animals were embolized as described above using a femoral artery cannulation.

Following the embolization procedure, the animals were treated with an NSAID analgesic (Metacam®) for 48 hours and then as needed. Three blood samples of approximately 5 mL each were drawn from each animal according to the schedule in Appendix A. The blood samples were used to evaluate the clinical laboratory parameters outlined in Section 5.6

The animals were euthanized as described in Section 5.3.3 immediately after the embolization was concluded. A gross examination of the target and non-target liver lobes was performed after they were surgically exposed. The tissues specified in section 5.7 were collected for histologic examination.

5.5.3 Acute Embolization Study of the Renal Artery. An acute study was conducted in two pigs (Pigs 9 and 10) targeting either the right or left renal artery (Pig 9 and Pig 10). The contralateral kidney served as both histologic and arteriographic control. Three blood samples of approximately 5 mL each were drawn from each animal the day prior to the embolization procedure, as specified in Appendix A. The blood samples were used to evaluate the clinical laboratory parameters outlined in Section 5.6

After embolization, the animals were sacrificed as described in Section 5.3.3. The kidneys were surgically exposed and a gross examination of the target and non-target kidney was performed. The tissues described in Section 5.7 were collected for histologic examination.

5.5.4 Acute Embolization Studies in the Hepatic Artery. An acute study was conducted in two pigs (Pigs 11 and 12) targeting the hepatic artery. Three blood samples of approximately 5 mL each were drawn from each animal the day prior to the embolization procedure, as specified in Appendix A. The blood samples were used to evaluate the clinical laboratory parameters outlined in Section 5.6.

After embolization, the animals were euthanized as described in Section 5.3.3. A gross examination of the target and non-target liver lobes was performed after they had been surgically exposed. Tissues specified in Section 5.7 were collected for histologic examination.

5.6 Clinical Laboratory Data

Table 2 shows the parameters that were measured at baseline and at the intervals post listed in the protocol study schedule (Appendix A). All clinical laboratory analyses were conducted at Central Laboratory for Veterinarians, Ltd. (Edmonton, AB). The data were reviewed by a qualified veterinary pathologist.

Table 2. Clinical Laboratory Parameters

Chemistry Albumin Albumin/Globulin Ratio Alkaline Phosphatase Anion Gap Blood Urea Nitrogen (BUN) BUN/Creatinine Ratio Calcium Calculated Osmolality Carbon Dioxide Chloride Creatinine Creatine Phosphokinase Gamma -GT Globulin Glucose Phosphorus Potassium AST (Sgot) ALT (Sgpt) Sodium Sodium/Potassium Ratio Sorbital Dehydrogenise - AO Total Bilirubin Total Protein Uric Acid	**Hematology** WBC and Differential Count RBC Count Hematocrit Hemoglobin Mean Corpuscular Volume Mean Corpuscular. Hemoglobin Mean Corpuscular. Hemoglobin Concentration Red Cell Distribution Width Platelet Count Mean Platelet Volume **Coagulation** Partial Thromboplastin Time Prothrombin Time Fibrinogen Degradation Products **Morphology** Platelet Morphology Fibrinogen Semi Quantitative RBC Morphology

5.7 Postmortem Examination

All animals were examined post mortem and select tissues were collected for histological examination. The collected tissues are listed in Table 3.

Tissue samples were processed and histological sections prepared by Histobest Inc. (Edmonton, AB) using standard procedures.

All carcasses were incinerated following post mortem examination and tissue collection.

Table 3. Tissues collected for histologic examination

Animal Treatment:	Renal Artery Embolization		Hepatic Artery Embolization	
Tissues Collected	**Acute Study**	**One Month Study**	**Acute Study**	**One Month Study**
Embolized renal artery	+	+	--	--
Embolized branch of the hepatic artery	--	--	+	+
Spleen	+	+	+	+
Kidneys	+	+	+	+
Adrenals	+	+	+	+
Liver Segment	+	+	+	+
Gall Bladder	+	+	+	+
Lungs	+	+	+	+
Heart	+	+	+	+
Brain	+	+	+	+
Eyes	+	+	+	+
Pancreas	+	+	+	+
Duodenum	+	+	+	+
Small Intestine	+	+	+	+
Large Intestine (with Rectum)	+	+	+	+
Stomach	+	+	+	+
Bladder	+	+	+	+
Gluteal Muscle	+	+	+	+
Diaphragm	+	+	+	+
Any abnormal tissues observed during gross examination	+	+	+	+

5.8. Statistical Analysis

An appropriate analysis of the safety and biological data developed in this preclinical study was performed. The statistical analysis was primarily descriptive.

Safety analyses were based on the clinical and laboratory effects observed in animals treated in this study. The analysis was primarily descriptive.

5.9. Key Personnel

Dr. Richard Owen, M.D., F.R.C.P.(C), an interventional radiologist at the University of Alberta Hospital, performed all device implantation procedures and made the determination that effective stasis of blood flow to the target organ had been achieved.

Dr. P. N. Nation, D.V.M., Ph.D., a board certified veterinary pathologist, performed all necropsies and interpreted all Clinical Laboratory data, gross pathologies and histological analyses. The resumes for Drs. Owen and Nation are included in Appendix R.

6. Results

6.1 Embolization.

The renal artery or one of its branches was embolized in 4 pigs at 10 weeks of age and 2 pigs at 15 weeks of age. The pigs embolized at 10 weeks of age were sacrificed at 14 weeks of age, one month after embolization (Chronic Renal Pigs 1 to 4). The pigs embolized at 15 weeks were sacrificed following treatment (Acute Renal Pigs 9 and 10). Only one kidney (left or right) or the pole of one kidney (upper or lower) was embolized in each animal. All animals were healthy at the time of embolization.

A branch of the hepatic artery feeding one or several lobes of the liver was embolized in 4 pigs at 11 weeks of age and 2 pigs at 15 weeks of age. The pigs treated at 11 weeks were sacrificed at 15 weeks of age, one month after embolization (Chronic Hepatic Pigs 5 to 8). The pigs treated at 15 weeks were sacrificed following treatment (Acute Hepatic Pigs 11 and 12).

All animals were healthy at the time of embolization and were treated (examined, weighed, and blood samples drawn) as scheduled in Appendix A. Individual and group mean weights are recorded in Appendix B. Data recorded during the embolization procedure are listed in Appendix C.

Table 4 shows the mean fluorographic time to achieve effective stasis at 10 and 11 weeks for each group of animals and individual fluorographic times at 15 weeks. The fluorographic times required to embolize the renal artery or one of its branches were similar at 10 weeks and at 15 weeks of age. The fluorographic times required to embolize one or more branches of the hepatic artery were also similar at 11 weeks and 15 weeks, although the embolization procedure for Pig 12 took longer than for Pig 11 (fluorographic time of 9.8 minutes *vs.* 3.1 minutes). The means of the data for the chronic treatment groups (N=4) are shown in Figure 1 with error bars indicating ± one standard deviation. The standard deviation could not be calculated for the acute treatment groups with two animals each.

Table 5 shows the mean and range of the number of vials required to achieve effective stasis in each group of animals. There is no difference in the average number of vials required to embolize the renal artery or one of its branches at 10 weeks (2 ± 0.8 vials) and at 15 weeks (2 vials). In contrast, the number of vials required to embolize one or more branches of the hepatic artery increased from 11 weeks (1.4 ± 0.5 vials) to 15 weeks (3 vials). These data are presented in Figure 2.

Table 4. Fluorographic time to achieve effective stasis in each organ system.

Treatment Group	Age of Pigs	Number of Pigs	Minutes (Mean ± 1 SD)
Acute Renal Artery	15 weeks	n = 2	5.6 (5.0, 6.2) minutes
Chronic Renal Artery	10 weeks	n = 4	7.2 ± 3.4 minutes
Acute Hepatic Artery	15 weeks	n = 2	5.3 (3.1, 9.8) minutes
Chronic Hepatic Artery	11 weeks	n = 4	3.4 ± 0.5 minutes

Figure 1. Fluorographic time to achieve effective stasis in each organ system.

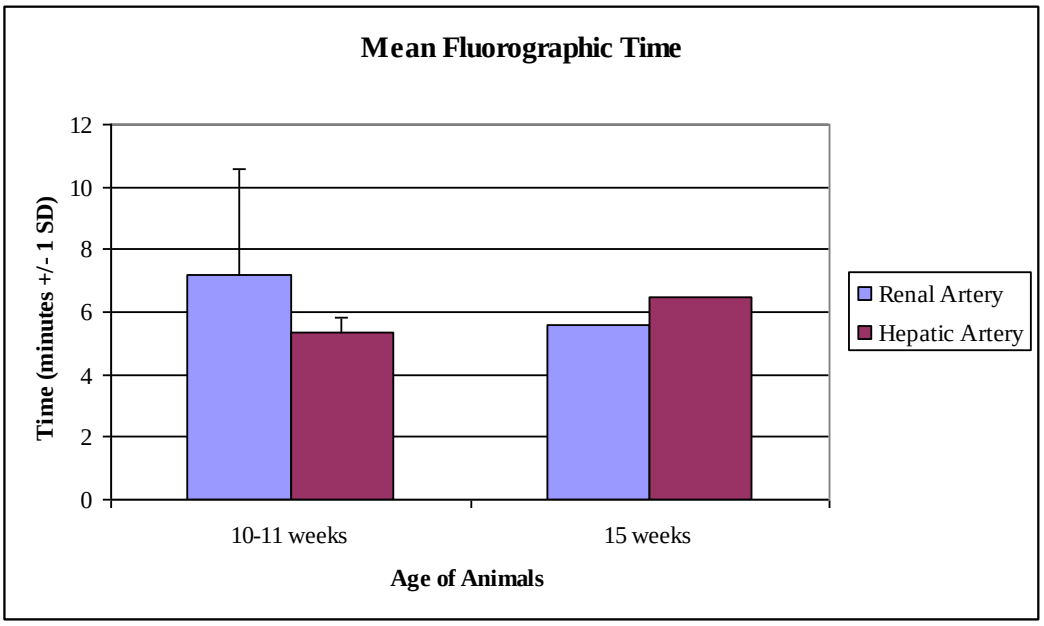
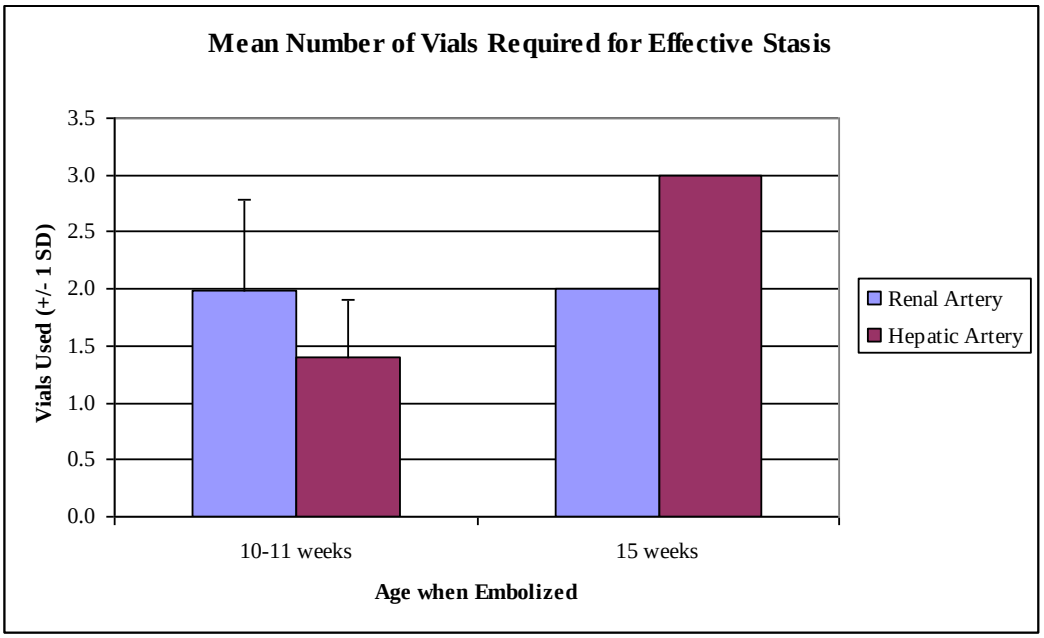


Table 5. Number of vials required to achieve effective stasis.

TreatmentGroup	Age of Pigs	Number of Pigs	Vials (Mean ± 1 SD)	Vials (Range)
Renal Artery	10 weeks	n = 4	2.0 ± 0.8	0.9 – 2.9
Renal Artery	15 weeks	n = 2	2	2
Hepatic Artery	11 weeks	n = 4	1.4 ± 0.5	1 – 2
Hepatic Artery	15 weeks	n = 2	3	3

Figure 2. Mean number of OCL 505 vials required for effective stasis.



6.2. Animal Health.

Chronic Renal Pig 3 was found lame in its pen 23 days after embolization and was sacrificed 4 days later, one day prior to its scheduled termination. Post mortem analysis revealed that this animal had an abscess in its left hind leg consistent with a deep puncture wound. This wound was unrelated to the embolization procedure. All other animals were in good health and were euthanized as scheduled.

6.3. Animal Weights.

All animals gained weight with time (Figure 3), although Chronic Kidney Pigs (Pigs 1 to 4) appear to gain weight at a slightly slower rate than the Chronic Hepatic Pigs (Pigs 5 to 8) and untreated Acute Pigs (9 to 12). This apparent difference is shown most clearly by comparing the mean weights for each group of pigs (Figure 4).

Note that Chronic Renal Pig 3 gained relatively little weight between the scheduled weighing days at 12 weeks and 14 weeks of age (two and four weeks post embolization, respectively) (Figure 3). This is consistent with this animal being found lame 23 days post embolization (approximately 13 weeks old)

All individual and average group mean weights are presented in Appendix B and graphically in Figures 3 and 4.

Figure 3. The weight of individual pigs by age.

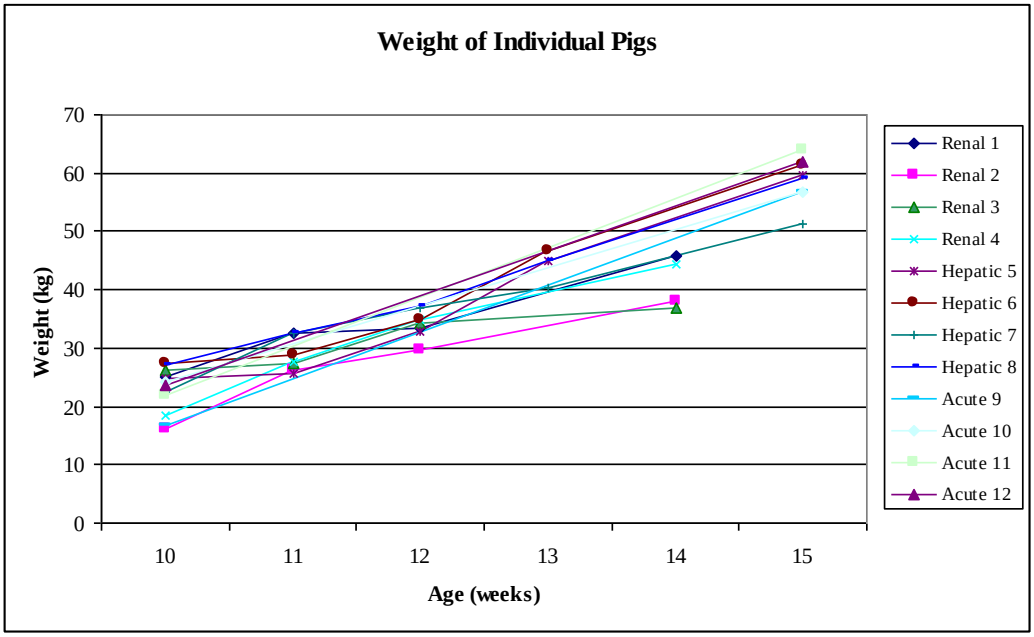
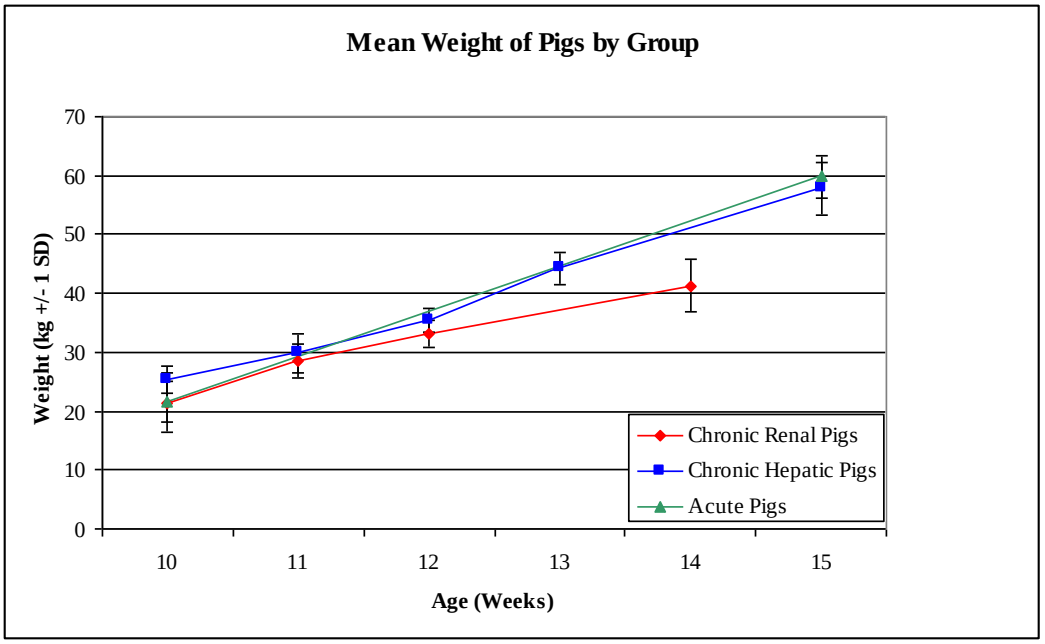


Figure 4. The mean weight (± SD) of each group of pigs by age.



Note: The error bars represent one standard deviation (SD).

6.4 Clinical Laboratory Data.

Blood samples were collected from the Acute treatment group of animals the day before surgery. Blood samples were collected from the Chronic treatment group the day before surgery, and again 1, 7, 14 and 28 days (1 month) after embolization. Clinical laboratory data outside the normal reference range are discussed below. Graphs of the arithmetic means outside the normal reference range are shown. The values for individual animals are shown where there are marked differences in the responses of animals within a group for a given parameter.

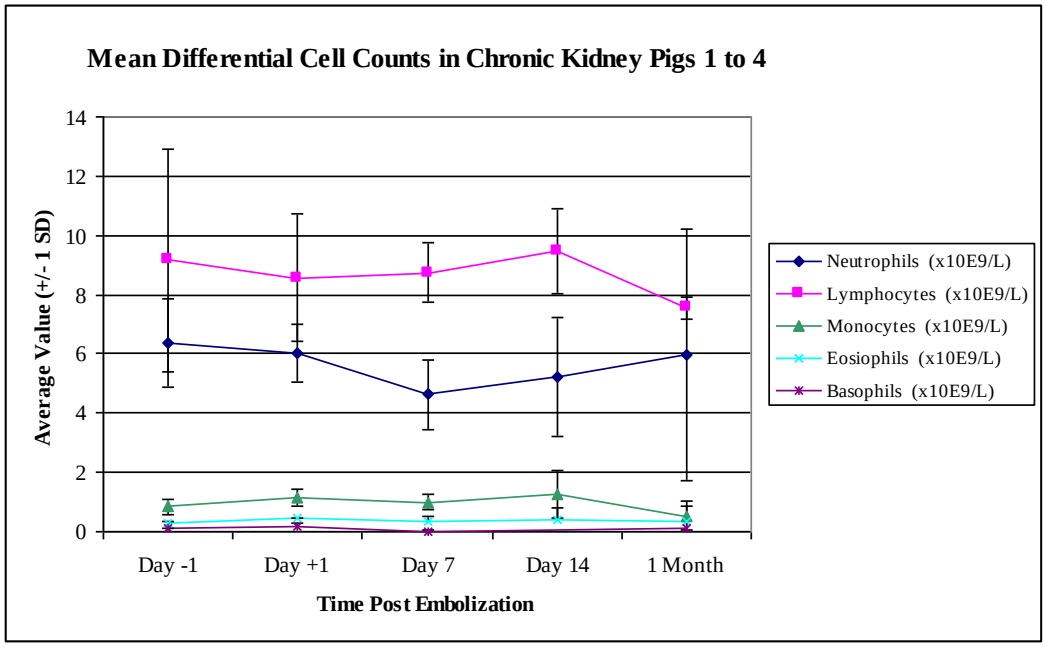
6.4.1. Hematology. One month after embolization, the Chronic Renal Pigs 1 to 4 Group had a mean neutrophil count similar to that of the earlier blood samples. However, the standard deviation of the neutrophil count at one month post embolization was larger than for previous samples (Figure 5). Examination of the cell counts in individual Chronic Renal Pigs (Figure 6) showed that the increased variation was due to the increased level of neutrophils in Chronic Renal Pig 3, the lame animal found to have an abscess in its hind leg.

6.4.2. Chemistry. The Chronic Kidney Pigs 1 to 4 Group had transient increases in Creatine and Uric Acid (Figures 7 and 8), Albumin and Sorbital Dehydrogenase (Figures 9 and 10), and AST (Figures 11 and 12). All values returned to normal levels by 7 days post embolization. Only the Chronic Kidney Group average data are shown for uric acid (Figure 7) and albumin (Figure 9) since the standard deviations were negligible for these parameters. All other changes are shown for individual animals (Figures 8, 10 and 12).

6.4.3. Coagulation. The Chronic Kidney Pigs 1 to 4 Group had transient increases in partial thromboplastin time and prothrombin time (Figures 13, 14 and 15). All values returned to normal levels by 7 days post embolization.

The Chronic Hepatic Pigs 5 to 8 Group had a transient increase in Partial Thromboplastin Time 1-7 days after embolization and an overall increase one month after embolization (Figure 16). All Chronic Hepatic Pigs had a slightly elevated Partial Thromboplastin Time one day after embolization (Figure 17). The increase seven days after embolization was due primarily to an increase in Chronic Hepatic Pig 6 (Figure 17). The overall increase in average Partial Thromboplastin Time observed one month after embolization (Figure 16) is consistent with the increase in Partial Thromboplastin Time observed in control animals as they age (Appendix O, Panel A).

Figure 5. Mean Differential Cell Count in Chronic Kidney Pigs 1 to 4



Source: Appendix L, Panel B.

Figure 6. Neutrophil Count in Individual Chronic Kidney Pigs 1 to 4

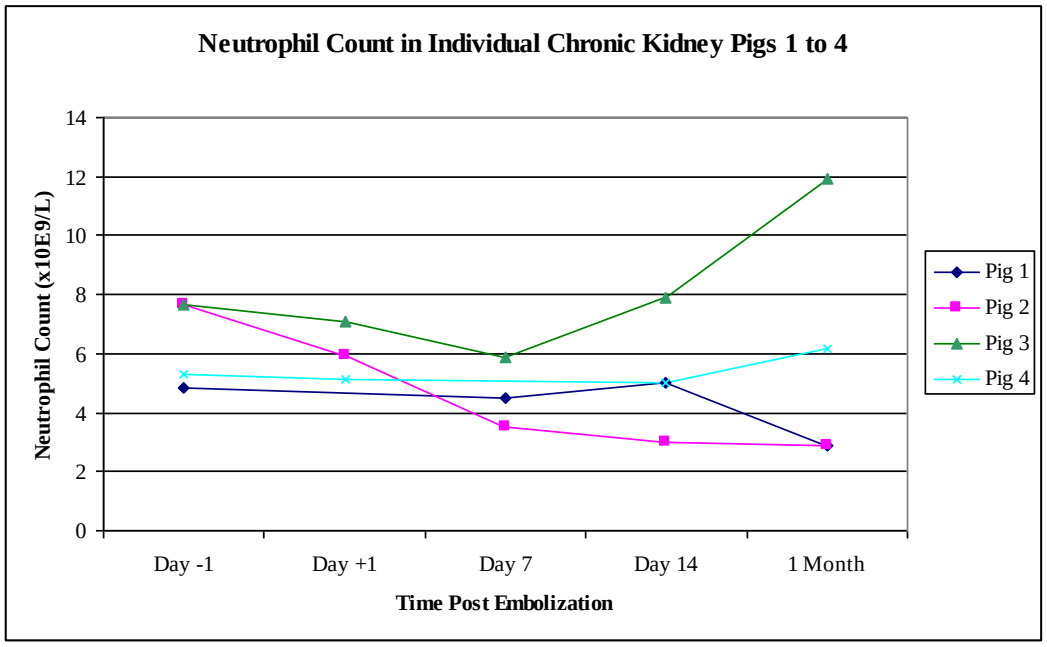
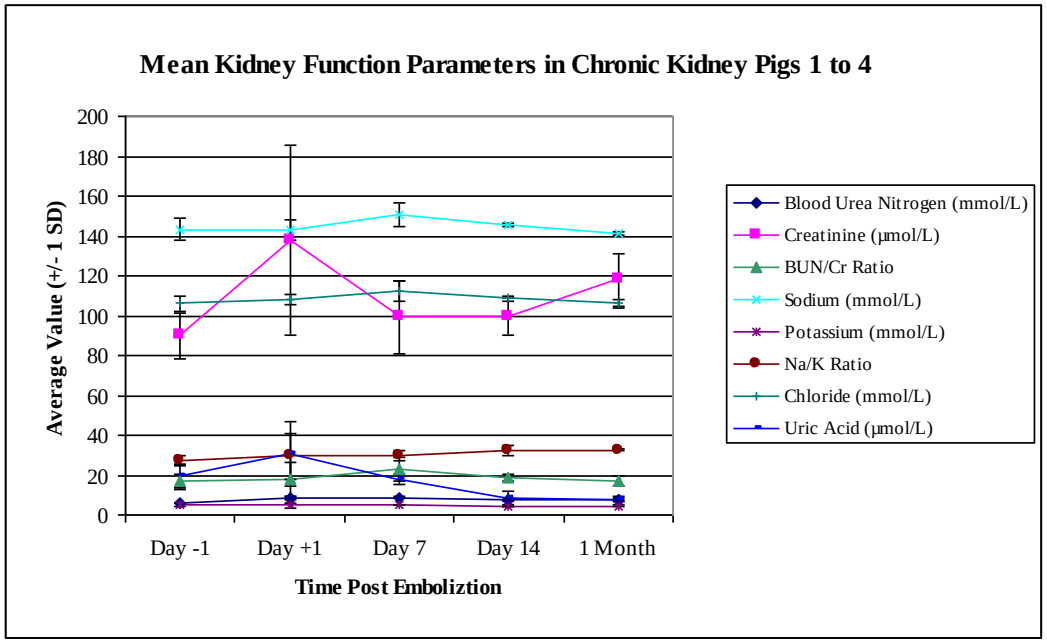


Figure 7. Mean Kidney Function Parameters in Chronic Kidney Pigs 1 to 4



Source: Appendix M, Panel B

Figure 8. Creatinine Levels in Individual Chronic Kidney Pigs

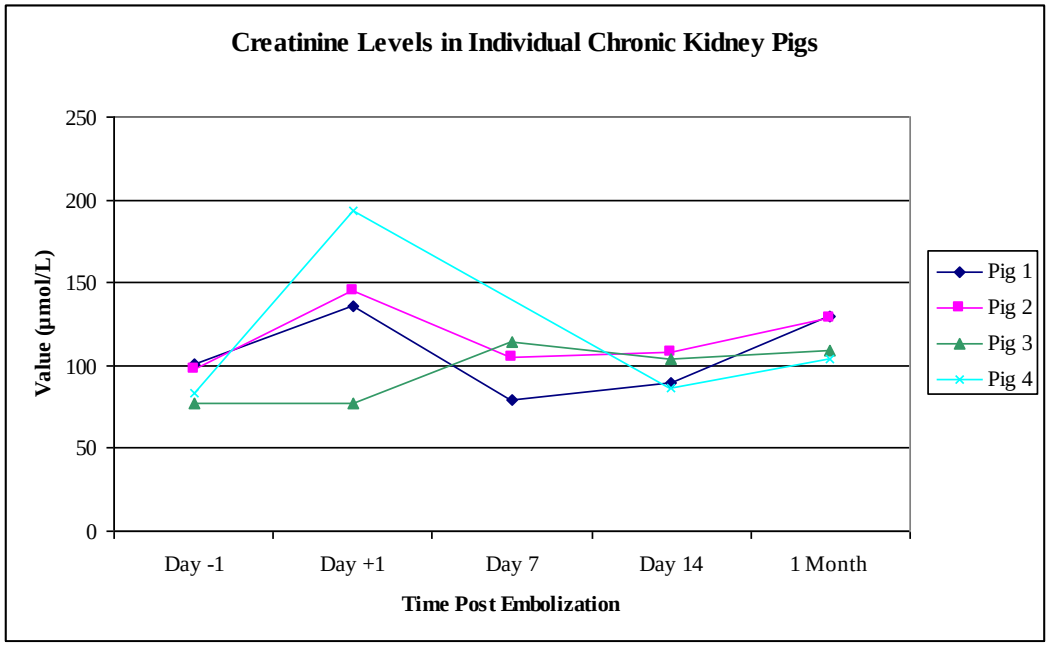
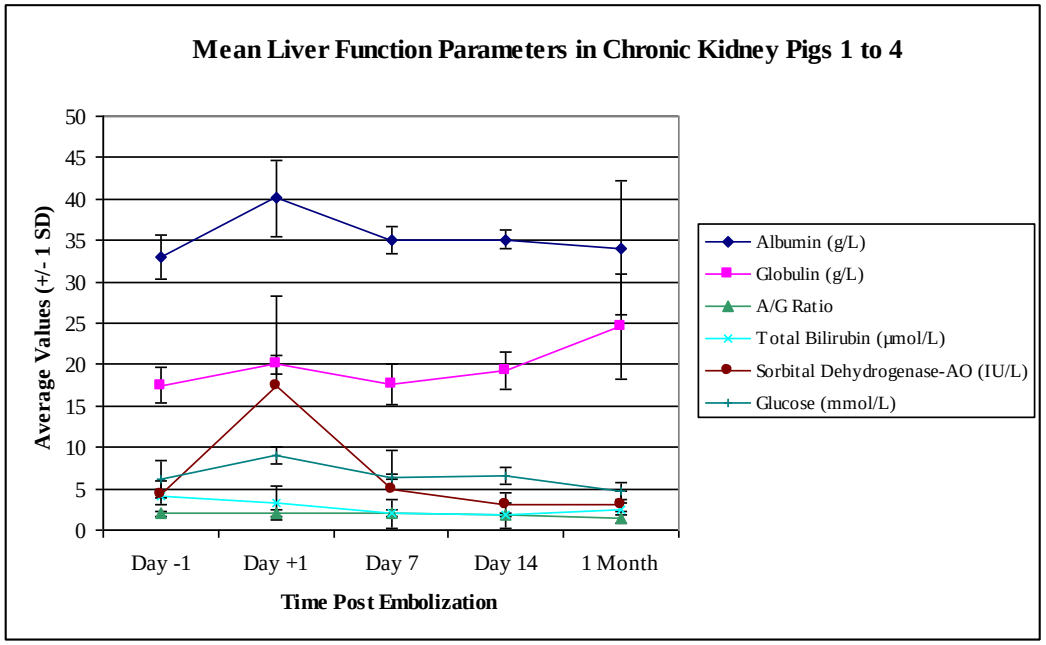


Figure 9. Mean Liver Function Parameters in Chronic Kidney Pigs 1 to 4



Source: Appendix N, Panel B

Figure 10. Levels of Sorbital Dehydrogenase-AO in Individual Chronic Kidney Pigs

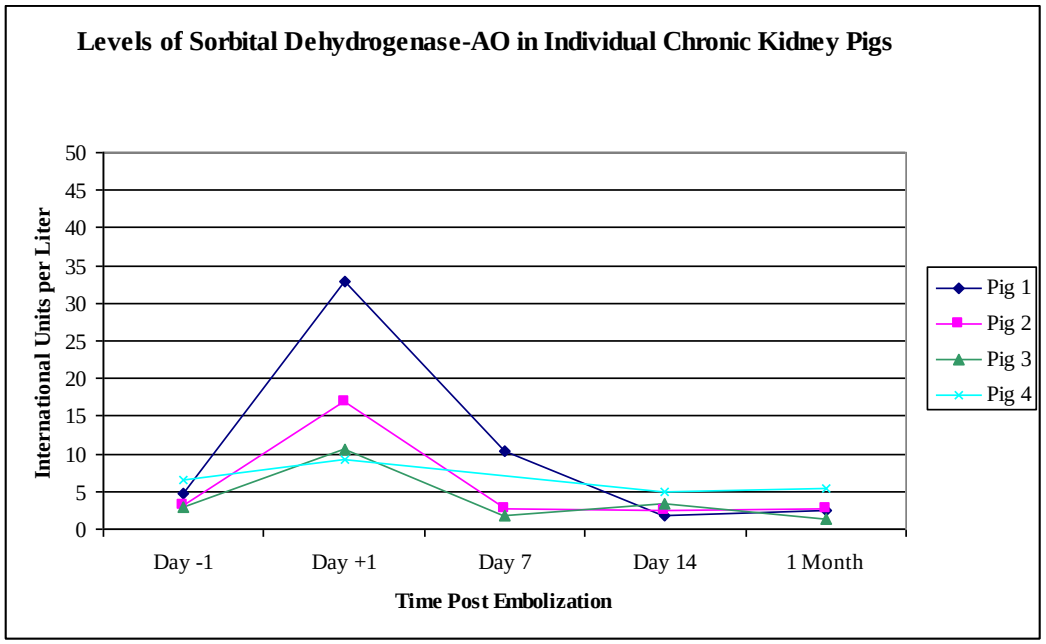
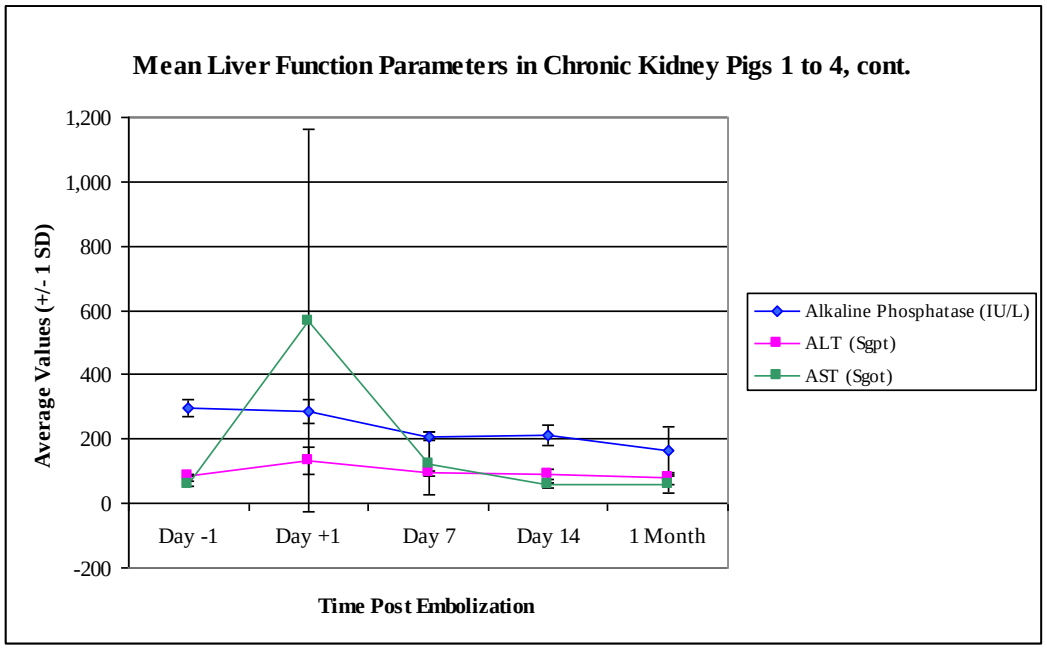


Figure 11. Mean Liver Function Parameters in Chronic Kidney Pigs 1 to 4, cont.



Source: Appendix N, Panel E.

Figure 12. AST (Sgot) Levels in Individual Chronic Kidney Pigs

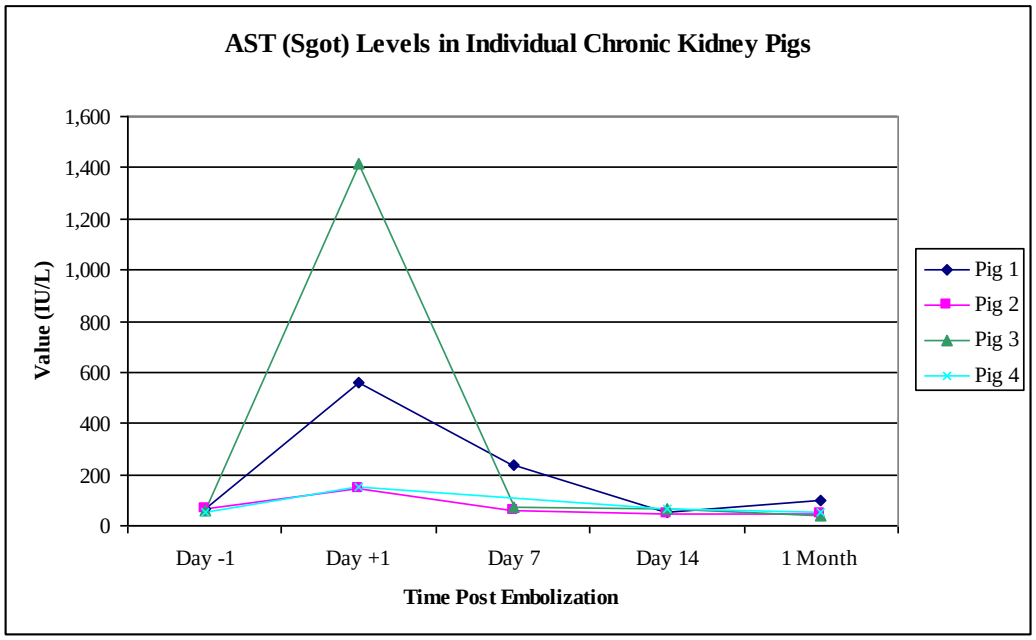
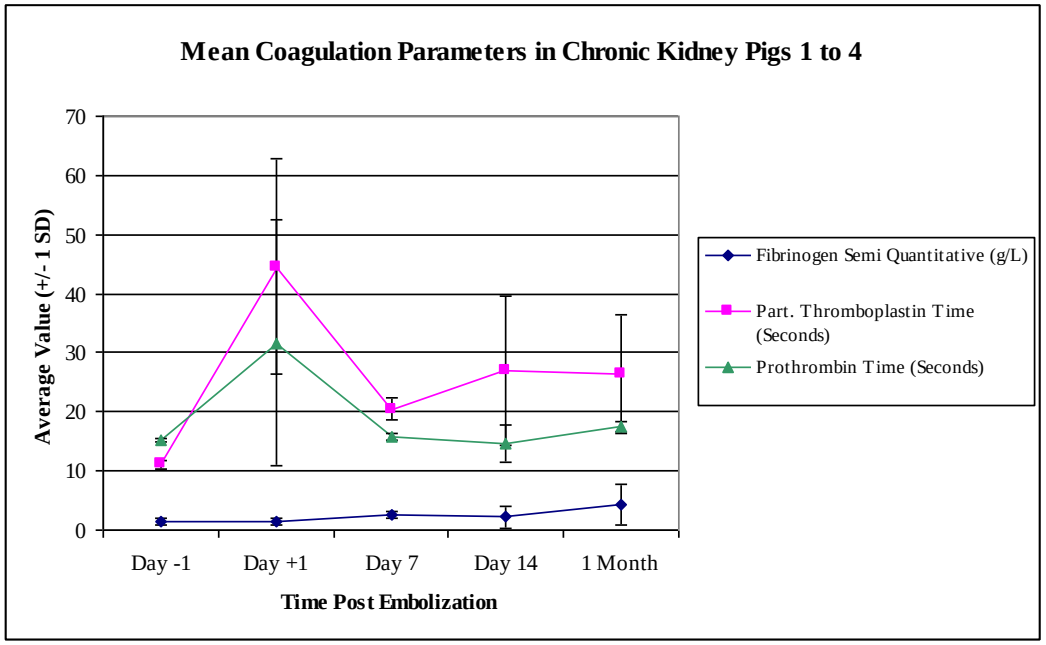


Figure 13. Mean Coagulation Parameters in Chronic Kidney Pigs 1 to 4



Source: Appendix O, Panel B.

Figure 14. Partial Thromboplastin Time in Individual Chronic Kidney Pigs

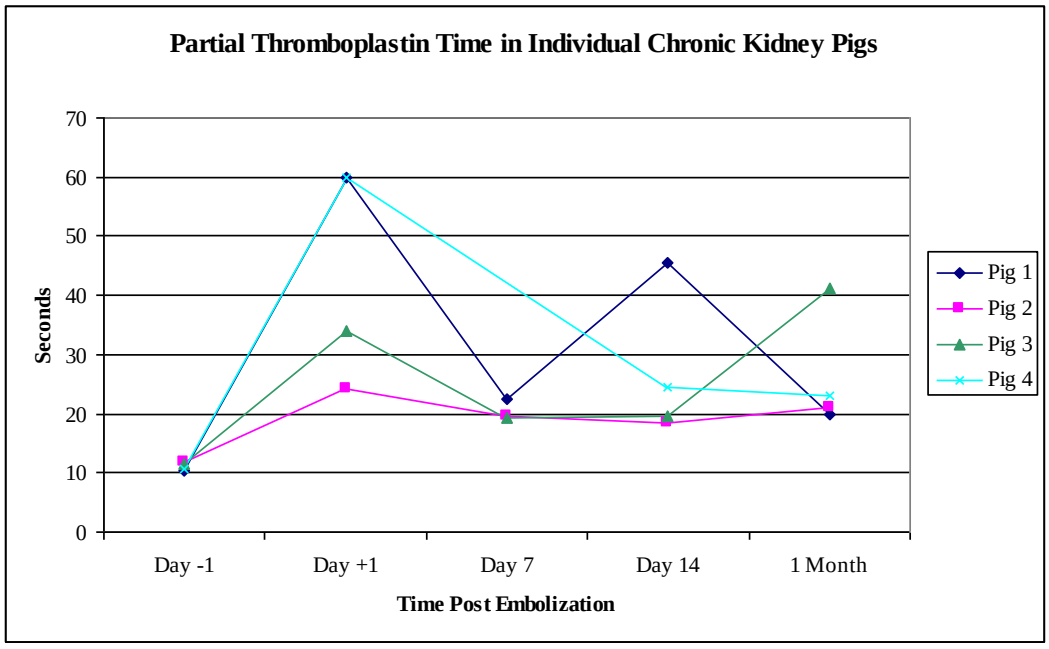


Figure 15. Prothrombin Time in Individual Chronic Kidney Pigs

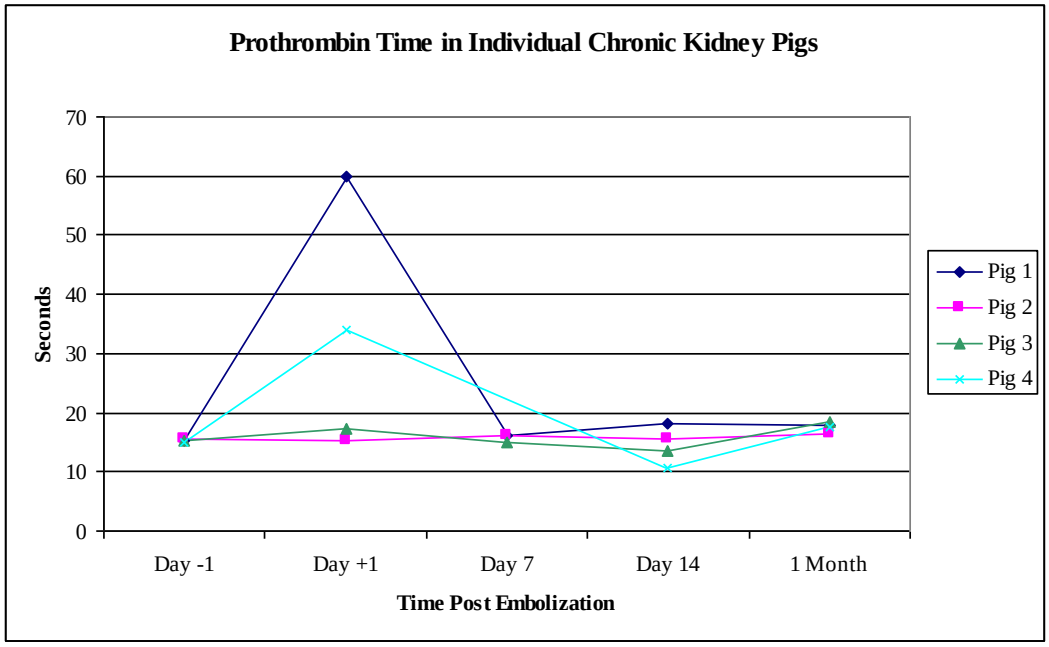
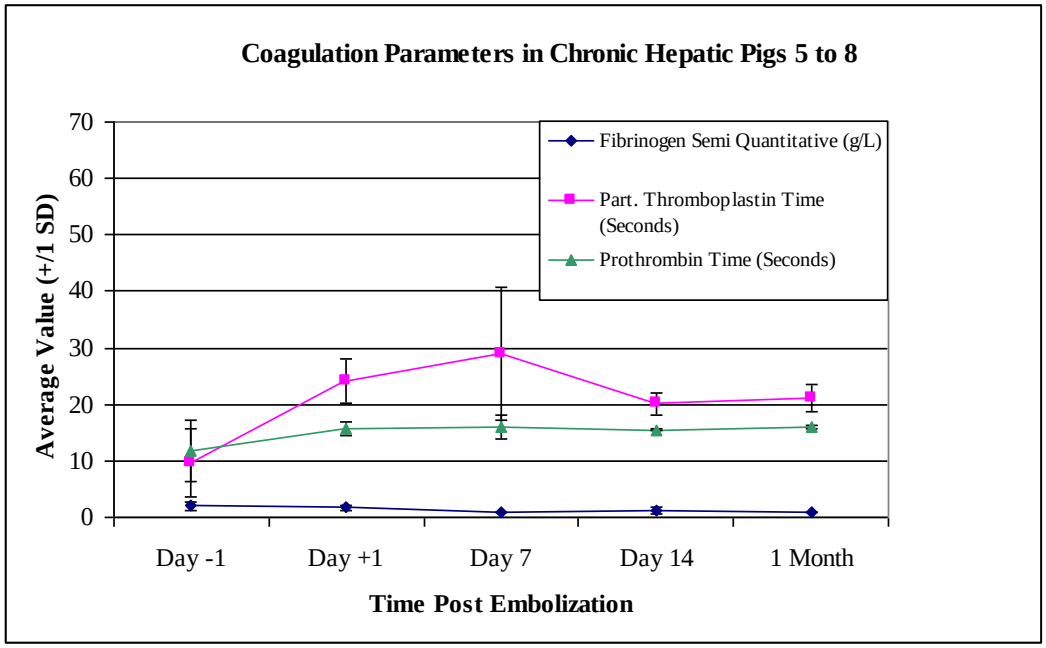
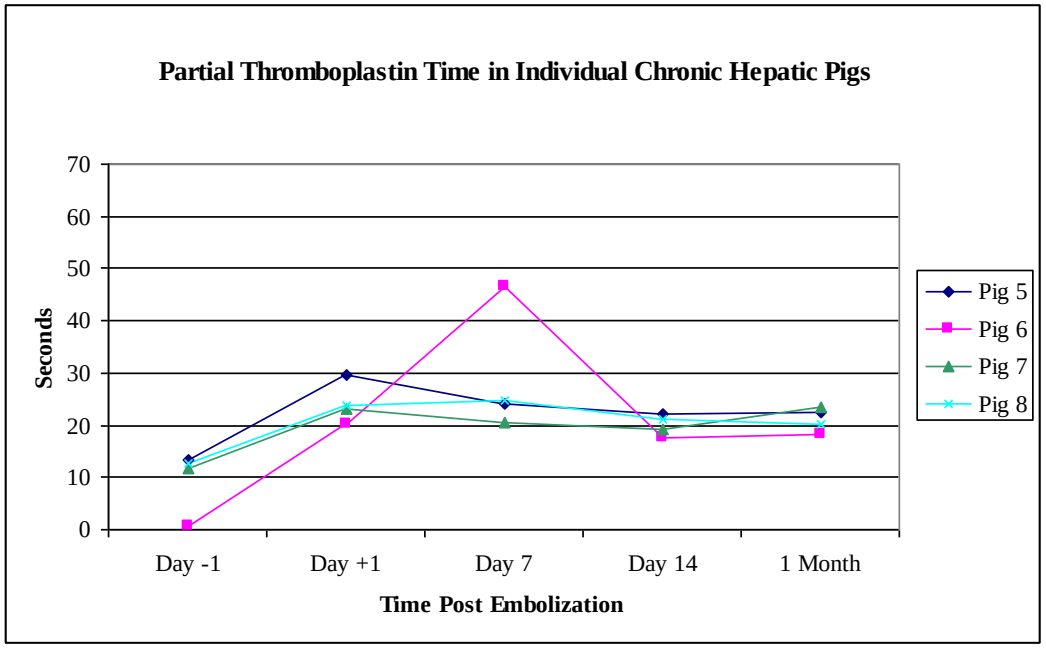


Figure 16. Coagulation Parameters in Chronic Hepatic Pigs 5 to 8



Source: Appendix O, Panel C.

Figure 17. Partial Thromboplastin Time in Individual Chronic Hepatic Pigs



6.4.4 Full Clinical Laboratory Data. The Clinical Laboratory data for each individual animal for all samples are provided in Appendix D together with normal reference ranges. The Clinical Laboratory data and the calculated means for all data points for all Chronic Renal Pigs 1 to 4 are provided by day sampling (Day -1, Day +1, Day 14 and Day 28) in Appendix E. Appendix F is a table of the Clinical Laboratory data (mean and standard deviations) for all days for Chronic Renal Pigs 1 to 4. The data for the Chronic Hepatic Pigs 5 to 8 are listed in Appendices G and H. The data for Acute Pigs 9 to 12 are listed in Appendix I. Data outside the normal range are shown in the tables in bold.

Graphs of the means of the Clinical Laboratory Data for each group of animals (Chronic Renal Pigs 1 to 4, Chronic Hepatic Pigs 5 to 8 and Pre-Treatment Values [Pigs 1 to 4 at 10 weeks old; Pigs 5 to 8 at 11 weeks old; and Pigs 9 to 12 at 15 weeks old]) are presented in Appendices J to O.

6.5 Postmortem Histological Findings.

6.5.1. Renal Artery Embolization.

6.5.1.1. Acute Animals. Embolization of the renal artery caused blanching of the treated kidney in Acute animals sacrificed after treatment. The contralateral kidney was unchanged. The treated renal artery or branch of the renal artery was visibly filled with the OCL 505 microspheres at the time of sacrifice and they could be felt through the arterial wall when it was palpated. The OCL 505 microspheres were only found in the treated vasculature.

Figure 18 is a representative photomicrograph of an acutely treated renal artery. The renal artery is visibly distended due to the administration of the OCL 505 microspheres. The microspheres were dislodged during tissue processing and none are present in the figure. There were no morphological changes observed in the acute tissues.

6.5.1.2. Chronic Animals. One month after embolization of the renal artery or one of its branches, the treated kidney was much smaller than the untreated contralateral control organ (Figure 19) in all Chronic Liver Pigs 1 to 4. This was due to morphological changes in the treated kidney, including atrophy of both the cortex and medulla (Figure 20). The untreated contralateral control kidney demonstrated compensatory hypertrophy.

Table 6 compares the length and width of treated and untreated kidneys from the Chronic Kidney Pigs 1 to 4. The longest and widest points of each kidney was measured with a ruler from an enlarged photograph of each pair of organs. Ten centimetres of the ruler in the photograph was then measured to calculate a conversion factor. This factor was used to calculate the final lengths and widths. The treated kidneys are 46% the length and 35% the width of the untreated kidneys.

Figure 21 shows a representative low-power (20x) cross-section of a kidney one month after embolization of the renal artery. This demonstrates the profound structural and morphological changes in the cortex and medulla observed grossly in Figure 20.

Figure 22 is a representative higher power (100x) photomicrograph of an occluded renal artery one month after embolization. The PLGA microspheres appear to be compressed and potentially fused together into large masses that completely occlude the artery. There are no discrete, round, OCL 505 microspheres observable one month after treatment. Fibrous connective tissue is clearly evident holding the PLGA mass in place.

A summary report of the gross post-mortem and histological findings for Chronic Kidney Pigs 1 to 4 and Acute Kidney Pigs 9 and 10 is provided in Appendix P.

6.5.2. Hepatic Artery Embolization.

6.5.2.1. Acute Animals. Embolization of the hepatic artery caused a faint blanching of the treated lobe of the liver in the acutely treated animals that were sacrificed immediately after treatment. The treated branch of the hepatic artery was visibly filled with the OCL 505 microspheres and they could be felt through the arterial wall when it was palpated. As with the renal artery, the acutely treated hepatic artery was visibly distended although all microspheres were lost during tissue preparation (data not shown).

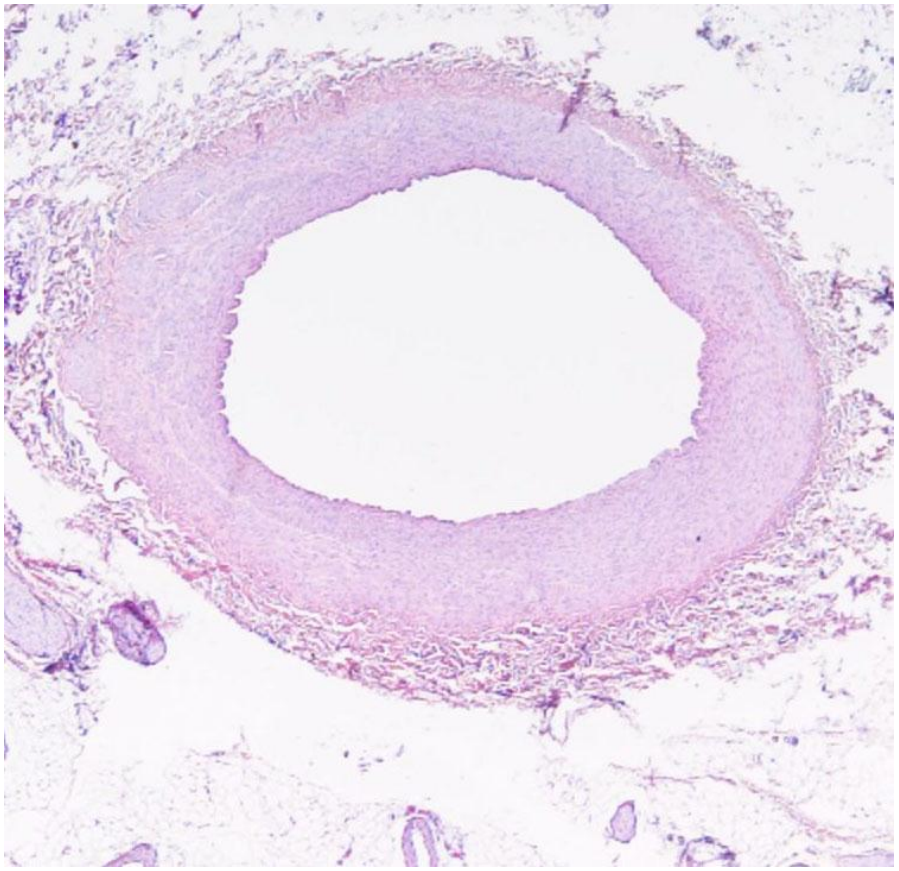
6.5.2.2. Chronic Animals. There were no gross morphological changes visible in the liver one month after embolization of one or more branches of the hepatic artery.

Figure 23 shows representative occluded hepatic arterioles one month after embolization. There are multiple occluded arterioles visible in the field. The liver tissue surrounding the occluded arterioles, although blanched to some extent, shows no sign of necrosis. Patent, non-occluded, arterioles filled with blood are also visible in the micrograph. The OCL 505 microspheres in the occluded arterioles are highly compressed, with a significant amount of fibrous connective tissue holding the microspheres in place, similar to that observed in the occluded renal artery (Figure 22).

OCL 505 microspheres were only found in the treated hepatic vasculature.

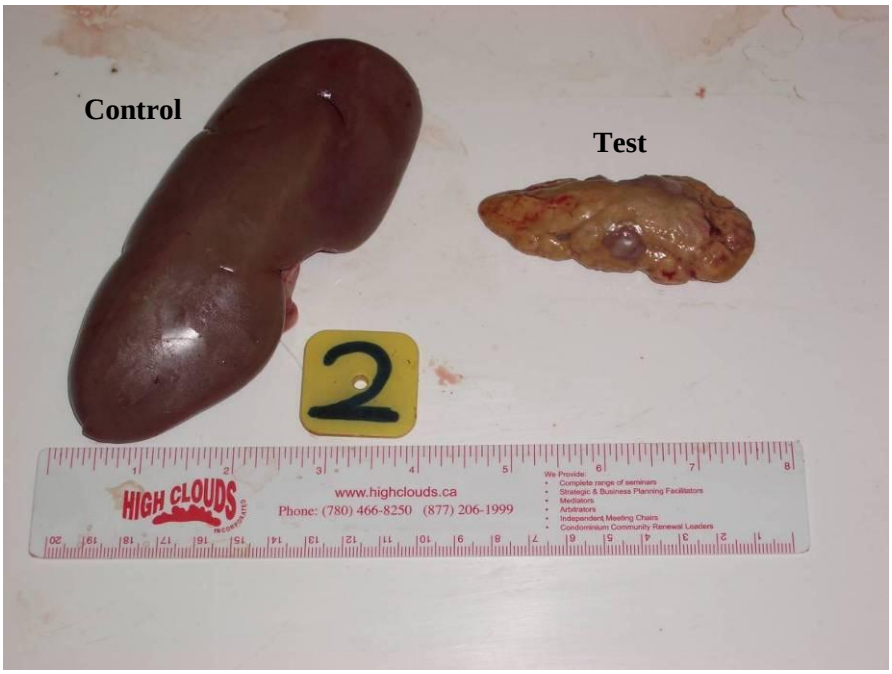
A summary report of the gross post-mortem and histological findings for Chronic Hepatic Pigs 5 to 8 and Acute Hepatic Pigs 11 and 12 is provided in Appendix Q.

Figure 18. OCL 505 microspheres in a treated renal artery of Acute Pig 10.



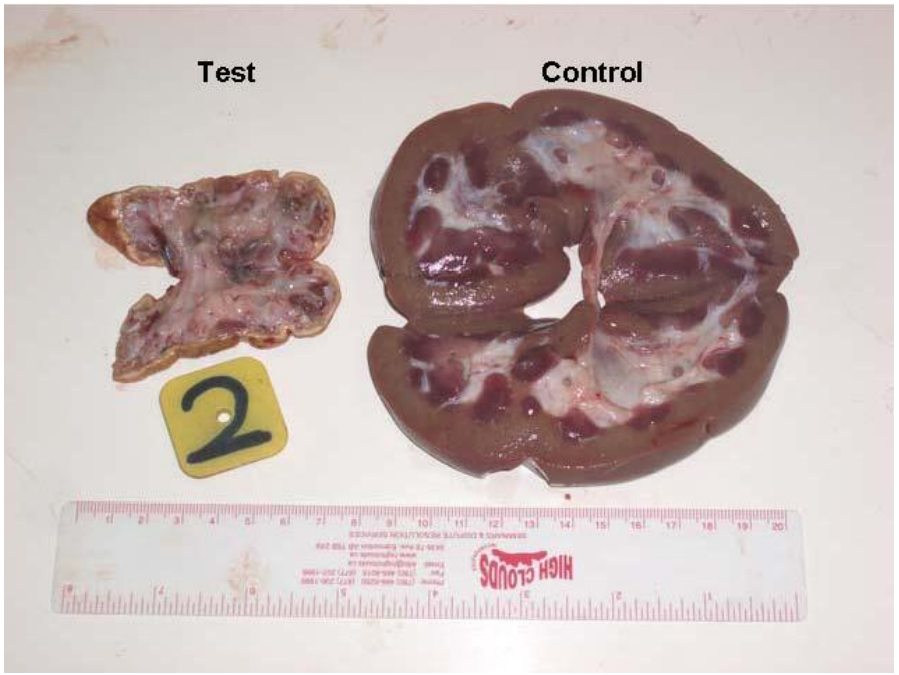
Photomicrograph of an H&E section from an acutely occluded renal artery. The microspheres have distended the artery, but were lost in processing as there is no matrix one hour after implantation to hold them in place. Magnification = 20x.

Figure 19. Comparison of treated and untreated kidneys from Chronic Kidney Pig 2 one month after embolization of the renal artery.



Gross comparison of treated and untreated kidneys.

Figure 20. Morphology of treated and untreated kidneys from Chronic Kidney Pig 2 one month after embolization of the renal artery.



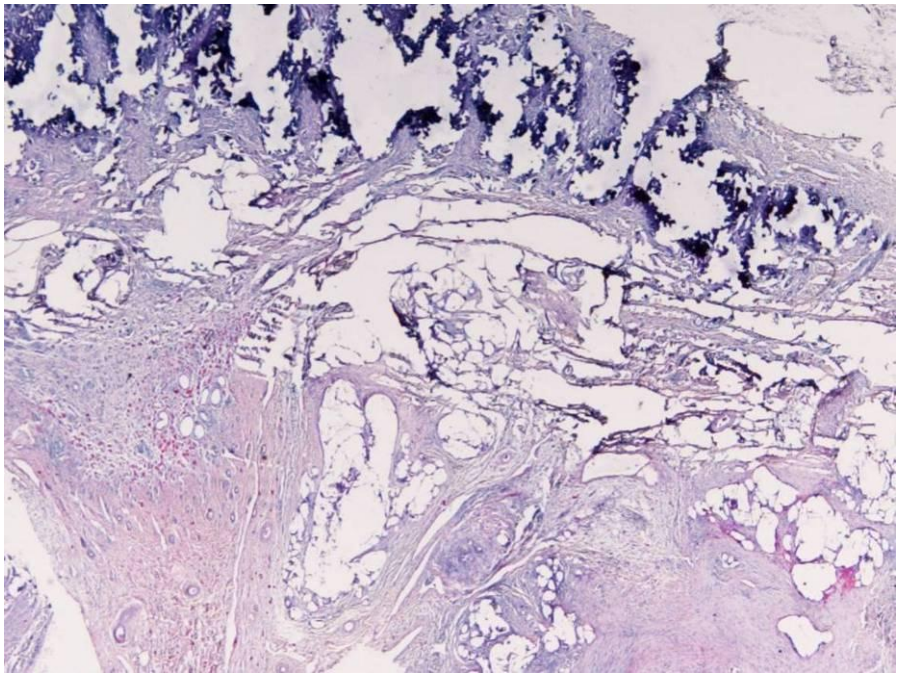
Gross comparison of treated and untreated kidneys. The renal artery was treated with a single intra-arterial administration of OCL 505. The organs have been bisected to show the significant morphological changes following occlusion, including the almost total atrophy of the cortex and partial atrophy of the medulla in the treated kidney in comparison to that of the contralateral control kidney from the same animal.

Table 6. Measurements of treated and untreated kidneys from Chronic Kidney Pigs 1 to 4.

Treated Kidney							
Pig	Longest Length (cm)[1]	Widest Width (cm)	Measurement of 10 cm for conversion	Conversion Factor[2]		Calculated Length[3]	Calculated Width
1	8.2	4.0	10.0 cm = 10.4 cm	0.96		7.88	3.85
2	8.5	3.3	10.0 cm = 10.6 cm	0.94		8.02	3.11
3	8.1	5.7	10.0 cm = 13.0 cm	0.77		6.23	4.38
4	6.3	3.2	10.0 cm = 8.4 cm	1.20		7.54	3.83
				Mean (± 1 SD) =		7.42 ± 0.82	3.79 ± 0.52
Contralateral Control Kidney							
Pig	Longest Length (cm)	Widest Width (cm)	Measurement of 10 cm for conversion	Conversion Factor		Calculated Length[3]	Calculated Width
1	13.6	7.1	10.0 cm = 10.4 cm	0.96		13.08	6.83
2	14.8	6.1	10.0 cm = 10.6 cm	0.94		12.76	5.26
3	14.0	6.3	10.0 cm = 13.0 cm	0.77		10.77	4.85
4	11.7	4.9	10.0 cm = 8.5 cm	1.18		13.76	5.76
				Mean (± 1 SD) =		12.89 ± 1.47	5.80 ± 0.81

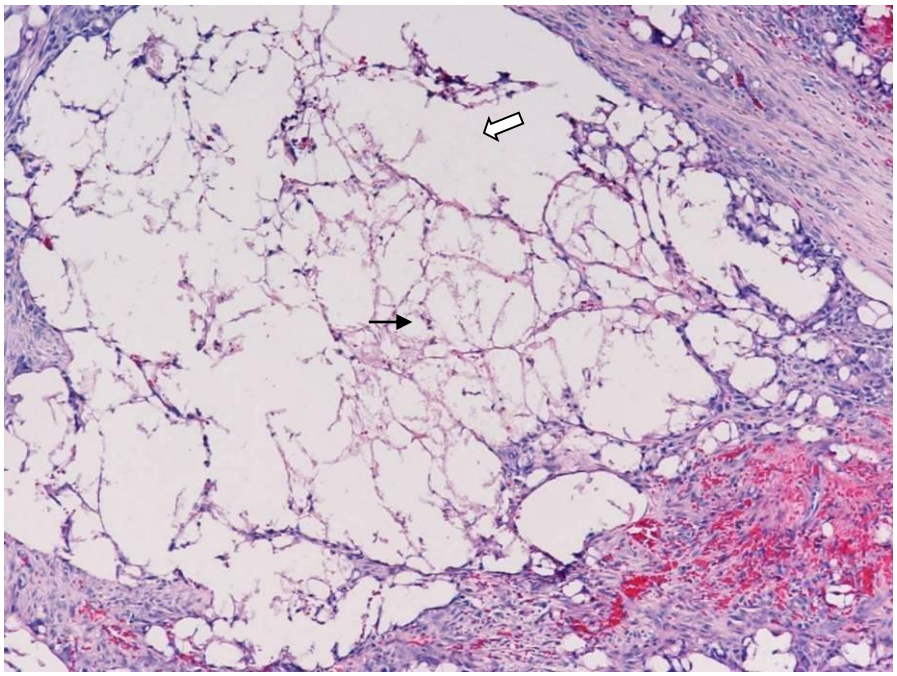
[1]The longest and widest points of the kidney measured on an enlarged photograph of each kidney pair.
[2]Ten cm on the ruler in the photograph divided by the length measured on the photograph.
[3]Length or width measured on the photograph multiplied by the conversion factor.

Figure 21. Kidney section from Chronic Kidney Pig 4



Microscopic morphology of the embolized kidney from Pig 4 one month after embolization. There is fibrosis and mineralization of the medulla with almost complete atrophy of the cortex. Magnification = 20x.

Figure 22. Occluded renal artery of Chronic Pig 2.



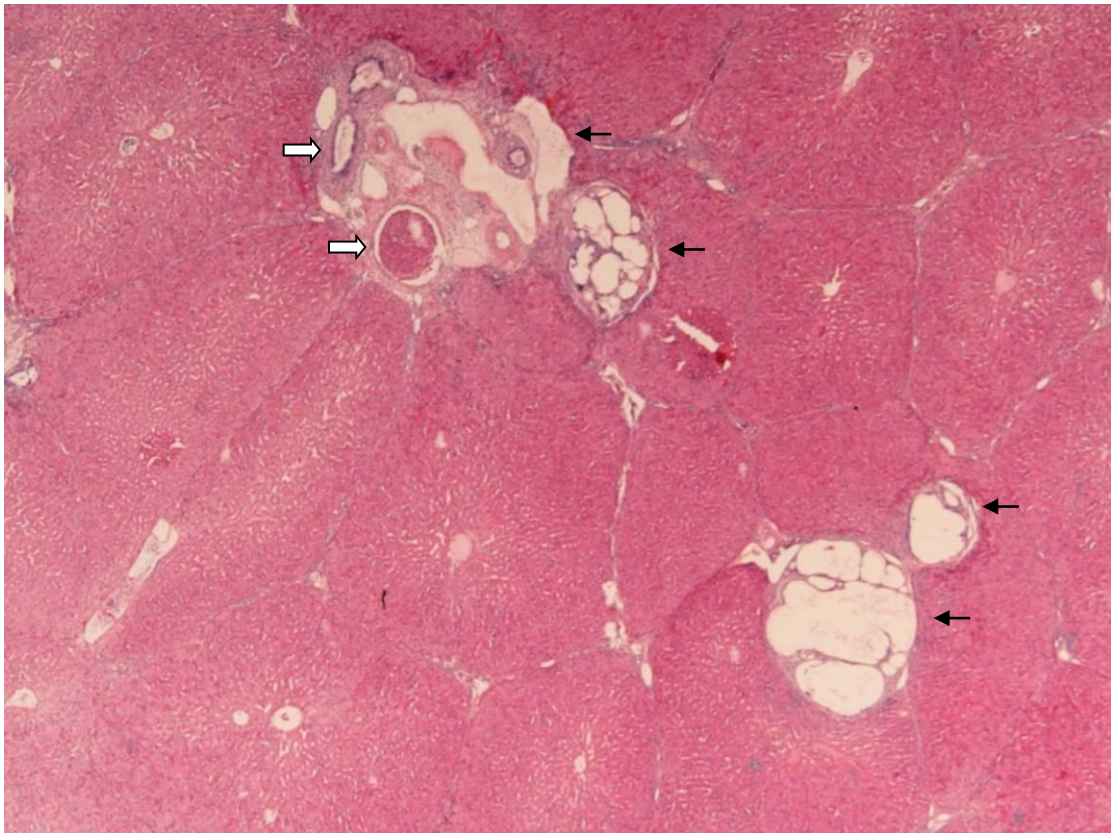
Photomicrograph of an occluded renal artery one month after implantation. There are thick bands of fibrous tissue (black arrow) surrounding and separating each microsphere or cluster of microspheres (white arrow). Deformity of the microspheres is evident. Red blood cells are visible in the lower right portion of the micrograph. Magnification = 100x.

7. Discussion

In this preclinical study of the safety and effectiveness of OCL505 as an artificial embolization device, the product was implanted in the renal and hepatic arteries of Durock-Yorkshire-Landrace cross pigs. In preparation for administration, the OCL 505 microspheres were suspended in a 3:1 ratio of saline to contrast medium (Appendix C), and the resulting suspension of microspheres was easily delivered through standard angiocatheters. The interventional radiologist performing the procedure noted that any blockages of the angiocatheter were easily cleared by simple flushing. One to three vials of the product were required to embolize the target vessel to effective stasis. An average of 2 vials was required to embolize the renal artery to effective stasis in 10 to 15 week old pigs. In contrast, an average of 1.4 and 3 vials was required to embolize the lobular branch of the hepatic artery to effective stasis in 11 and 15 week old pigs, respectively (Table 4).

Twelve pigs were treated in this study. Four pigs (Chronic Kidney Pigs 1 to 4) were implanted at 10 weeks of age, four pigs (Chronic Hepatic Pigs 5 to 8) were implanted at 11 weeks of age, and four pigs (Acute Kidney Pigs 9 and 10 and Acute Hepatic Pigs 11 and 12) were implanted at 15 weeks of age. The animals in the Acute Kidney and Acute Hepatic Treatment Groups were sacrificed immediately after the implantation procedure, whereas the animals in the Chronic Kidney and Chronic Hepatic Treatment Groups were sacrificed one month post implantation.

Figure 23. OCL 505 microspheres in the liver of Chronic Pig 8 one month after embolization.



Photomicrograph of occluded hepatic arterioles (black arrows point to examples). Bands of fibrous tissue invest each microsphere or cluster of microspheres, forming a matrix that occludes the arterioles. The liver is potentially blanched in surrounding areas, but there is no evidence of infarction in the tissue. Patent, non-occluded arterioles are also present (white arrows). Magnification = 20x.

Implantation of OCL 505 caused decreased blood flow in the implanted artery and caused blanching of the downstream kidney or segment of the liver. Following implantation, the treated arteries became rigid and visibly distended (Figure 18), and the microspheres could be palpated through the vessel wall.

One month after implantation, the treated arteries were completely occluded. On histological examination, thick bands of fibrous tissue surrounded and separated each microsphere or cluster of microspheres. The appearance of the microspheres in both the renal and hepatic arteries was similar (Figure 22, 100x magnification, and Figure 23, 20x magnification). The microspheres were compressed and distorted, which is consistent with the microspheres undergoing degradation. There was no evidence of recanalization in either the renal or hepatic arteries.

Treated kidneys were smaller than the contralateral untreated kidneys one month post embolization (Figure 19). On histological examination, the treated kidney had

undergone significant morphological changes, including the almost total atrophy of the cortex and partial atrophy of the medulla (Figures 20 and 21).

Immediately following the embolization of a single lobe of the porcine liver, blanching of the treated lobe was noted. However, in contrast to the atrophy that occurred in the embolized porcine kidney, there were no significant long-term morphological changes associated with the embolization of the liver. Despite the evidence that the treated arteries were completely occluded at one month post occlusion (Figure 23), there was no evidence of infarction, which was considered to be due to the nature of the dual arterial and portal blood supply to the liver parenchyma.

All animals recovered quickly and uneventfully after surgery. A number of transitory changes in clinical chemistry parameters were observed in the Chronic Kidney Pigs, including elevated creatinine (Figures 7 and 8), uric acid (Figure 7), albumin (Figure 9) sorbital dehydrogenase-AO (Figures 9 and 10), AST (SGOT) levels (Figures 11 and 12) as well as prolonged partial thromboplastin (Figures 13 and 14) and prothrombin times (Figures 13 and 15). Since these changes were observed in the Chronic Kidney Pigs one day after surgery, and often in one or two animals within the group, the changes were considered to be due to the initial stress from the functional loss of one kidney rather than to implantation of OCL505 itself. Only one animal in the Chronic Hepatic Pig Group had a prolonged partial thromboplastin time seven days after implantation (Figure 17). All clinical laboratory changes resolved with time.

As a consequence of an abscess associated with a puncture wound in a hind leg of Chronic Kidney Pig 3, this animal had an elevated neutrophil count 14 to 21 days after implantation (Figures 5 and 6). This change in neutrophil count was therefore considered to be unrelated to implantation of OCL 505.

All pigs gained weight throughout the study. However, the animals in the Chronic Kidney Pig group gained weight more slowly than those animals in the Chronic Hepatic Pig or untreated Acute Pig groups (Figure 4). This suggests that the functional loss of one kidney and the metabolic demands to remove tissue breakdown by-products impacted the rate of weight gain. However, several other factors also contributed to this difference in weight gain. Firstly, the Chronic Kidney Pigs 2 and 4 weighed 6 to 9 kg less than other Chronic Kidney or Hepatic Pigs prior to treatment. Therefore, the Chronic Kidney Pig group had an initial mean weight that was less than that of the Chronic Hepatic Pigs (Appendix B). Chronic Kidney Pigs 2 and 4 gained weight during the study, but always weighed less than animals in the other two groups (Figure 3). Secondly, the weight gain differences may have been due in part to the age and size of the animals when treated. Young pigs gain weight very rapidly (the Chronic Hepatic Pigs had a mean weight gain of 4.4 kg between the ages of 10 weeks and 11 weeks [Appendix B]). This additional bulk in the Chronic Hepatic Pigs at 12 weeks of age may have helped buffer the impact of surgery on the animals. Finally, Chronic Kidney Pig 3 had a leg abscess, which affected its ability to move

and eat and therefore caused it to gain weight more slowly than the animals in its group (Figure 3).

Occlusin® 505 AED was found to be safe and effective as an embolotherapeutic agent as tested. Additional work is warranted with this device.

8. Conclusions

Primary Objective:

(a) OCL 505 was safe and effective for use as an artificial embolization device as tested.

Secondary Objectives:

(a) OCL 505 microspheres were spherical immediately after implantation but showed signs of particle remodelling one month after implantation. The remodelling was the result of the microspheres undergoing biodegradation and reabsorption.

(b) No significant systemic toxicity was observed following implantation. Transient elevations were observed in several clinical laboratory parameters that were attributed to the functional loss of one kidney or of the surgical procedure rather than as a reaction to the implantation of OCL 505. All clinical laboratory parameters that were out of the normal range returned to normal within 7 to 14 days after implantation.

(c) Implantation of OCL 505 caused striking morphological changes in the embolized kidney but no observed infarction of the liver parenchyma. The resistance of the liver to infarction was considered due to its dual blood supply.

(d) No evidence of recanalization was observed one month after implantation of OCL 505 in arteries supplying the kidney or lobes of the liver.

(e) OCL 505 was readily and consistently suspended to neutral buoyancy in contrast media and Sodium Chloride Injection. The resuspended device was easy to administer through standard 5-French angiocatheters.

9. References

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5. Zimmerman A, Schubiger PA, Mettler D, Geiger L, Triller J, Rosler H. Renal pathology after arterial yttrium-90 microsphere administration in pigs. Invest Rad. 1995; 12: 716-723.

Appendix A. Study Timeline and Flow Chart

Pigs 1 – 4 (Renal Artery Embolization)														
Time from Embolization	**DAYS**											**WEEKS**		**MONTH**
	---	**-7**	**-1**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**2**	**3**	**1**
Animal Age (Weeks)		**9**		**10**							**11**	**12**	**13**	**14**
Daily Observation		X	X	X	X	X	X	X	X	X	X	X	X	X
Acclimatization		X												
Physical Exam & Vital Signs			X	X[1]	X						X	X		X
Body Weight			X								X	X		X
Bleeding & Laboratory Testing			X		X						X	X		X
Angiography				X										
Embolization				X										
Metacam[2]				X	X									
Necropsy														X
Gross Evaluation														X
Histology														X
Pigs 5 to 8 (Hepatic Artery Embolization)														
Time from Embolization	**DAYS**											**WEEKS**		**MONTH**
	-14	**-7**	**-1**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**2**	**3**	**1**
Animal Age (Weeks)	**9**	**10**		**11**							**12**	**13**	**14**	**15**
Daily Observation	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Acclimatization	X	X												
Physical Exam & Vital Signs		X	X	X[1]	X						X	X		X
Body Weight		X	X								X	X		X
Bleeding & Laboratory Testing			X		X						X	X		X
Angiography				X										
Embolization				X										
Metacam[2]				X	X									
Necropsy														X
Gross Evaluation														X
Histology														X

[1]Physical Exam (only) one hour post-embolization

[2]Metacam was administered for the first two days, and then as needed for analgesia

Appendix A. Study Timeline and Flow Chart, cont.

Pigs 9 – 12 (Acute Renal and Hepatic Embolizations)													
Time from Embolization	**DAYS**										**WEEKS**		**MONTH**
	-35	**-28**	**-1**	**0**									
Animal Age (Weeks)	**9**	**10**		**15**									
Daily Observation	X	X	X										
Acclimatization	X												
Physical Exam & Vital Signs		X	X										
Body Weight		X	X										
Bleeding & Laboratory Testing		X	X										
Angiography			X										
Embolization				X									
Necropsy				X									
Gross Evaluation				X									
Histology				X									

Appendix B. Individual Animal Weights

Weight of the individual animals in kilograms on the specified date and day of the study.

Date	15 May 07	22 May 07	29 May 07	06 Jun 07	13 Jun 07	19 Jun 07
Day[1]	Day -1	Day 7	Day 14	---	1 Month	---
Age	10 Weeks	11 Weeks	12 Weeks	13 Weeks	14 Weeks	15 Weeks
Pig 1	25.0	32.6	33.5	---	45.7	---
Pig 2	16.0	26.2	29.7	---	37.9	---
Pig 3	26.2	27.5	34.4	---	36.9	---
Pig 4	18.5	27.7	34.9	---	44.5	---
Mean	21.43	28.50	33.13	---	41.25	---
1 Std	4.95	2.81	2.36	---	4.49	---
Day	Day -7	Day -1	Day 7	Day 14	---	1 Month
Pig 5	24.9	25.6	32.8	44.8	---	59.5
Pig 6	27.3	28.9	35.0	46.8	---	61.5
Pig 7	22.4	32.5	36.9	40.4	---	51.3
Pig 8	27.0	32.5	37.1	44.9	---	59
Mean	25.40	29.88	35.45	44.23	---	57.83
1 Std	2.27	3.32	2.00	2.71	---	4.48
Day	Day -35	---	---	---	---	Day -1
Pig 9	16.7	---	---	---	---	56.8
Pig 10	24.3	---	---	---	---	56.7
Pig 11	21.9	---	---	---	---	63.9
Pig 12	23.5	---	---	---	---	61.8
Mean	21.60	---	---	---	---	59.80
1 Std	3.42	---	---	---	---	3.62

[1]Study Day relative to embolization. Day -7, 7 days prior to embolization, Day -1 = 24 hours before embolization, Day 7 = one week post embolization, Day 14 = 2 weeks post embolization, and 1Month = 4 weeks post embolization.

Appendix C. Embolization Information for All Animals

Animal ID	Pig 1	Pig 2	Pig 3	Pig 4	Pig 5	Pig 6	Pig 7	Pig 8	Pig 9	Pig 10	Pig 11	Pig 12
Order of Surgery	4	3	2	1	5	6	7	8	9	10	11	12
Date of Surgery	16 May 2007	16 May 2007	16 May 2007	16 May 2007	23 May 2007	23 May 2007	23 May 2007	23 May 2007	20 June 2007	20 June 2007	20 June 2007	20 June 2007
Animal Age at Surgery	10 Weeks	10 Weeks	10 Weeks	10 Weeks	11 Weeks	11 Weeks	11 Weeks	11 Weeks	15 Weeks	15 Weeks	15 Weeks	15 Weeks
Animal Age at Sacrifice	14 Weeks	14 Weeks	14 Weeks	14 Weeks	15 Weeks	15 Weeks	15 Weeks	15 Weeks	15 Weeks	15 Weeks	15 Weeks	15 Weeks
Route of Embolization	Femoral Artery	Femoral Artery	Femoral Artery	Femoral Artery	Femoral Artery	Femoral Artery	Femoral Artery	Femoral Artery	Brachial Artery	Brachial Artery	Brachial Artery	Brachial Artery
Artery Embolized	Renal	Renal	Renal	Renal	Hepatic	Hepatic	Hepatic	Hepatic	Renal	Renal	Hepatic	Hepatic
Organ Occluded	Left Kidney (LP)[1]	Right Kidney (UP)[2]	Right Kidney (Whole)	Left Kidney (Whole)	Anterior left lobe of Spleen	Left segments 2,3 of Spleen	Left hepatic arterial branch	Right anterior hepatic arterial branch	Left Kidney (Whole)	Left Kidney (UP)	Anterior hepatic main branch	Right Branches of Spleen
Contrast Agent	Omni 300	Omni 300	Omni 300	Omni 300	Omni 240	Omni 240	Omni 240	Omni 240	Omni 300	Omni 300	Omni 300	Omni 300
Saline per Vial (mL)	5	5[3], 5[2]	5, 5	10, 10, 5[4]	8.3	8	8, 8	8, 8	10, 10	10, 5	5, 5, 5	15, 7.5
Contrast Agent per Vial (mL)	15	15, 15	15, 15	30,30,15	28	25	30, 30	30, 30	30, 30	30, 15	15,15,15	45, 22.5
Total Volume per Vial (mL)	20	20, 20	20, 20	40,40,20	36	33	38, 38	38, 38	40, 40	40, 20	20	30
Vials Diluted	1	2	2	3	1	1	2	2	2	2	3	3
Total Volume (mL)	20	40	40	100	36	36	76	76	80	60	60	90
Volume for Effective Stasis (mL)	19.5	40	40	98	36	36	62	76	80	60	60	90
Total Vials Used	0.98	2.00	2.00	2.94	1.00	1.00	1.63	2.00	2.00	2.00	3.00	3.00
Time to embolize (min)	8	17	15	23	10	9	12	10	DNR[5]	DNR	DNR	DNR
Fluorography Time (min)	3.8	DNR	7.1	10.6	5.6	5.6	DNR	4.8	5	6.2	3.1	9.8
Hands On	1:50	12:39	11:05	9:47	9:35	11:10	12:15	14:10	9:20	10:55	11:50	13:25
Hands Off	2:17	13:20	11:45	10:28	DNR	11:40	DNR	14:35	10:25	11:12	12:15	13:55
Total Surgery Time (h)	0:27	0:41	0:40	0:41	DNR	0:30	DNR	0:25	1:05	0:17	0:25	0:30
Start Anesthesia	13:35	12:21	10:43	9:25	9:15	10:55	11:45	13:50	8:55	10:40	11:28	1:05
Back in pen	14:17	13:30	11:45	10:28	10:40	11:40	12:40	14:30	DNR	DNR	DNR	DNR
Total Procedure Time (h)	0:42	1:09	1:02	1:03	1:25	0:45	0:55	0:40	DNR	DNR	DNR	DNR

[1]Lower Pole; [2]Upper Pole; [3]mLs per first vial; mLs per second vial; [4]mLs per third vial; [5]Did not record.

Appendix D. Clinical Laboratory Data for Individual Animals

D1. Clinical Laboratory Data for Chronic Renal Pig 1

D2. Clinical Laboratory Data for Chronic Renal Pig 2

D3. Clinical Laboratory Data for Chronic Renal Pig 3

D4. Clinical Laboratory Data for Chronic Renal Pig 4

D5. Clinical Laboratory Data for Chronic Hepatic Pig 5

D6. Clinical Laboratory Data for Chronic Hepatic Pig 6

D7. Clinical Laboratory Data for Chronic Hepatic Pig 7

D8. Clinical Laboratory Data for Chronic Hepatic Pig 8

D9. Clinical Laboratory Data for Pigs 9 to 12

Appendix D1. Clinical Laboratory Data for Chronic Renal Pig 1.

Time Post Embolization	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Hematology							
White Cell Count	14.6	NS[1]	15.41	16.8	**10.31**[2]	x10E9/L	11.0 - 21.0
Red Cell Count	6.93	NS	6.13	6.42	6.9	x10E12/L	5.10 - 8.00
Hemoglobin	129	NS	116	119	125	g/L	90 - 150
Hematocrit	0.386	NS	**0.336**	**0.347**	0.37	L/L	0.36 - 0.48
Mean Corp Vol	55.7	NS	54.8	54.1	53.6	fl	52 - 66
Mean Corp Hemoglobin	18.6	NS	18.9	18.5	18.1	pg	17.0 - 24.0
Mean Corp Hemoglobin Conc	334	NS	345	342	338	g/L	300 - 360
RDW	21	NS	20.5	19	21.1	%CV	Reported Value
Platelet CNT	460	NS	530	493	389	x10E9/L	100 - 900
Mean Platelet Volume	NR[3]	NS	NR	23.8	18.4	fl	6.7-9.9
Differential Cell Count							
% Neutrophils	33	NS	29	30	**28**	%	Reported Value
% Lymphocytes	60	NS	63	60	68	%	Reported Value
% Monocytes	4	NS	**8**	**9**	2	%	Reported Value
% Eosinophils	1	NS	NR	1	1	%	Reported Value
% Basophils	1	NS	NR	NR	1	%	Reported Value
Absolute Differential Values							
Neutrophils	4.85	NS	4.47	5.04	**2.88**	x10E9/L	3.00 - 14.00
Lymphocytes	8.79	NS	9.71	10.08	7.05	x10E9/L	3.8 - 14.50
Monocytes	0.603	NS	**1.23**	**1.51**	0.21	x10E9/L	0 - 1.000
Eosinophils	0.198	NS	NR	0.17	0.075	x10E9/L	0 - 1.500
Basophils	0.134	NS	NR	NR	0.094	x10E9/L	0 - 0.500
Chemistry							
Glucose	**4.5**	**9.5**	6.6	5.2	**4.5**	mmol/L	4.7 - 8.3
Blood Urea Nitrogen	5.9	8	9	8	8.1	mmol/L	3.5 - 10.6
Creatinine	100.9	135.8	79	100.2	129.4	µmol/L	75 - 205
BUN/Cr Ratio	15	15	29	20	16	Ratio	Reported Value
Sodium	137	145	144	144	142	mmol/L	135 - 150
Potassium	4.4	6	5.4	4.2	4.3	mmol/L	4.0 - 6.7
Na/K Ratio	31	24	27	34	33	Ratio	Reported Value
Chloride	102	110	107	109	105	mmol/L	94 - 110
Carbon Dioxide	20.6	**16.6**	**27.4**	**32.8**	**31.5**	mmol/L	18 - 26
Anion Gap	19	24	15	6	10	mmol/L	10-20
Calcium	2.41	2.09	2.52	2.45	2.49	mmol/L	1.73 - 2.83
Phosphorus	**3.26**	**3.2**	**3.23**	2.74	**3.25**	mmol/L	1.65 - 2.85
Total Protein	**50**	**62**	**52**	**54**	**61**	g/L	70 - 89
Albumin	**35.22**	**42.57**	**36.84**	**34.38**	**38.96**	g/L	19 - 32
Globulin	**15**	**19**	**15**	**20**	**22**	g/L	35 - 54
A/G Ratio	**2.4**	**2.2**	**2.4**	**1.8**	**1.8**	Ratio	0.4 - 1.4
Total Bilirubin	5	1	0	3	INV	µmol/L	0 - 6
Alkaline Phosphatase	263	270	223	**165**	235	IU/L	180 - 460
ALT (Sgpt)	83	124	96	76	104	IU/L	Reported Value
Gamma gt	**58**	**60**	**57**	**44**	**53**	IU/L	8.0 - 40
Creatine Phosphokinase	**1,747**	**24,648**	**13,569**	**5,578**	**11,757**	IU/L	00 - 125
Calculated Osmolality	273	298	293	289	285	mmol/kg	NP[4]
AST (Sgot)	64	**562**	**237**	53	97	IU/L	30 - 100
Sorbital Dehydrogenase-AO	4.7	32.9	10.4	1.8	2.4	IU/L	Reported Value
Uric Acid	14	23	19	4	7	µmol/L	Reported Value
Date of Bleed[5]	16 May	17 May	24 May	30 May	13 Jun		

Appendix D1. Clinical Laboratory Data for Chronic Renal Pig 1, cont.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Ranges
Morphology and Coagulation Parameters							
Platelets	Adequate	NS	Adequate	Adequate	Adequate	Reported Value	Adequate
RBC Morph	**See Below**	NS	**See Below**	**See Below**	**See Below**	Reported Value	Normal
Aniso	1+	NS	NR	NR	1+	Reported Value	NP
Poik	3+	NS	2+	3+	3+	Reported Value	NP
Polychrom	1+	NS	NR	NR		Reported Value	NP
Fibrinogen Degradation Products	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	**Positive**	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	Observation	Negative
Fibrinogen Semi Quantitative	2	---	2	1	1	g/L	1.0 - 3.0
Part. Thromboplastin Time	**10.3**	**>60**	22.5	**45.5**	**20**	second	21.0 - 36.0
Prothrombin Time	**15.4**	**>60**	**16**	**18.2**	**17.8**	second	10.0 - 15.0
Date of Bleed	16 May	17 May	24 May	30 May	13 Jun		

[1] No Sample
[2] Numbers in bold are outside of the reference range
[3] Not Reported
[4] Not Provided

Appendix D2. Clinical Laboratory Data for Chronic Renal Pig 2

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Hematology							
White Cell Count	13.01	13.746	12.5	12.4	11.11	x10E9/L	11.0 - 21.0
Red Cell Count	5.84	6.91	5.69	6.49	6.97	x10E12/L	5.10 - 8.00
Hemoglobin	108	128	104	118	129	g/L	90 - 150
Hematocrit	**0.315**[1]	0.377	**0.312**	**0.357**	0.377	L/L	0.36 - 0.48
Mean Corp Vol	53.9	54.6	54.8	55	54.1	fl	52 - 66
Mean Corp Hemoglobin	18.5	18.5	18.3	18.1	18.5	pg	17.0 - 24.0
Mean Corp Hemoglobin Conc	343	338	334	329	343	g/L	300 - 360
RDW	19.3	19.7	19.7	20.9	20	%CV	Reported Value
Platelet CNT	357	381	485	379	370	x10E9/L	100 - 900
Mean Platelet Volume	19.7	22.7	24.7	NR[2]	NR	fl	6.7-9.9
Differential Cell Count							
% Neutrophils	59	43	28	**24**	**26**	%	Reported Value
% Lymphocytes	34	46	62	60	71	%	Reported Value
% Monocytes	7	7	6	8	2	%	Reported Value
% Eosinophils	NR	3	4	8	1	%	Reported Value
% Basophils	NR	0	0	NR	NR	%	Reported Value
Absolute Differential Values							
Neutrophils	7.68	5.95	3.52	**2.98**	**2.89**	x10E9/L	3.00 - 14.00
Lymphocytes	4.42	6.39	7.71	7.44	7.89	x10E9/L	3.8 - 14.50
Monocytes	0.91	0.906	0.706	0.99	0.22	x10E9/L	0 - 1.000
Eosinophils	NR	0.467	0.484	0.99	0.11	x10E9/L	0 - 1.500
Basophils	NR	0.033	0.014	NR	NR	x10E9/L	0 - 0.500
Chemistry							
Glucose	**4.1**	7.8	6.5	6.3	**3.5**	mmol/L	4.7 - 8.3
Blood Urea Nitrogen	5.6	8.1	9.2	7.5	8.7	mmol/L	3.5 - 10.6
Creatinine	97.7	145.4	105	108.3	129	µmol/L	75 - 205
BUN/Cr Ratio	14	14	22	17	17	Ratio	Reported Value
Sodium	140	147	**154**	145	140	mmol/L	135 - 150
Potassium	5.1	4	5	4.3	4.4	mmol/L	4.0 - 6.7
Na/K Ratio	27	37	31	34	32	Ratio	Reported Value
Chloride	104	110	**116**	109	104	mmol/L	94 - 110
Carbon Dioxide	**29.4**	24.3	**33**	**32.4**	**28.1**	mmol/L	18 - 26
Anion Gap	12	17	10	8	12	mmol/L	10-20
Calcium	2.59	2.53	2.7	2.67	2.55	mmol/L	1.73 - 2.83
Phosphorus	**3.73**	2.72	**3.36**	**3.02**	**3.15**	mmol/L	1.65 - 2.85
Total Protein	**46**	**56**	**52**	**54**	**61**	g/L	70 - 89
Albumin	29.18	**34.77**	**34.38**	**36.65**	**42.81**	g/L	19 - 32
Globulin	**17**	**21**	**18**	**17**	**18**	g/L	35 - 54
A/G Ratio	**1.7**	**1.6**	**2**	**2.1**	**2.4**	Ratio	0.4 - 1.4
Total Bilirubin	INV	4	3	3	INV	µmol/L	0 - 6
Alkaline Phosphatase	289	256	208	224	213	IU/L	180 - 460
ALT (Sgpt)	86	100	102	93	74	IU/L	Reported Value
Gamma gt	**56**	**73**	**66**	**65**	**68**	IU/L	8.0 - 40
Creatine Phosphokinase	**2,753**	**1,700**	**4,337**	**1,250**	**3,871**	IU/L	00 - 125
Calculated Osmolality	280	297	311	291	281	mmol/kg	NP[3]
AST (Sgot)	68	**144**	62	45	44	IU/L	30 - 100
Sorbital Dehydrogenase-AO	3.2	16.8	2.8	2.4	2.7	IU/L	Reported Value
Uric Acid	28	21	15	9	9	µmol/L	Reported Value
Date of Bleed[4]	16 May	17 May	24 May	30 May	13 Jun		

Appendix D2. Clinical Laboratory Data for Chronic Renal Pig 2, cont.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate	Adequate	Reported Value	Adequate
RBC Morph	**See Below**	**See Below**	**See Below**	**See Below**	**See below**	Reported Value	Normal
Aniso	2+	2+	NR	NR	1+	Reported Value	NP
Poik	3+	3+	2+	3+	3+	Reported Value	NP
Polychrom	1+	NR	NR	NR	NR	Reported Value	NP
Fibrinogen Degradation Products	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	**Positive**	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	Observation	Negative
Fibrinogen Semi Quantitative	1	2	3	1	3	g/L	1.0 - 3.0
Part. Thromboplastin Time	**11.7**	24.3	**19.6**	**18.5**	21	second	21.0 - 36.0
Prothrombin Time	**15.6**	**15.2**	**16**	**15.5**	**16.5**	second	10.0 - 15.0
Date of Bleed	16 May	17 May	24 May	30 May	13 Jun		

[1] Numbers in bold are outside of the reference range
[2] Not Reported
[3] Not Provided
[4] Year of Bleed: 2007

Appendix D3. Clinical Laboratory Data for Chronic Renal Pig 3.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Hematology							
White Cell Count	19.1	19.439	16	20.2	20.9	x10E9/L	11.0 - 21.0
Red Cell Count	7.02	7.86	6.27	6.65	6.49	x10E12/L	5.10 - 8.00
Hemoglobin	126	135	106	114	106	g/L	90 - 150
Hematocrit	0.377	0.417	**0.321**[1]	**0.342**	**0.318**	L/L	0.36 - 0.48
Mean Corp Vol	53.7	53	**51.2**	**51.4**	**48.9**	fl	52 - 66
Mean Corp Hemoglobin	18	17.1	**16.8**	17.2	**16.4**	pg	17.0 - 24.0
Mean Corp Hemoglobin Conc	335	323	329	334	335	g/L	300 - 360
RDW	21.1	21.2	19.4	21.5	21.9	%CV	Reported Value
Platelet CNT	653	675	870	650	864	x10E9/L	100 - 900
Mean Platelet Volume	17.2	15.8	14.2	21.4	12.8	fl	6.7-9.9
Differential Cell Count							
% Neutrophils	40	36	37	39	57	%	Reported Value
% Lymphocytes	52	55	55	48	37	%	Reported Value
% Monocytes	**6**	**5**	**7**	**11**	**6**	%	Reported Value
% Eosinophils	2	2	1	2	NR[2]	%	Reported Value
% Basophils	NR	1	0	NR	NR	%	Reported Value
Absolute Differential Values							
Neutrophils	7.64	7.06	5.88	7.88	11.92	x10E9/L	3.00 - 14.00
Lymphocytes	9.93	10.7	8.79	9.7	7.73	x10E9/L	3.8 - 14.50
Monocytes	**1.15**	**1.05**	**1.05**	**2.22**	**1.25**	x10E9/L	0 - 1.000
Eosinophils	0.38	0.463	0.208	0.4	NR	x10E9/L	0 - 1.500
Basophils	NR	0.166	0.039	NR	NR	x10E9/L	0 - 0.500
Chemistry							
Glucose	7.3	**8.4**	6.1	6.7	5.9	mmol/L	4.7 - 8.3
Blood Urea Nitrogen	6.4	9.2	8.1	7.6	6.5	mmol/L	3.5 - 10.6
Creatinine	77.4	77	114.2	104	109.5	µmol/L	75 - 205
BUN/Cr Ratio	21	30	18	18	15	Ratio	Reported Value
Sodium	148	136	**154**	146	141	mmol/L	135 - 150
Potassium	6.2	**8.5**	4.9	4.4	4.3	mmol/L	4.0 - 6.7
Na/K Ratio	24	16	31	33	33	Ratio	Reported Value
Chloride	109	107	**114**	107	108	mmol/L	94 - 110
Carbon Dioxide	**27.5**	**11.4**	**32.6**	**28.6**	25.5	mmol/L	18 - 26
Anion Gap	18	26	12	15	12	mmol/L	10-20
Calcium	2.82	2.32	2.77	2.59	2.27	mmol/L	1.73 - 2.83
Phosphorus	**3.87**	**4**	**3.34**	**3.15**	2.54	mmol/L	1.65 - 2.85
Total Protein	**54**	**64**	**54**	**58**	**59**	g/L	70 - 89
Albumin	**34.41**	**45.03**	**33.91**	**35.58**	26.08	g/L	19 - 32
Globulin	**20**	**19**	**20**	**22**	**33**	g/L	35 - 54
A/G Ratio	**1.8**	**2.4**	**1.7**	**1.6**	0.8	Ratio	0.4 - 1.4
Total Bilirubin	3	hem	3	1	2	µmol/L	0 - 6
Alkaline Phosphatase	318	340	197	235	**72**	IU/L	180 - 460
ALT (Sgpt)	84	198	84	84	62	IU/L	Reported Value
Gamma gt	**65**	**106**	**59**	**58**	37	IU/L	8.0 - 40
Creatine Phosphokinase	**2,647**	**22,729**	**2,775**	**3,189**	**1,085**	IU/L	00 - 125
Calculated Osmolality	301	286	310	294	283	mmol/kg	NP[3]
AST (Sgot)	61	**1,414**	71	64	41	IU/L	30 - 100
Sorbital Dehydrogenase-AO	2.9	10.5	1.8	3.3	1.3	IU/L	Reported Value
Uric Acid	17	55	20	7	7	µmol/L	Reported Value
Date of Bleed[4]	15 May	17 May	24 May	30 May	12 Jun		

Appendix D3. Clinical Laboratory Data for Chronic Renal Pig 3, cont.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate	**Increased**	Reported Value	Adequate
RBC Morph	**See Below**	**See Below**	**See Below**	**See Below**	**See Below**	Reported Value	Normal
Aniso	1+	1+	1+	NR	1+	Reported Value	NP
Poik	3+	3+	3+	3+	2+	Reported Value	NP
Polychrom	1+	NR	NR	NR	NR	Reported Value	NP
Fibrinogen Degradation Products	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	**Positive**	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	Observation	Negative
Fibrinogen Semi Quantitative	1	1	3	**5**	**9**	g/L	1.0 - 3.0
Part. Thromboplastin Time	**11.4**	34	**19.3**	**19.6**	**41.3**	second	21.0 - 36.0
Prothrombin Time	**15.2**	**17.4**	15	13.6	**18.5**	second	10.0 - 15.0
Date of Bleed	15 May	17 May	24 May	30 May	12 Jun		

[1] Numbers in bold are outside of the reference range
[2] Not Reported
[3] Not Provided
[4] Year of Bleed: 2007

Appendix D4. Clinical Laboratory Data for Chronic Renal Pig 4.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Hematology							
White Cell Count	19.9	15.836	NS[1]	16.2	15.11	x10E9/L	11.0 - 21.0
Red Cell Count	**8.06**[2]	7.7	NS	6.5	6.66	x10E12/L	5.10 - 8.00
Hemoglobin	141	138	NS	114	117	g/L	90 - 150
Hematocrit	0.454	0.416	NS	**0.351**	**0.348**	L/L	0.36 - 0.48
Mean Corp Vol	56.2	54	NS	54	52.3	fl	52 - 66
Mean Corp Hemoglobin	17.5	17.9	NS	17.5	17.5	pg	17.0 - 24.0
Mean Corp Hemoglobin Conc	311	332	NS	325	335	g/L	300 - 360
RDW	21.6	21.7	NS	19.6	19	%CV	Reported Value
Platelet CNT	229	363	NS	508	487	x10E9/L	100 - 900
Mean Platelet Volume	NR	NR	NS	21.1	19.1	fl	6.7-9.9
Differential Cell Count							
% Neutrophils	27	32	NS	31	41	%	Reported Value
% Lymphocytes	68	54	NS	66	50	%	Reported Value
% Monocytes	3	**9**	NS	2	3	%	Reported Value
% Eosinophils	1	2	NS	1	6	%	Reported Value
% Basophils	1	2	NS	NR[3]	NR	%	Reported Value
Absolute Differential Values							
Neutrophils	5.3	5.1	NS	5.03	6.19	x10E9/L	3.00 - 14.00
Lymphocytes	13.5	8.6	NS	10.69	7.56	x10E9/L	3.8 - 14.50
Monocytes	0.696	**1.48**	NS	0.32	0.45	x10E9/L	0 - 1.000
Eosinophils	0.26	0.391	NS	0.16	0.91	x10E9/L	0 - 1.500
Basophils	0.117	0.265	NS	NR	NR	x10E9/L	0 - 0.500
Chemistry							
Glucose	**8.8**	**10.2**	NS	7.7	5.3	mmol/L	4.7 - 8.3
Blood Urea Nitrogen	5.9	8.8	NS	7.1	8.6	mmol/L	3.5 - 10.6
Creatinine	83.4	193.1	NS	86.2	104.4	µmol/L	75 - 205
BUN/Cr Ratio	18	11	NS	21	21	Ratio	Reported Value
Sodium	148	144	NS	146	142	mmol/L	135 - 150
Potassium	5.4	**3.5**	NS	5	4.3	mmol/L	4.0 - 6.7
Na/K Ratio	27	41	NS	29	33	Ratio	Reported Value
Chloride	109	105	NS	110	108	mmol/L	94 - 110
Carbon Dioxide	21.4	19.6	NS	**28.9**	**28.5**	mmol/L	18 - 26
Anion Gap	23	23	NS	12	10	mmol/L	10-20
Calcium	**2.94**	2.39	NS	2.48	2.44	mmol/L	1.73 - 2.83
Phosphorus	**3.93**	**3.05**	NS	**3.16**	**2.89**	mmol/L	1.65 - 2.85
Total Protein	**51**	**59**	NS	**52**	**54**	g/L	70 - 89
Albumin	**33.44**	**37.89**	NS	**33.95**	**28.57**	g/L	19 - 32
Globulin	**18**	**21**	NS	**18**	**25**	g/L	35 - 54
A/G Ratio	**1.9**	**1.8**	NS	**1.9**	1.1	Ratio	0.4 - 1.4
Total Bilirubin	4	5	NS	0	3	µmol/L	0 - 6
Alkaline Phosphatase	317	281	NS	224	**144**	IU/L	180 - 460
ALT (Sgpt)	90	112	NS	115	72	IU/L	Reported Value
Gamma gt	**60**	**64**	NS	**61**	**45**	IU/L	8.0 - 40
Creatine Phosphokinase	**1,587**	**1,493**	NS	**2,416**	**4,520**	IU/L	00 - 125
Calculated Osmolality	300	293	NS	296	286	mmol/kg	NP[4]
AST (Sgot)	53	**154**	NS	65	52	IU/L	30 - 100
Sorbital Dehydrogenase-AO	6.5	9.2	NS	4.9	5.5	IU/L	Reported Value
Uric Acid	18	24	NS	13	7	µmol/L	Reported Value
Date of Bleed[5]	15 May	17 May	24 May	30 May	13 Jun		

Appendix D4. Clinical Laboratory Data for Chronic Renal Pig 4.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Morphology and Coagulation Parameters							
Platelets	Increased	Adequate	NS	Adequate	Adequate	Reported Value	Adequate
RBC Morph	**See Below**	**See Below**	NS	**See Below**	**See Below**	Reported Value	Normal
Aniso	1+	1+	NS	NR	1+	Reported Value	NP
Poik	3+	3+	NS	3+	3+	Reported Value	NP
Polychrom	1+	NR	NS	NR	1+	Reported Value	NP
Fibrinogen Degradation Products	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	NS	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	Observation	Negative
Fibrinogen Semi Quantitative	2	1	NS	2	**4**	g/L	1.0 - 3.0
Part. Thromboplastin Time	**10.8**	**>60**	NS	24.6	23.1	second	21.0 - 36.0
Prothrombin Time	15	**34.1**	NS	10.7	**17.5**	second	10.0 - 15.0
Date of Bleed	15 May	17 May	24 May	30 May	13 Jun		

[1] No Sample
[2] Numbers in bold are outside of the reference range
[3] Not Reported
[4] Not Provided
[5] Year of Bleed: 2007

Appendix D5. Clinical Laboratory Data for Chronic Hepatic Pig 5.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Hematology							
White Cell Count	15	15.8	14.9	17.8	17.91	x10E9/L	11.0 - 21.0
Red Cell Count	6.36	7.74	7.8	7.95	7.73	x10E12/L	5.10 - 8.00
Hemoglobin	107	129	128	135	129	g/L	90 - 150
Hematocrit	**0.319**[1]	0.39	0.393	0.396	0.385	L/L	0.36 - 0.48
Mean Corp Vol	**50.2**	**50.4**	**50.4**	**49.8**	**49.8**	fl	52 - 66
Mean Corp Hemoglobin	**16.7**	**16.6**	**16.4**	**16.9**	**16.7**	pg	17.0 - 24.0
Mean Corp Hemoglobin Conc	334	330	326	340	336	g/L	300 - 360
RDW	20.6	20.9	21.4	22.3	21.4	%CV	Reported Value
Platelet CNT	439	514	648	499	458	x10E9/L	100 - 900
Mean Platelet Volume	20.5	18.2	16.7	19.7	19.2	fl	6.7-9.9
Differential Cell Count							
% Neutrophils	39	26	**11**	37	20	%	Reported Value
% Lymphocytes	56	66	80	51	71	%	Reported Value
% Monocytes	3	5	6	5	4	%	Reported Value
% Eosinophils	2	3	3	7	5	%	Reported Value
% Basophils	NR[2]	0	NR	NR	NR	%	Reported Value
Absolute Differential Values							
Neutrophils	5.85	4.08	**1.64**	6.58	3.57	x10E9/L	3.00 - 14.00
Lymphocytes	8.4	10.5	11.92	9.08	12.72	x10E9/L	3.8 - 14.50
Monocytes	0.45	0.733	0.89	0.89	0.72	x10E9/L	0 - 1.000
Eosinophils	0.3	0.399	0.45	1.25	0.9	x10E9/L	0 - 1.500
Basophils	NR	0.057	NR	NR	NR	x10E9/L	0 - 0.500
Chemistry							
Glucose	5.4	7.5	6.6	5.3	5.4	mmol/L	4.7 - 8.3
Blood Urea Nitrogen (BUN)	4.1	4.6	4.5	5.4	5.5	mmol/L	3.5 - 10.6
Creatinine	111.4	95.7	98.2	105.9	112.3	µmol/L	75 - 205
BUN/Cr Ratio	9	12	12	13	12	Ratio	Reported Value
Sodium	147	**154**	144	147	147	mmol/L	135 - 150
Potassium	5.1	4	4.3	4.1	4.2	mmol/L	4.0 - 6.7
Na/K Ratio	29	39	33	36	35	Ratio	Reported Value
Chloride	**112**	**117**	108	107	107	mmol/L	94 - 110
Carbon Dioxide	**28.5**	**26.5**	**31.4**	**31.6**	**35.7**	mmol/L	18 - 26
Anion Gap	12	15	9	13	9	mmol/L	10-20
Calcium	2.38	2.59	2.5	2.54	2.47	mmol/L	1.73 - 2.83
Phosphorus	**3.81**	**3.62**	**3.32**	**3.41**	**3.47**	mmol/L	1.65 - 2.85
Total Protein	**46**	**53**	**53**	**61**	**61**	g/L	70 - 89
Albumin	31.3	**36.88**	**37.35**	**38.92**	**39.29**	g/L	19 - 32
Globulin	**15**	**16**	**16**	**22**	**22**	g/L	35 - 54
A/G Ratio	**2.1**	**2.3**	**2.4**	**1.8**	**1.8**	Ratio	0.4 - 1.4
Total Bilirubin	4	3	3	4	3	µmol/L	0 - 6
Alkaline Phosphatase	341	345	320	279	249	IU/L	180 - 460
ALT (Sgpt)	73	81	68	55	59	IU/L	Reported Value
Gamma gt	**55**	**60**	**59**	**59**	**53**	IU/L	8.0 - 40
Creatine Phosphokinase	**874**	**1,226**	**3,280**	**762**	**1,503**	IU/L	00 - 125
Calculated Osmolality	292	306	287	292	292	mmol/kg	NP[3]
AST (Sgot)	51	51	82	39	43	IU/L	30 - 100
Sorbital Dehydrogenase-AO	4.2	1.8	2.5	2.4	4.7	IU/L	Reported Value
Uric Acid	13	15	8	3	2	µmol/L	Reported Value
Date of Bleed[4]	23-May	24-May	30-May	06-Jun	19-Jun		

Appendix D5. Clinical Laboratory Data for Chronic Hepatic Pig 5, cont.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate	Adequate	Reported Value	Adequate
RBC Morph	**See Below**	**See Below**	**See Below**	**See Below**	**See Below**	Reported Value	Normal
Aniso	NR	1+	NR	1+	1+	Reported Value	NP
Poik	3+	3+	3+	3+	3+	Reported Value	NP
Polychrom	NR	NR	NR	NR	1+	Reported Value	NP
Fibrinogen Degradation Products	**Positive**	**Positive**	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	**Positive**	Observation	Negative
Fibrinogen Semi Quantitative	3	2	1	1	1	g/L	1.0 - 3.0
Part. Thromboplastin Time	**13.4**	29.7	24	22	22.5	second	21.0 - 36.0
Prothrombin Time	13.7	**16.9**	**15.8**	**15.7**	**16**	second	10.0 - 15.0
Date of Bleed	23-May	24-May	30-May	06-Jun	19-Jun		

[1] Numbers in bold are outside of the reference range
[2] Not Reported
[3] Not Provided
[4] Year of Bleed: 2007

Appendix D6. Clinical Laboratory Data for Chronic Hepatic Pig 6.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Hematology							
White Cell Count	**8.99**[1]	**10.71**	**12.7**	16.31	20.91	x10E9/L	11.0 - 21.0
Red Cell Count	5.33	6.4	6.31	6.18	6.4	x10E12/L	5.10 - 8.00
Hemoglobin	108	125	123	124	126	g/L	90 - 150
Hematocrit	**0.315**	0.375	0.373	**0.355**	0.371	L/L	0.36 - 0.48
Mean Corp Vol	59	58.7	59.1	57.5	58	fl	52 - 66
Mean Corp Hemoglobin	20.2	19.6	19.5	20.1	19.7	pg	17.0 - 24.0
Mean Corp Hemoglobin Conc	342	334	330	349	339	g/L	300 - 360
RDW	19	19	19.6	19.1	20	%CV	Reported Value
Platelet CNT	287	529	469	368	391	x10E9/L	100 - 900
Mean Platelet Volume	16.2	28.6	29.8	23.9	24.3	fl	6.7-9.9
Differential Cell Count							
% Neutrophils	**21**	32	30	41	37	%	Reported Value
% Lymphocytes	74	56	61	51	57	%	Reported Value
% Monocytes	3	**10**	**8**	**7**	3	%	Reported Value
% Eosinophils	2	2	1	1	3	%	Reported Value
% Basophils	NR[2]	NR	NR	NR	NR	%	Reported Value
Absolute Differential Values							
Neutrophils	**1.89**	3.43	3.8	6.69	7.73	x10E9/L	3.00 - 14.00
Lymphocytes	6.65	6	7.75	8.32	11.92	x10E9/L	3.8 - 14.50
Monocytes	0.27	**1.07**	**1.02**	**1.14**	0.63	x10E9/L	0 - 1.000
Eosinophils	0.18	0.21	0.13	0.16	0.63	x10E9/L	0 - 1.500
Basophils	NR	NR	NR	NR	NR	x10E9/L	0 - 0.500
Chemistry							
Glucose	**2**	5.9	6.7	5.6	4.9	mmol/L	4.7 - 8.3
Blood Urea Nitrogen (BUN)	6.6	6.5	7.3	8.2	8.9	mmol/L	3.5 - 10.6
Creatinine	90	83.3	80.2	85	88.4	µmol/L	75 - 205
BUN/Cr Ratio	18	20	23	24	25	Ratio	Reported Value
Sodium	148	**157**	146	145	143	mmol/L	135 - 150
Potassium	4.7	4.6	4.6	4.6	4.7	mmol/L	4.0 - 6.7
Na/K Ratio	31	34	32	32	30	Ratio	Reported Value
Chloride	**111**	**118**	109	107	106	mmol/L	94 - 110
Carbon Dioxide	**28.3**	**32.4**	**34.9**	**34.1**	**32.3**	mmol/L	18 - 26
Anion Gap	13	11	7	9	9	mmol/L	10-20
Calcium	2.33	2.61	2.54	2.57	2.45	mmol/L	1.73 - 2.83
Phosphorus	**3.73**	**3.07**	**2.92**	**3.08**	**3.01**	mmol/L	1.65 - 2.85
Total Protein	**49**	**59**	**57**	**60**	**62**	g/L	70 - 89
Albumin	30.3	**37.64**	**36.24**	**36.59**	**34.2**	g/L	19 - 32
Globulin	**19**	**21**	**21**	**23**	**28**	g/L	35 - 54
A/G Ratio	**1.6**	**1.8**	**1.7**	**1.6**	1.2	Ratio	0.4 - 1.4
Total Bilirubin	3	3	3	4	2	µmol/L	0 - 6
Alkaline Phosphatase	261	297	260	232	211	IU/L	180 - 460
ALT (Sgpt)	89	98	86	78	79	IU/L	Reported Value
Gamma gt	**38**	**42**	40	**44**	**41**	IU/L	8.0 - 40
Creatine Phosphokinase	**735**	**679**	**1,574**	**5,693**	**1,444**	IU/L	00 - 125
Calculated Osmolality	293	313	294	292	289	mmol/kg	NP[3]
AST (Sgot)	38	35	46	48	41	IU/L	30 - 100
Sorbital Dehydrogenase-AO	1.1	1.7	2.4	2.1	2.2	IU/L	Reported Value
Uric Acid	16	10	11	0	3	µmol/L	Reported Value
Date of Bleed[4]	23 May	24 May	30 May	06 Jun	19 Jun		

Appendix D6. Clinical Laboratory Data for Chronic Hepatic Pig 6, cont.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate	Adequate	Reported Value	Adequate
RBC Morph	**See Below**	**See Below**	**See Below**	**See Below**	**See Below**	Reported Value	Normal
Aniso	NR	NR	1+	1+	1+	Reported Value	NP
Poik	3+	3+	2+	3+	3+	Reported Value	NP
Polychrom	NR	NR	NR	NR	1+	Reported Value	NP
Fibrinogen Degradation Products	**Positive**	**Positive**	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	**Positive**	Observation	Negative
Fibrinogen Semi Quantitative	1	1	1	1	1	g/L	1.0 - 3.0
Part. Thromboplastin Time	**0.8**	**20.1**	**46.4**	**17.7**	**18.1**	second	21.0 - 36.0
Prothrombin Time	**3.7**	**16.2**	**19**	**15.3**	**15.6**	second	10.0 - 15.0
Date of Bleed	23 May	24 May	30 May	06 Jun	19 Jun		

[1] Numbers in bold are outside of the reference range
[2] Not Reported
[3] Not Provided
[4] Year of Bleed: 2007

Appendix D7. Clinical Laboratory Data for Chronic Hepatic Pig 7.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Hematology							
White Cell Count	**8.22**[1]	13	11	13.1	14.41	x10E9/L	11.0 - 21.0
Red Cell Count	5.86	6.4	6.41	6.09	6.21	x10E12/L	5.10 - 8.00
Hemoglobin	113	126	124	122	127	g/L	90 - 150
Hematocrit	**0.34**	0.38	0.377	**0.358**	0.373	L/L	0.36 - 0.48
Mean Corp Vol	58	59.5	58.9	58.9	60	fl	52 - 66
Mean Corp Hemoglobin	19.4	19.7	19.3	20.1	20.5	pg	17.0 - 24.0
Mean Corp Hemoglobin Conc	334	331	328	341	341	g/L	300 - 360
RDW	20.1	19.8	19.8	20.5	18.2	%CV	Reported Value
Platelet CNT	165	434	420	206	411	x10E9/L	100 - 900
Mean Platelet Volume	17.6	19.3	16.9	NR[2]	23	fl	6.7-9.9
Differential Cell Count							
% Neutrophils	**3**	**14**	**21**	33	**20**	%	Reported Value
% Lymphocytes	85	76	74	60	72	%	Reported Value
% Monocytes	6	7	3	5	5	%	Reported Value
% Eosinophils	6	3	2	1	1	%	Reported Value
% Basophils	NR	NR	NR	0	1	%	Reported Value
Absolute Differential Values							
Neutrophils	**0.25**	**1.82**	**2.31**	4.33	**2.93**	x10E9/L	3.00 - 14.00
Lymphocytes	6.99	9.88	8.14	7.88	10.4	x10E9/L	3.8 - 14.50
Monocytes	0.49	0.91	0.33	0.608	0.759	x10E9/L	0 - 1.000
Eosinophils	0.49	0.39	0.22	0.174	0.133	x10E9/L	0 - 1.500
Basophils	NR	NR	NR	0.064	0.18	x10E9/L	0 - 0.500
Chemistry							
Glucose	**4.1**	**8.7**	6.9	7	5.5	mmol/L	4.7 - 8.3
Blood Urea Nitrogen (BUN)	4.5	4	6.1	6.3	5.1	mmol/L	3.5 - 10.6
Creatinine	76.1	81.8	76.8	**73.5**	78	µmol/L	75 - 205
BUN/Cr Ratio	15	12	20	22	16	Ratio	Reported Value
Sodium	**152**	**156**	144	144	143	mmol/L	135 - 150
Potassium	4.7	4.2	4.3	4.1	**3.9**	mmol/L	4.0 - 6.7
Na/K Ratio	32	37	33	35	37	Ratio	Reported Value
Chloride	**113**	**120**	**111**	107	105	mmol/L	94 - 110
Carbon Dioxide	**29.7**	**27.7**	**33.2**	**31.6**	**31.7**	mmol/L	18 - 26
Anion Gap	14	13	4	10	10	mmol/L	10-20
Calcium	2.38	2.59	2.53	2.63	2.51	mmol/L	1.73 - 2.83
Phosphorus	**3.87**	**3.21**	**3.19**	**3.19**	**3.24**	mmol/L	1.65 - 2.85
Total Protein	**55**	**59**	**58**	**59**	**59**	g/L	70 - 89
Albumin	**36**	**39.05**	**38.04**	**39.97**	**37.87**	g/L	19 - 32
Globulin	**19**	**20**	**20**	**19**	**21**	g/L	35 - 54
A/G Ratio	**1.9**	**2**	**1.9**	**2.1**	**1.8**	Ratio	0.4 - 1.4
Total Bilirubin	5	3	2	4	2	µmol/L	0 - 6
Alkaline Phosphatase	217	195	206	223	202	IU/L	180 - 460
ALT (Sgpt)	74	77	60	62	63	IU/L	Reported Value
Gamma gt	32	35	32	32	32	IU/L	8.0 - 40
Creatine Phosphokinase	**2,365**	**580**	**1,348**	**1,639**	**2,372**	IU/L	00 - 125
Calculated Osmolality	300	311	289	289	284	mmol/kg	NP[3]
AST (Sgot)	58	52	53	43	67	IU/L	30 - 100
Sorbital Dehydrogenase-AO	0.9	3.3	2.4	2.8	2.2	IU/L	Reported Value
Uric Acid	7	3	0	2	0	µmol/L	Reported Value
Date of Bleed[4]	23 May	24 May	30 May	06 Jun	19 Jun		

Appendix D7. Clinical Laboratory Data for Pig Chronic Hepatic 7, cont.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate	Adequate	Reported Value	Adequate
RBC Morph	**See Below**	**See Below**	**See Below**	**See Below**	**See Below**	Reported Value	Normal
Aniso	NR	1+	NR	1+	1+	Reported Value	NP
Poik	3+	3+	3+	3+	3+	Reported Value	NP
Polychrom	NR	NR	NR	2+	NR	Reported Value	NP
Fibrinogen Degradation Products	**Positive**	**Positive**	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	**Positive**	Observation	Negative
Fibrinogen Semi Quantitative	2	2	1	1	1	g/L	1.0 - 3.0
Part. Thromboplastin Time	**11.8**	23	**20.6**	**19.3**	23.3	second	21.0 - 36.0
Prothrombin Time	**15.8**	13.9	14.1	**15.5**	**16**	second	10.0 - 15.0
Date of Bleed	23 May	24 May	30 May	06 Jun	19 Jun		

[1] Numbers in bold are outside of the reference range
[2] Not Reported
[3] Not Provided
[4] Year of Bleed: 2007

Appendix D8. Clinical Laboratory Data for Chronic Hepatic Pig 8.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Hematology							
White Cell Count	14.11	11.9	15.6	14.4	15.21	x10E9/L	11.0 - 21.0
Red Cell Count	6.33	7.4	7.17	7.06	6.73	x10E12/L	5.10 - 8.00
Hemoglobin	113	131	126	123	117	g/L	90 - 150
Hematocrit	**0.334**[1]	0.398	0.38	0.365	**0.351**	L/L	0.36 - 0.48
Mean Corp Vol	52.8	53.8	53	**51.7**	52.2	fl	52 - 66
Mean Corp Hemoglobin	17.9	17.7	17.6	17.4	17.4	pg	17.0 - 24.0
Mean Corp Hemoglobin Conc	339	329	331	337	333	g/L	300 - 360
RDW	17.9	19.8	20.4	20.1	20.9	%CV	Reported Value
Platelet CNT	527	599	493	493	393	x10E9/L	100 - 900
Mean Platelet Volume	14.4	15	15.7	12.9	13.9	fl	6.7-9.9
Differential Cell Count							
% Neutrophils	**4**	**12**	38	33	26	%	Reported Value
% Lymphocytes	88	73	50	48	68	%	Reported Value
% Monocytes	6	6	6	**12**	2	%	Reported Value
% Eosinophils	2	8	6	4	4	%	Reported Value
% Basophils	NR[2]	1	NR	3	NR	%	Reported Value
Absolute Differential Values							
Neutrophils	**0.56**	**1.43**	5.92	4.70	3.96	x10E9/L	3.00 - 14.00
Lymphocytes	12.42	8.69	7.8	6.93	10.34	x10E9/L	3.8 - 14.50
Monocytes	0.85	0.71	0.94	**1.72**	0.3	x10E9/L	0 - 1.000
Eosinophils	0.28	0.95	0.94	0.549	0.61	x10E9/L	0 - 1.500
Basophils	NR	0.12	NR	0.474	NR	x10E9/L	0 - 0.500
Chemistry							
Glucose	**3.3**	7	6.3	5.7	5.2	mmol/L	4.7 - 8.3
Blood Urea Nitrogen (BUN)	4.9	6	6	7.2	6	mmol/L	3.5 - 10.6
Creatinine	101.4	92.2	89.6	95.9	96.1	µmol/L	75 - 205
BUN/Cr Ratio	12	16	17	19	16	Ratio	Reported Value
Sodium	146	150	148	144	142	mmol/L	135 - 150
Potassium	4.1	4	4.4	4.2	**3.7**	mmol/L	4.0 - 6.7
Na/K Ratio	36	38	34	34	38	Ratio	Reported Value
Chloride	109	**111**	**112**	108	105	mmol/L	94 - 110
Carbon Dioxide	**29.1**	**26.5**	**29.8**	**27.7**	**31.3**	mmol/L	18 - 26
Anion Gap	12	17	11	13	9	mmol/L	10-20
Calcium	2.57	2.79	2.69	2.68	2.56	mmol/L	1.73 - 2.83
Phosphorus	**3.46**	**3.27**	**3.03**	**2.93**	2.75	mmol/L	1.65 - 2.85
Total Protein	**49**	**57**	**56**	**63**	**66**	g/L	70 - 89
Albumin	**36.38**	**42.91**	**39.62**	**38.24**	**36.42**	g/L	19 - 32
Globulin	**13**	**14**	**16**	**25**	**30**	g/L	35 - 54
A/G Ratio	**2.9**	**3**	**2.4**	**1.5**	1.2	Ratio	0.4 - 1.4
Total Bilirubin	4	3	3	4	2	µmol/L	0 - 6
Alkaline Phosphatase	261	268	236	204	237	IU/L	180 - 460
ALT (Sgpt)	84	89	74	71	80	IU/L	Reported Value
Gamma gt	**43**	**55**	**57**	**66**	**53**	IU/L	8.0 - 40
Creatine Phosphokinase	**728**	**673**	**1,055**	**4,911**	**1,577**	IU/L	00 - 125
Calculated Osmolality	287	299	296	289	282	mmol/kg	NP[3]
AST (Sgot)	89	53	58	61	56	IU/L	30 - 100
Sorbital Dehydrogenase-AO	11.5	2.1	3.8	4.3	2.9	IU/L	Reported Value
Uric Acid	14	18	5	3	2	µmol/L	Reported Value
Date of Bleed[4]	23 May	24 May	30 May	06 Jun	19 Jun		

Appendix D8. Clinical Laboratory Data for Chronic Hepatic Pig 8, cont.

Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Units	Reference Range
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate	Adequate	Reported Value	Adequate
RBC Morph	**See Below**	**See Below**	**See Below**	**See Below**	**See Below**	Reported Value	Normal
Aniso	NR	1+	NR	NR	1+	Reported Value	NP
Poik	3+	2+	3+	3+	3+	Reported Value	NP
Polychrom	NR	1+	NR	---	1+	Reported Value	NP
Fibrinogen Degradation Products	**Positive**	**Positive**	**Positive @1:2, 1:8**	**Positive @1:2, 1:8**	**Positive**	Observation	Negative
Fibrinogen Semi Quantitative	2	2	1	2	1	g/L	1.0 - 3.0
Part. Thromboplastin Time	**12.7**	23.7	24.7	21.3	**20.3**	second	21.0 - 36.0
Prothrombin Time	13.7	**15.8**	**15.5**	**15.6**	**16.5**	second	10.0 - 15.0
Date of Bleed	23 May	24 May	30 May	06 Jun	19 Jun		

[1] Numbers in bold are outside of the reference range
[2] Not Reported
[3] Not Provided
[4] Year of Bleed: 2007

Appendix D9. Clinical Laboratory Data for Acute Pigs 9 – 12.

	Pig 9	Pig 10	Pig 11	Pig 12	Units	Reference Range
Day of Bleed	Day -1	Day -1	Day -1	Day -1		
Hematology						
White Cell Count	25.81	14.8	16.412	19.7	x10E9/L	11.0 - 21.0
Red Cell Count	7.73	7.41	6.47	7.54	x10E12/L	5.10 - 8.00
Hemoglobin	142	139	124	133	g/L	90 - 150
Hematocrit	0.43	0.412	0.371	0.405	L/L	0.36 - 0.48
Mean Corp Volume	55.7	55.7	57.3	53.7	fl	52 - 66
Mean Corp Hemoglobin	18.4	18.8	19.1	17.7	pg	17.0 - 24.0
Mean Corp Hemoglobin Conc	331	337	333	329	g/L	300 - 360
RDW	19.7	20.5	19.2	22.5	%CV	Reported Value
Platelet CNT	422	280	509	491	x10E9/L	100 - 900
Mean Platelet Volume	20.7	NR[2]	15.9	16.3	fl	6.7-9.9
Differential Cell Count						
% Neutrophils	22	23	30	26	%	Reported Value
% Lymphocytes	**68**[1]	67	59	63	%	Reported Value
% Monocytes	**9**	6	**8**	7	%	Reported Value
% Eosinophils	1	2	1	2	%	Reported Value
% Basophils	NR	2	1	1	%	Reported Value
Absolute Differential Values						
Neutrophils	5.68	3.45	4.92	5.05	x10E9/L	3.00 - 14.00
Lymphocytes	**17.55**	9.93	9.75	12.5	x10E9/L	3.8 - 14.50
Monocytes	**2.32**	0.913	**1.28**	**1.43**	x10E9/L	0 - 1.000
Eosinophils	0.26	0.237	0.232	0.442	x10E9/L	0 - 1.500
Basophils	NR	0.228	0.23	0.212	x10E9/L	0 - 0.500
Chemistry						
Glucose	6.4	6.3	6.7	**8.5**	mmol/L	4.7 - 8.3
Blood Urea Nitrogen	8.2	8.5	10.2	**11.9**	mmol/L	3.5 - 10.6
Creatinine	115.8	118.5	102.9	130.5	µmol/L	75 - 205
BUN/Cr Ratio	18	18	25	23	Ratio	Reported Value
Sodium	147	146	146	146	mmol/L	135 - 150
Potassium	4.3	4	3.9	4.3	mmol/L	4.0 - 6.7
Na/K Ratio	34	37	37	34	Ratio	Reported Value
Chloride	108	108	106	107	mmol/L	94 - 110
Carbon Dioxide	26	**27.1**	**30.3**	18.7	mmol/L	18 - 26
Anion Gap	17	15	14	25	mmol/L	10-20
Calcium	2.63	2.52	2.47	2.66	mmol/L	1.73 - 2.83
Phosphorus	**3.19**	**3.08**	**3.09**	**3.64**	mmol/L	1.65 - 2.85
Total Protein	**63**	**65**	**62**	**65**	g/L	70 - 89
Albumin	**40.44**	**40.8**	**41.27**	**41.9**	g/L	19 - 32
Globulin	**23**	**24**	**21**	**23**	g/L	35 - 54
A/G Ratio	**1.8**	**1.7**	**2**	**1.8**	Ratio	0.4 - 1.4
Total Bilirubin	3	2	2	3	µmol/L	0 - 6
Alkaline Phosphatase	**163**	187	294	209	IU/L	180 - 460
ALT (Sgpt)	78	86	66	62	IU/L	Reported Value
Gamma gt	**60**	**64**	33	**58**	IU/L	8.0 - 40
Creatine Phosphokinase	**2,379**	**1,669**	**2,918**	**726**	IU/L	00 - 125
Calculated Osmolality	296	294	296	300	mmol/kg	NP[3]
AST (Sgot)	44	45	66	53	IU/L	30 - 100
Sorbital Dehydrogenase-AO	5.7	3.7	3.1	9.3	IU/L	Reported Value
Uric Acid	0	6	4	13	µmol/L	Reported Value
Date of Bleed[4]	19 Jun	19 Jun	19 Jun	19 Jun		

Appendix D9. Clinical Laboratory Data for Acute Pigs 9 – 12, cont.

	Pig 9	Pig 10	Pig 11	Pig 12	Units	Reference Range
Day of Bleed	Day -1	Day -1	Day -1	Day -1		
Morphology and Coagulation Parameters						
Platelets	Adequate	Adequate	Adequate	Adequate	Reported Value	Adequate
RBC Morph	**See Below**	**See Below**	**See Below**	**See Below**	Reported Value	Normal
Aniso	1+	1+	1+	1+	Reported Value	NP
Poik	3+	3+	3+	3+	Reported Value	NP
Polychrom	1+	1+	1+	1+	Reported Value	NP
Fibrinogen Degradation Products	**Positive**	**Positive**	**Positive**	**Positive**	Observation	Negative
Fibrinogen Semi Quantitative	1	2	1	1	g/L	1.0 - 3.0
Part. Thromboplastin Time	23.1	21.5	22.3	27	second	21.0 - 36.0
Prothrombin Time	**16**	**16.1**	**15.3**	**16.3**	second	10.0 - 15.0
Date of Bleed	19 Jun	19 Jun	19 Jun	19 Jun		

[1] Numbers in bold are outside of the reference range
[2] Not Reported
[3] Not Provided
[4] Year of Bleed: 2007

Appendix E. Summary Clinical Data for Chronic Renal Pigs 1 to 4

Appendix E1. Clinical Laboratory Data for Chronic Renal Pigs 1 to 4 on Day -1

Appendix E2. Clinical Laboratory Data for Chronic Renal Pigs 1 to 4 on Day +1

Appendix E3. Clinical Laboratory Data for Chronic Renal Pigs 1 to 4 on Day 7

Appendix E4. Clinical Laboratory Data for Chronic Renal Pigs 1 to 4 on Day 14

Appendix E5. Clinical Laboratory Data for Chronic Renal Pigs 1 to 4 at 1 Month

Appendix E1. Clinical Laboratory Data for Chronic Renal Pigs 1 to 4 on Day -1

Animal Number:	Pig 1	Pig 2	Pig 3	Pig 4		Mean	STDEV
Time Post Embolization	Day -1	Day -1	Day -1	Day -1		Day -1	Day -1
Hematology							
White Cell Count	14.6	13.01	19.1	19.9		16.65	3.37
Red Cell Count	6.93	5.84	7.02	8.06		6.96	0.91
Hemoglobin	129	108	126	141		126.00	13.64
Hematocrit	0.386	0.315	0.377	0.454		0.38	0.06
Mean Corp Vol	55.7	53.9	53.7	56.2		54.88	1.26
Mean Corp Hemoglobin	18.6	18.5	18	17.5		18.15	0.51
Mean Corp Hemoglobin Conc	334	343	335	311		330.75	13.77
RDW	21	19.3	21.1	21.6		20.75	1.00
Platelet CNT	460	357	653	229		424.75	179.12
Mean Platelet Volume	NR[1]	19.7	17.2	NR		18.45	1.77
Differential Cell Count							
% Neutrophils	33	59	40	27		39.75	13.89
% Lymphocytes	60	34	52	68		53.50	14.55
% Monocytes	4	7	6	3		5.00	1.83
% Eosinophils	1	NR	2	1		1.33	0.58
% Basophils	1	NR	NR	1		1.00	0.00
Absolute Differential Values							
Neutrophils	4.85	7.68	7.64	5.3		6.37	1.50
Lymphocytes	8.79	4.42	9.93	13.5		9.16	3.74
Monocytes	0.603	0.91	1.15	0.696		0.84	0.24
Eosinophils	0.198	NR	0.38	0.26		0.28	0.09
Basophils	0.134	NR	NR	0.117		0.13	0.01
Chemistry							
Glucose	4.5	4.1	7.3	8.8		6.18	2.26
Blood Urea Nitrogen (BUN)	5.9	5.6	6.4	5.9		5.95	0.33
Creatinine	100.9	97.7	77.4	83.4		89.85	11.26
BUN/Cr Ratio	15	14	21	18		17.00	3.16
Sodium	137	140	148	148		143.25	5.62
Potassium	4.4	5.1	6.2	5.4		5.28	0.75
Na/K Ratio	31	27	24	27		27.25	2.87
Chloride	102	104	109	109		106.00	3.56
Carbon Dioxide	20.6	29.4	27.5	21.4		24.73	4.38
Anion Gap	19	12	18	23		18.00	4.55
Calcium	2.41	2.59	2.82	2.94		2.69	0.24
Phosphorus	3.26	3.73	3.87	3.93		3.70	0.30
Total Protein	50	46	54	51		50.25	3.30
Albumin	35.22	29.18	34.41	33.44		33.06	2.69
Globulin	15	17	20	18		17.50	2.08
A/G Ratio	2.4	1.7	1.8	1.9		1.95	0.31
Total Bilirubin	5	INV	3	4		4.00	1.00
Alkaline Phosphatase	263	289	318	317		296.75	26.21
ALT (Sgpt)	83	86	84	90		85.75	3.10
Gamma gt	58	56	65	60		59.75	3.86
Creatine Phosphokinase	1,747	2,753	2,647	1,587		2,183.50	601.53
Calculated Osmolality	273	280	301	300		288.50	14.15
AST (Sgot)	64	68	61	53		61.50	6.35
Sorbital Dehydrogenase-AO	4.7	3.2	2.9	6.5		4.33	1.65
Uric Acid	14	28	17	18		19.25	6.08

Appendix E1. Clinical Laboratory Data for Chronic Renal Pigs 1 to 4 on Day -1, cont.

Animal Number:	Pig 1	Pig 2	Pig 3	Pig 4		Mean	STDEV
Time Post Embolization	Day -1	Day -1	Day -1	Day -1		Day -1	Day -1
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Increased		NA[2]	NA
RBC Morph	See Below	See Below	See Below	See Below		NA	NA
Aniso	1+	2+	1+	1+		NA	NA
Poik	3+	3+	3+	3+		NA	NA
Polychrom	1+	1+	1+	1+		NA	NA
Fibrinogen Degradation	Positive	Positive	Positive	Positive		NA	NA
Fibrinogen Semi Quantitative	2	1	1	2		1.50	0.58
Part. Thromboplastin Time	10.3	11.7	11.4	10.8		11.05	0.62
Prothrombin Time	15.4	15.6	15.2	15		15.30	0.26

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV.

Appendix E2. Clinical Laboratory Data for Chronic Renal Pigs 1 – 4 on Day +1

Animal Number:	Pig 1	Pig 2	Pig 3	Pig 4		Mean	STDEV
Time Post Embolization	Day +1	Day +1	Day +1	Day +1		Day +1	Day +1
Hematology							
White Cell Count	NR[1]	13.746	19.439	15.836		16.34	2.88
Red Cell Count	NR	6.91	7.86	7.7		7.49	0.51
Hemoglobin	NR	128	135	138		133.67	5.13
Hematocrit	NR	0.377	0.417	0.416		0.40	0.02
Mean Corp Vol	NR	54.6	53	54		53.87	0.81
Mean Corp Hemoglobin	NR	18.5	17.1	17.9		17.83	0.70
Mean Corp Hemoglobin Conc	NR	338	323	332		331.00	7.55
RDW	NR	19.7	21.2	21.7		20.87	1.04
Platelet CNT	NR	381	675	363		473.00	175.17
Mean Platelet Volume	NR	22.7	15.8	NR		19.25	4.88
Differential Cell Count							
% Neutrophils	NR	43	36	32		37.00	5.57
% Lymphocytes	NR	46	55	54		51.67	4.93
% Monocytes	NR	7	5	9		7.00	2.00
% Eosinophils	NR	3	2	2		2.33	0.58
% Basophils	NR	0	1	2		1.00	1.00
Absolute Differential Values							
Neutrophils	NR	5.95	7.06	5.1		6.04	0.98
Lymphocytes	NR	6.39	10.7	8.6		8.56	2.16
Monocytes	NR	0.906	1.05	1.48		1.15	0.30
Eosinophils	NR	0.467	0.463	0.391		0.44	0.04
Basophils	NR	0.033	0.166	0.265		0.15	0.12
Chemistry							
Glucose	9.5	7.8	8.4	10.2		8.98	1.08
Blood Urea Nitrogen (BUN)	8	8.1	9.2	8.8		8.53	0.57
Creatinine	135.8	145.4	77	193.1		137.83	47.67
BUN/Cr Ratio	15	14	30	11		17.50	8.50
Sodium	145	147	136	144		143.00	4.83
Potassium	6	4	8.5	3.5		5.50	2.27
Na/K Ratio	24	37	16	41		29.50	11.56
Chloride	110	110	107	105		108.00	2.45
Carbon Dioxide	16.6	24.3	11.4	19.6		17.98	5.41
Anion Gap	24	17	26	23		22.50	3.87
Calcium	2.09	2.53	2.32	2.39		2.33	0.18
Phosphorus	3.2	2.72	4	3.05		3.24	0.54
Total Protein	62	56	64	59		60.25	3.50
Albumin	42.57	34.77	45.03	37.89		40.07	4.61
Globulin	19	21	19	21		20.00	1.15
A/G Ratio	2.2	1.6	2.4	1.8		2.00	0.37
Total Bilirubin	1	4	hemolyzed	5		3.33	2.08
Alkaline Phosphatase	270	256	340	281		286.75	36.94
ALT (Sgpt)	124	100	198	112		133.50	44.10
Gamma gt	60	73	106	64		75.75	20.89
Creatine Phosphokinase	24,648	1,700	22,729	1,493		12,642.50	12,779.14
Calculated Osmolality	298	297	286	293		293.50	5.45
AST (Sgot)	562	144	1414	154		568.50	596.36
Sorbital Dehydrogenase-AO	32.9	16.8	10.5	9.2		17.35	10.89
Uric Acid	23	21	55	24		30.75	16.21

Appendix E2. Clinical Laboratory Data for Pigs 1 – 4 on Day +1, cont.

Animal Number:	Pig 1	Pig 2	Pig 3	Pig 4		Mean	STDEV
Time Post Embolization	Day +1	Day +1	Day +1	Day +1		Day +1	Day +1
Morphology and Coagulation Parameters							
Platelets	NR	Adequate	Adequate	Adequate		NA[2]	NA
RBC Morph	NR	See	See Below	See		NA	NA
Aniso	NR	2+	1+	1+		NA	NA
Poik	NR	3+	3+	3+		NA	NA
Polychrom	NR	NR	NR	NR		NA	NA
Fibrinogen Degradation Products	Positive @1:2, 1:8	Positive @1:2, 1:8	Positive @1:2, 1:8	Positive @1:2, 1:8		NA	NA
Fibrinogen Semi Quantitative	NR	2	1	1		1.33	0.58
Part. Thromboplastin Time	**60**[3]	24.3	34	**60**		44.58	18.25
Prothrombin Time	**60**	15.2	17.4	34.1		31.68	20.68

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV
[3]The values in bold were reported as being >60 (Appendix D, Clinical Laboratory Data for Individual Animals). Since the true value is unknown, they are given here as "60" for the purposes of calculating mean and standard deviation.

Appendix E3. Clinical Laboratory Data for Chronic Renal Pigs 1 to 4 on Day 7

Animal Number:	Pig 1	Pig 2	Pig 3	Pig 4		Mean	STDEV
Time Post Embolization	Day 7	Day 7	Day 7	Day 7		Day 7	Day 7
Hematology							
White Cell Count	15.41	12.5	16	NS[2]		14.64	1.87
Red Cell Count	6.13	5.69	6.27	NS		6.03	0.30
Hemoglobin	116	104	106	NS		108.67	6.43
Hematocrit	0.336	0.312	0.321	NS		0.32	0.01
Mean Corp Vol	54.8	54.8	51.2	NS		53.60	2.08
Mean Corp Hemoglobin	18.9	18.3	16.8	NS		18.00	1.08
Mean Corp Hemoglobin Conc	345	334	329	NS		336.00	8.19
RDW	20.5	19.7	19.4	NS		19.87	0.57
Platelet CNT	530	485	870	NS		628.33	210.50
Mean Platelet Volume	NR[1]	24.7	14.2	NS		19.45	7.42
Differential Cell Count							
% Neutrophils	29	28	37	NS		31.33	4.93
% Lymphocytes	63	62	55	NS		60.00	4.36
% Monocytes	8	6	7	NS		7.00	1.00
% Eosinophils	NR	4	1	NS		2.50	2.12
% Basophils	NR	0	0	NS		0.00	0.00
Absolute Differential Values							
Neutrophils	4.47	3.52	5.88	NS		4.62	1.19
Lymphocytes	9.71	7.71	8.79	NS		8.74	1.00
Monocytes	1.23	0.706	1.05	NS		1.00	0.27
Eosinophils	NR	0.484	0.208	NS		0.35	0.20
Basophils	NR	0.014	0.039	NS		0.03	0.02
Chemistry							
Glucose	6.6	6.5	6.1	NS		6.40	0.26
Blood Urea Nitrogen (BUN)	9	9.2	8.1	NS		8.77	0.59
Creatinine	79	105	114.2	NS		99.40	18.26
BUN/Cr Ratio	29	22	18	NS		23.00	5.57
Sodium	144	154	154	NS		150.67	5.77
Potassium	5.4	5	4.9	NS		5.10	0.26
Na/K Ratio	27	31	31	NS		29.67	2.31
Chloride	107	116	114	NS		112.33	4.73
Carbon Dioxide	27.4	33	32.6	NS		31.00	3.12
Anion Gap	15	10	12	NS		12.33	2.52
Calcium	2.52	2.7	2.77	NS		2.66	0.13
Phosphorus	3.23	3.36	3.34	NS		3.31	0.07
Total Protein	52	52	54	NS		52.67	1.15
Albumin	36.84	34.38	33.91	NS		35.04	1.57
Globulin	15	18	20	NS		17.67	2.52
A/G Ratio	2.4	2	1.7	NS		2.03	0.35
Total Bilirubin	0	3	3	NS		2.00	1.73
Alkaline Phosphatase	223	208	197	NS		209.33	13.05
ALT (Sgpt)	96	102	84	NS		94.00	9.17
Gamma gt	57	66	59	NS		60.67	4.73
Creatine Phosphokinase	13,569	4,337	2,775	NS		6,893.67	5,833.53
Calculated Osmolality	293	311	310	NS		304.67	10.12
AST (Sgot)	237	62	71	NS		123.33	98.54
Sorbital Dehydrogenase-AO	10.4	2.8	1.8	NS		5.00	4.70
Uric Acid	19	15	20	NS		18.00	2.65

Appendix E3. Clinical Laboratory Data for Chronic Renal Pigs 1 – 4 on Day 7, cont.

Animal Number:	Pig 1	Pig 2	Pig 3	Pig 4		Mean	STDEV
Time Post Embolization	Day 7	Day 7	Day 7	Day 7		Day 7	Day 7
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	NS		NA[3]	NA
RBC Morph	See Below	See Below	See Below	NS		NA	NA
Aniso	NR	NR	1+	NS		NA	NA
Poik	2+	2+	3+	NS		NA	NA
Polychrom	NR	NR	NR	NS		NA	NA
Fibrinogen Degradation Products	Positive	Positive	Positive	NS		NA	NA
Fibrinogen Semi Quantitative	2	3	3	NS		2.67	0.58
Part. Thromboplastin Time	22.5	19.6	19.3	NS		20.47	1.77
Prothrombin Time	16	16	15	NS		15.67	0.58

[1] Not Reported
[2] No Sample
[3] Not Applicable to calculate Mean and STDEV

Appendix E4. Clinical Laboratory Data for Chronic Renal Pigs 1 – 4 on Day 14

Animal Number:	Pig 1	Pig 2	Pig 3	Pig 4		Mean	STDEV
Time Post Embolization	Day 14	Day 14	Day 14	Day 14		Day 14	Day 14
Hematology							
White Cell Count	16.8	12.4	20.2	16.2		16.40	3.20
Red Cell Count	6.42	6.49	6.65	6.5		6.52	0.10
Hemoglobin	119	118	114	114		116.25	2.63
Hematocrit	0.347	0.357	0.342	0.351		0.35	0.01
Mean Corp Vol	54.1	55	51.4	54		53.63	1.55
Mean Corp Hemoglobin	18.5	18.1	17.2	17.5		17.83	0.59
Mean Corp Hemoglobin Conc	342	329	334	325		332.50	7.33
RDW	19	20.9	21.5	19.6		20.25	1.15
Platelet CNT	493	379	650	508		507.50	111.10
Mean Platelet Volume	23.8	NR[1]	21.4	21.1		22.10	1.48
Differential Cell Count							
% Neutrophils	30	24	39	31		31.00	6.16
% Lymphocytes	60	60	48	66		58.50	7.55
% Monocytes	9	8	11	2		7.50	3.87
% Eosinophils	1	8	2	1		3.00	3.37
% Basophils	NR	NR	NR	NR		0.00	0.00
Absolute Differential Values							
Neutrophils	5.04	2.98	7.88	5.03		5.23	2.01
Lymphocytes	10.08	7.44	9.7	10.69		9.48	1.42
Monocytes	1.51	0.99	2.22	0.32		1.26	0.80
Eosinophils	0.17	0.99	0.4	0.16		0.43	0.39
Basophils	NR	NR	NR	NR		0.00	0.00
Chemistry							
Glucose	5.2	6.3	6.7	7.7		6.48	1.03
Blood Urea Nitrogen (BUN)	8	7.5	7.6	7.1		7.55	0.37
Creatinine	100.2	108.3	104	86.2		99.68	9.57
BUN/Cr Ratio	20	17	18	21		19.00	1.83
Sodium	144	145	146	146		145.25	0.96
Potassium	4.2	4.3	4.4	5		4.48	0.36
Na/K Ratio	34	34	33	29		32.50	2.38
Chloride	109	109	107	110		108.75	1.26
Carbon Dioxide	32.8	32.4	28.6	28.9		30.68	2.23
Anion Gap	6	8	15	12		10.25	4.03
Calcium	2.45	2.67	2.59	2.48		2.55	0.10
Phosphorus	2.74	3.02	3.15	3.16		3.02	0.20
Total Protein	54	54	58	52		54.50	2.52
Albumin	34.38	36.65	35.58	33.95		35.14	1.22
Globulin	20	17	22	18		19.25	2.22
A/G Ratio	1.8	2.1	1.6	1.9		1.85	0.21
Total Bilirubin	3	3	1	0		1.75	1.50
Alkaline Phosphatase	165	224	235	224		212.00	31.76
ALT (Sgpt)	76	93	84	115		92.00	16.83
Gamma gt	44	65	58	61		57.00	9.13
Creatine Phosphokinase	5,578	1,250	3,189	2,416		3,108.25	1,829.25
Calculated Osmolality	289	291	294	296		292.50	3.11
AST (Sgot)	53	45	64	65		56.75	9.54
Sorbital Dehydrogenase-AO	1.8	2.4	3.3	4.9		3.10	1.35
Uric Acid	4	9	7	13		8.25	3.77

Appendix E4. Clinical Laboratory Data for Chronic Renal Pigs 1 – 4 on Day 14, cont.

Animal Number:	Pig 1	Pig 2	Pig 3	Pig 4		Mean	STDEV
Time Post Embolization	Day 14	Day 14	Day 14	Day 14		Day 14	Day 14
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate		NA[2]	NA
RBC Morph	See Below	See Below	See Below	See Below		NA	NA
Aniso	NR	NR	NR	NR		NA	NA
Poik	3+	3+	3+	3+		NA	NA
Polychrom	NR	NR	NR	NR		NA	NA
Fibrinogen Degradation Products	Positive @1:2, 1:8	Positive @1:2, 1:8	Positive @1:2, 1:8	Positive @1:2, 1:8		NA	NA
Fibrinogen Semi Quantitative	1	1	5	2		2.25	1.89
Part. Thromboplastin Time	45.5	18.5	19.6	24.6		27.05	12.58
Prothrombin Time	18.2	15.5	13.6	10.7		14.50	3.16

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV

Appendix E5. Clinical Laboratory Data for Chronic Renal Pigs 1 – 4 at 1 Month

Animal Number:	Pig 1	Pig 2	Pig 3	Pig 4		Mean	STDEV
Time Post Embolization	1 Month	1 Month	1 Month	1 Month		1 Month	1 Month
Hematology							
White Cell Count	10.31	11.11	20.9	15.11		14.36	4.84
Red Cell Count	6.9	6.97	6.49	6.66		6.76	0.22
Hemoglobin	125	129	106	117		119.25	10.14
Hematocrit	0.37	0.377	0.318	0.348		0.35	0.03
Mean Corp Vol	53.6	54.1	48.9	52.3		52.23	2.34
Mean Corp Hemoglobin	18.1	18.5	16.4	17.5		17.63	0.91
Mean Corp Hemoglobin Conc	338	343	335	335		337.75	3.77
RDW	21.1	20	21.9	19		20.50	1.27
Platelet CNT	389	370	864	487		527.50	230.12
Mean Platelet Volume	18.4	NR[1]	12.8	19.1		16.77	3.45
Differential Cell Count							
% Neutrophils	28	26	57	41		38.00	14.31
% Lymphocytes	68	71	37	50		56.50	15.97
% Monocytes	2	2	6	3		3.25	1.89
% Eosinophils	1	1	NR	6		2.67	2.89
% Basophils	1	NR	NR	NR		1.00	0.00
Absolute Differential Values							
Neutrophils	2.88	2.89	11.92	6.19		5.97	4.26
Lymphocytes	7.05	7.89	7.73	7.56		7.56	0.36
Monocytes	0.21	0.22	1.25	0.45		0.53	0.49
Eosinophils	0.075	0.11	NR	0.91		0.37	0.47
Basophils	0.094	NR	NR	NR		0.09	0.00
Chemistry							
Glucose	4.5	3.5	5.9	5.3		4.80	1.04
Blood Urea Nitrogen (BUN)	8.1	8.7	6.5	8.6		7.98	1.02
Creatinine	129.4	129	109.5	104.4		118.08	13.01
BUN/Cr Ratio	16	17	15	21		17.25	2.63
Sodium	142	140	141	142		141.25	0.96
Potassium	4.3	4.4	4.3	4.3		4.33	0.05
Na/K Ratio	33	32	33	33		32.75	0.50
Chloride	105	104	108	108		106.25	2.06
Carbon Dioxide	31.5	28.1	25.5	28.5		28.40	2.46
Anion Gap	10	12	12	10		11.00	1.15
Calcium	2.49	2.55	2.27	2.44		2.44	0.12
Phosphorus	3.25	3.15	2.54	2.89		2.96	0.32
Total Protein	61	61	59	54		58.75	3.30
Albumin	38.96	42.81	26.08	28.57		34.11	8.05
Globulin	22	18	33	25		24.50	6.35
A/G Ratio	1.8	2.4	0.8	1.1		1.53	0.72
Total Bilirubin	INV	INV	2	3		2.50	0.71
Alkaline Phosphatase	235	213	72	144		166.00	73.69
ALT (Sgpt)	104	74	62	72		78.00	18.11
Gamma gt	53	68	37	45		50.75	13.23
Creatine Phosphokinase	11,757	3,871	1,085	4,520		5,308.25	4,550.06
Calculated Osmolality	285	281	283	286		283.75	2.22
AST (Sgot)	97	44	41	52		58.50	26.08
Sorbital Dehydrogenase-AO	2.4	2.7	1.3	5.5		2.98	1.79
Uric Acid	7	9	7	7		7.50	1.00

Appendix E5. Clinical Laboratory Data for Chronic Renal Pigs 1 – 4 at 1 Month, cont.

Animal Number:	Pig 1	Pig 2	Pig 3	Pig 4		Mean	STDEV
Time Post Embolization	1 Month	1 Month	1 Month	1 Month		1 Month	1 Month
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Increased	Adequate		NA[2]	NA
RBC Morph	See Below	See below	See Below	See Below		NA	NA
Aniso	1+	1+	1+	1+		NA	NA
Poik	3+	3+	2+	3+		NA	NA
Polychrom	0	NR	NR	1+		NA	NA
Fibrinogen Degradation Products	Positive @1:2, 1:8	Positive @1:2, 1:8	Positive @1:2, 1:8	Positive @1:2, 1:8		NA	NA
Fibrinogen Semi Quantitative	1	3	9	4		4.25	3.40
Part. Thromboplastin Time	20	21	41.3	23.1		26.35	10.05
Prothrombin Time	17.8	16.5	18.5	17.5		17.58	0.83

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV

Appendix F. Means for Clinical Laboratory Data of Chronic Renal Pigs 1 to 4

	Means for Pigs 1 to 4					Standard Deviations for Pigs 1 to 4				
Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Day -1	Day +1	Day 7	Day 14	1 Month
Hematology										
White Cell Count	1 6.65	16.34	14.64	16.40	14.36	3.37	2.88	1.87	3.20	4.84
Red Cell Count	6.96	7.49	6.03	6.52	6.76	0.91	0.51	0.30	0.10	0.22
Hemoglobin	126.00	133.67	108.67	116.25	119.25	13.64	5.13	6.43	2.63	10.14
Hematocrit	0.38	0.40	0.32	0.35	0.35	0.06	0.02	0.01	0.01	0.03
Mean Corp Vol	54.88	53.87	53.60	53.63	52.23	1.26	0.81	2.08	1.55	2.34
Mean Corp Hemoglobin	18.15	17.83	18.00	17.83	17.63	0.51	0.70	1.08	0.59	0.91
Mean Corp Hemoglobin Conc	330.75	331.00	336.00	332.50	337.75	13.77	7.55	8.19	7.33	3.77
RDW	20.75	20.87	19.87	20.25	20.50	1.00	1.04	0.57	1.15	1.27
Platelet CNT	424.75	473.00	628.33	507.50	527.50	179.12	175.17	210.50	111.10	230.12
Mean Platelet Volume	18.45	19.25	19.45	22.10	16.77	1.77	4.88	7.42	1.48	3.45
Differential Cell Count										
% Neutrophils	39.75	37.00	31.33	31.00	38.00	13.89	5.57	4.93	6.16	14.31
% Lymphocytes	53.50	51.67	60.00	58.50	56.50	14.55	4.93	4.36	7.55	15.97
% Monocytes	5.00	7.00	7.00	7.50	3.25	1.83	2.00	1.00	3.87	1.89
% Eosinophils	1.33	2.33	2.50	3.00	2.67	0.58	0.58	2.12	3.37	2.89
% Basophils	1.00	1.00	0.00	NR[1]	1.00	---	1.00	---	NR	NR
Absolute Differential Values										
Neutrophils	6.37	6.04	4.62	5.23	5.97	1.50	0.98	1.19	2.01	4.26
Lymphocytes	9.16	8.56	8.74	9.48	7.56	3.74	2.16	1.00	1.42	0.36
Monocytes	0.84	1.15	1.00	1.26	0.53	0.24	0.30	0.27	0.80	0.49
Eosinophils	0.28	0.44	0.35	0.43	0.37	0.09	0.04	0.20	0.39	0.47
Basophils	0.13	0.15	0.03	NR	0.09	0.01	0.12	0.02	NR	NR
Chemistry										
Glucose	6.18	8.98	6.40	6.48	4.80	2.26	1.08	0.26	1.03	1.04
Blood Urea Nitrogen	5.95	8.53	8.77	7.55	7.98	0.33	0.57	0.59	0.37	1.02
Creatinine	89.85	137.83	99.40	99.68	118.08	11.26	47.67	18.26	9.57	13.01
BUN/Cr Ratio	17.00	17.50	23.00	19.00	17.25	3.16	8.50	5.57	1.83	2.63
Sodium	143.25	143.00	150.67	145.25	141.25	5.62	4.83	5.77	0.96	0.96
Potassium	5.28	5.50	5.10	4.48	4.33	0.75	2.27	0.26	0.36	0.05
Na/K Ratio	27.25	29.50	29.67	32.50	32.75	2.87	11.56	2.31	2.38	0.50
Chloride	106.00	108.00	112.33	108.75	106.25	3.56	2.45	4.73	1.26	2.06
Carbon Dioxide	24.73	17.98	31.00	30.68	28.40	4.38	5.41	3.12	2.23	2.46
Anion Gap	18.00	22.50	12.33	10.25	11.00	4.55	3.87	2.52	4.03	1.15
Calcium	2.69	2.33	2.66	2.55	2.44	0.24	0.18	0.13	0.10	0.12
Phosphorus	3.70	3.24	3.31	3.02	2.96	0.30	0.54	0.07	0.20	0.32
Total Protein	50.25	60.25	52.67	54.50	58.75	3.30	3.50	1.15	2.52	3.30
Albumin	33.06	40.07	35.04	35.14	34.11	2.69	4.61	1.57	1.22	8.05
Globulin	17.50	20.00	17.67	19.25	24.50	2.08	1.15	2.52	2.22	6.35
A/G Ratio	1.95	2.00	2.03	1.85	1.53	0.31	0.37	0.35	0.21	0.72
Total Bilirubin	4.00	3.33	2.00	1.75	2.50	1.00	2.08	1.73	1.50	0.71
Alkaline Phosphatase	296.75	286.75	209.33	212.00	166.00	26.21	36.94	13.05	31.76	73.69
ALT (Sgpt)	85.75	133.50	94.00	92.00	78.00	3.10	44.10	9.17	16.83	18.11
Gamma gt	59.75	75.75	60.67	57.00	50.75	3.86	20.89	4.73	9.13	13.23
Creatine Phosphokinase	2,183.50	12,642.50	6,893.67	3,108.25	5,308.25	601.53	12,779.14	5,833.53	1,829.25	4,550.06
Calculated Osmolality	288.50	293.50	304.67	292.50	283.75	14.15	5.45	10.12	3.11	2.22
AST (Sgot)	61.50	568.50	123.33	56.75	58.50	6.35	596.36	98.54	9.54	26.08
Sorbital Dehydrogenase-AO	4.33	17.35	5.00	3.10	2.98	1.65	10.89	4.70	1.35	1.79
Uric Acid	19.25	30.75	18.00	8.25	7.50	6.08	16.21	2.65	3.77	1.00

Appendix F. Means for Clinical Laboratory Data of Chronic Renal Pigs 1 to 4, cont.

	Means for Pigs 1 to 4					Standard Deviations for Pigs 1 to 4				
Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Day -1	Day +1	Day 7	Day 14	1 Month
Morphology and Coagulation Parameters										
Platelets	NA[2]	NA	NA	NA	NA	NA	NA	NA	NA	NA
RBC Morph	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Aniso	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Poik	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Polychrom	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Fibrinogen Degradation Products	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Fibrinogen Semi Quantitative	1.50	1.33	2.67	2.25	4.25	0.58	0.58	0.58	1.89	3.40
Part. Thromboplastin Time	11.05	44.58	20.47	27.05	26.35	0.62	18.25	1.77	12.58	10.05
Prothrombin Time	15.30	31.68	15.67	14.50	17.58	0.26	20.68	0.58	3.16	0.83

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV

Appendix G. Summary Clinical Data for Chronic Hepatic Pigs 5 to 8

Appendix G1. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day -1

Appendix G2. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day +1

Appendix G3. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day 7

Appendix G4. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day 14

Appendix G5. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 at 1 Month

Appendix G1. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day -1

Animal Number:	Pig 5	Pig 6	Pig 7	Pig 8		Mean	STDEV
Day of Bleed	Day -1	Day -1	Day -1	Day -1		Day - 1	Day -1
Hematology							
White Cell Count	15	8.99	8.22	14.11		11.58	3.47
Red Cell Count	6.36	5.33	5.86	6.33		5.97	0.48
Hemoglobin	107	108	113	113		110.25	3.20
Hematocrit	0.319	0.315	0.34	0.334		0.33	0.01
Mean Corp Vol	50.2	59	58	52.8		55.00	4.20
Mean Corp Hemoglobin	16.7	20.2	19.4	17.9		18.55	1.56
Mean Corp Hemoglobin Conc	334	342	334	339		337.25	3.95
RDW	20.6	19	20.1	17.9		19.40	1.20
Platelet CNT	439	287	165	527		354.50	160.59
Mean Platelet Volume	20.5	16.2	17.6	14.4		17.18	2.57
Differential Cell Count							
% Neutrophils	39	21	3	4		16.75	16.98
% Lymphocytes	56	74	85	88		75.75	14.48
% Monocytes	3	3	6	6		4.50	1.73
% Eosinophils	2	2	6	2		3.00	2.00
% Basophils	NR[1]	NR	NR	NR		NR	NR
Absolute Differential Values							
Neutrophils	5.85	1.89	0.25	0.56		2.14	2.58
Lymphocytes	8.4	6.65	6.99	12.42		8.62	2.65
Monocytes	0.45	0.27	0.49	0.85		0.52	0.24
Eosinophils	0.3	0.18	0.49	0.28		0.31	0.13
Basophils	NR	NR	NR	NR		NR	NR
Chemistry							
Glucose	5.4	2	4.1	3.3		3.70	1.43
Blood Urea Nitrogen (BUN)	4.1	6.6	4.5	4.9		5.03	1.10
Creatinine	111.4	90	76.1	101.4		94.73	15.19
BUN/Cr Ratio	9	18	15	12		13.50	3.87
Sodium	147	148	152	146		148.25	2.63
Potassium	5.1	4.7	4.7	4.1		4.65	0.41
Na/K Ratio	29	31	32	36		32.00	2.94
Chloride	112	111	113	109		111.25	1.71
Carbon Dioxide	28.5	28.3	29.7	29.1		28.90	0.63
Anion Gap	12	13	14	12		12.75	0.96
Calcium	2.38	2.33	2.38	2.57		2.42	0.11
Phosphorus	3.81	3.73	3.87	3.46		3.72	0.18
Total Protein	46	49	55	49		49.75	3.77
Albumin	31.3	30.3	36	36.38		33.50	3.14
Globulin	15	19	19	13		16.50	3.00
A/G Ratio	2.1	1.6	1.9	2.9		2.13	0.56
Total Bilirubin	4	3	5	4		4.00	0.82
Alkaline Phosphatase	341	261	217	261		270.00	51.68
ALT (Sgpt)	73	89	74	84		80.00	7.79
Gamma gt	55	38	32	43		42.00	9.76
Creatine Phosphokinase	874	735	2,365	728		1,175.50	795.85
Calculated Osmolality	292	293	300	287		293.00	5.35
AST (Sgot)	51	38	58	89		59.00	21.65
Sorbital Dehydrogenase-AO	4.2	1.1	0.9	11.5		4.43	4.95
Uric Acid	13	16	7	14		12.50	3.87

Appendix G1. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day -1, cont.

Animal Number:	Pig 5	Pig 6	Pig 7	Pig 8		Mean	STDEV
Day of Bleed	Day -1	Day -1	Day -1	Day -1		Day - 1	Day -1
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate		NA[2]	NA
RBC Morph	See Below	See Below	See Below	See Below		NA	NA
Aniso	NR	NR	NR	NR		NA	NA
Poik	3+	3+	3+	3+		NA	NA
Polychrom	NR	NR	NR	NR		NA	NA
Fibrinogen Degradation Products	Positive	Positive	Positive	Positive		NA	NA
Fibrinogen Semi Quantitative	3	1	2	2		2.00	0.82
Part. Thromboplastin Time	13.4	0.8	11.8	12.7		9.68	5.95
Prothrombin Time	13.7	3.7	15.8	13.7		11.73	5.44

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV

Appendix G2. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day+1

Animal Number:	Pig 5	Pig 6	Pig 7	Pig 8		Mean	STDEV
Date of Bleed	Day +1	Day +1	Day +1	Day +1		Day +1	Day +1
Hematology							
White Cell Count	15.8	10.71	13	11.9		12.85	2.18
Red Cell Count	7.74	6.4	6.4	7.4		6.99	0.69
Hemoglobin	129	125	126	131		127.75	2.75
Hematocrit	0.39	0.375	0.38	0.398		0.39	0.01
Mean Corp Vol	50.4	58.7	59.5	53.8		55.60	4.29
Mean Corp Hemoglobin	16.6	19.6	19.7	17.7		18.40	1.51
Mean Corp Hemoglobin Conc	330	334	331	329		331.00	2.16
RDW	20.9	19	19.8	19.8		19.88	0.78
Platelet CNT	514	529	434	599		519.00	67.70
Mean Platelet Volume	18.2	28.6	19.3	15		20.28	5.84
Differential Cell Count							
% Neutrophils	26	32	14	12		21.00	9.59
% Lymphocytes	66	56	76	73		67.75	8.88
% Monocytes	5	10	7	6		7.00	2.16
% Eosinophils	3	2	3	8		4.00	2.71
% Basophils	0	NR[1]	NR	1		0.50	0.71
Absolute Differential Values							
Neutrophils	4.08	3.43	1.82	1.43		2.69	1.27
Lymphocytes	10.5	6	9.88	8.69		8.77	1.99
Monocytes	0.733	1.07	0.91	0.71		0.86	0.17
Eosinophils	0.399	0.21	0.39	0.95		0.49	0.32
Basophils	0.057	NR	NR	0.12		0.09	0.04
Chemistry							
Glucose	7.5	5.9	8.7	7		7.28	1.16
Blood Urea Nitrogen (BUN)	4.6	6.5	4	6		5.28	1.17
Creatinine	95.7	83.3	81.8	92.2		88.25	6.76
BUN/Cr Ratio	12	20	12	16		15.00	3.83
Sodium	154	157	156	150		154.25	3.10
Potassium	4	4.6	4.2	4		4.20	0.28
Na/K Ratio	39	34	37	38		37.00	2.16
Chloride	117	118	120	111		116.50	3.87
Carbon Dioxide	26.5	32.4	27.7	26.5		28.28	2.81
Anion Gap	15	11	13	17		14.00	2.58
Calcium	2.59	2.61	2.59	2.79		2.65	0.10
Phosphorus	3.62	3.07	3.21	3.27		3.29	0.23
Total Protein	53	59	59	57		57.00	2.83
Albumin	36.88	37.64	39.05	42.91		39.12	2.68
Globulin	16	21	20	14		17.75	3.30
A/G Ratio	2.3	1.8	2	3		2.28	0.53
Total Bilirubin	3	3	3	3		3.00	0.00
Alkaline Phosphatase	345	297	195	268		276.25	62.79
ALT (Sgpt)	81	98	77	89		86.25	9.29
Gamma gt	60	42	35	55		48.00	11.52
Creatine Phosphokinase	1,226	679	580	673		789.50	294.51
Calculated Osmolality	306	313	311	299		307.25	6.24
AST (Sgot)	51	35	52	53		47.75	8.54
Sorbital Dehydrogenase-AO	1.8	1.7	3.3	2.1		2.23	0.74
Uric Acid	15	10	3	18		11.50	6.56

Appendix G2. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day+1

Animal Number:	Pig 5	Pig 6	Pig 7	Pig 8		Mean	STDEV
Date of Bleed	Day +1	Day +1	Day +1	Day +1		Day +1	Day +1
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate		NA[2]	NA
RBC Morph	See Below	See Below	See Below	See Below		NA	NA
Aniso	1+	NR	1+	1+		NA	NA
Poik	3+	3+	3+	2+		NA	NA
Polychrom	NR	NR	NR	1+		NA	NA
Fibrinogen Degradation Products	Positive	Positive	Positive	Positive		NA	NA
Fibrinogen Semi Quantitative	2	1	2	2		1.75	0.50
Part. Thromboplastin Time	29.7	20.1	23	23.7		24.13	4.03
Prothrombin Time	16.9	16.2	13.9	15.8		15.70	1.28

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV

Appendix G3. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day 7

Animal Number:	Pig 5	Pig 6	Pig 7	Pig 8		Mean	STDEV
Date of Bleed	Day 7	Day 7	Day 7	Day 7		Day 7	Day 7
Hematology							
White Cell Count	14.9	12.7	11	15.6		13.55	2.10
Red Cell Count	7.8	6.31	6.41	7.17		6.92	0.70
Hemoglobin	128	123	124	126		125.25	2.22
Hematocrit	0.393	0.373	0.377	0.38		0.38	0.01
Mean Corp Vol	50.4	59.1	58.9	53		55.35	4.35
Mean Corp Hemoglobin	16.4	19.5	19.3	17.6		18.20	1.47
Mean Corp Hemoglobin Conc	326	330	328	331		328.75	2.22
RDW	21.4	19.6	19.8	20.4		20.30	0.81
Platelet CNT	648	469	420	493		507.50	98.47
Mean Platelet Volume	16.7	29.8	16.9	15.7		19.78	6.70
Differential Cell Count							
% Neutrophils	11	30	21	38		25.00	11.63
% Lymphocytes	80	61	74	50		66.25	13.43
% Monocytes	6	8	3	6		5.75	2.06
% Eosinophils	3	1	2	6		3.00	2.16
% Basophils	NR[1]	NR	NR	NR		NR	NR
Absolute Differential Values							
Neutrophils	1.64	3.8	2.31	5.92		3.42	1.90
Lymphocytes	11.92	7.75	8.14	7.8		8.90	2.02
Monocytes	0.89	1.02	0.33	0.94		0.80	0.31
Eosinophils	0.45	0.13	0.22	0.94		0.44	0.36
Basophils	NR	NR	NR	NR		NR	NR
Chemistry							
Glucose	6.6	6.7	6.9	6.3		6.63	0.25
Blood Urea Nitrogen (BUN)	4.5	7.3	6.1	6		5.98	1.15
Creatinine	98.2	80.2	76.8	89.6		86.20	9.66
BUN/Cr Ratio	12	23	20	17		18.00	4.69
Sodium	144	146	144	148		145.50	1.91
Potassium	4.3	4.6	4.3	4.4		4.40	0.14
Na/K Ratio	33	32	33	34		33.00	0.82
Chloride	108	109	111	112		110.00	1.83
Carbon Dioxide	31.4	34.9	33.2	29.8		32.33	2.21
Anion Gap	9	7	4	11		7.75	2.99
Calcium	2.5	2.54	2.53	2.69		2.57	0.09
Phosphorus	3.32	2.92	3.19	3.03		3.12	0.18
Total Protein	53	57	58	56		56.00	2.16
Albumin	37.35	36.24	38.04	39.62		37.81	1.41
Globulin	16	21	20	16		18.25	2.63
A/G Ratio	2.4	1.7	1.9	2.4		2.10	0.36
Total Bilirubin	3	3	2	3		2.75	0.50
Alkaline Phosphatase	320	260	206	236		255.50	48.34
ALT (Sgpt)	68	86	60	74		72.00	10.95
Gamma gt	59	40	32	57		47.00	13.14
Creatine Phosphokinase	3,280	1,574	1,348	1,055		1,814.25	1,000.00
Calculated Osmolality	287	294	289	296		291.50	4.20
AST (Sgot)	82	46	53	58		59.75	15.63
Sorbital Dehydrogenase-AO	2.5	2.4	2.4	3.8		2.78	0.68
Uric Acid	8	11	0	5		6.00	4.69

Appendix G3. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day 7, cont.

Animal Number:	Pig 5	Pig 6	Pig 7	Pig 8		Mean	STDEV
Date of Bleed	Day 7	Day 7	Day 7	Day 7		Day 7	Day 7
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate		NA[2]	NA
RBC Morph	See Below	See Below	See Below	See Below		NA	NA
Aniso	NR	1+	NR	NR		NA	NA
Poik	3+	2+	3+	3+		NA	NA
Polychrom	NR	NR	NR	NR		NA	NA
Fibrinogen Degradation Products	Positive @1:2, 1:8	Positive @1:2, 1:8	Positive @1:2, 1:8	Positive @1:2, 1:8		NA	NA
Fibrinogen Semi Quantitative	1	1	1	1		1.00	0.00
Part. Thromboplastin Time	24	46.4	20.6	24.7		28.93	11.79
Prothrombin Time	15.8	19	14.1	15.5		16.10	2.07

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV

Appendix G4. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day 14

Animal Number:	Pig 5	Pig 6	Pig 7	Pig 8		Mean	STDEV
Date of Bleed	Day 14	Day 14	Day 14	Day 14		Day 14	Day 14
Hematology							
White Cell Count	17.8	16.31	13.1	14.4		15.40	2.07
Red Cell Count	7.95	6.18	6.09	7.06		6.82	0.87
Hemoglobin	135	124	122	123		126.00	6.06
Hematocrit	0.396	0.355	0.358	0.365		0.37	0.02
Mean Corp Vol	49.8	57.5	58.9	51.7		54.48	4.41
Mean Corp Hemoglobin	16.9	20.1	20.1	17.4		18.63	1.72
Mean Corp Hemoglobin Conc	340	349	341	337		341.75	5.12
RDW	22.3	19.1	20.5	20.1		20.50	1.34
Platelet CNT	499	368	206	493		391.50	137.62
Mean Platelet Volume	19.7	23.9	NR[1]	12.9		18.83	5.55
Differential Cell Count							
% Neutrophils	37	41	33	33		36.00	3.83
% Lymphocytes	51	51	60	48		52.50	5.20
% Monocytes	5	7	5	12		7.25	3.30
% Eosinophils	7	1	1	4		3.25	2.87
% Basophils	NR	NR	0	3		1.50	2.12
Absolute Differential Values							
Neutrophils	6.58	6.69	4.33	4.7		5.58	1.23
Lymphocytes	9.08	8.32	7.88	6.93		8.05	0.90
Monocytes	0.89	1.14	0.608	1.72		1.09	0.47
Eosinophils	1.25	0.16	0.174	0.549		0.53	0.51
Basophils	NR	NR	0.064	0.474		0.27	0.29
Chemistry							
Glucose	5.3	5.6	7	5.7		5.90	0.75
Blood Urea Nitrogen (BUN)	5.4	8.2	6.3	7.2		6.78	1.20
Creatinine	105.9	85	73.5	95.9		90.08	13.96
BUN/Cr Ratio	13	24	22	19		19.50	4.80
Sodium	147	145	144	144		145.00	1.41
Potassium	4.1	4.6	4.1	4.2		4.25	0.24
Na/K Ratio	36	32	35	34		34.25	1.71
Chloride	107	107	107	108		107.25	0.50
Carbon Dioxide	31.6	34.1	31.6	27.7		31.25	2.64
Anion Gap	13	9	10	13		11.25	2.06
Calcium	2.54	2.57	2.63	2.68		2.61	0.06
Phosphorus	3.41	3.08	3.19	2.93		3.15	0.20
Total Protein	61	60	59	63		60.75	1.71
Albumin	38.92	36.59	39.97	38.24		38.43	1.42
Globulin	22	23	19	25		22.25	2.50
A/G Ratio	1.8	1.6	2.1	1.5		1.75	0.26
Total Bilirubin	4	4	4	4		4.00	0.00
Alkaline Phosphatase	279	232	223	204		234.50	31.88
ALT (Sgpt)	55	78	62	71		66.50	10.08
Gamma gt	59	44	32	66		50.25	15.24
Creatine Phosphokinase	762	5,693	1,639	4,911		3,251	2,416
Calculated Osmolality	292	292	289	289		290.50	1.73
AST (Sgot)	39	48	43	61		47.75	9.57
Sorbital Dehydrogenase-AO	2.4	2.1	2.8	4.3		2.90	0.98
Uric Acid	3	0	2	3		2.00	1.41

Appendix G4. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 on Day 14, cont.

Animal Number:	Pig 5	Pig 6	Pig 7	Pig 8		Mean	STDEV
Date of Bleed	Day 14	Day 14	Day 14	Day 14		Day 14	Day 14
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate		NA[2]	NA
RBC Morph	See Below	See Below	See Below	See Below		NA	NA
Aniso	1+	1+	1+	NR		NA	NA
Poik	3+	3+	3+	3+		NA	NA
Polychrom	NR	NR	2+	---		NA	NA
Fibrinogen Degradation Products	Positive @1:2, 1:8	Positive @1:2, 1:8	Positive @1:2, 1:8	Positive @1:2, 1:8		NA	NA
Fibrinogen Semi Quantitative	1	1	1	2		1.25	0.50
Part. Thromboplastin Time	22	17.7	19.3	21.3		20.08	1.95
Prothrombin Time	15.7	15.3	15.5	15.6		15.53	0.17

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV

Appendix G5. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 at 1 Month

Animal Number:	Pig 5	Pig 6	Pig 7	Pig 8		Mean	STDEV
Date of Bleed	1 Month	1 Month	1 Month	1 Month		1 Month	1 Month
Hematology							
White Cell Count	17.91	20.91	14.41	15.21		17.11	2.94
Red Cell Count	7.73	6.4	6.21	6.73		6.77	0.68
Hemoglobin	129	126	127	117		124.75	5.32
Hematocrit	0.385	0.371	0.373	0.351		0.37	0.01
Mean Corp Vol	49.8	58	60	52.2		55.00	4.79
Mean Corp Hemoglobin	16.7	19.7	20.5	17.4		18.58	1.81
Mean Corp Hemoglobin Conc	336	339	341	333		337.25	3.50
RDW	21.4	20	18.2	20.9		20.13	1.41
Platelet CNT	458	391	411	393		413.25	31.16
Mean Platelet Volume	19.2	24.3	23	13.9		20.10	4.67
Differential Cell Count							
% Neutrophils	20	37	20	26		25.75	8.02
% Lymphocytes	71	57	72	68		67.00	6.88
% Monocytes	4	3	5	2		3.50	1.29
% Eosinophils	5	3	1	4		3.25	1.71
% Basophils	NR[1]	NR	1	NR		1.00	NR
Absolute Differential Values							
Neutrophils	3.57	7.73	2.93	3.96		4.55	2.16
Lymphocytes	12.72	11.92	10.4	10.34		11.35	1.17
Monocytes	0.72	0.63	0.759	0.3		0.60	0.21
Eosinophils	0.9	0.63	0.133	0.61		0.57	0.32
Basophils	NR	NR	0.18	NR		0.18	NR
Chemistry							
Glucose	5.4	4.9	5.5	5.2		5.25	0.26
Blood Urea Nitrogen (BUN)	5.5	8.9	5.1	6		6.38	1.72
Creatinine	112.3	88.4	78	96.1		93.70	14.45
BUN/Cr Ratio	12	25	16	16		17.25	5.50
Sodium	147	143	143	142		143.75	2.22
Potassium	4.2	4.7	3.9	3.7		4.13	0.43
Na/K Ratio	35	30	37	38		35.00	3.56
Chloride	107	106	105	105		105.75	0.96
Carbon Dioxide	35.7	32.3	31.7	31.3		32.75	2.01
Anion Gap	9	9	10	9		9.25	0.50
Calcium	2.47	2.45	2.51	2.56		2.50	0.05
Phosphorus	3.47	3.01	3.24	2.75		3.12	0.31
Total Protein	61	62	59	66		62.00	2.94
Albumin	39.29	34.2	37.87	36.42		36.95	2.17
Globulin	22	28	21	30		25.25	4.43
A/G Ratio	1.8	1.2	1.8	1.2		1.50	0.35
Total Bilirubin	3	2	2	2		2.25	0.50
Alkaline Phosphatase	249	211	202	237		224.75	21.95
ALT (Sgpt)	59	79	63	80		70.25	10.81
Gamma gt	53	41	32	53		44.75	10.21
Creatine Phosphokinase	1,503	1,444	2,372	1,577		1,724.00	435.41
Calculated Osmolality	292	289	284	282		286.75	4.57
AST (Sgot)	43	41	67	56		51.75	12.15
Sorbital Dehydrogenase-AO	4.7	2.2	2.2	2.9		3.00	1.18
Uric Acid	2	3	0	2		1.75	1.26

Appendix G5. Clinical Laboratory Data for Chronic Hepatic Pigs 5 to 8 at 1 Month, cont.

Animal Number:	Pig 5	Pig 6	Pig 7	Pig 8		Mean	STDEV
Date of Bleed	1 Month	1 Month	1 Month	1 Month		1 Month	1 Month
Morphology and Coagulation Parameters							
Platelets	Adequate	Adequate	Adequate	Adequate		NA[2]	NA
RBC Morph	See Below	See Below	See Below	See Below		NA	NA
Aniso	1+	1+	1+	1+		NA	NA
Poik	3+	3+	3+	3+		NA	NA
Polychrom	1+	1+	NR	1+		NA	NA
Fibrinogen Degradation Products	Positive	Positive	Positive	Positive		NA	NA
Fibrinogen Semi Quantitative	1	1	1	1		1.00	0.00
Part. Thromboplastin Time	22.5	18.1	23.3	20.3		21.05	2.34
Prothrombin Time	16	15.6	16	16.5		16.03	0.37

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV

Appendix H. Means for Clinical Laboratory Data in Chronic Hepatic Pigs 5 to 8

	Mean Values for Pigs 5 to 8					One Standard Deviation for Pigs 5 to 8				
Day of Bleed	Day -1	Day +1	Day 7	Day 14	1 Month	Day -1	Day +1	Day 7	Day 14	1 Month
Hematology										
White Cell Count	11.58	12.85	13.55	15.40	17.11	3.47	2.18	2.10	2.07	2.94
Red Cell Count	5.97	6.99	6.92	6.82	6.77	0.48	0.69	0.70	0.87	0.68
Hemoglobin	110.25	127.75	125.25	126.00	124.75	3.20	2.75	2.22	6.06	5.32
Hematocrit	0.33	0.39	0.38	0.37	0.37	0.01	0.01	0.01	0.02	0.01
Mean Corp Vol	55.00	55.60	55.35	54.48	55.00	4.20	4.29	4.35	4.41	4.79
Mean Corp Hemoglobin	18.55	18.40	18.20	18.63	18.58	1.56	1.51	1.47	1.72	1.81
Mean Corp Hemoglobin Conc	337.25	331.00	328.75	341.75	337.25	3.95	2.16	2.22	5.12	3.50
RDW	19.40	19.88	20.30	20.50	20.13	1.20	0.78	0.81	1.34	1.41
Platelet CNT	354.50	519.00	507.50	391.50	413.25	160.59	67.70	98.47	137.62	31.16
Mean Platelet Volume	17.18	20.28	19.78	18.83	20.10	2.57	5.84	6.70	5.55	4.67
Differential Cell Count										
% Neutrophils	16.75	21.00	25.00	36.00	25.75	16.98	9.59	11.63	3.83	8.02
% Lymphocytes	75.75	67.75	66.25	52.50	67.00	14.48	8.88	13.43	5.20	6.88
% Monocytes	4.50	7.00	5.75	7.25	3.50	1.73	2.16	2.06	3.30	1.29
% Eosinophils	3.00	4.00	3.00	3.25	3.25	2.00	2.71	2.16	2.87	1.71
% Basophils	NR	0.50	NR	1.50	1.00	NR	0.71	NR	2.12	NR
Absolute Differential Values										
Neutrophils	2.14	2.69	3.42	5.58	4.55	2.58	1.27	1.90	1.23	2.16
Lymphocytes	8.62	8.77	8.90	8.05	11.35	2.65	1.99	2.02	0.90	1.17
Monocytes	0.52	0.86	0.80	1.09	0.60	0.24	0.17	0.31	0.47	0.21
Eosinophils	0.31	0.49	0.44	0.53	0.57	0.13	0.32	0.36	0.51	0.32
Basophils	NR[1]	0.09	NR	0.27	0.18	NR	0.04	NR	0.29	NR
Chemistry										
Glucose	3.70	7.28	6.63	5.90	5.25	1.43	1.16	0.25	0.75	0.26
Blood Urea Nitrogen (BUN)	5.03	5.28	5.98	6.78	6.38	1.10	1.17	1.15	1.20	1.72
Creatinine	94.73	88.25	86.20	90.08	93.70	15.19	6.76	9.66	13.96	14.45
BUN/Cr Ratio	13.50	15.00	18.00	19.50	17.25	3.87	3.83	4.69	4.80	5.50
Sodium	148.25	154.25	145.50	145.00	143.75	2.63	3.10	1.91	1.41	2.22
Potassium	4.65	4.20	4.40	4.25	4.13	0.41	0.28	0.14	0.24	0.43
Na/K Ratio	32.00	37.00	33.00	34.25	35.00	2.94	2.16	0.82	1.71	3.56
Chloride	111.25	116.50	110.00	107.25	105.75	1.71	3.87	1.83	0.50	0.96
Carbon Dioxide	28.90	28.28	32.33	31.25	32.75	0.63	2.81	2.21	2.64	2.01
Anion Gap	12.75	14.00	7.75	11.25	9.25	0.96	2.58	2.99	2.06	0.50
Calcium	2.42	2.65	2.57	2.61	2.50	0.11	0.10	0.09	0.06	0.05
Phosphorus	3.72	3.29	3.12	3.15	3.12	0.18	0.23	0.18	0.20	0.31
Total Protein	49.75	57.00	56.00	60.75	62.00	3.77	2.83	2.16	1.71	2.94
Albumin	33.50	39.12	37.81	38.43	36.95	3.14	2.68	1.41	1.42	2.17
Globulin	16.50	17.75	18.25	22.25	25.25	3.00	3.30	2.63	2.50	4.43
A/G Ratio	2.13	2.28	2.10	1.75	1.50	0.56	0.53	0.36	0.26	0.35
Total Bilirubin	4.00	3.00	2.75	4.00	2.25	0.82	0.00	0.50	0.00	0.50
Alkaline Phosphatase	270.00	276.25	255.50	234.50	224.75	51.68	62.79	48.34	31.88	21.95
ALT (Sgpt)	80.00	86.25	72.00	66.50	70.25	7.79	9.29	10.95	10.08	10.81
Gamma gt	42.00	48.00	47.00	50.25	44.75	9.76	11.52	13.14	15.24	10.21
Creatine Phosphokinase	1,175.50	789.50	1,814.25	3,251.25	1,724.00	795.85	294.51	1,000.00	2,416.10	435.41
Calculated Osmolality	293.00	307.25	291.50	290.50	286.75	5.35	6.24	4.20	1.73	4.57
AST (Sgot)	59.00	47.75	59.75	47.75	51.75	21.65	8.54	15.63	9.57	12.15
Sorbital Dehydrogenase-AO	4.43	2.23	2.78	2.90	3.00	4.95	0.74	0.68	0.98	1.18
Uric Acid	12.50	11.50	6.00	2.00	1.75	3.87	6.56	4.69	1.41	1.26

Appendix H. Means for Clinical Laboratory Data of Chronic Hepatic Pigs 5 to 8, cont.

	Mean Values for Pigs 5 to 8					One Standard Deviation for Pigs 5 to 8				
Day of Bleed		Day +1	Day 7	Day 14	1 Month	Day -1	Day +1	Day 7	Day 14	1 Month
Morphology and Coagulation Parameters										
Platelets	NA[2]	NA	NA	NA	NA	NA	NA	NA	NA	NA
RBC Morph	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Aniso	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Poik	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Polychrom	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Fibrinogen Degradation Products	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Fibrinogen Semi Quantitative	2.00	1.75	1.00	1.25	1.00	0.82	0.50	0.00	0.50	0.00
Part. Thromboplastin Time	9.68	24.13	28.93	20.08	21.05	5.95	4.03	11.79	1.95	2.34
Prothrombin Time	11.73	15.70	16.10	15.53	16.03	5.44	1.28	2.07	0.17	0.37

[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV

Appendix I. Summary Clinical Data by Date of Bleed for Acute Pigs 9 to 12

Animal Number:	Pig 9	Pig 10	Pig 11	Pig 12		Mean	STDEV
Date of Bleed	Day -1	Day -1	Day -1	Day -1		Day -1	Day -1
Hematology							
White Cell Count	25.81	14.8	16.412	19.7		19.18	4.87
Red Cell Count	7.73	7.41	6.47	7.54		7.29	0.56
Hemoglobin	142	139	124	133		134.50	7.94
Hematocrit	0.43	0.412	0.371	0.405		0.40	0.02
Mean Corp Vol	55.7	55.7	57.3	53.7		55.60	1.47
Mean Corp Hemoglobin	18.4	18.8	19.1	17.7		18.50	0.61
Mean Corp Hemoglobin Conc	331	337	333	329		332.50	3.42
RDW	19.7	20.5	19.2	22.5		20.48	1.45
Platelet CNT	422	280	509	491		425.50	104.00
Mean Platelet Volume	20.7	NR[1]	15.9	16.3		17.63	2.66
Differential Cell Count							
% Neutrophils	22	23	30	26		25.25	3.59
% Lymphocytes	68	67	59	63		64.25	4.11
% Monocytes	9	6	8	7		7.50	1.29
% Eosinophils	1	2	1	2		1.50	0.58
% Basophils	NR	2	1	1		1.33	0.58
Absolute Differential Values							
Neutrophils	5.68	3.45	4.92	5.05		4.78	0.94
Lymphocytes	17.55	9.93	9.75	12.5		12.43	3.64
Monocytes	2.32	0.913	1.28	1.43		1.49	0.60
Eosinophils	0.26	0.237	0.232	0.442		0.29	0.10
Basophils	NR	0.228	0.23	0.212		0.22	0.01
Chemistry							
Glucose	6.4	6.3	6.7	8.5		6.98	1.03
Blood Urea Nitrogen (BUN)	8.2	8.5	10.2	11.9		9.70	1.71
Creatinine	115.8	118.5	102.9	130.5		116.93	11.32
BUN/Cr Ratio	18	18	25	23		21.00	3.56
Sodium	147	146	146	146		146.25	0.50
Potassium	4.3	4	3.9	4.3		4.13	0.21
Na/K Ratio	34	37	37	34		35.50	1.73
Chloride	108	108	106	107		107.25	0.96
Carbon Dioxide	26	27.1	30.3	18.7		25.53	4.90
Anion Gap	17	15	14	25		17.75	4.99
Calcium	2.63	2.52	2.47	2.66		2.57	0.09
Phosphorus	3.19	3.08	3.09	3.64		3.25	0.26
Total Protein	63	65	62	65		63.75	1.50
Albumin	40.44	40.8	41.27	41.9		41.10	0.63
Globulin	23	24	21	23		22.75	1.26
A/G Ratio	1.8	1.7	2	1.8		1.83	0.13
Total Bilirubin	3	2	2	3		2.50	0.58
Alkaline Phosphatase	163	187	294	209		213.25	57.02
ALT (Sgpt)	78	86	66	62		73.00	11.02
Gamma gt	60	64	33	58		53.75	14.06
Creatine Phosphokinase	2,379	1,669	2,918	726		1,923.00	947.85
Calculated Osmolality	296	294	296	300		296.50	2.52
AST (Sgot)	44	45	66	53		52.00	10.17
Sorbital Dehydrogenase-AO	5.7	3.7	3.1	9.3		5.45	2.80
Uric Acid	0	6	4	13		5.75	5.44

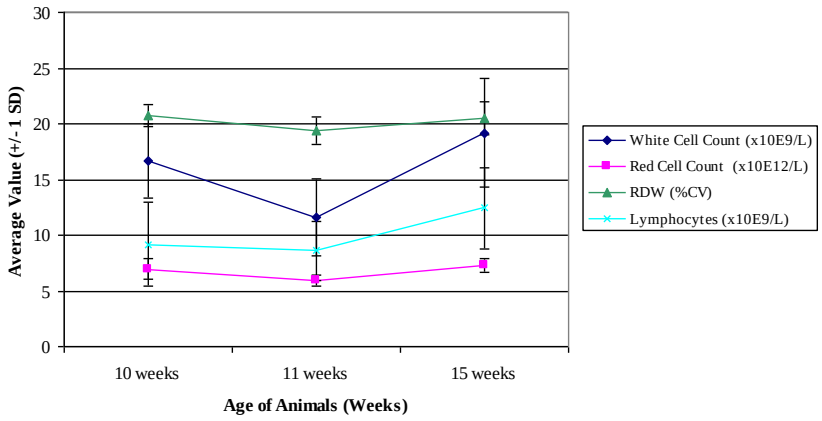
Appendix I. Clinical Laboratory Data for Acute Pigs 9 to 12 on Day -1, cont.

Animal Number:	Pig 9	Pig 10	Pig 11	Pig 12		Mean	STDEV
Date of Bleed	Day -1	Day -1	Day -1	Day -1		Day -1	Day -1
Platelets	Adequate	Adequate	Adequate	Adequate		NA[2]	NA
RBC Morph	See Below	See Below	See Below	See Below		NA	NA
Aniso	1+	1+	1+	1+		NA	NA
Poik	3+	3+	3+	3+		NA	NA
Polychrom	1+	1+	1+	1+		NA	NA
Fibrinogen Degradation Products	Positive	Positive	Positive	Positive		NA	NA
Fibrinogen Semi Quantitative	1	2	1	1		1.25	0.50
Part. Thromboplastin Time	23.1	21.5	22.3	27		23.48	2.44
Prothrombin Time	16	16.1	15.3	16.3		15.93	0.43

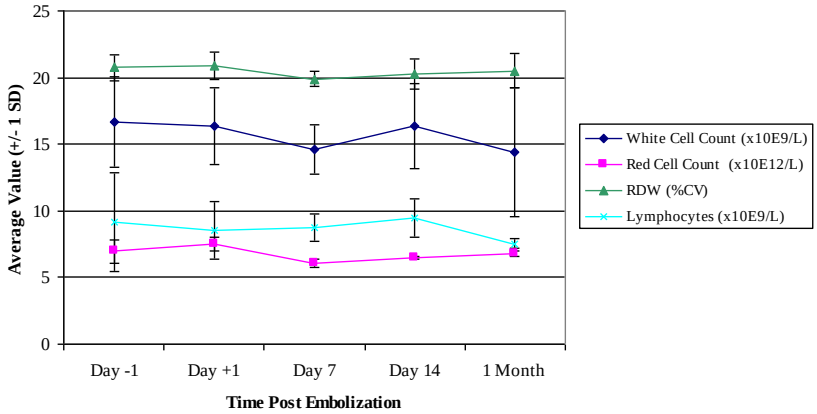
[1] Not Reported
[2] Not Applicable to calculate Mean and STDEV

Appendix J. Graphs of Hematology Parameters

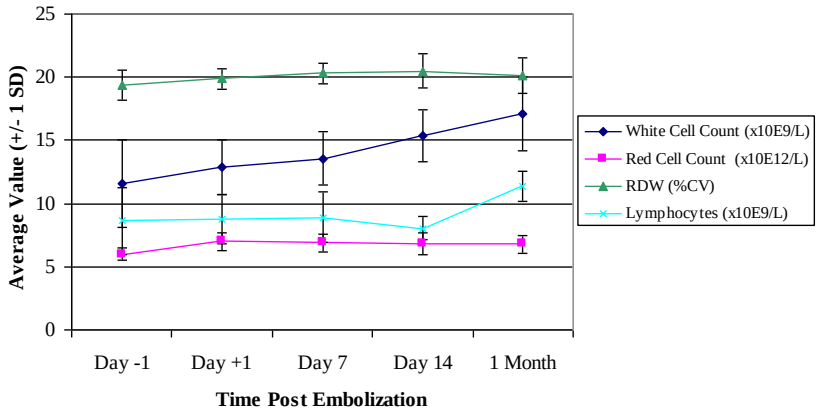
A. Mean Pre-Treatment Hematology Parameters



B. Mean Hematology Parameters in Chronic Kidney Pigs 1 to 4

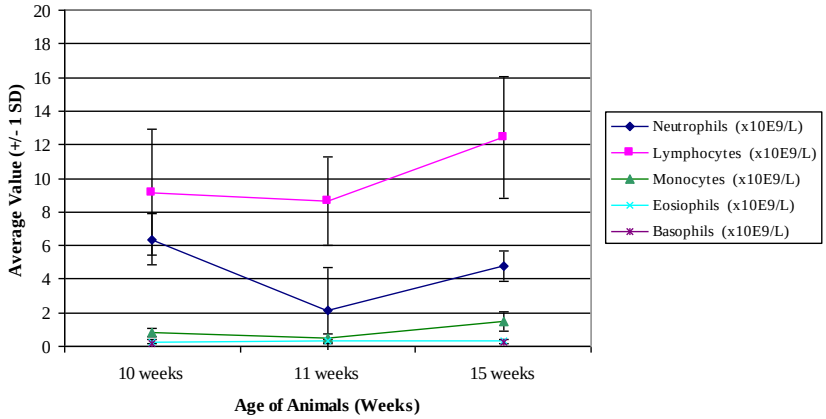


C. Mean Hematology Parameters in Chronic Hepatic Pigs 5 to 8

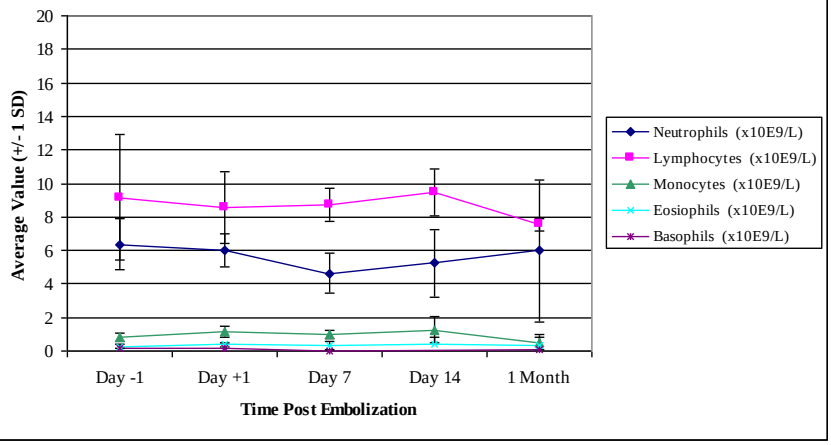


Appendix K. Graphs of Differential Cell Counts

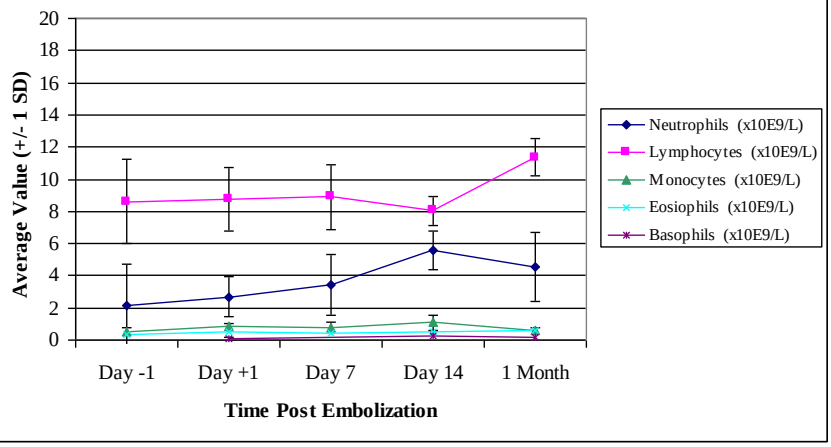
A. Mean Pre-Treatment Differential Cell Count



B. Mean Differential Cell Counts in Chronic Kidney Pigs 1 to 4

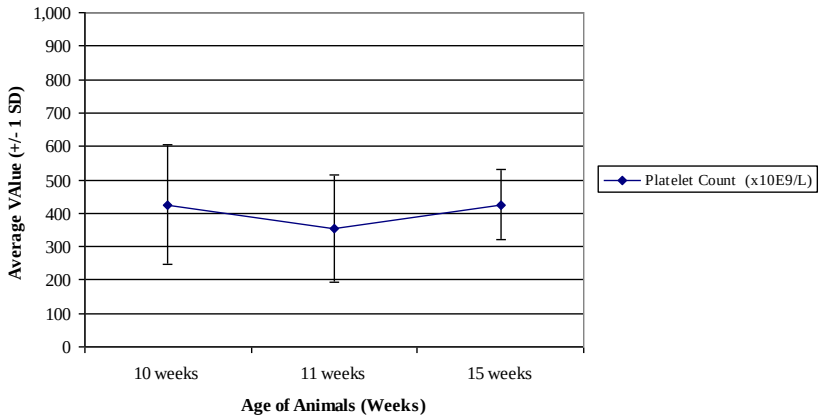


C. Mean Differential Cell Count in Chronic Hepatic Pigs 5 to 8

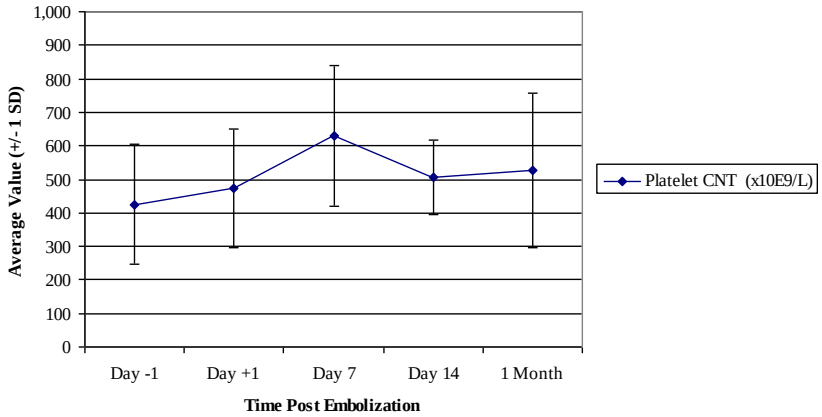


Appendix L. Graphs of Platelet Counts

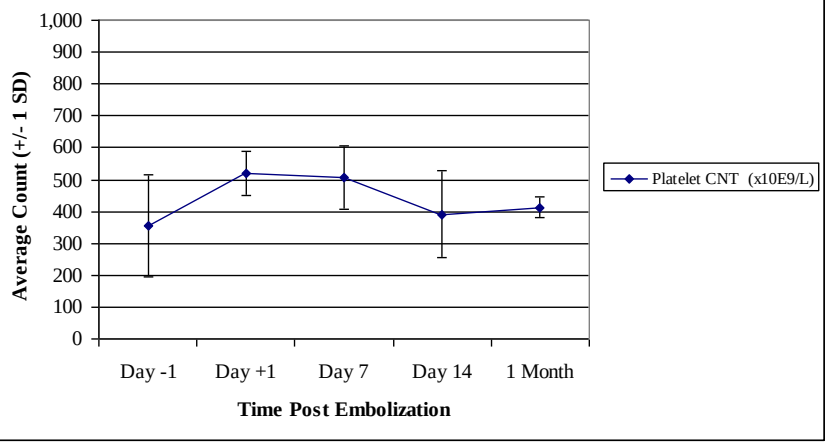
A. Mean Pre-Treatment Platelet Count



B. Mean Platelet Counts in Chronic Kidney Pigs 1 to 4

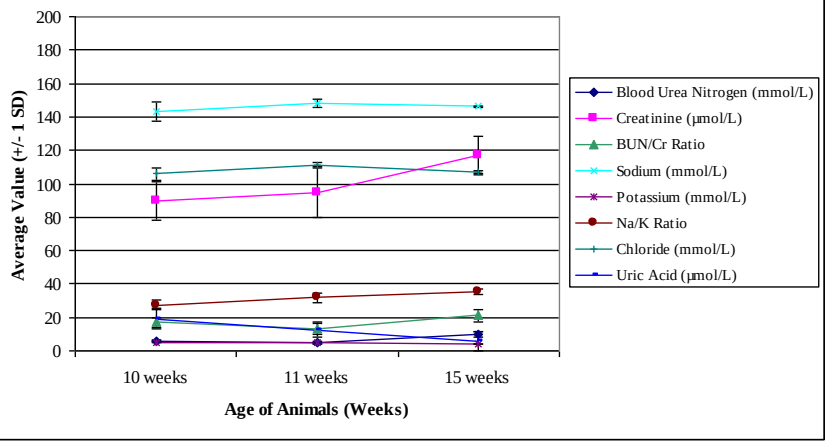


C. Mean Platelet Count in Chronic Hepatic Pigs 5 to 8

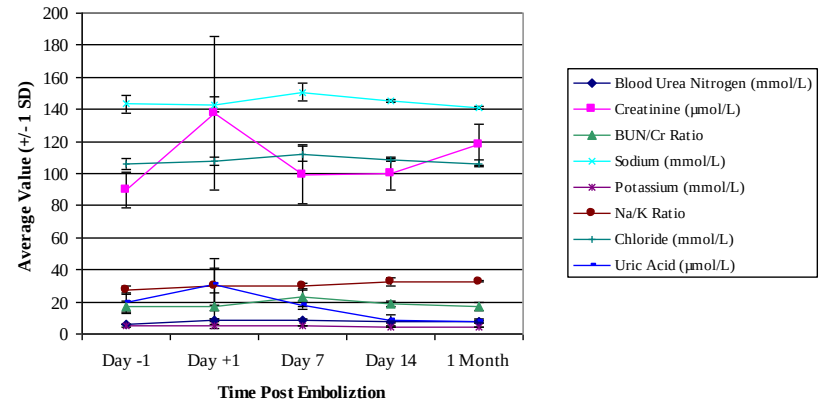


Appendix M. Graphs of Kidney Function Parameters

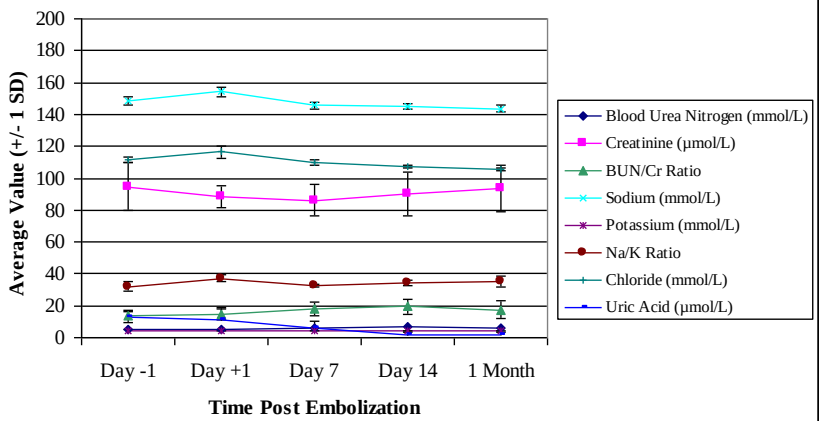
A. Mean Pre-Treatment Kidney Function Parameters



B. Mean Kidney Function Parameters in Chronic Kidney Pigs 1 to 4

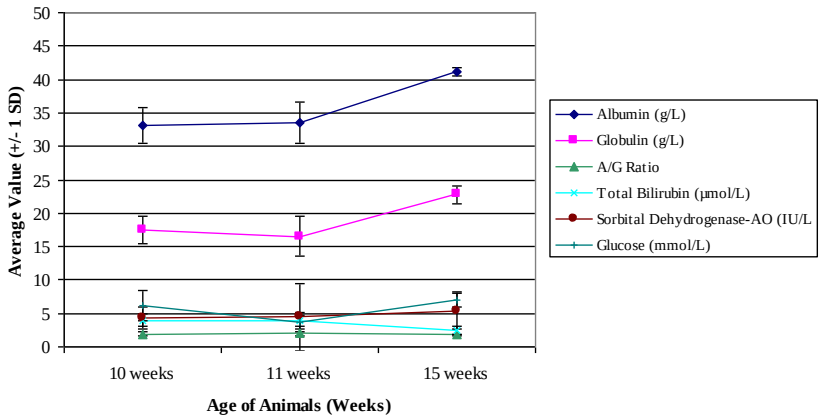


C. Mean Kidney Function Parameters in Chronic Hepatic Pigs 5 to 8

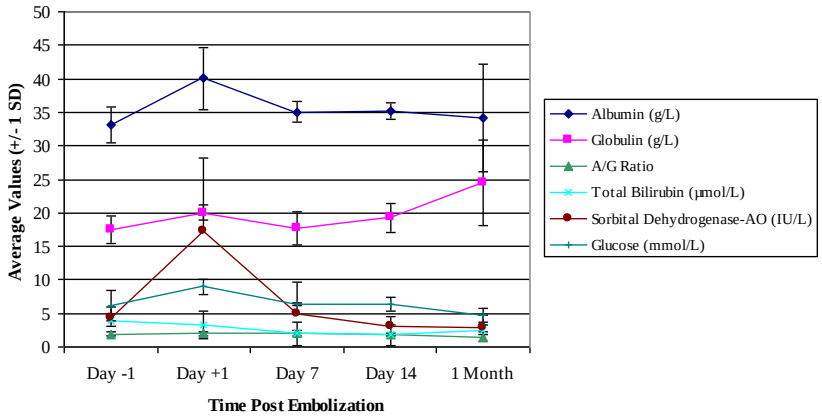


Appendix N. Graphs of Liver Function Parameters

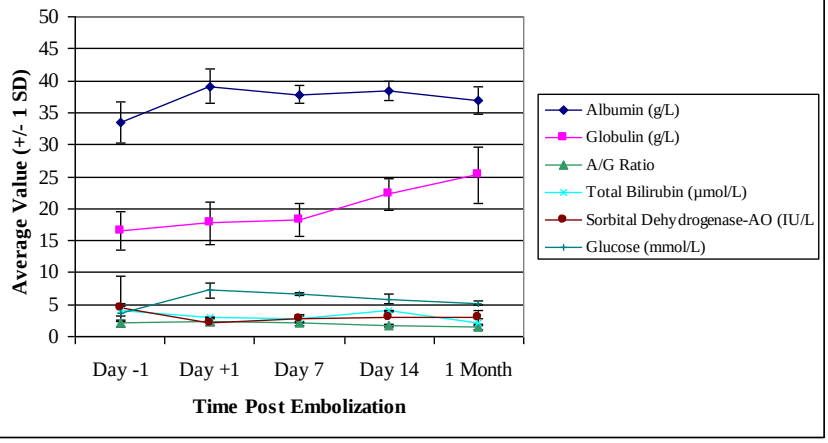
A. Mean Pre-Treatment Liver Function Parameters



B. Mean Liver Function Parameters in Chronic Kidney Pigs 1 to 4

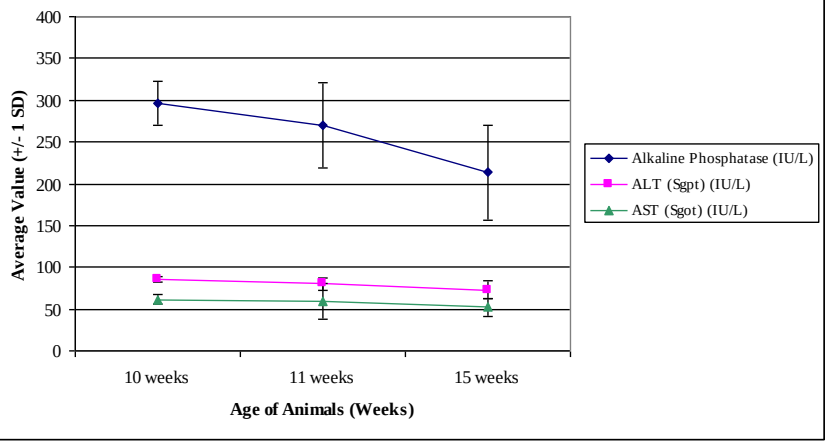


C. Mean Liver Function Parameters in Chronic Hepatic Pigs 5 to 8

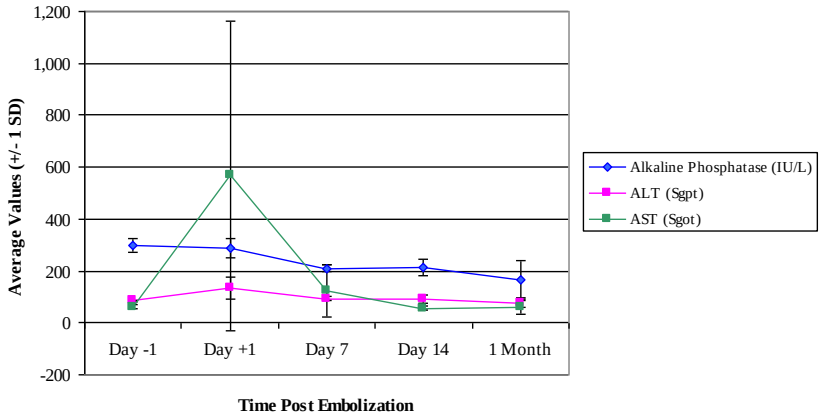


Appendix N. Graphs of Liver Function Parameters, cont.

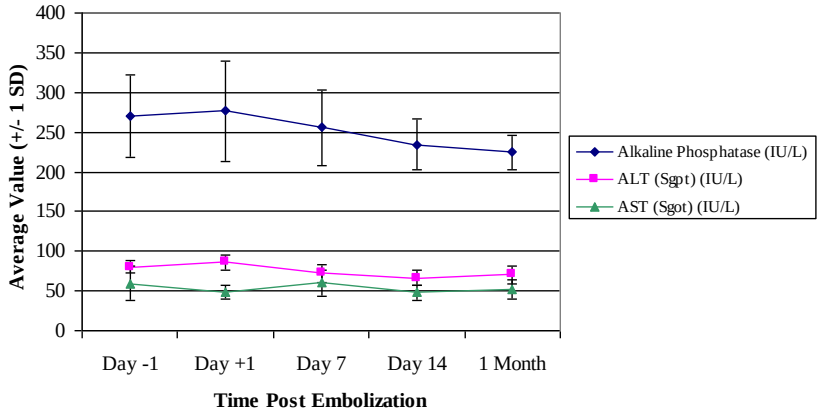
D. Mean Pre-Treatment Liver Function Parameters, cont.



E. Mean Liver Function Parameters in Chronic Kidney Pigs 1 to 4, cont.

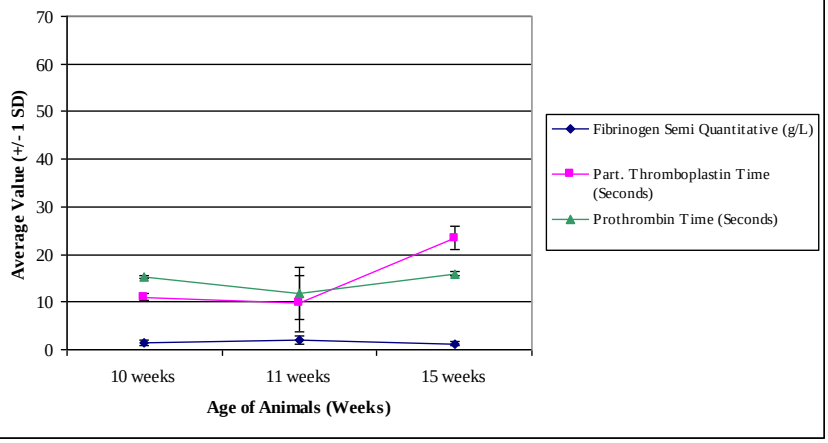


F. Mean Liver Function Parameters in Chronic Hepatic Pigs 5 to 8, cont.

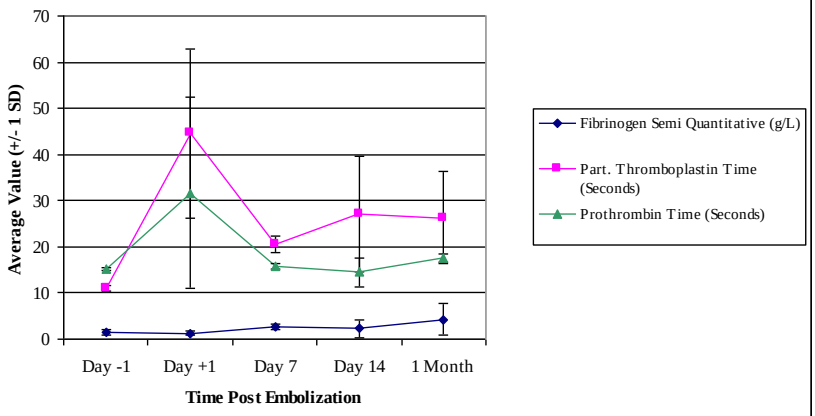


Appendix O. Graphs of Coagulation Parameters

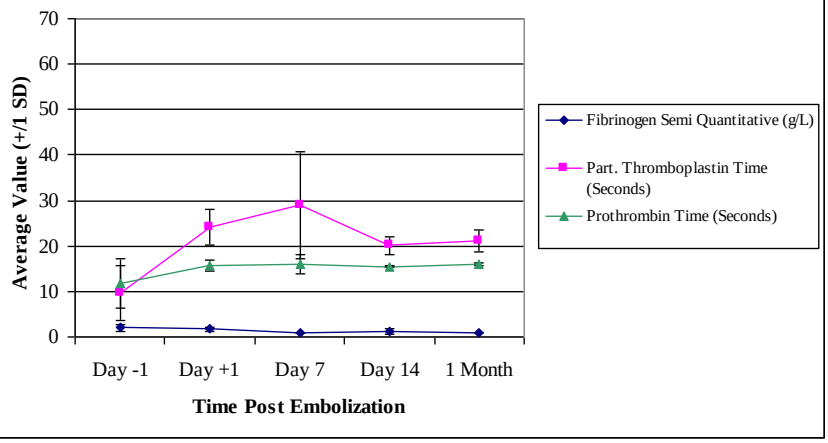
A. Mean Pre-Treatment Coagulation Parameters



B. Mean Coagulation Parameters in Chronic Kidney Pigs 1 to 4



C. Mean Coagulation Parameters in Chronic Hepatic Pigs 5 to 8



Appendix P. Summary Gross Postmortem and Histological Report for Acute and Chronic Renal Artery Embolization Pigs 1 to 4, 9 and 10

One renal artery of each of pigs 1 to 4, and 10 was injected with microspheres. The other renal artery served as a control in each animal. Pigs 1 to 4 were euthanized one month following injection, while pigs 9 and 10 were euthanized a few minutes following injection. A postmortem examination was performed on each pig immediately following euthanasia, and a standard set of tissues was collected for microscopic examination.

Pigs 9 and 10 were found to have irregular pale mottling of the cortex of microsphere injected kidneys. Microspheres were readily identified in the injected renal artery of each animal, and fully occluded the lumen. Upon incision of the injected artery microspheres would roll out of the vessel. Microscopic examination of the injected renal artery and kidney demonstrated dilation of the larger branches of the renal artery where microspheres had become impacted, but the microspheres themselves had been dislodged in the processes of manipulation of the tissues for slide preparation. No evidence of microspheres penetrating beyond the arcuate arteries of the injected kidney was found, and none of the other organs examined were found to contain any evidence of microspheres in their vasculature.

Pigs 1 to 4, euthanized one month following injection demonstrated dramatic changes. The injected renal arteries were firm, and the lumen of each artery contained a solid fibrous core of material that was completely occluding the artery. Such fibrous cores were present up to the level of the arcuate arteries. There was complete atrophy of the cortex of injected kidneys, with diffuse mineralization and fibrosis of the remaining tissue. The affected kidneys were shrunken to approximately 1/5 of their expected volume. Microscopically, the injected renal arteries contained a matrix of fibrous connective tissue in which were embedded the remains of the injected microspheres. The latter were distorted and smaller than when injected, and varied in size. These changes suggested that they were undergoing some degree of resorption. There was a mild foreign body reaction to the microspheres with small numbers of macrophages and occasional giant cells attempting to ingest them. There was no evidence of microspheres in any of the other organs that were examined microscopically.

Appendix Q. Summary Gross Postmortem and Histological Report for Acute and Chronic Hepatic Artery Embolization Pigs 5 to 8, 11 and 12

A branch of the hepatic artery chosen at the discretion of the consulting radiologist, of each of pigs 5 to 8, 11 and 12 was injected with microspheres. Pigs 5 – 8 were euthanized one month following injection, while pigs 11 and 12 were euthanized a few minutes following injection. A postmortem examination was performed on each pig immediately following euthanasia, and a standard set of tissues was collected for microscopic examination.

Pigs 11 and 12 were found to have irregular pale discolouration of the parenchyma, especially of the peripheral areas of the middle two lobes and the left lateral lobe of pig 11, and throughout the parenchyma of pig 12. Microspheres could be identified in the injected hepatic artery of each animal with careful dissection, and fully occluded the lumen of the distal branches in which they lodged. Upon incision of the injected artery microspheres would roll out of the vessel. Microscopic examination of the injected areas of hepatic artery demonstrated dilation of the branches of the artery where microspheres had become impacted, but the microspheres themselves had been dislodged in the processes of manipulation of the tissues for slide preparation. No evidence of microspheres penetrating beyond the distal branches of the hepatic artery was found. Evidence of microspheres was not found in the hepatic sinusoids, and none of the other organs examined were found to contain any evidence of microspheres in their vasculature.

Pigs 5 to 8, euthanized one month following injection demonstrated dramatic changes. The injected branches of the hepatic arteries were firm, and the lumen of each artery contained a solid fibrous core of material that was completely occluding the artery. Occluded vessels had a firm, cord-like feel, and could not be compressed. In contrast to the kidneys, which had undergone complete atrophy, the livers were unaffected by occlusion of the distal branches of the hepatic arteries. In two pigs the hepatic parenchyma was entirely normal, while in the other two the parenchyma of the edges of both of the left middle and of the left lateral lobes was pale. This pale colour extended approximately ¼ of the way towards the middle of each lobe.

Microscopically, the injected hepatic arteries were almost identical to the injected renal arteries of the other group of pigs. Injected arteries contained a matrix of fibrous connective tissue in which were embedded the remains of the injected microspheres. The microspheres were distorted and smaller than when injected, and varied in size. These changes suggested that they were undergoing some degree of resorption. There was a mild foreign body reaction to the microspheres with small numbers of macrophages and occasional giant cells attempting to ingest them. There was no evidence of microspheres in the hepatic sinusoids, nor in any of the other organs that were examined microscopically.

Appendix R. Resumes of Key Personnel

CURRICULUM VITAE – Dr. Richard J T Owen

HOME ADDRESS: R.R. 260
Spruce Grove, Alberta
T7Y 1B1
Phone: (780) 407 6907 / (780) 407 1210
Fax: (780) 407 6176
e-mail drrichardowen@tbwifi.ca
BUSINESS ADDRESS: Radiology and Diagnostic Imaging
Walter C. Mackenzie Health Sciences Centre
University of Alberta Hospital
8440 – 112 Street
Edmonton, Alberta
Canada, T6G 2B7
CITIZENSHIP: Dual - British/Canadian
AGE: 45 Years

EDUCATION:

1987: University of Wales College of Medicine, Wales, MB b Ch
1991: Royal College of Physcians, England, MRCP (UK)
1996: Royal College of Radiologists, England, FRCR (UK)
1997: Royal College of Radiologists, England, CCST
2001: Medical Council of Canada, LMCC

LICENCES: College of Physicians & Surgeons of Alberta (2000) No: S09603
General Medical Council, London (1987) No: 3257166
RADIOLOGY RESIDENCY*:* Leicester teaching hospitals training scheme: 1991-96.
FELLOWSHIP TRAINING: Interventional Radiology, Calgary, Alberta; 1996-97
WORK EXPERIENCE:

June 2003-Present University Appointment: Assistant Professor, Department of Radiology and Diagnostic Imaging, Faculty of Medicine, University of Alberta, Edmonton, Canada. Staff Radiologist (Specialist Intervention), Medical Imaging Consultants, Edmonton.

Feb 2000 – Present Departments of Radiology; Grey Nuns Hospital, Royal Alexandra and University of Alberta Hospitals.

During my time in Edmonton I have continued my research interests and development of interventional radiology. I have introduced several new techniques (such as hepatic artery chemoembolization, radioembolization and pre-op portal vein embolization) and further developed established techniques (Broviac catheter placement, portacath placements, uterine artery embolization and gonadal vein embolization). I am actively involved in the clinical islet cell programme, was responsible for the Journal club for 2 years, act as the director for the fellowship programme and the mentor for the interventional fellow. I am the chairman of the regional Angio-interventional subgroup and represent radiology at the GI tumour group and the transplant group.

Jul 1997 –Jan 2000 Consultant in Radiology (Specialist intervention), Freeman Hospital, Newcastle, UK.
Academic appointment: Clinical Lecturer.

The Freeman Hospital has one of the largest vascular units in the UK and is a tertiary care center for several specialities. The hospital also houses the Northern region Liver and renal transplant services. The interventional service encompasses all specialties and modalities and during my appointment I consolidated my clinical experience in all areas.

During the post I set up a Central Venous line placement service, initiated the fellowship programme, become actively involved in the endovascular aortic stent trial and in the TIPSS trial.
Together with my colleague Dr Rose we established the Freeman as a training site for the Cook aortic endograft and ran several training courses.
I set up 2 randomised trials involving central venous catheter placement and subintimal angioplasty and was the college tutor for the 8 trainees attached to radiology.
In addition to the interventional commitment I had sessions in ultrasound, CT, General reporting and bariums as well as shared time in MRI.
Areas of Clinical experience:

a) Diagnostic arteriography and venography in all areas (including neuro-radiology)
b) Arterial and venous angioplasty, vascular stents, thrombolysis and embolisation techniques.
c) Specialist procedures in renal and mesenteric domains.
d) Placement of central venous catheters, dialysis access and A/V fistulae maintenance.
e) Cholangiography, hepatic chemo and radio embolisation, stent placements and portosystemic shunts.
f) Aortic stent grafts
g) Biopsy and drainage procedures
h) Specialist urological procedures
I) Combined procedures in Interventional theatre
J) Gynaecological interventions including uterine artery embolization.
K) Islet transplantation

July 1996 - June 1997	Fellow (Interventional Radiology) Foothills Hospital, University of Calgary, Canada
Sep1991 - June 1996	Registrar (Radiology Resident) Leicester Royal Infirmary, Leicester Training Scheme, UK
July – Sep 1991	Registrar (Medicine). Glenfield General Hospital, Leicester, UK
Feb - July 1991	Senior House Officer (Accident & Emergency). Nuneaton General Hospital, Warwickshire, UK
Aug 1990 - Jan 1991	Senior House Officer (Obstetrics and Gynaecology). Nuneaton Maternity Hospital, Warwickshire, UK
Aug 1988 - Jan 1990	Senior House Officer (Internal Medicine). Nuneaton General Hospital, Warwickshire, UK
Aug 1987 - July 1988	House Physician/Surgeon. Cardiff Royal Infirmary (Surgery) Newport General Hospital (Medicine) University of Wales College of Medicine, Cardiff, UK

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10. Sensier Y, Fishwick G, Owen R et al. A comparison between colour duplex ultrasonography and arteriography for imaging infrapopliteal arterial lesions. *Eur J Vasc End Surg* 1998 15(1) 44-50.
11. Gordon A C, Saliken J C, Johns D, Owen R et al. US guided puncture of the internal jugular vein: complications and anatomic considerations. *JVIR* 1998 9(2) 333-338
12. Dresner S M, Banergee B, Owen R, Lees T A. A popliteal aneurysm caused by an avulsion fracture of the femur: A case presenting with deep venous thrombosis. *Eur J Vasc End Surg; 1999; 17: 180-182*
13. Mahallati H, Owen RJT. Therapeutic embolization of a pseudoaneurysm of the Superior Gluteal artery occurring as a complication of bone marrow biopsy. Can Assoc Radiol J. 1999 50(4):265-267
14. Saliken JC, Gray RR, Donnelly BJ, Owen RJT et al. Extraprostatic biopsy improves the staging of localized prostate cancer. Can Assoc Radiol J. 2000;51(2):114-120
15. Owen RJT, Rose JDG. Endovascular Treatment of a portal vein tear during TIPSS. *CVIR*. 2000 Mar; 23(2) 230-232
16. Butler TJ, Jackson RW, Robson JY, Owen RJ, Delves HT, Sieniawska CE, Rose JD. In vivo degradation of tungsten embolisation coils. Br J Radiol. 2000 Jun;73(870):601-3
17. Owen RJ, Jackson R, Loose HW, Lees TA, Dunlop P, Rose JD. Percutaneous Ablation of an Internal Iliac Aneurysm Using Tissue Adhesive. *CVIR* 2000 Sep;23 (5): 389-391
18. Owen RJ, Haslam PJ, Elliot ST, Rose JD, Loose HW. Percutaneous Ablation of Peripheral Pseudoaneurysms using thrombin: A simple and effective solution. *CVIR* 2000 Nov-Dec;23 (6): 441-446
19. Casey JJ, Lakey JRT, Ryan EA, Paty BW, Owen R et al. Portal venous pressure changes following sequential clinical islet transplantation. *Transplantation* 2002 ;74(7):913-915
20. 20. Owen RJ, Ryan EA, O'Kelly K, Lakey JR, McCarthy MC, Paty BW, Bigam DL, Kneteman NM, Korbutt GS, Rajotte RV, Shapiro AM. Percutaneous transhepatic pancreatic islet cell transplantation in type 1 diabetes: Radiologic aspects. *Radiology* 2003 Oct;229 (1):165-170
21. Penner RM, Owen RJ, Williams CN. Diagnosis of a bleeding Dieulafoy lesion on computed tomography and its subsequent embolization. Can J Gastroenterol. 2004 Aug;18(8):525-7
22. Villiger P, Ryan EA, Owen R, O'Kelly K, Oberholzer J, Al Saif F, Kin T, Wang H, Larsen I, Blitz SL, Menon V, Senior P, Bigam DL, Paty B, Kneteman NM, Lakey JR, Shapiro AM. Prevention of bleeding after islet transplantation: lessons learned from a multivariate analysis of 132 cases at a single institution. Am J Transplant. 2005 Dec;5(12):2992-8.
23. Baerlocher MO, McLaren K, Collingwood P, Giroux MF, Owen R, Poole A, Pugash R, Asch MR; Canadian Interventional Radiology Association. Conclusions and recommendations from the position paper on interventional radiology in Canada. Can Assoc Radiol J. 2007 Feb;58(1):11-4.
24. Suchak AA, O'Kelly K, Al Saif F, Shapiro AM, Owen RJ. Hepatic artery-portal venous fistula after percutaneous intraportal islet cell transplant. Transplantation. 2007 Mar 15;83(5):669-70.
25. Benko A, Fraser-Hill M, Magner P, Capusten B, Barrett B, Myers A, Owen RJ; Canadian Association of Radiologists. Canadian Association of Radiologists: consensus guidelines for the prevention of contrast-induced nephropathy. Can Assoc Radiol J. 2007 Apr;58(2):79-87.
26. Xiao Z, Dickey D, Owen RJ, Tulip J, Moore R. Interstitial photodynamic therapy of the canine prostate using intra-arterial administration of photosensitizer and computerized pulsed light delivery J Urol. 2007 Jul;178(1):308-13. Epub 2007 May 17.
27. Moore RB, Xiao Z, Owen RJ, Ashforth R, Dickey D, Helps C, Tulip J. Photodynamic Therapy of the Canine Prostate: Intra-arterial Drug Delivery. Cardiovasc Intervent Radiol. 2007 Oct 26;

28. Mahajan A, Rao G, Lees G, Owen R. A case of successful ablation of a gastrophrenic fistula with n-Butyl-2-Cyanocrylate. *Can J Gastroenterol.* 2008 Jan;22(1):69-70.
29. Chung J, Owen RJ. Using inferior vena cava filters to prevent pulmonary embolism. *Can Fam Physician.* 2008 Jan;54(1):49-55.
30. 30. Baerlocher MO, Owen R, Poole A, Giroux MF. Interventional radiology deserves formal recognition as a distinct medical subspecialty: a statement from the Canadian Interventional Radiology Association. *J Vasc Interv Radiol.* 2008 Jan;19(1):9-12.
31. Moore RB, Xiao Z, Owen RJ, Ashforth R, Dickey D, Helps C, Tulip J. Photodynamic Therapy of the Canine Prostate: Intra-arterial Drug Delivery. *CVIR.* 2008 Jan (1)31 164-176
32. Chung J, Owen R, Turnbull R, Chyczij H, Winkelaar G, Gibney N. Endovascular repair in traumatic thoracic aortic injuries: comparison with open surgical repair. J Vasc Interv Radiol. 2008 Apr;19(4):479-86.

ABSTRACTS / PRESENTATIONS:

1. Lamont A L, Owen R J T, Brookes J. Postnatal Investigation And Early Management Of Prenatally Diagnosed Hydronephrosis. *European Society of Paediatric Radiology* - June 1994, Brussels.
2. Owen R J T, Lamont A L, Brookes J. Postnatal Investigation And Early Management Of Prenatally Diagnosed Hydronephrosis. *Scientific Meeting, Royal College of Radiologists* - 13th September 1994, Norwich.
3. Owen R J T, Hickey F, Finlay D B. A Survey Of Metatarsal Fractures In Children. Poster/Presentation, *Roentgen Centenary Congress,* 12th-16th June 1995. Birmingham.
4. Kunkler R B, Owen R J T, Kockelbergh R C. Bone Scintigraphy In The Management Of Bladder Cancer. *American Urological Association 4th May 1996, USA.*
5. Owen R J T, Eslar C, Finlay D B. How significant is bone bruising on MRI of the knee. BIR/RCR meeting May 1996.
6. Owen R J T, Harper W M, Finlay D B, Belton I P. Isotope Bone Scans In Patients With Painful Knee Replacements: Do They Alter Management? Poster/Presentation, BIR/RCR May 1996.
7. Owen R J, Saliken J C, Johns D G, Donnely B, Wiseman D, Gray R R. Cryosurgery 18 Month follow up. *SCVIR. Washington USA*. 8th-13th March 1997

8 - 10. Owen R J, Saliken J C, Johns D G, Donnely B, Wiseman D, Gray R R. Sextant prostatic biopsy comparison with clinical staging. *SCVIR Washington DC*, March 12 1997, Society of Cryosurgery. Hawaii Feb 1997, CAR Meeting1997

11 - 12. Owen R J, Saliken J C, Johns D G, Donnely B, Wiseman D, Gray R R. Evaluation of an extended prostate biopsy protocol. *Society of Cryosurgery*. Hawaii Feb 1996, CAR 1997

13. Owen R J, Gordon A C, Saliken J C, Johns D, et al. US guided puncture of the internal jugular vein: complications and anatomic considerations. *Northern Radiology meeting. Newcastle upon Tyne* , March 1998.
14. Owen R J, Gordon A C, Gray R, So B. A Comparative study of Temporary and Tunnelled Haemodialysis Catheter Survival. *Northern Radiology meeting. Newcastle upon Tyne,* March 1998.
15. Owen R J, Gordon A C, Gray R, Saliken J C. Central Venous Catheters for Haemodialysis. *Northern Radiology meeting. Newcastle upon Tyne,* March 1998.
16. Akomolafe B, Owen RJT et al. Angioplasty of the Profunda Femoris artery. South African Vascular Society, South Africa Aug 1999.

17 – 18. Owen R J, Elliott S, Rose J, Loose H. The Percutaneous Ablation of Pseudoaneurysms Using Thrombin: A Simple and Effective Solution. *Northern Vascular Society*, Windermere Oct 1999, *BSIR*, Manchester Nov 1999.
19. Owen R J, Chidambaram V, Manas D, Jackson R, Rose J. Endoluminal Revascularisation of Clotted native and Synthetic Arteriovenous Fistulae. *BSIR*, Manchester, Nov 1999
20. Jackson RW, Butler T, Robson JY, Owen RJT, Delves HT, Sieniawska, Rose JDG. In Vivo Degradation of Tungsten Embolisation Coils. *BSIR*, Manchester, Nov 1999
21-22. Owen RJT, Dunlop P, Lees TA, Wyatt MJ, Jones NA, Lambert D, Rose JDG. Combined Surgical and Radiological Procedures: The way Forward *BSIR*, Manchester, Nov 1999. *VSS* Nov 1999.
23. Owen RJ, Jackson R, Chidambaram V, Haslam PJ, Manas D. Surgical versus radiological placement of ash dialysis catheters: A randomised study. *SCVIR* San Diego March 2000
24. Owen RJ, Gray RR. Complex Case Presentation: Embolisation of Hepatic Artery Aneurysm with SMA Stent placement. *BSIR*, Newcastle, Nov 2000.
25. Owen RJ, Ryan EA, O'Kelly K, Shapiro AMJ. Percutaneous Transhepatic Pancreatic Islet Cell Transplantation in Type 1 Diabetes. *BSIR*, Cardiff Nov 2001
26. Owen RJ, Ashforth R, Logie L, Bailey B. Peripherally Inserted Catheters for Home Parenteral Therapy Program: A Survival Study. *BSIR*, Cardiff Nov 2001
27. Owen RJ, Shapiro AMJ Ryan EA, O'Kelly K, Lakey JR. Percutaneous Transhepatic Pancreatic Islet Cell Transplantation in Type 1 Diabetes. *CVIR*, Lucerne Oct 2002
28. McNally DM, Owen RJ, Sherlock R. Endovascular Management And Outcome Of Acquired Uterine Artery Arteriovenous Malformations. *SIR* Salt lake Mar 2003.
29. Owen RJ, McNally DM, Ryan EA, Ackerman T, Shapiro AM. Trans Hepatic Portal Vein Puncture In Islet Cell Transplantation: Should The Tract Be Embolized? *SIR* Salt lake Mar 2003 (Poster).
30. Owen RJ, Shapiro AMJ Ryan EA, O'Kelly K, Lakey JR. Percutaneous Transhepatic Pancreatic Islet Cell Transplantation in Type 1 Diabetes (Extended Results). *SIR* Salt Lake Mar 2003.
31. Barker SJ, Owen RJ, O'Kelly K, Lewanczuk RZ, Hamilton PG. Primary Hyperaldosteronism and the Preoperative Role of Selective Adrenal Vein Sampling. *International Congress of Radiology*. Montreal June 2004 (Poster)
32. Bhargava R, Ackermann T, Owen R, Shapiro A, Ryan E, Lakey J, Paty B, Senior P. Islet Transplantation: A pictorial Essay of Late Changes in the Abdomen. *Canadian Association of Radiologists.* 2005 Sep.
33. Mahajan A, Ashforth R, Olson J, Owen R. The Efficacy Of Ok-432 Sclerotherapy For The Treatment Of Pediatric Lymphatic Malformations. *SIR* Toronto Mar 2006
34. Owen RJ, Mercer J, Moliniari M, Wada R, Rajotte RV, Shapiro A.M. Portal Vein Embolization of Radiolabelled Polyvinyl Alcohol Particles in a Porcine Model: Hepatic Distribution. *SIR* Toronto Mar 2006
35. Lambert RG, Siminoski KG, Dhillon SS, Ashforth RA, Schaffler GC, Owen RT et al. Efficacy of a Canadian Percutaneous vertebroplasty Programme. *SIR* Toronto Mar 2006
36. Chung J, Owen RJ, Winkelaar GB, Turnbull RG. Technical Considerations in the Endovascular Repair of Acute and Chronic Traumatic Aortic Injuries. Electronic Poster. *SIR* Seattle Mar 2007

37. Chung J, Owen RJ, Winkelaar GB, Turnbull RG. Endovascular repair of Acute and Chronic Traumatic Thoracic Aortic Injuries: A Comparative Study with Open Surgery. *SIR* Seattle Mar 2007
38. Chung J, Owen RJ, Winkelaar GB, Turnbull RG. Endovascular repair of Acute and Chronic Traumatic Thoracic Aortic Injuries: A Comparative Study with Open Surgery. *Western Vascular society* Victoria Nov 2007

INVITED PRESENTATIONS / VISITING LECTURER

Canadian Association of Medical Radiation Technologists. Lectures on Ultrasound guided injection of pseudoaneurysms & Vascular stents: Calgary, Alberta June 2001

Leicester Royal infirmary (UK); Lecture on Islet cell transplantation in diabetes and teaching sessions with residents. Visiting Lecturer July 2003

Radiological Society of North America. Invited speaker on Islet cell transplantation Chicago December 2003

Society of Interventional Radiology. Moderator scientific session (Hepatic Interventions) Phoenix March 2004

Alberta Society of Radiation Technologists. Speaker Edmonton (Islet cell transplantation in diabetes) May 2004

Cardiovascular and Interventional Society of Europe. Invited speaker Barcelona (Hepatic intervention session) Sept 2004

Calgary. Resident research day Invited speaker (thrombosed dialysis access management) and judge May 2005

Canadian Interventional Radiology Association. AGM Company sponsored forum (Cutting balloon) June 2005

Society of Interventional Radiology. Invited speaker Toronto (Contrast nephropathy a radiologists perspective) March 2006

Winnipeg Endovascular Forum. Invited speaker (Cutting balloon) June 2006

Society of interventional radiology. Invited speaker on islet cell transplantation. Seattle March 2007

Winnipeg Endovascular forum. Invited Speaker on Endovascular treatment of trauma and upper limb interventions. Apr 2007

Canadian Interventional Radiology Association. AM Organizer and Invited speaker on thrombolysis in renal access grafts and on the use of glue in IR. May 2007

Canadian Interventional Radiology Association. AM Organizer and Invited speaker on Use of contrast agents in renal failure and complicated case presentations. May 2008

Cross Cancer Institute. Invited speaker on vertebral body augmentation. June 2008

GRANT APPLICATIONS / FUNDING / AWARDS:

Principle Investigator - Pump priming grant from the Royal College of Radiologists 1999 (£6000) Subintimal Angioplasty Versus Conventional Intra-Luminal Angioplasty In Superficial Femoral Artery Occlusions. Owen RJT, Lees T, Rose JDG.

Principle Investigator - Char Amersham award 2003 ($12000). Portal Vein Embolization Of Radiolabelled Polyvinyl Alcohol Particles In A Porcine Model.

Co-investigator – National Cancer Institute of Canada; Operating grant. 2004 Novel Intravesical Molecular Therapy for superficial Bladder Cancer.

Co-Investigator – Alta Chem Pharma; Operating grant. 2004 Development of Hypocrellin B SO17 for Photodynamic Therapy (PDT) of Prostate Cancer.

Co – Investigator - ViRexx Medical Corp. Operating grant. Development of new embolotherapeutic agent – A Preclinical Study of the safety and Efficacy of OCL-501 in a porcine splenic infarct model.

Site principle investigator in multinational multicentre trial – Phase III study of Ytrium labeled particles in embolization in advanced HCC – Nordion MDS sponsor.

Principle investigator - local trial – Animal safety study of a new embolic agent, ViRexx Corp/ sponsor ($50,000)
Site PI CORAL (NIH Study) Cardiovascular outcomes in renal artery lesions. NIH sponsored
Co-Investigator (P Tandon) Pro biotics and their effects on portal pressures. Local funding
I have also been able to gain funding from several commercial companies to assist ancillary staff in attending educational meetings as well as assisting in the procurement of funding for the radiology research nurse programme.

RESEARCH IN PROGRESS:

Embolization of traumatic uterine AV malformations
Portal vein embolization of radiolabelled polyvinyl alcohol particles in a porcine model
The use of von Willebrand factor as an embolization agent in an animal model
The use of a novel embolic agent in an animal model
The use of tissue adhesive in percutaneous islet cell transplantation procedures
Long term results of angioplasty in hemodialysis fistula using the 'cutting balloon'
Radioembolization, trans arterial Chemoembolization in liver tumors
Photodynamic therapy

SOCIETY MEMBERSHIPS:

Royal College of Radiologists (UK), since 1991
Royal college of Physicians (UK), since 1991
British Society of Interventional Radiology, since 1995
Society of Interventional Radiology, since 1996
Cardiovascular and Interventional Radiological Society of Europe, since 1998
Alberta Medical Association, since 2000
Canadian Medical Association, since 2000
Canadian Interventional Radiology Association, since 2001

NATIONAL BODIES:

Treasurer for Canadian Interventional Radiology Association, since June 2004
Programme Chair 2007 AGM Canadian interventional Radiology Association – Banff Alberta, Canada
Programme Chair 2008 AGM Canadian interventional Radiology Association – Montreal, Quebec, Canada

Recreational activities:

Soccer player and coach, Golf, Squash, Swimming, Snow boarding, Gardening and fishing

CURRICULUM VITAE – DR. P.N. NATION

HOME ADDRESS: 18208 Ellerslie Road
Edmonton, Alberta
T6W 1A5
(780) 430-8128

BUSINESS ADDRESS: Animal Pathology Services (APS) Ltd.,
18208 Ellerslie Road,
Edmonton,
Alberta T6W 1A5
(780) 720-5378

CITIZENSHIP: Canadian

AGE: 58 Years

EDUCATION:

1967	St. Andrew's College, Aurora, ON	Senior Matriculation (Honors)
1972	Simon Fraser University, Burnaby, BC	BSc. (Biology)
1974	University of Saskatchewan, Saskatoon, SK	DVM
1976	University of Saskatchewan, Saskatoon, SK	MVSc (Veterinary Pathology)
1980	Diplomate of American College of Veterinary	Dipl. ACVP Pathologists
1987	Faculty of Medicine, University of Calgary, Calgary, AB	Ph.D. (Neurotoxicology)

UNDERGRADUATE AWARDS:

1972 Louis Hewitt Award in Public Health and Epidemiology
1973 Co-recipient of Pfizer Co. Award for Academics and Leadership
1974 Class of '74 Public Relations Award
Pitman Moore Award for Scholastic, Social and Athletic Achievement
Canadian Veterinary Medical Association Award for Contribution to the Profession

GRADUATE AWARDS:

1975 Co-recipient of Rogar STB graduate Student Award
1986 Canadian Pharmacology Society Graduate Student Award

OTHER:

2004 Alberta Veterinarian of the Year

WORK EXPERIENCE:

June 1 1974 - May 31, 1976 Professional Associate I
Dept of Veterinary Pathology
Western College of Veterinary Medicine
University of Saskatchewan
Saskatoon, Sask. S7N 0W0

A service/training position performing duties in general veterinary diagnostic pathology, all species, high component of comparative pathology/physiology

July 1 1976 - Sept 1 1976 Visiting Veterinary Pathologist
Department of Pathobiology
University of Connecticut, Storrs,
Connecticut USA

Term academic veterinary diagnostic position

Oct 1976 - Sept 1980 Veterinarian II

Animal Health Division
Alberta Agriculture:
Fairview (1976 - 1978)
Airdrie (1978 - 1980)

Veterinary diagnostic pathology position having service, educational and research components. All species were examined with emphasis on food producing animals, horses, pets and zoo species.

Sept 1980 - Feb 1985 — Head, Regional Animal Health Laboratory
Animal Health Division
Alberta Agriculture
P.O. Bag 1
Airdrie, Alberta T4B 2C1

Veterinary diagnostic pathology position supervising a staff of ten permanent and up to five part-time employees in addition to performing service, educational and research activities as previously.

Feb 1985 - July 1987 — Fellow of the Alberta Heritage Fund for Medical Research
Dept of Pharmacology and Therapeutics
Faculty of Medicine, University of Calgary
3330 Hospital Drive N.W.
Calgary, AB T2N 4N1

Research position held while conducting neurotoxicology study for PhD thesis. Thesis title "Drug Interactions on Neuronal Membranes."

July 1987 - Dec 1991 — Head, Pathology Branch
Alberta Agriculture O.S. Longman Bldg
6909 - 116 Street
Edmonton, AB T6H 4P2

Middle management position supervising six laboratory managers and a laboratory scientist at four separate locations in the province. Total staff size of 41 permanent positions. Budget $2.1 million.

Dec 1991 – Dec 1999 — Comparative Pathologist
Health Science Lab Animal Services
Room 140 Heritage Medical Research Centre
University of Alberta, Edmonton, AB T6G 2S2

President Veterinary Pathology Laboratory
9520 – 27 Avenue, Edmonton, AB T6N 1B2

Full time service position in lab animal services in the University of Alberta providing diagnostic assistance and advice to medical researchers concerning laboratory animals. Professional services were sub-contracted by the University of Alberta to Veterinary Pathology Laboratory, a private veterinary diagnostic laboratory servicing North-central Alberta. This particular contract involved providing clinical pathology and anatomic services to veterinary practitioners concentrating on the traditional companion animal and food producing species but also including exotics, lab animals and avians.

Dec 1999 – April 2005	Director, Health Science Lab Animal Services Room 140 Heritage Medical Research Centre University of Alberta Edmonton, AB T6G 2S2
April 2005 – present	President Animal Pathology Services APS Ltd. 18208 Ellerslie Road, Edmonton, AB T6W 1A5
1979 - 1985	Adjunct Assistant Professor Dept of Pathology, Faculty of Medicine University of Calgary 3330 Hospital Drive N.W. Calgary, AB T2N 1N4
1999 – Present	Adjunct Associate Professor, Dept of Pathology and Laboratory Medicine, University of Alberta Edmonton, AB T6G 2S2

ACADEMIC COMMITTEE ACTIVITIES:

1989 - 1992	Member of two graduate student committees at University of Calgary.
1990 - 1991	Executive secretary of Alberta Agriculture Research Institute "Poultry, Pork and other livestock" research grant scientific review committee.
1990 - 1991	Northern Bison Management Board.
1992 – Present	Animal Health Technician Program Advisory Committee, Lakeland College,Vermilion, Alberta.
1993 – 2005	Member of the Faculty (of Agriculture) Animal Policy and Welfare Committee, University of Alberta
1998 - 2005	Member of the University (of Alberta) Animal Policy and Welfare Committee
1999 - 2005	Member of the Health Sciences Animal Policy and Welfare Committee

PROFESSIONAL ASSOCIATION ACTIVITIES:

A. PAST

1973	President of Western Veterinary Medical Students' Association.
1974 - 1976	Member of Saskatchewan Veterinary Medical Association.
1974 - 1976	Member of Public Relation Committee, Saskatchewan VMA
1978 - 1982	Chairman of Continuing Education Committee Alberta VMA
1983	Academic Program Chairman for the Canadian Veterinary Medical Association annual convention.
1974 - 1981	Member of Wildlife Disease Association
1974 - 1982	Member of American Veterinary Medical Association
1984	President, Canadian Association of Veterinary Pathologists
1988	President, Western Conference of Veterinary Diagnostic Pathologists
1994	President of Western Conference of Veterinary Diagnostic Pathologists
1999	Chairman of Practice Inspection Committee, Alberta, VMA

B. PRESENT

Licensed to practice veterinary medicine in Alberta.
Member of Canadian Veterinary Medical Association 1974 to present.
Member of Alberta Veterinary Medical Association 1977 to present.
Member of Canadian Association of Veterinary Pathologists 1976 to present.
Member of American College of Veterinary Pathologists 1980 to present.
Certified specialist in veterinary pathology, CVMA, 1981 to present.
Member of Canadian Association of Laboratory Animal Science 1995 to present
Member of Canadian Association of Laboratory Animal Medicine 1995 to present
Member, Registration Committee, Alberta VMA
Member, Council of the Alberta VMA

PUBLICATIONS:

1. Nation P.N. and Allen J.R. Antibodies to Toxoplasma gondii in Saskatchewan cats, sheep and cattle. Can Vet J. 17:308-310. 1976
2. Nation P.N. and Wobeser G. Renal coccidiosis in wild ducks in Saskatchewan. J Wildlife Diseases. 13:370-375. 1977.
3. Nation P.N. Epistaxis of guttural pouch origin in horses: pathology of three cases. Can Vet J. 19:194-197. 1978
4. Nation P.N. and Dies K.H. Capillaria hepatica in a horse. Can Vet J. 19:315-316. 1978.
5. Nation P.N., Benn M.H., Roth S.H. and Wilkens J.L. Clinical signs and site of action of the larkspur alkaloid methyllycaconitine in calves after parental administration. Can Vet J. 23:264-266. 1982
6. Nation P.N., Crowe S.P., and Harries W.N. Clinical signs and pathology of accidental monesin poisoning in sheep. Can Vet J. 23:323-326. 1982.
7. Nation P.N. Salmonella dublin septicemia in two littermate puppies. Can Vet J. 25:324-326. 1984.
8. Frelier P.F., Leininger R.W., Armstrong L.D., Nation P.N. and Povey R.C. Suspected parvovirus infection in porcupines. J Amer Vet Med Assn. 185:1291-1294. 1984
9. Nation P.N. and Calder W.A. Necrosis of the brain in calves following dehorning. Can Vet J. 1985
10. Nation P.N. and Klavano G.G. Osteopetrosis in foals. Can Vet J. 27:74-77. 1986
11. Nation P.N., McNabb L.G., Roth S.H. The effects of a suitable solvent for neuropharmacological experiments with water soluble compounds. Proc West Pharmacol. Soc. 29:167-170. 1986
12. Nation P.N. and Roth S.H. Complex effects of the insecticide permethrin on an isolated sensory neuron. Proc West Pharmacol. Soc. 30:343-347. 1987
13. Nation P.N. and Roth S.H. The effects of neomycin on membrane properties and discharge activity of an isolated sensory neuron. C J Phys Pharmacol. 66:27-31. 1988.
14. Nation P.N. Alsike clover poisoning in horses: a review. Can Vet J. 30:410-715. 1989.
15. Nation P.N. and Williams E.S. Maggots, mutilations and myth: patterns of post-mortem scavenging of the bovine carcass. Can Vet J. 30:742-747. 1989.

Chalmers G.A., Nation P.N. and Pritchard J. Terminal ileitis in lambs. Can Vet J. 31:292-295. 1990.

17. Buret A., Gall D.G., Nation P.N., and Olson M.E. Intestinal protozoa and epithelial cell kinetics, structure and function. Parasitology Today. 6:375-380. 1990.
18. Nation P.N. Hepatic disease in Alberta horses: A retrospective study of "alsike clover poisoning" (1973-1988) Can Vet J. 32:602-607. 1991.
19. Opgenorth A., Graham K., Nation P.N., Strayer D., and McFadden G. Deletion analysis of two tandomly arranged virulent genes in mycsoma virus, M11L and mycsoma growth factor. J Virol. 66:4720-4731. 1992.
20. Nation P.N. Veterinarians in Alberta universities. Chapter 14, p. 167-176 in D.W. MacDonald, Ed. A short history of the veterinary profession in Alberta. 1955-90. Alberta Vet. Med. Assn. 1993.
21. Nation P.N. and Roth S.H. Synergistic effects of monensin in combination with permethrin or neomycin on neuronal activity. Vet and Human Toxicology. 35:414-418. 1993.
22. Opgenorth A., Nation N., Graham K., and McFadden G. Transforming growth factor alpha, Shope fibroma growth factor, and vaccinia growth factor can replace myxoma growth factor in the induction of myxomatosis in rabbits. Virol. 192:701-9. 1993.
23. Macen J.L., Upton C., Nation N., and McFadden G. SERP1, a serine proteinase inhibitor encoded by myxoma virus, is a secreted glycoprotein that interferes with inflammation. Virol. 195:348-63. 1993.
24. Yan Wei-dong, Perk M., Nation P.N., Power R.F., Liu L., Jiang X., and Lucas A. Fluorescence spectroscopic detection of virus-induced atherosclerosis. Proc SPIE 1993.
25. Mossman, K., Nation, P.N., Macen, J., Garbutt, M., Lucas, A., McFadden, G. Myxoma virus M-T7, a secreted homologue of the interferon – gamma receptor, is a critical virulence factor for the development of myxomatosis in European rabbits. Virol. 215:17-30. 1996
26. Maksymowych, W.P., Nation, P.N., Nash, P., Macen, J., Lucas, A., McFadden, G., Russell, A.S. Amelioration of antigen-induced arthritis in rabbits treated with a secreted viral serine proteinase inhibitor. J Rheum 23:878-882. 1996
27. Morck, D.W., Merrill, J.K., Gard, M.S., McKay, S.G., Olson, M.E., Nation, P.N. Treatment of experimentally induced pneumonia pasteurellosis of young calves with tilmicosin. Can Vet J. Res. 61:187-192. 1997
28. Lucas, A.R., Liu, L., Macen, J., Nash, P. Dai, E., Etches, W., Stewart, M., Graham, K., Humen, D., Hobman, M.L., Nation, P.N., McFadden, G. A virus encoded serine proteinase inhibitor, SERP-1, inhibits atherosclerotic plaque development following balloon angioplasty. Circulation 1997.
29. Dai E, Stewart M, Ritchie B, Mesaeli N, Raha S, Kolodziejczyk D, Hobman ML, Liu LY, Etches W, Nation N, Michelak M, Lucas A. Calreticulin, a potential vascular regulaory protein, reduces intimal hyperplasia after arterial injury. Arterioscler Thromb Vasc Biol. 17:2359-68. 1997.
30. Szarka RJ, Wang N, Gordon L, Nation PN, Smith RH. A murine model of pulmonary damage induced by lipopolysaccharide via intranasal instillation. J Immunol Methods 202:49-57. 1997.

31. Lucas, A., Dai, E., Liu, L.Y., Nation, P.N. Atherosclerosis in Marek's disease virus infected hypercholesterolemic roosters is reduced by HMG CoA reductase and ACE inhibitor therapy. Cardiovascular Res. 38:237-246. 1998.
32. Nation, P.N., Fanning, A.E., Hopf, H.C., Church, T.L. Observations on animal and human health during the outbreak of *Mycobacterium bovis* in game farm wapiti in Alberta. Can Vet J. 40:113-117. 1999.
31. Christov, A., Dai., E., Liu, L., Miller, L.W., Nash, P., Lalani, A., McFadden, G., Nation, P.N., Lucas, A., Tulip, J. Detection of transplant vasculopathy in a rat aortic allograft model by fluorescence spectroscopic optical analysis. Lasers in Surgery and Medicine. 24: 346-59. 1999.
32. Chisholm, J.W., Nation, P.N., Dolphin, P.J., Agellon, L.B. High plasma cholesterol in drug-induced cholestasis is associated with enhanced hepatic cholesterol synthesis. Amer J Physiol. 276: 1165-1173 1999.
33. Miller L.W., Dai E., Nash P., Lui L., Icton C., Klironomous D., Fan L., Nation N., Zhong R., McFadden G., Lucas A. Inhibition of Transplant Vasculopathy in a Rat Aortic Allograft Model After Infusion of an Anti-Inflammatory Viral Serpin. Circulation 101: 1598-1605. 1999.
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Appendix S. Revisions

Original Report Date: 18 July 2008

Date	Comments	Initials
12 Nov 2009	Changed the report by 1. specifying the catheter used for embolization, 2. describing selection of the treated renal artery, 3. adding language to show that the selected micrographs were representative of all animals, 4. changing the report date, version number and sponsor company, and 5. Correcting typographical and minor formatting errors. Changes were made in response to an external review by a regulatory consultant.	
1 Dec 2011	Changed the report by 1. corrected the dose of Excel per 20 May 10 email from B. Tchir and 2. changed the report date and version number	