7102

#10

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Group Art Unit: 335
MICHAEL D. DAKE, ET AL.	)	Examiner: J. P. LACYK
Serial No.: 07/484,117	)	
Filed: February 23, 1990	)	
For: RADIOACTIVE CATHETER	)	Pasadena, California

11/13/91

DECLARATION OF STEPHEN N. OESTERLE

Honorable Commissioner of
Patents and Trademarks
Washington, D. C. 20231

Sir:

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE U.S. POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO: COMMISSIONER OF PATENTS AND TRADEMARKS, WASHINGTON, D.C. 20231, ON

October 23, 1991
10/23/91
(DATE SIGNED)

I, Professor Stephen N. Oesterle, declare:

MY BACKGROUND

1. I am currently Associate Professor of Medicine (cardiology), Director, Catherization and Coronary Intervention Laboratories, Georgetown University Medical Center, Washington, D.C.

2. I received my Bachelor of Arts in chemistry, summa cum laude, from Harvard College, Cambridge, Massachusetts, with a Phi Betta Kappa award, in 1973. In 1977 I received my M.D., cum laude, from Yale University, New Haven, Connecticut.

3. My further qualifications are detailed in the attached curriculum vitae, which correctly and accurately presents my education, faculty and hospital appointments, professional and honorary society memberships, teaching assignments, fellowship programs of which I have been a director, and some of my publications. As indicated in my curriculum vitae, I have been assistant professor of medicine at Stanford University, Stanford, California. I am a fellow of the Society for Cardiac Angiography and Interventions; a fellow of the American College of Cardiology; and founding member and treasurer of the American Society of Cardiovascular Interventions.

4. In short, I am an expert in cardiology, and particularly interventional cardiology.

EXPERIMENTAL WORK

5. A device according to the present invention was constructed and tested for reliability and safety for delivery of radiation to the coronary vasculature in dogs. The methodology used, and the device used, was as described in the example portion of the present application.

6. The attached data sheets provide experimental information, namely the number of rads delivered during the test to the dogs. In general, the radiation was delivered for less

than 30 minutes. About two months after the experimental work, tissue samples from the coronary arteries of the dogs were microscopically examined. The tissues examined were control (non-treated) tissue, radiated tissue, and radiated and denuded (angioplasty) tissue. Histology reports for the treated tissue are attached to this declaration. In the reports, the following abbreviations were used:

LAD - left anterior descending coronary artery

LCx - circumflex coronary artery

RCA - right coronary artery

7. The results of the tests indicate that intraluminal radiation treatment of a coronary artery of a mammal can safely and effectively be accomplished.

UTILITY

8. A person of ordinary skill in the art relating to coronary intervention would believe the present invention has utility, namely that it can prevent restenosis. I conclude this based on the following evidence:

(a) The experimental results discussed above.

(b) The fact that keloid growth, which is the growth of scar tissue, can be prevented in many cases through the use of radiation therapy. Examples of articles that teach this are the Borok et al. article, "Role of Ionizing Irradiation For

393 Keloids", and Kovalic, et al., "Radiation Therapy Following Keloidectomy: A 20-Year Experience".

(c) The major component of restenosis is scar tissue. This is discussed in such articles as Faxon et al., "Mechanism of Angioplasty and Its Relation to Restenosis".

Thus, the claim for utility for the present invention is believable on its face to those of ordinary skill in the art.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application and any patent or patents resulting therefrom.

Date: 10/22/91

By: _____
Stephen N. Oesterle, M.D.

Dog 2228

LCX-1 [radiation only]	Areas of denudation of endothelium. Vessel patent. Very mild intimal hyperplasia. One area of vessel disruption is probably artefact.
LCX-2	tangential cut through vessel - cannot adequately assess.
LAD-1 [denudation & radiation]	vessel patent - small area of very mild intimal hyperplasia.
LAD-2	vessel patent - mild intimal hyperplasia.
Marginal [control]	Small vessel, but intact; normal.

2238

Protocol: RAD IATED STUDY

Number: 89-11-04

Investigators: Oesterle
Kloner
Dawson

USC # 2675

DATE: 2-5-90

Weight 67 lbs

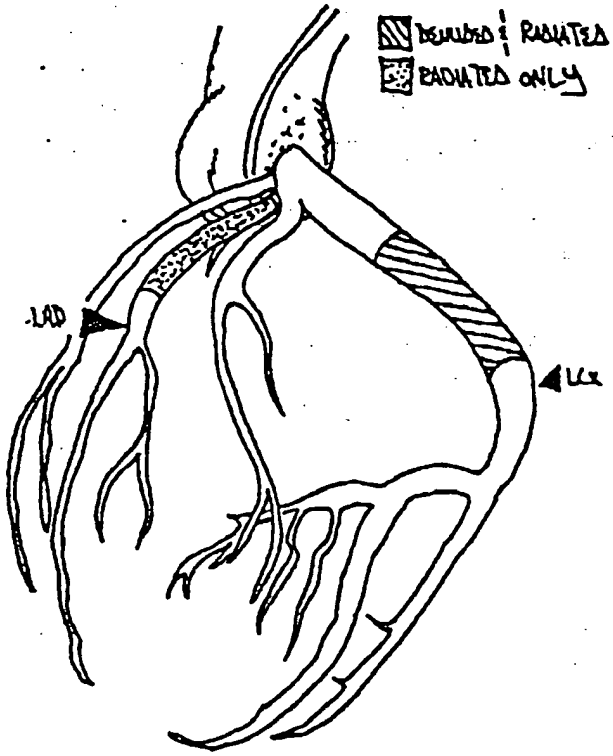
Sex: ♂ ♀

Drugs
Sodium Pentobarbital _____ ml
15mg Morphine
Heparin 4600 units
Buotal -50
Protamine - 3500 units

Isotopes **Generation**

None	☒	
Ce	☐	_____
Ru	☐	_____
Nb	☐	_____
Bin #		_____

Dead ☐
KCl under deep anesthesia ☐
Other _____



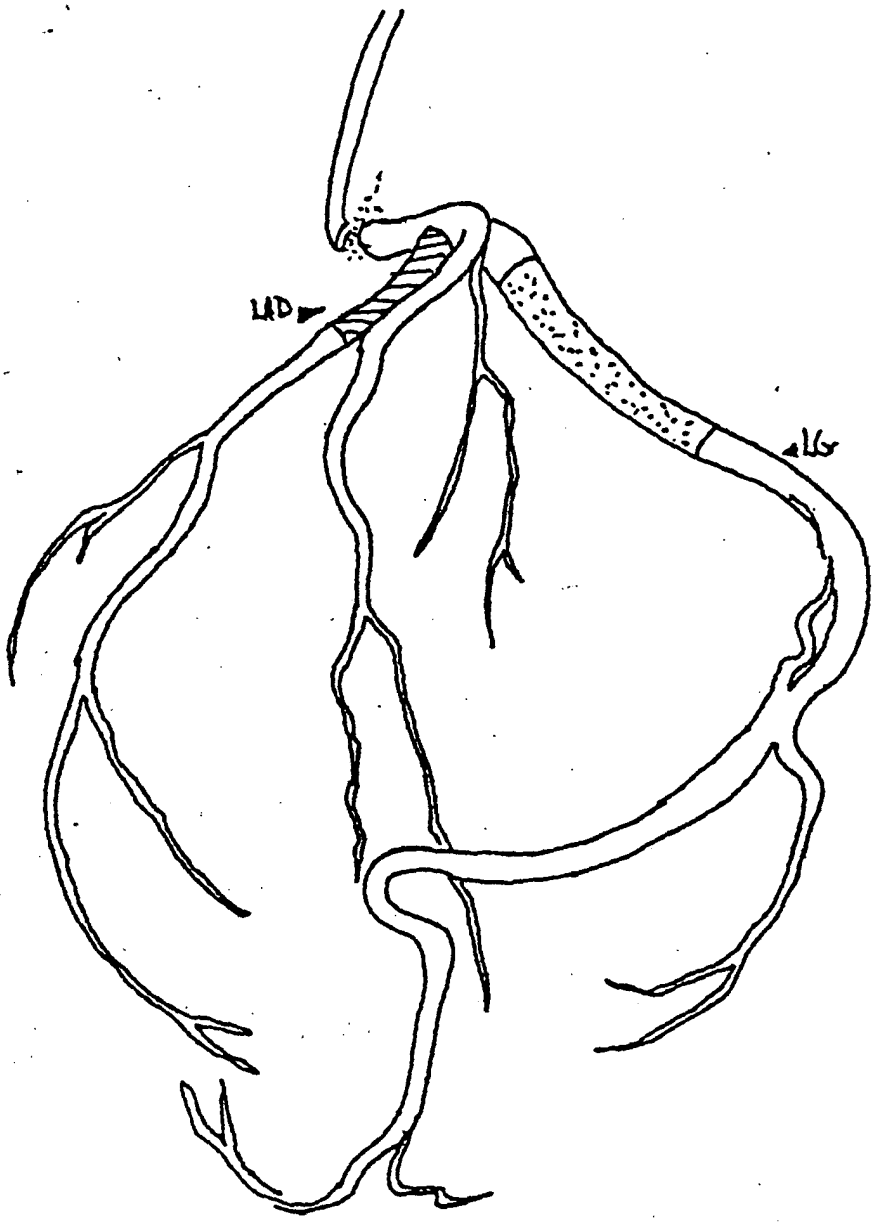
☐ ANIMAL DRAPED IN USUAL STERILE FASHION / (R) GROIN PREPED
☐ RFA ISOLATED & EXPOSED; SUSPENDED BY PROX & DISTAL UMBILICAL TAPE TRACTION
☐ PUNCTURE PER COOK NEEDLE; 6FR SHEATH W/ INTRODUCTION RFA
☒ SYSTEMIC HEPARINIZATION PER 4,600 U BOLUS IVP

☐ 10:05 BASELINE HEMODYNAMIC RECORDING DONE
☐ 10:10 PROXIMAL LCx: 3.0 ACX BALLOON INFLATION x2 [NO IRRADIATOR USED]
☐ 10:15 DOSIOS CATHETER PLACED PROXIMAL LAD
☐ 10:16 IRRIDIUM #12 "SEEDS" [32 MINS: 500RADS @ 5cm] PLACED PROX LAD [ACROSS 1ST DIAG]
☐ 10:38 2cc Na+ PENTOBARB IVP
☐ 10:41 5cc Na+ PENTOBARB IVP
☐ 10:48 CINE ANGIOGRAPHY DEMONSTRATES GOOD DISTAL RUN-OFF & "SEED" PROXIMAL PROX LAD
☐ 10:50 IRRIDIUM SEEDS W PROX LCx for 32 MINS [500RADS @ 5cm
☐ 11:00 5cc Na+ PENTOBARB IVP
☐ 11:10 4cc Na+ PENTOBARB IVP
☐ 11:20 "SEEDS" W/DRAWN LCx / CINE ANGIOGRAPHY REVEALS GOOD FLOW —● ___35___ mg PROTAMINE 50cm IVP
☐ 11:30 ARTERIOTOMY CLOSED BY & INTERRUPTED 5-0 PROLENE SUTURE
☐ MUSCLE / FASCIA / SKIN APPROXIMATED & RUNNING 2.0 VICRYL
☐ NO HEMATOMA / WOUND IS DRY
☐ ANIMAL RETURNED TO HOLDING AREA IN STABLE CND.

Photographs ☐
Roll # _____

DOG / 2228

TU / 16 JAN 96



DEMARCATION / RADIATION

RADIATION ONLY

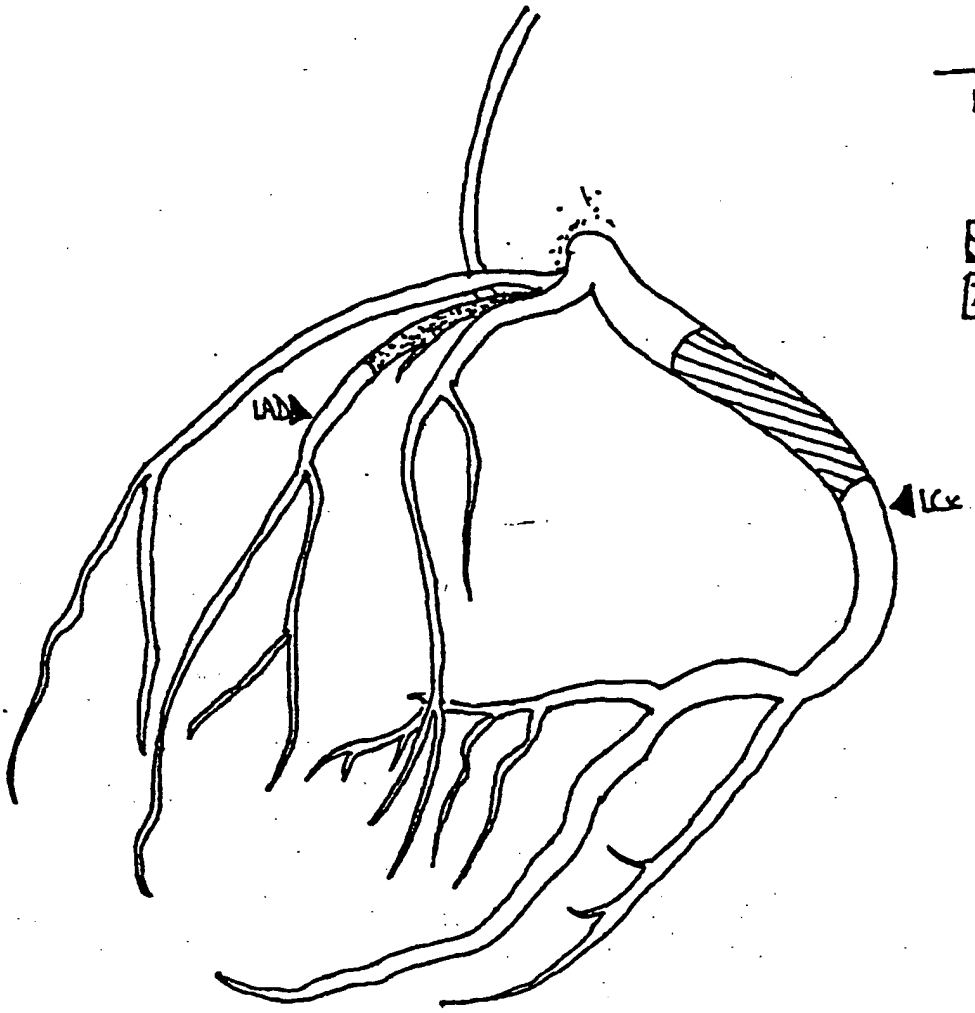
Dog 2238

LAD-1	(Radiated only) Normal
LAD-2	(Radiated only) Some denudation of endothelium
Marginal	(Control) Normal
LCX-1	(Radiation and denudation) denuded endothelium; occasional neutrophils adherent to intima
LCX-2	(Radiation & denudation) area of denudation; vessel otherwise intact

Dog 2239

LAD-1	(Denuded and radiated) endothelium denuded, vessel otherwise intact
LAD-2	(Denuded and radiated) endothelium denuded; area of neutrophil infiltration into wall of vessel plus nuclear dust. Some edema or necrosis in media of this same area.
Marginal	(Control) Normal
LCX-1	(Radiated only) areas where elastic lamina appear lifted off of the vessel; areas where elastic lamina appears split. Some platelet and ? fibrin adherent to intima; few neutrophils adherent to intima.
LCX-2	(Radiated Only) Some denudation. Elastic lamina cut tangentially.

Dog / 2238
mw / 6 FEB 90



DAMAGE/RADIATION
RADIATION ONLY

2239

Protocol: Radiation Study

Investigators: Oesterle / Dawson
Klover

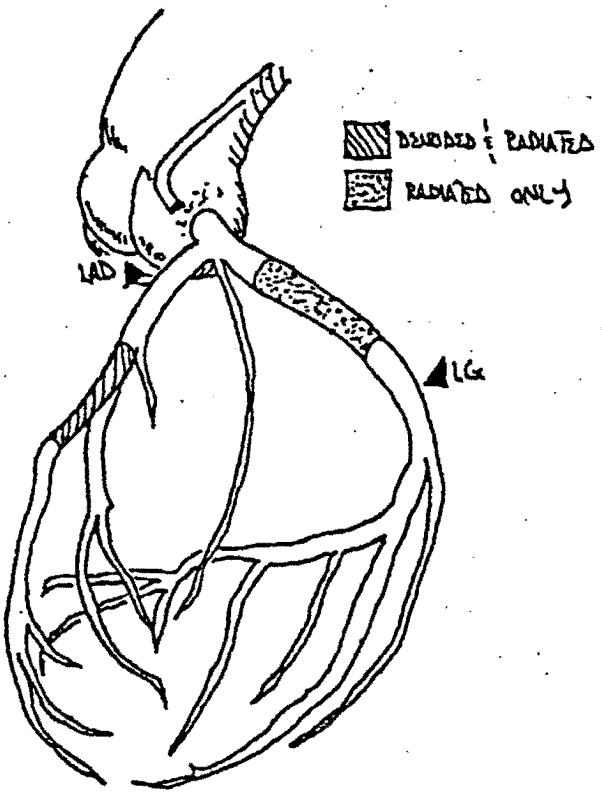
Number: 89-11-04
USC #: 2676
DATE: 2-5-90
Weight: 46 lbs
Sex: ♂ ♀

Drugs
Sodium Pentobarbital _____ ml
15mg Morphine
Heparin 3000 units
Biotal - 50 cc
Protamine - 25mg

Isotopes — **Generation**

None	☒	
Ce	☐	_____
Ru	☐	_____
Nb	☐	_____
Bin #		_____

Dead ☐
KCl under deep anesthesia ☐
Other _____

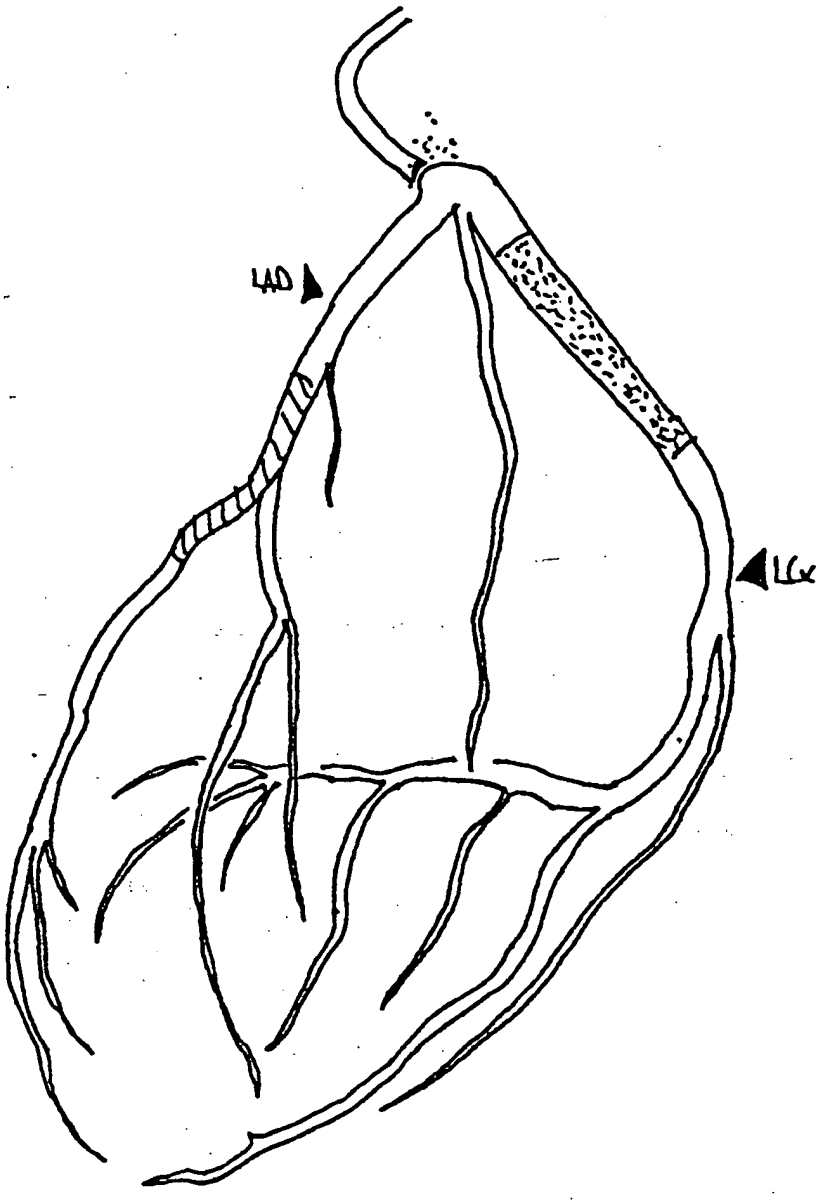


☐ Animal group shaved, prepped, draped in usual sterile fashion
☐ RFA isolated & exposed sufficiently by prox & distal um bilical tapes
☐ 8Fr sheath introduction per RFA puncture & BS sec Femoral heparinization (3000 unit bolus)
☐ 12:40 Baseline Hemodynamics done
☐ 12:45 Prox LAD: 2.5 mm Hartzler balloon inflation
☐ 12:52 Iridium 192 "seeds" placed prox LAD
[32 mins: 500 rads @ 5mm]
☐ 12:50 5cc Na⁺ Pentobarb IVP
☐ 13:24 "Hot" catheter w/drawn LAD / cine rec: good distal run off
☐ 13:26 Dummy positioned in prox LCx; subsequent "seed" delivery prox LCx
[32 mins: 500 rads @ 5mm]
☐ 13:45 3cc Na⁺ Pentobarb IVP
* note: ↑ arterial "oozing" along sheath insertion site: sheath anchored by single 2-0 silk ties to skin.
☐ 13:58 Hot catheter w/drawn cineangiographic pre-formed [good flow].
- 25mg Protamine IVP
☐ 14:00 Arteriotomy closed per multiple interrupted / purse-string 5-0 Prolene sutures
☐ 14:15 Skin along w/ underlying tissue approximated using 2.0 running chromic _____ RD

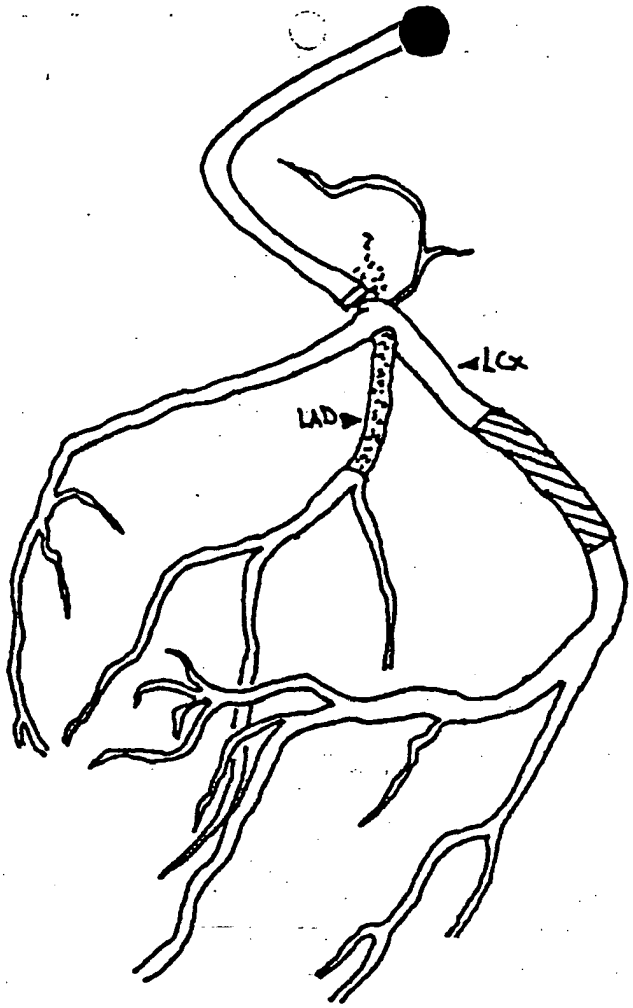
Photographs ☐ -
Roll # _____

☐ Animal awake & returned to Holding Area as such.

Jog / 2239
mw / 6 6B 90



DOUBLE ⅓ RADIATION
RADIATION ONLY



DOG / 2227
MW / 15 JAN 90

DESCRIPTION / RADIATION
RADIATION ONLY

2227

Protocol: Oostube-radiation study

Investigators: Gestake / Kune
Mehrle / Alkon / graves

Number:

USC # 2654

DATE: 1/15-16/86

Weight 41 lbs / 186 kg

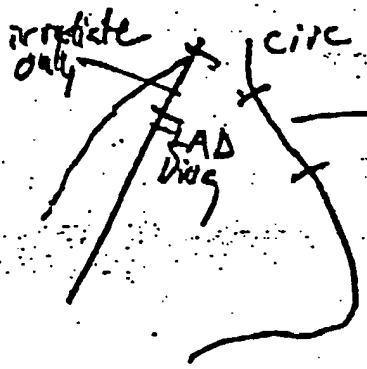
Sex: ♂ ♀

Drugs
Sodium Pentobarbital ____ ml
Thiamylal
Heparin - 25000
Protamine - 50 mg

Isotopes — Generation

None ☐
Ce ☐
Ru ☐
Nb ☐
Bin # ____

Dead ☐
KCl under deep anesthesia ☐
Other ____



Prox circ denuded with 3.0 balloon
35 sec x 2

iridium - 20 min - 600 rads @ 5 mm.

circ - denudation + radiation
20 min

LAD diag - radiation only
20 min

Photographs ☐
Roll # ____

Dog #2229

LCX-1 [denudation & radiation]	vessel patent - one small area of vessel appears disrupted- this may be artefact. Mild to moderate intimal hyperplasia. Some neutrophils adhering to intima.
LCX-2	vessel patent - areas of denudation - intimal hyperplasia - mild - moderate.
LAD-1 [radiation only]	vessel patent - areas of denudation - very mild intimal hyperplasia.
LAD-2	vessel patent - moderate intimal hyperplasia.
Marginal [Control]	Normal

2229

Protocol: Osteole - Radiation Study

Investigators: Osteole

Number:

USC # 2645

DATE: 1-16-98

Weight 60 lbs

Sex: ♂ ♀

Drugs
Sodium Pentobarbital 6 ml
Sustal - 15mg Morphine
Heparin 4200 units

Isotopes - Generation

None	☒	
Ce	☐	
Ru	☐	
Nb	☐	
Bin #		

Dead ☐
KCl under deep anesthesia ☐
Other

@ 3.0 ACS-ACX BALLOON PREPPED / .014 WIRE SHAPED

@ 3.0 Balloon Cx at 1:26 PM

@ Mid-Cx for denudation
LCx DENUDED FOR 4 55 SECS @ 4 ATMOSPHERES

@ 1:32 radiation catheter in place

@ PLACED IN MID-LCX

Denuded mid-dx

1:03 PROXIMAL LAD; IRIDIUM 192 SEEDS PLACED PROXIMAL TO VESSEL

@ 1:29 SEEDS W/DRAWN PROX LAD

@ FINAL CINE PERFORMED; DEMONSTRATES VASOSPASM CORONARY WASH-OUT

@ 6FR SHEATH W/DRAWN / UMBILICAL TAPE USED TO MAINTAIN VESSEL STASIS

@ ARTERIOTOMY CLOSED VIA PURSE STRING SUTURE OF 5.0 PROLENE

@ UNDERLYING FASCIA (2°) + SKIN CLOSED VIA 2.0 VICRYL

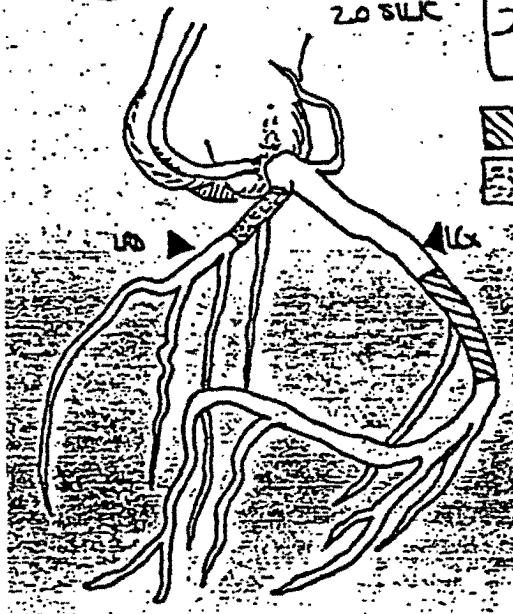
@ WOUND IS DRY & NO HEMATOMA NOTED

@ ANIMAL RETURNED TO RECOVERY A/O

No ECG tracing generating

@ ANIMAL SEDATED W 15mg IM S ⊕ ___ mg SUSTAL
@ ANIMAL INTUBATED IN LAB / TRANSFERRED TO TABLE & INTUBATED
@ (R) GROIN PREPPED · DRAPED IN STERILE FASHION
@ 2% LIDOCAINE ADMINISTRATION SUB-Q (R) GROIN
@ (R) INGUINAL FOLD INCISED LONGITUDINALLY
@ BLUNT DISSECTION TO EXPOSE / ISOLATED (R) FA/FV
@ INTRODUCTION GUIDE WIRE THRU POTTS NEEDLE
@ 8FR SHEATH CANNULATION RFA
@ SHEATH ANCHORED PER SINGLE 2.0 SILK

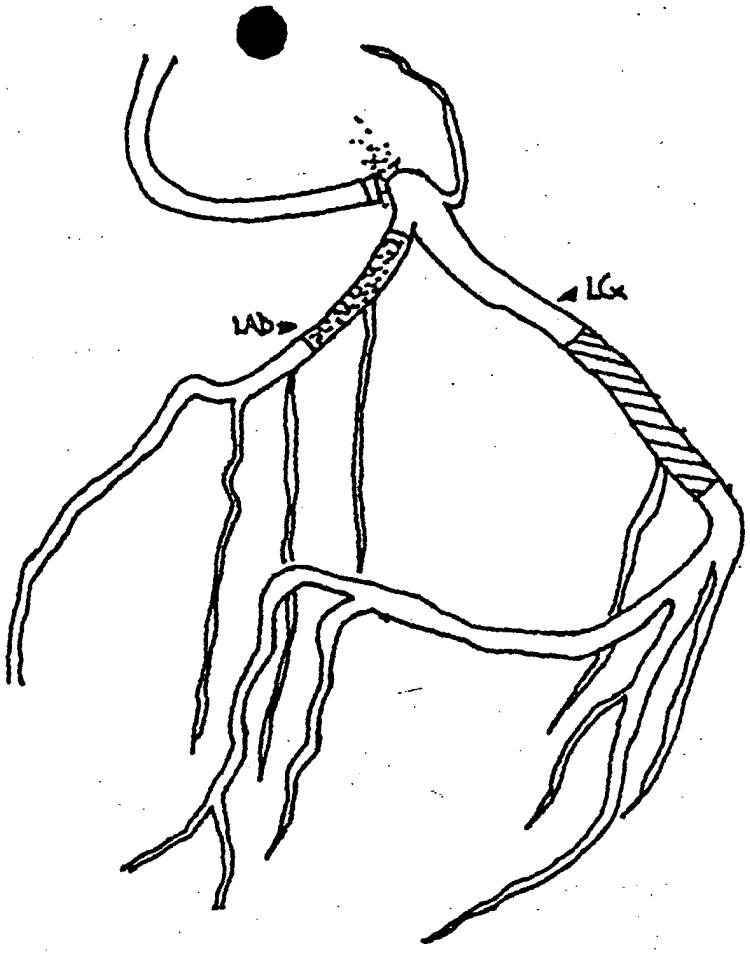
Iridium
26 minutes
each 500 RAD @ 5 M.M



DENUDATION & RADIATION
RADIATION ONLY

Photographs ☐
Roll #

Doc/2229
Tu/16 JAN 90



DEMARCATION / RADIATION
RADIATION ONLY

2226

Protocol: Gestule - radiation study

Investigators: Ozsteule / Klone
Aiken / Ahmed / Gamer

Number:

USC # 2655

DATE: 1/15/96

Weight 421bs / 19.1kg

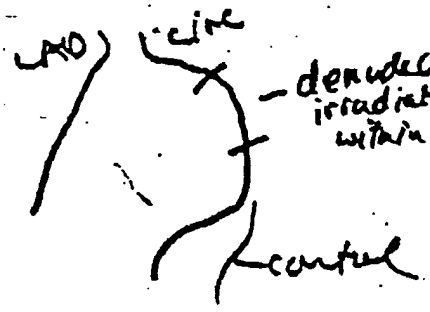
Sex: ♂ ♀

Drugs
Sodium Pentobarbital ____ ml
Heparin 2800 U.
Ketamylad.
Atropine 0.4 mg
protamine gang

Isotopes		Generation
None	☐	
Ce	☐	
Ru	☐	
Nb	☐	
	Bin #	

Dead ☐
KCl under deep anesthesia ☐
Other ____

26 mm - 500 RADS at 5 mg - iridium seeds
inflate 2.5 balloon prox. circ. 45 sec x2
seeds placed in circ 10:17
out 10:43



could not advance catheter into LAD. - some spasm of LAD
take distal circ measurement

Photographs ☐
Roll # ____

Dog / 2226
mv / 15 JAN 90

IRRADIATION / RADIATION

Protocol: Restenosis Study

Investigators: _____

Number: _____

USC # 2633

DATE: 12-11-89

Weight 46 lbs 2 oz

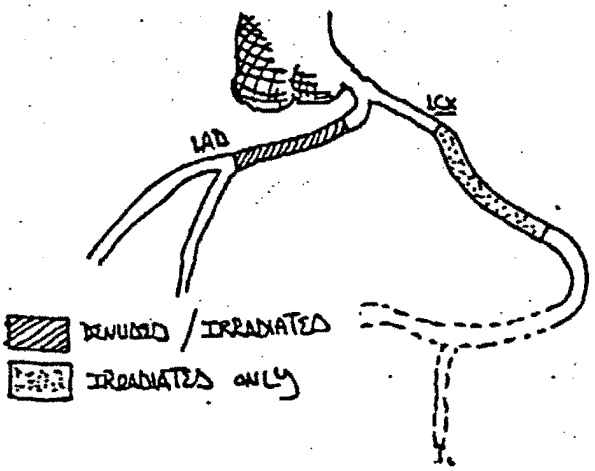
Sex: ♂ ♀

Drugs
Sodium Pentobarbital _____ ml
Brutal - 40 cc
Heparin 3000 units
Mefamins 20mg IVP

Isotopes **Generation**

None	☒	
Ce	☐	_____
Ru	☐	_____
Nb	☐	_____
	Bin #	_____

Dead ☐
KCl under deep anesthesia ☐
Other _____



☑ 1% LIDOCAINE ADM SUB-Q (L) GROIN
☑ PERCUTANEOUS INTRODUCTION 8FR INTRODUCTION INSTRUMENT
☑ SYSTEMATIC HEPARINIZATION FOR 3,000 U BOLUS IVP
☑ (L) COL AS CANNULATION FOR 8FR GUIDE
☑ LAD Balloon @ 11:57 } 100% e in Satin
BALLOON: 2.5 MS CATHETER IN PROX LAD CIRCUMFLEX
☑ Iridium Catheter in LAD 12:05
"HOT TIP" CATHETER ADVANCED ALONG FOR DOSIMETRIC INFUSION CATHETER
☑ Iridium catheter in Cx 12:30
DELIVERY 600 RADS IN 11 MINS.
☑ CORONARY SPASM NOTED DISTAL TO IRIDIUM CATHETER DURING LAD IRRADIATION.
○ POSSIBLY 2° TO INJECTION SOLN ON GUIDING CATHETER
○ POSSIBLY SPASM INDUCED BY IRIDIUM CATHETER
☑ GOOD DISTAL RUN-OFF NOTED (R) CATHETER IS W/DRAWN.
○ NOTE: ANIMAL IS BRADYCARDIC
☑ CATHETER W/DRAWN: FINAL CINE ANGIOGRAPHY PERFORMED TO DEMONSTRATE GOOD FLOW.

☑ 20mg Phenamine Administered IVP PRIOR TO 8FR INTRODUCTION INSTRUMENT W/DRAWN
☑ DIGITAL PRESSURE APPLIED TO (L) FEMORAL ARTERY FOR HEMOSTASIS (2° TO SUCCESSFUL PERCUTANEOUS INTRODUCTION).
☑ 15 MIN MANUAL PRESSURE APPLIED TO (L) FA, SLT LARGE HEMATOMA DEVELOPED.
☑ ANIMAL TRANSFERRED TO POST ANESTHESIA RECOVERY AREA

Photographs ☐ -
Roll # _____

12/12/89 Hearts dissected. No gross abn noted in vessels.

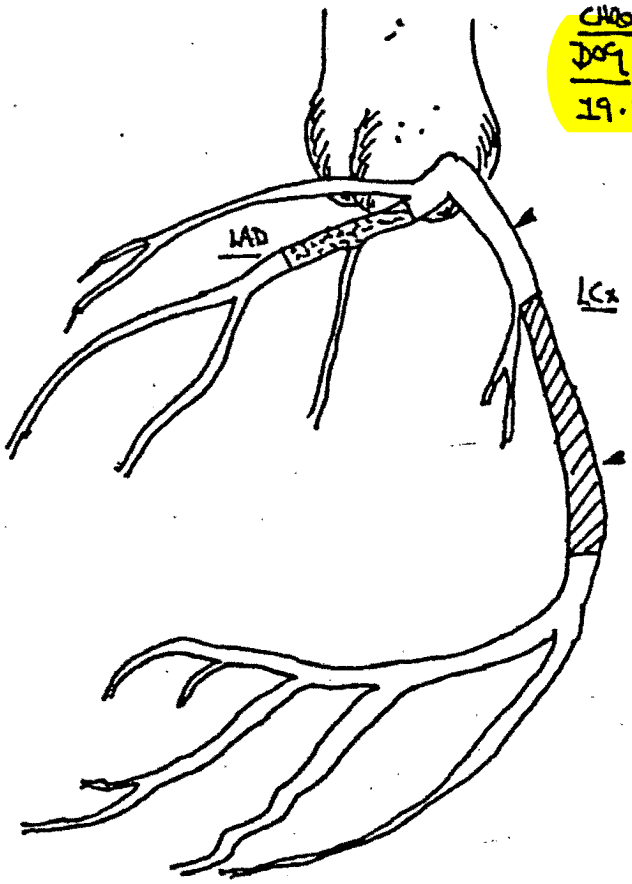
Dr. Kloner's Path Reading

April 5, 1990

2206 - Chronic

Circ - 2 (Denude, radiate)	vessel patent intima & endothelium intact.
2206 Circ - 1	vessel patent, mild intimal hyperplasia (about 5 cell layers think) on one side of vessel only.
2206 Marginal (Control)	Normal
2206 LAD -1 (Radiate)	Vessel patent intimal hyperplasia about 3-4 cell layers thick on one side of vessel. On the other side - peculiar network of ? fibrin and ? neointimal cells.
2206 LAD - 2	Appears Normal.

CHRONIC
DOG /2206
19 · DEC · 89



DENUDED & IRRADIATED
IRRADIATED ONLY

2238

Protocol: RAD IATRO STUDY

Number: 89-11-04

Investigators: Oesterle
Kloner
Dawson

USC # 2675

DATE: 2-5-90

Weight 67 lbs

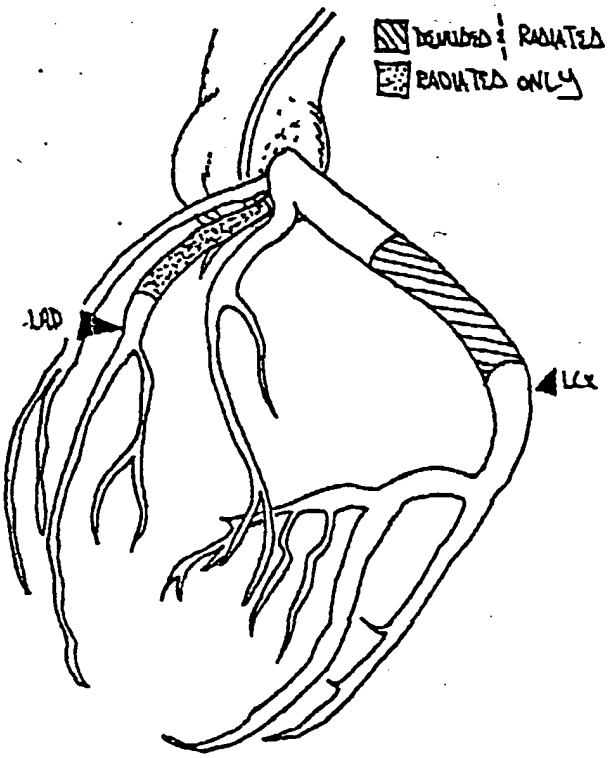
Sex: ♂ ♀

Drugs
Sodium Pentobarbital _____ ml
15mg Morphine
Heparin 4600 units
Buital -50
Protamine - 3500 units

Isotopes **Generation**

None	☒	
Ce	☐	_____
Ru	☐	_____
Nb	☐	_____
Bin #		_____

Dead ☐
KCl under deep anesthesia ☐
Other _____



☐ ANIMAL DRAPED IN USUAL STERILE FASHION / (R) GROIN PREPED
☐ RFA ISOLATED & EXPOSED ; SUSPENDED BY PROX & DISTAL UMBILICAL TAPE TRACTION
☐ PUNCTURE PER COOK NEEDLE ; 8Fr SHEATH W/ PRODUCTION RFA
☒ SYSTEMIC HEPARINIZATION PER 4,600 U BOLUS IVP

☐ 10:05 BASELINE HEMODYNAMIC RECORDING DONE
☐ 10:10 PROXIMAL LCx : 3.0 ACX BALLOON INFLATION x 2 [NO INDICATOR USED]
☐ 10:15 DOBBOS CATHETER PLACED PROXIMAL LAD
☐ 10:16 IRRIDIUM 192 "SEEDS" [32 MINS : 5000 RADS @ 5mm] PLACED PROX LAD [ACROSS 1ST DIAG]
☐ 10:38 2cc Na+ PENTOBARB IVP
☐ 10:41 5cc Na+ PENTOBARB IVP
☐ 10:48 CINE ANGIOGRAPHY DEMONSTRATES GOOD DISTAL RUN-OFF & "SEED" REMOVAL PROX LAD
☐ 10:50 IRRIDIUM SEEDS IN PROX LCx for 32 MINS [5000 RADS @ 5mm
☐ 11:00 5cc Na+ PENTOBARB IVP
☐ 11:10 4 cc Na+ PENTOBARB IVP
☐ 11:20 "SEEDS" W/DRAWN LCx / CINE ANGIOGRAPHY REVEALS GOOD FLOW ——— 35 mg PROTAMINE ADMIN IVP
☐ 11:30 ARTERIOTOMY CLOSED BY 3 INTERRUPTED 5-0 PROLENE SUTURES
☐ MUSCLE / FASCIA / SKIN APPROXIMATED & RUNNING 2.0 VICRYL
☐ NO HEMATOMA / WOUND IS DRY
☐ ANIMAL RETURNED TO HOLDING AREA IN STABLE CND.

Photographs ☐ -
Roll # _____

2228

Protocol: Oestrule : Radiation Study

Investigators: Oestrule

Number:

USC #: 2634

DATE: 1-11-90

Weight: 5-3 lbs

Sex: ♂ ♀

Drugs

Sodium Pentobarbital 6 ml

3600 units heparin + 15 mg Morphine

30 cc Surital

Isotopes — Generation

None	☑	
Ce	☐	
Ru	☐	
Nb	☐	
	Bin #	

Dead ☐

KCl under deep anesthesia ☐

Other

ⓐ ANIMAL (R) GROIN SHAVED, PREPPED & DRAPED IN USUAL STERILE F

ⓐ 2% LIDOCAINE SUB-Q (R) GROIN / INCISION (R) JUGULAR FOLD

ⓐ CUTDOWN (R) FEMORAL ARTERY / 8FR CANNULATION

ⓐ HEPARIN @ 3.0 balloon tipped catheter

Time: at 10:10 end: 10:13

LOCATION: MID-LAD

ⓐ Prop'd Cx ; BEGIN RADIATION, 10:19 AM

[Iridium 26 minutes each / 500 RAD @ 5m

ⓐ PROX Cx : END RADIATION ; 10:45 AM

ⓐ MID LAD : BEGIN RADIATION ;
END RADIATION ;

[INTRODUCTION IRRIDIUM 192 "SEEDS" : 500 RADS / 5mm]

ⓐ FINAL CINEANGIOGRAPHIC SHOT DEMONSTRATES GOOD DISTAL RUN

ⓐ PROX & DISTAL TENSION APPLIED TO VASCULAR TIES AS 8FR SHEATH W/D
FROM ARTERIAL CIRCULATION.

ⓐ HEPARIN REVERSED 2 30 mg BOLUS PROTAMINE (L) INTERNAL JUGULAR

ⓐ (R) FEM ARTERIOTOMY CLOSED VIA INTERRUPTED 5.0 PROLENE
- MILD - MODERATE OOZING NOTICED PRIOR TO SKIN APPROXIMATION
- 2.0 VICRYL SUTURES PLACED W WOUND

ⓐ SKIN CLOSED VIA RUNNING 2.0 VICRYL

ⓐ ANIMAL EXTUBATED PRIOR TO CLOSURE 2° HYPER-VENTILATION ABSENT E.T. TUBE

ⓐ ANIMAL TRANSFERRED TO RECOVERY AREA IN SATISFACTORY CND. NO HE
TORMA APPARENTED

Photographs ☐

Roll #

ⓐ HEPARINIZATION = 3600 UNIT BOLUS IVP

No. ECG tracings obtained

January 25, 1990

HISTOLOGY FOR DR. OESTERLE'S RADIATION STUDY
(ROBERT A. KLONER'S READING)

2205 Circumflex	Irradiated, nondenuded.
Slides 1:	One area appears denuded with a few neutrophils attached to the surface. Can't rule out some artifactual loss of intima. Some of intima cut tangentially. Media intact.
2205 LAD	Irradiated, denuded.
Slide 1:	Areas of denudation White cells attached to intima Media appears intact
Slide 2:	As above. Area of intima disrupted with probable platelet deposition. Blood in lumen of vessel ? post mortem clot. One area of vessel has round-cell infiltration beneath elastic lamina.
2205 Marginal	Portion of intima appears detached (looks artifactual) A few isolated white cells adjacent to intima. Media intact. Otherwise looks normal.

Protocol: Osteele radiation study

Investigators: Osteele
Pappas, Minah, Aiken
Klein, Garver

Number:

USC # 2623

DATE: 12/18/89

Weight 38 lbs

Sex: ♂ ♀

Drugs
Sodium Pentobarbital ____ ml
Buotal - (sunital 3.0 cc
Heparin 3000 U
Pralmine 20mg IVP @ 11:05AM

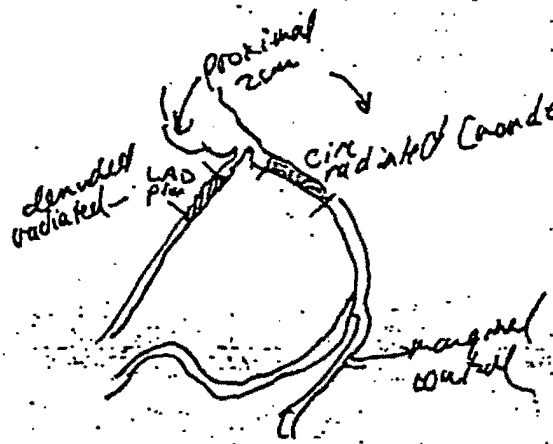
Isotopes (as flow) **Generation**

None	☒	
Ce	☐	____
Ru	☐	____
Nb	☐	____
	Bin #	____

Dead ☐
KCl under deep anesthesia ☐
Other ____

☑ UNSUCCESSFUL (R) FA PERCUTANEOUS PUNCTURE
☑ (L) FA W/DOWN (2) VISUAL ARTERIAL PUNCTURE
☑ 8FR SHEATH INTRODUCTION (L) FA
☑ 3000 U HEPARINIZATION PER IV BOLUS
☑ 8FR GUIDE CANNULATION OF (L) CORONARY
☑ LAD - angioplasty - proximal - 1 min. injection
☑ irridium 192. ~~1700~~ 2280 rads at 3mm in 11 min
○ prox. LAD radiated. 10:27 — 10:38
☑ Circ radiated 10:40 — 10:58 . 5100 rads at 3mm (11 min)
☑ 20mg PRALMINE ADMINISTERED
☑ CATHETER W/DRAWN
☑ SHEATH W/DRAWN
☑ ARTERIOTOMY CLOSED PER INTERRUPTED 5-0 PROLENE PURSE STRING SUTURES
☑ TISSUES APPROXIMATE ! SKIN CLOSED PER 2-0 VICRYL SUTURES
☑ ANIMAL TRANSFERRED TO RECOVERY AREA

▨ DRUGS + IRRADIATION
▨ IRRADIATION ONLY



☑ Post radiation angiogram time
Demonstrates good distal run off

Photographs ☐
Roll # ____

12/27/89 - hearts dissected - no gross abn in vessels.

Study: #2226 (01/15/90)

LCX - denuded, radiated

1. areas of endothelium denudation leaving exposed elastic lamina

2. endothelium denuded in areas. One small zone of hemorrhage and edema in media with some neutrophils in adventitia of this area.

Marginal- Endothelium intact. Some artefact on one side of vessel.

Study 2227 (01/15/90)

LCX - denuded, radiated

1. large portions of vessel denuded with overlying thin layer of probable thrombus, (RBC's, platelets, few WBC's).

2. As above; one area has edema, disruption and possible necrosis of the media. Small amount of hemorrhage in vessel wall with neutrophils as well.

LAD - radiated, not denuded.

1. Some areas of denudation.

2. As above. Some areas where thin layer of platelets, RBC's overly intima.

Marginal-Control
Normal

January 25, 1990

HISTOLOGY FOR DR. OESTERLE'S RADIATION STUDY (ROBERT A. KLONER'S READING)

2204 Circumflex	Radiated, nondenuded
Slides 1 and 2:	While most of the vessel appears intact there is one area making up about 15-20% of the circumference which appears to have lost the endothelium. In the media of this area are some neutrophils and degenerated neutrophil nuclei ("nuclear dust"). There is also some hemorrhage, edema and possibly necrosis in the media of this area.
2204 Marginal	Control Normal
2204 LAD	Radiated - denuded
Slide 1:	Much of, but not all of the endothelial lining is removed, leaving an exposed elastic lamina. There is a focal zone of hemorrhage into the media and neutrophil infiltration; again, some degenerated neutrophil nuclei.
Slide 2:	Endothelial denudation, otherwise media appears intact.

THE AMERICAN MEDICAL ASSOCIATION

FAMILY MEDICAL GUIDE

Editor-in-Chief
Jeffrey R.M. Kunz, MD

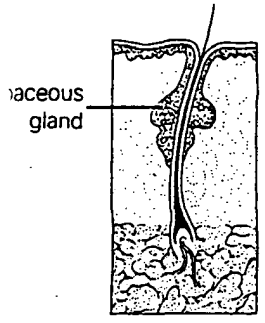
RANDOM HOUSE
NEW YORK

teach you to clean it with a mild antiseptic, and cover it with a dressing. This should be done frequently.

If the ulcer fails to heal, your physician may coat it with a white paste and then bandage it up. In some cases this still fails to clear up the problem, and you may be advised to go into the hospital for a few weeks. There you can rest in bed in the proper position, and your ulcer will be constantly observed and treated as necessary. To hasten healing, a skin graft (see Box, previous page) may be needed.

Sebaceous cysts

See p.242, **Visual aids to diagnosis, 40.**



A sebaceous gland is a tiny gland that lies just beneath the skin and produces an oily, waxy substance to keep the skin supple. A sebaceous cyst develops when the gland fills with a thick "cheesy" fluid that slowly accumulates. The cyst then grows slowly over many years. It can be seen as a pale lump beneath the skin. Such cysts are most often found in the scalp. In some cysts there is a narrow pore connecting the cyst and the skin surface. This pore is marked by a tiny, dark dot.

Sebaceous cysts usually occur singly. They are often painless and harmless, are quite common, and are often first noticed in young adults. The cause of these cysts is not known.

What are the risks?

If bacteria enter the pore, the cyst becomes infected. It then becomes enlarged, red, inflamed and tender. It may eventually burst and release foul-smelling pus. After this, the inflammation recedes but the cyst still remains and may become reinfected later. The cyst may also break beneath the skin. This causes a great deal of redness and pain. As the cyst heals, scar tissue may develop, and this may make it difficult to remove the cyst through surgery.

What should be done?

Most people with small cysts simply accept them. If a cyst becomes infected, or if you want one removed because it is unsightly, see your physician. *Antibiotics* are usually prescribed for an infected cyst. An obtrusive cyst can be removed by surgery in a simple outpatient operation, for which you may be given a local anesthetic. If, however, even a small part of the cyst is left behind, and this is sometimes unavoidable, it can recur.

Keloid

See p.241, **Visual aids to diagnosis, 34.**

A keloid is a scar that grows excessively. It can occur after an operation, a burn, a vaccination, severe acne (see p.708), or even the piercing of an ear lobe. At first the scar seems normal, but after several months it grows and becomes noticeably larger and thicker. Occasionally, for some reason, a keloid develops after a very minor scratch.

Keloids are harmless, but they can itch, and they sometimes cause deformity. They are quite common in people with black skin, but rare in those with light skin.

What should be done?

Some keloids stop growing, or even disappear, for no apparent reason. If you want one treated for cosmetic reasons, consult your physician, who will probably inject a steroid medication into it. This sometimes makes it smaller. An alternative is *X-ray* treatment. A keloid cannot simply be cut out. This would leave a scar that might turn into another keloid. Removing the keloid and treating the new scar with injections, X-rays, or both may result in only a small scar.

Lichen planus

See p.441, **Visual aids to diagnosis, 33.**

Lichen planus is an itchy skin rash of unknown origin. It is either small, shiny, reddish spots that appear suddenly, often on the wrists, or patches of thickened, discolored skin that gradually fade and leave a brown mark. Another type of lichen planus is a light, lacy pattern of slightly raised tissue in moist areas such as the vulva and also the inside of the mouth (see Oral lichen planus, p.452). Lichen planus can also make fingernails and toenails ridged.

Lichen planus is most common in middle-

What is the treatment?

should consult your physician, because there are many other skin conditions, some of them serious, that resemble lichen planus.

Most of the time, a dermatologist (skin specialist) can diagnose lichen planus on sight. If the diagnosis is in doubt, you may have to undergo a *biopsy*, in which a sample of skin is removed and examined. *Steroid* ointment usually relieves the irritation and reduces the rash. But the rash often returns and

2240 - Marg. -	Vessel patent. Few neutrophils attached to intima.
2240-Diag. 1 [radiated only]	Severe intimal hyperplasia; lumen is narrowed by about 10%. Many neutrophils observed in vessel lumen. Cannot R/O early thrombus.
2240-Diag. 2 - [radiated only]	Severe intimal hyperplasia; about a 20-30% concentric luminal narrowing. Very impressive disease. Possible early thrombus.
2240 LCX - 1 [denuded & radiated]	Vessel patent. Very mild intimal hyperplasia.
2240 LCX - 2 [denuded & radiated]	Vessel patent. Very mild intimal hyperplasia.

Protocol: IRRADIUM 192 [redacted]

Investigators: [redacted] · KLOVER · et al.

Number: 84-11-04

USC # 2641

DATE: 2-7-90

Weight 65LBS

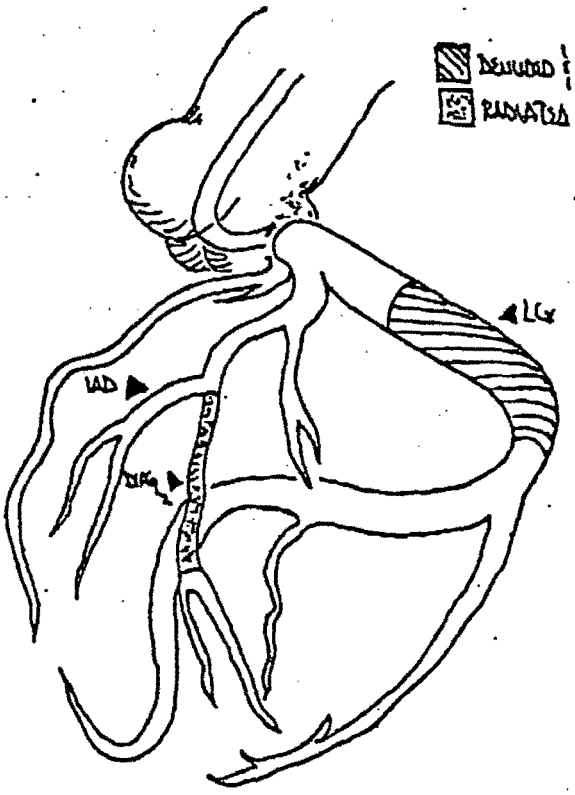
Sex: ♂ ♀

Drugs
Sodium Pentobarbital _____ ml
15mg Morphine
Hyparin - 4500 units
Biotal
Protamine

Isotopes		Generation
None	☐	
Ce	☐	_____
Ru	☐	_____
Nb	☐	_____
	Bin #	_____

*NOTE: ANIMAL IN RIGHT DECUBITUS POSITION ; IMAGES @ 30° LAO ANGULATION

Dead ☐
KCl under deep anesthesia ☐
Other _____



☐ ANIMAL SCRUBBED & ABOUT HANDS ; TAKEN TO CATH LAB WHERE MINERAL OIL PREPPED / DRAPED IN STERILE FASHION.

☐ LONGITUDINAL INGUINAL (R) INCISION MADE / RFA EXPOSED & ISOLATED SUSPENDED BY PROX & DISTAL UMBILICAL TAPE

☐ 8FR SHEATH INTRODUCTION RFA PER 18G NEEDLE PUNCTURE ; SHEATH ANCHORED BY SINGLE 2-0 SILK TIE — * CONSIDER COPE ABOUT SHEATH THROUGHOUT STUDY

☐ SYSTEMIC HEPARINIZATION PER 4500U HEPARIN BOLUS

☐ 10:04 BASELINE HEMODYNAMICS [500 RADS]

☐ 10:10 INFLATION x2 @ 3.0 HARTZER ACX BALLOON IN MID-LCx
* NOTE: HUGE LCx SYSTEM @ 3.0mm ALONG COURSE TO MID-PDA

☐ 10:14 DORROS CATHETER PLACED mid LCx / CATHETER FLUSHED & HEPARIN-SALINE SOLN

☐ 10:15 IRRIDIUM 192 CATHETER PLACED IN MID-LCx
[32 mins : 500 RADS @ 5mm]

☐ 10:40 3cc 1% PENTOBARB ADMIN IVP

☐ 10:45 "HOT" CATHETER W/DRAWN / HEMODYNAMICS DONE / ANGIO = GOOD DISTAL FLOW

☐ 10:51 DORROS MANIPULATED W/O 2nd DIAG of LAD

☐ 10:52 "SEEDS" IN LAD DIAG BR [DIAG 1]
[32 mins : 500 RADS @ 5mm]

☐ 11:24 CATHETER W/DRAWN / HEMODYNAMICS DONE / CINE SHOWS GOOD DISTAL RUN-OFF

☐ TECHNICAL DIFFICULTY IN CLOSING ARTERIOTOMY [5.0 PROLENE EMPLOYED]

Photographs ☐
Roll # _____

☐ HEPARIN REVERSED & 35mg PROTAMINE IVP

☐ SKIN CLOSED & 2.0 VICRYL SUTURE

☐ ANIMAL TAKEN TO HOLDING AREA

Lab notes
8/21/91

2241

Protocol: Iridium Study

Investigators: Oesterle, Klonar

Number: 89-11-04

USC #

DATE: 2-7-90

Weight

Sex: ♂ ♀

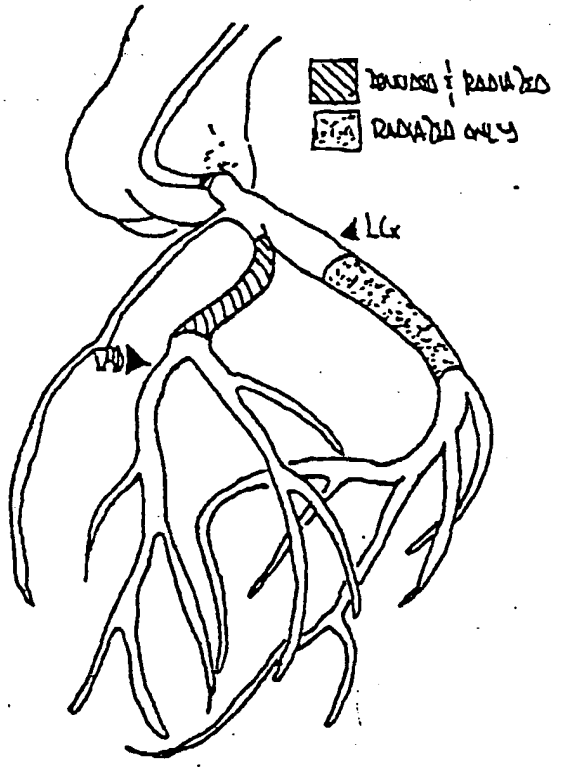
Drugs
Sodium Pentobarbital _____ ml
15 mg Morphine
Heparin
Bidal
Protamine

Isotopes — **Generation**

None	☐	
Ce	☐	_____
Ru	☐	_____
Nb	☐	_____
	Bin #	_____

*NOTE: ANIMAL IN (R) DECUBITUS POSITION ; IMAGED IN 30° LAO PROJECTION

Dead ☐
KCl under deep anesthesia ☐
Other _____

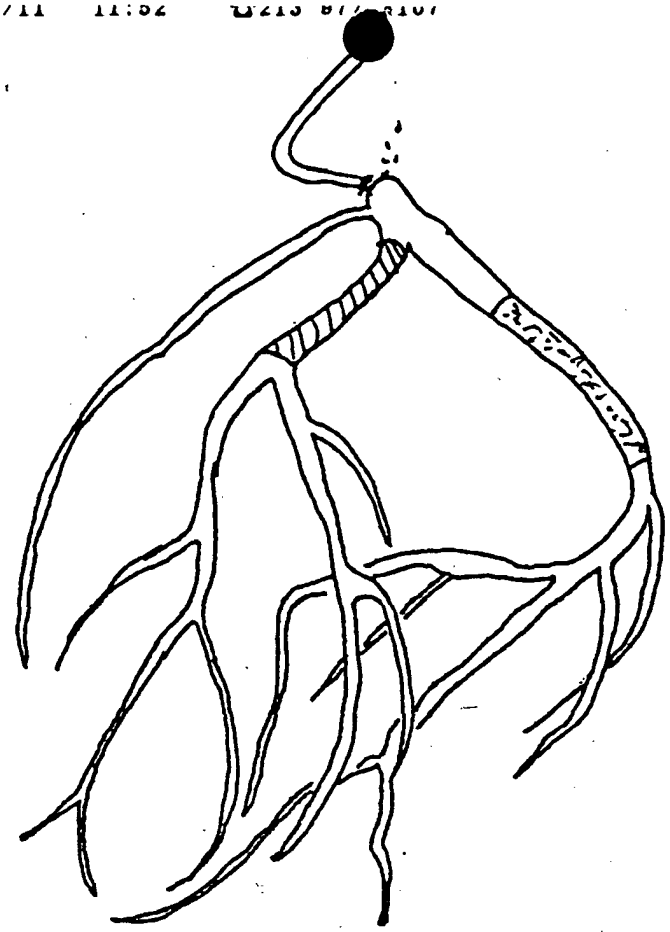


☐ ANIMAL SEDATED / SHAVED & TRANSPORTED TO LABS
☐ BILATERAL GROIN PREPPED / DRAPED IN USUAL STERILE FASHION
☐ (R) INGUINAL INCISION MADE / & BLUNT DISSECTION THE R FEM ART WAS ISOLATED & SUSPENDED BELOW UMBILICAL TAPES
☐ 6Fr SHEATH INTRODUCED TO RFA & ANCHORED TO SKIN BY SINGLE 2.0 TIE — # DOME ∓ ALONG TRACT AFFORDED ADEQUATE HEMOSTASIS
☐ ANIMAL SYSTEMMICALLY HEPARINIZED THE 3500 UNIT BOLUS IA
☐ 13:28 OPENING [BASELINE] HEMODYNAMICS RECORDED ON 250
☐ 13:35 2.5 μ BALLOON INFLATED x2 IN PROX LAD [PRIOR TO LRG 1ST DIAG BR]
☐ 13:41 IRRIDIUM 192 CATHETER ADVANCED TO LEVEL OF PROX LAD for 32 MINS [500 RADS @ 5cm]
☐ 13:50 0.5mg ATROPINE IVP
☐ 14:02 5cc NS+ PENTOBARB IVP
☐ 14:13 "HOT" CATHETER W/DRAWN FROM PROX LAD
☐ 14:15 DOSIMETRIC GUIDE PLACED PROX LCx & SUBSEQUENT "SEED WIRE" @ 14:17 HR [32 MINS: 500 RADS @ 5cm]
☐ 14:49 IRIDIUM CATHETER REMOVED FROM PROX LCx / HEMODYNAMICS PERFORMED AS WELL AS FINAL CINE ANGIOGRAPHY [DEMONSTRATED GOOD FLOW].
☐ SHEATH W/DRAWN ; ARTERIOTOMY SUTURED BY 5.0 PROLENE INTERRUPTED TIES
☐ ANIMAL'S HEPARIN IS REVERSED & ABX of _____ mg PENTOBARB IVS
☐ 5.0 VICRYL USED TO APPROX SUBQ FASCIA · MUSCLE & SKIN
☐ ANIMAL STABLE & RETURNED TO HOLDING AREA

Photographs ☐
Roll # _____

2241 - Marg.-	Normal.
2241 - LAD 1 [denuded & radiated]	Red cells and a few white cells adherent to intima. Vessel patent.
2241 - LAD 2 [denuded & radiated]	Severe intimal hyperplasia; lumen narrowed by about 25%.
2241 - LCX - 1 [radiated only]	Vessel patent. Mild to moderate intimal hyperplasia.
2241 - LCX - 2 [radiated only]	Mild to moderate intimal hyperplasia. Vessel patent.

Dog 2241
12 / 7 Feb 90



Bruised + Radiation

Radiation only

2207

Protocol: Oestrale : Radiation study

Investigators: Oesterle, Mehaffey, Dawson, Allen, Garner, Kloner

Number:

USC # 2616

DATE: 12/19/89

Weight 68 lbs / 30.9 kg

Sex ♂ ♀

Drugs

Sodium Pentobarbital ... ml

Brietal - 40 ml

Heparin - 4600 units

Protamine 46 mg

15mg Mo-Dine

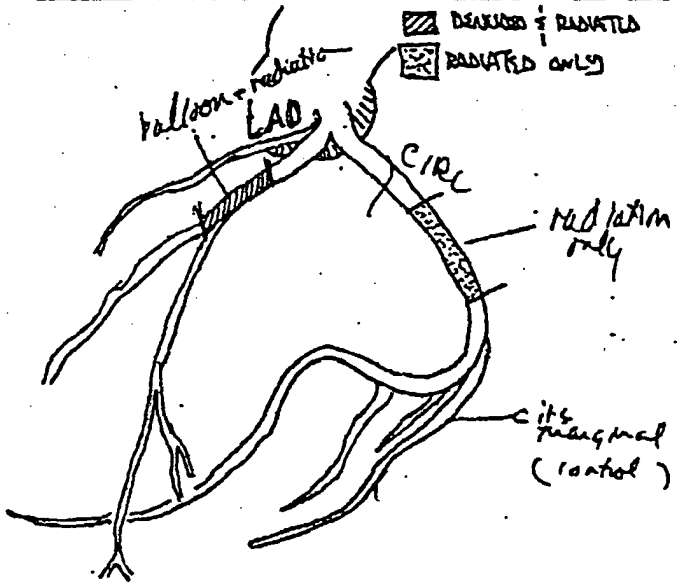
Isotopes **Generation**

None	☒	
Ce	☐	
Ru	☐	
Nb	☐	
Bin #		

Dead ☐

KCl under deep anesthesia ☐

Other



☑ LIDOCAINE INFILTRATION (R) GROIN

☑ PERCUTANEOUS INTRODUCTION 8F SHEATH TO (R) FA FOR SELDINGER TECHNIQUE ; 4600 U SYSTEMIC HEPARINIZATION

☑ angioplasty balloon 25 sulp (12 generation) for 1 min in proximal LAD denudation

☑ 11:59 AM - 12:19 irridium in prox. LAD. ← blue catheter prior to first large diagonal ○ CINE C 12:09 } GOOD FLOW CINE C 12:19 }

☑ 12:23 AM — 12:42 irridium in mid circ. — no denudation

CINE ANGIO @ 12:53 & 12:42 DEMONSTRATES GOOD RUN-OFF

☑ CATHETER W/DRAWN : FINAL CINE PERFORMED ANIMAL IN SEVERE TACHYCARDIA

☑ 46mg PROTAMINE ADMINISTERED

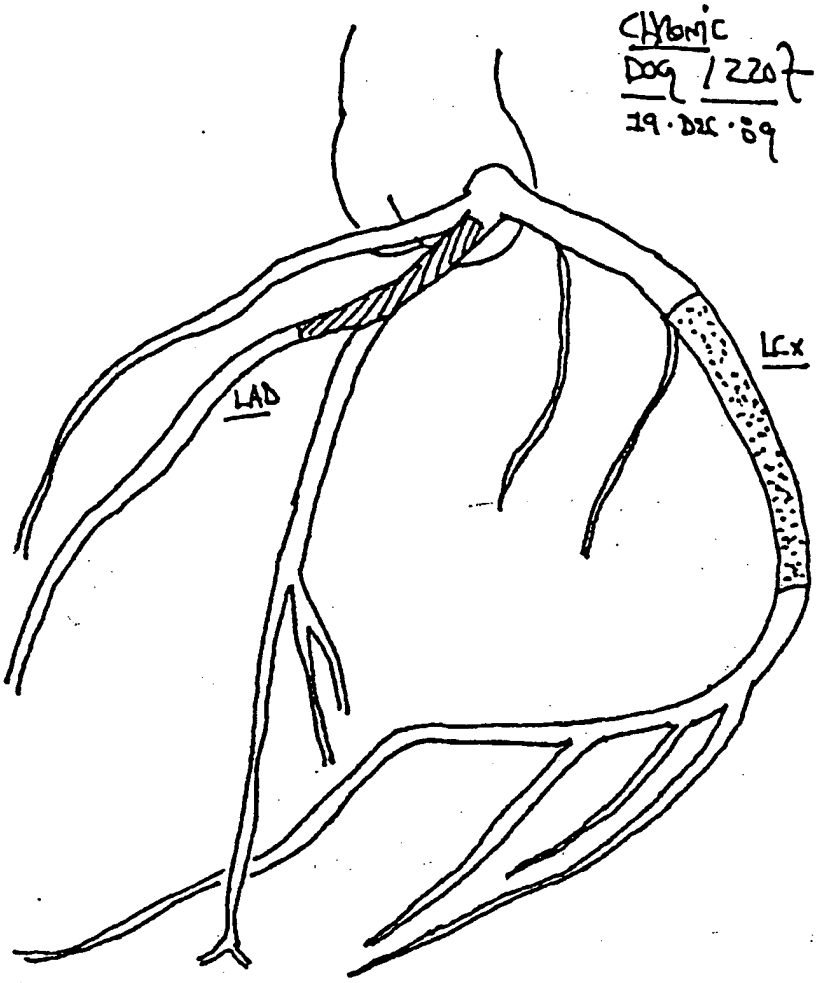
☑ SHEATH W/DRAWN ; DIGITAL PRESSURE APPLIED (R) GROIN FOR HEMOSTASIS (15min.)

☑ NO HEMATOMA

Photographs ☐

Roll #

CHRONIC
DOG / 2207
19 · DEC · 89



DENUDED & IRRADIATED
IRRADIATED ONLY

Dr. Kloners's path reading

April 5, 1990

2207 Chronic	
2207 Marginal	Poor slide. Small arteriole branch appears normal; no large vessel.
2207 LAD 1 (denude & radiate)	Vessel patent. Zone of intimal hyperplasia in one area. Intima appears lifted off of vessel ? artefact.
2207 *LAD 2	Vessel narrowed by about 40% by severe intimal hyperplasia. Very striking finding.
2207 CIRC-1 (Radiate only)	Moderate intimal hyperplasia but vessel patent.
2207 CIRC 2	Normal.

Protocol: 00812 : RADIA[redacted]3004

Investigators: ~~Brotzer~~ Oesterle
Hirsch, Dawson, Aiken
Klonen, Gaver

[redacted] Number:

USC # 2630

DATE: 12·19·89

Weight 82 lbs / 37.5 kg

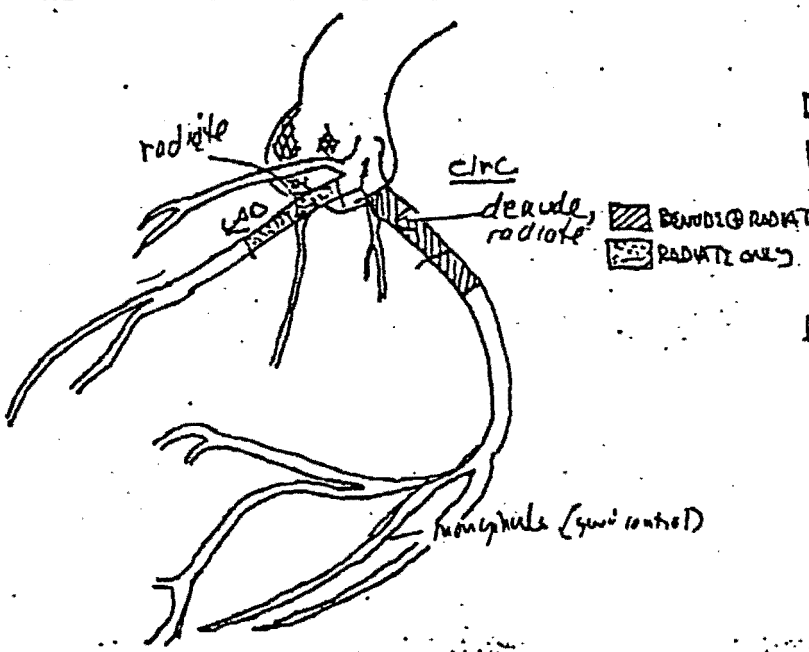
Sex ♂ ♀

Drugs
Sodium Pentobarbital ____ ml
Biotal - 40
Heparin 4500 U
protamine 40 mg.
15 mg Morphine

Isotopes — **Generation**

None	☑	
Ce	☐	____
Ru	☐	____
Nb	☐	____
	Bin #	____

Dead ☐
KCl under deep anesthesia ☐
Other ____



☑ 1% LIDOCAINE 40cm SUB-Q (R) GROIN
☑ PERCUTANEOUS INTRODUCTION 8FR SHEATH (R) FM
☑ 4500 U SYSTEMIC HEPARINIZATION
☑ angioplasty balloon inflated proximal circ 1.5 min.
3.0 balloon : ACS SULPIT
☑ doppler catheter in LCX
☑ irridium - 500 rads at 5 mm (19 min)
@ in at 10:07 AM — 10:26] circ
ANGIO @ 10:17 / ANGIO @ 10:26
GOOD DISTAL RUN-OFF DEMONSTRATED
☑ irridium - 500 rads at 5 mm
10:33 — 10:52 19 min.] LAD
ANGIO @ 10:43 / 10:52 = GOOD DISTAL FLOW
☑ final clin - good flow
CATHETER W/DRAWN W/O CLOTS
☑ Yomey PROAMINE JVP
☑ ANIMAL TRANSPORTED TO RECOVERY WHERE SHEATH W/DRAWN & SUBSEQUENT BRIZIAL PRESSURE APPLIED (R) GROIN FOR HEMOSTASIS

☑ HEMOSTASIS ACHIEVED W/ MANUAL PRESSURE — NO HEMATOMA NOTED

Photographs ☐
Roll # ____

CURRICULUM VITAE

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1983	Subspecialty Board, Cardiovascular Medicine

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