DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

6 MAY 2016

MEMORANDUM FOR ST
ATTN: KEVIN WU

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Graft-Impacted Tacrolimus-Eluting Hydrogels Prolong Survival After Vascularized Composite Allografts** presented at/published to **Association of Surgeons Great Britain and Ireland 11-13 May 2016** with MDWI 41-108, and has been assigned local file #**16194.**

2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.

4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

INSTRUCTIONS

USE ONLY THE MOST CURRENT 59 MDW FORM 3039 LOCATED ON AF E-PUBLISHING

1. The author must complete page two of this form:
   a. In Section 2, add the funding source for your study [e.g., 59 MDW CRD Graduate Health Sciences Education (GHSE) (SG5 O&M); SG5 R&D; Tri-Service Nursing Research Program (TSNRP); Defense Medical Research & Development Program (DMRDP); NIH; Congressionally Directed Medical Research Program (CDMRP) ; Grants; etc.]

   b. In Section 2, there may be funding available for journal costs, if your department is not paying for figures, tables or photographs for your publication. Please state "YES" or "NO" in Section 2 of the form, if you need publication funding support.

2. Print your name, rank/grade, sign and date the form in the author's signature block or use an electronic signature.

3. Attach a copy of the 59 MDW IRB or IACUC approval letter for the research related study. If this is a technical publication/presentation, state the type (e.g. case report, QA/QI study, program evaluation study, informational report/briefing, etc.) in the "Protocol Title" box.

4. Attach a copy of your abstract, paper, poster and other supporting documentation.

5. Save and forward, via email, the processing form and all supporting documentation to your unit commander, program director or immediate supervisor for review/approval.

6. On page 2, have either your unit commander, program director or immediate supervisor:
   a. Print their name, rank/grade, title; sign and date the form in the approving authority's signature block or use an electronic signature.

7. Submit your completed form and all supporting documentation to the CRD for processing (59crdpubspres@us.af.mil). If you have any questions or concerns, please contact the 59 CRD/ Publications and Presentations Section at 292-7141 for assistance.

8. The 59 CRD/Publications and Presentations Section will route the request form to clinical investigations, 502 ISG/JAC (Ethics Review) and Public Affairs (59 MDW/PA) for review and then forward you a final letter of approval or disapproval.

9. Once your manuscript, poster or presentation has been approved for a one-time public release, you may proceed with your publication or presentation submission activities, as stated on this form. **Note:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.

10. If your manuscript is accepted for scientific publication, please contact the 59 CRD/Publications and Presentations Section at 292-7141. This information is reported to the 59 MDW/CC. All medical research or technical information publications/presentations must be reported to the Defense Technical Information Center (DITC). See 59 MDWI 41-108, *Presentation and Publication of Medical and Technical Papers*, for additional information.

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement:
"The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement for research involving humans:
"The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402."

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement for research involving animals, as required by AFMAN 40-401_IP :
"The experiments reported herein were conducted according to the principles set forth in the National Institute of Health Publication No. 80-23, Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966, as amended."

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1. TO: CLINICAL RESEARCH	2. FROM: (Author's Name, Rank, Grade, Office Symbol)	3. GME/GHSE STUDENT:	4. PROTOCOL NUMBER:
	Kevin Wu, CTR	☒ YES ☐ NO	NAVY15-09

5. PROTOCOL TITLE: (**NOTE:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)

Vascularized Composite Allotransplantation (VCA) in Swine (Sus scrofa) for Optimization of Reconstruction of Battlefield Injuries Using the

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:

Graft-Implanted Tacrolimus-Eluting Hydrogels Prolong Survival After Vascularized Composite AllograftsT

7. FUNDING RECEIVED FOR THIS STUDY? ☒ YES ☐ NO FUNDING SOURCE: AFMSA/ 59MDW ST

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: ☐ YES ☒ NO

9. IS THIS MATERIAL CLASSIFIED? ☐ YES ☒ NO

10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.?
☐ YES ☒ NO **NOTE:** If the answer is YES then attach a copy of the Agreement to the Publications/Presentations Request Form.

11. MATERIAL IS FOR: ☐ DOMESTIC RELEASE ☒ FOREIGN RELEASE
CHECK APPROPRIATE BOX OR BOXES FOR APPROVAL WITH THIS REQUEST. ATTACH COPY OF MATERIAL TO BE PUBLISHED/PRESENTED.

☐ 11a. PUBLICATION/JOURNAL (List intended publication/journal.)

☐ 11b. PUBLISHED ABSTRACT (List intended journal.)

☐ 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.)

☐ 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meting.)
Association of Surgeons of Great Britain and Ireland/ 11-13 May 2016

☐ 11e. OTHER (Describe: name of meeting, city, state, and date of meeting.)

12. EXPECTED DATE WHEN YOU WILL NEED THE CRD TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC
NOTE: All publications/presentations are required to be placed in the Defense Technical Information Center (DTIC).

DATE: May 10, 2016

13. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email)	14. DUTY PHONE/PAGER NUMBER
Corpus Raul S, raul.s.corpus.ctr@mail.mil	2105394404

15. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.

LAST NAME, FIRST NAME AND M.I.	GRADE/RANK	SQUADRON/GROUP/OFFICE SYMBOL	INSTITUTION (If not 59 MDW)
a. Primary/Corresponding Author Kevin Wu	CTR	59MDW ST RESTOR	
b. Renford Cindass	O-3	59MDW ST RESTOR	
c. Shari Lawson	CTR	59MDW ST RESTOR	
d. Mark Roth			FHCRC
e. Vijay Gorantla			UPITT
f. Michael Davis	O-5	59MDW ST RESTOR	

I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401_IP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.

16. AUTHOR'S PRINTED NAME, RANK, GRADE	17. AUTHOR'S SIGNATURE	18. DATE
Kevin Wu, CTR		April 26, 2016
19. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE	**20. APPROVING AUTHORITY'S SIGNATURE**	**21. DATE**
Michael R Davis, Lt Col, Director-RESTOR, Deputy Commander		April 26, 2016

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1st ENDORSEMENT (59 MDW/SGVU Use Only)

TO: Clinical Research Division 59 MDW/CRD Contact 292-7141 for email instructions.	22. DATE RECEIVED 4/26/2016	23. ASSIGNED PROCESSING REQUEST FILE NUMBER 16194
24. DATE REVIEWED 29 Apr 2016		25. DATE FORWARDED TO 502 ISG/JAC

26. AUTHOR CONTACTED FOR RECOMMENDED OR NECESSARY CHANGES: ☒ NO ☐ YES If yes, give date. _____ ☐ N/A

27. COMMENTS ☒ APPROVED ☐ DISAPPROVED

The presentation is approved. The presentation should receive a legal ethics review since it is being given to a foreign audience.

28. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	29. REVIEWER SIGNATURE	30. DATE
Rocky Calcote, PhD, Clinical Res. Administrator	CALCOTE.ROCKY.D.1178245844 Digitally signed by CALCOTE.ROCKY.D.1178245844 DN: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=CALCOTE.ROCKY.D.1178245844 Date: 2016.04.29 07:02:22 -05'00'	

2nd ENDORSEMENT (502 ISG/JAC Use Only)

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34. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	35. REVIEWER SIGNATURE	36. DATE

3rd ENDORSEMENT (59 MDW/PA Use Only)

37. DATE RECEIVED 6 May 2016	38. DATE FORWARDED TO 59 MDW/SGVU 6 May 2016

39. COMMENTS ☑ APPROVED (In compliance with security and policy review directives.) ☐ DISAPPROVED

40. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	41. REVIEWER SIGNATURE	42. DATE
Christopher Carwile, TSgt/E-6, NCOIC, PA	CARWILE.CHRISTOPHER.STEWART.1280477229 Digitally signed by CARWILE.CHRISTOPHER.STEWART.1280477229 DN: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=CARWILE.CHRISTOPHER.STEWART.1280477229 Date: 2016.05.06 11:15:14 -05'00'	6 May 2016

4th ENDORSEMENT (59 MDW/SGVU Use Only)

43. DATE RECEIVED	44. SENIOR AUTHOR NOTIFIED BY PHONE OF APPROVAL OR DISAPPROVAL ☐ YES ☐ NO ☐ COULD NOT BE REACHED ☐ LEFT MESSAGE

45. COMMENTS ☐ APPROVED ☐ DISAPPROVED

46. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	47. REVIEWER SIGNATURE	48. DATE

Graft-Implanted Tacrolimus-Eluting Hydrogels Prolong Survival After Vascularized Composite Allografts

Kevin Wu, Renford Cindass, Shari Lawson Jerry R Spencer, Mark Roth,

VS Gorantla, Michael R Davis

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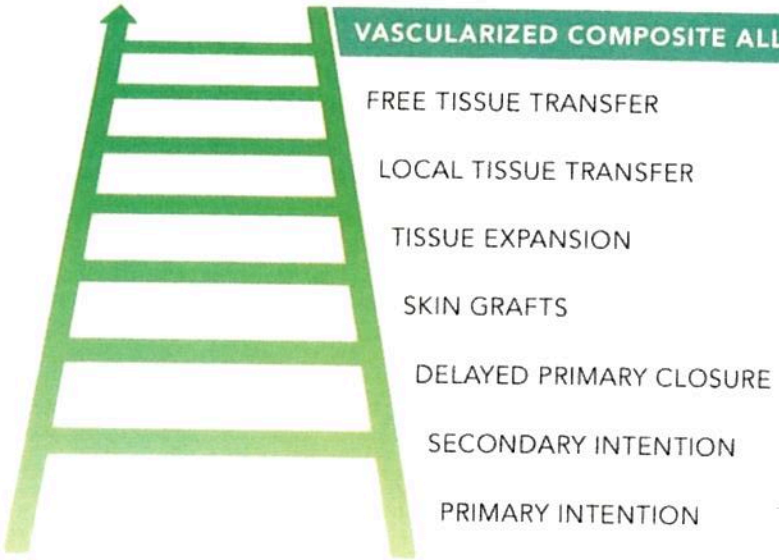
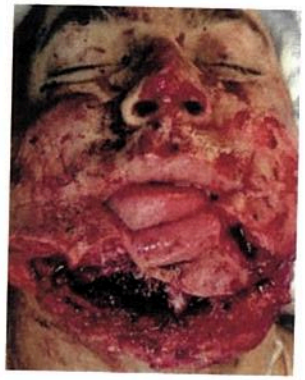
Disclaimer

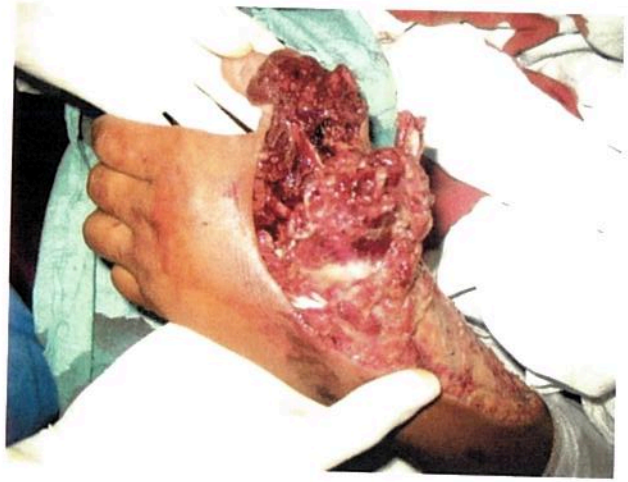
The views expressed are those of the authors and do not reflext the official view or policy of the Department of Defense, Department of the Army, Department of the Air Force or its Components.

The experiments reported herein were conducted according to the principles set forth in the National Institute of Health Publication 80-23, Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966, as amended

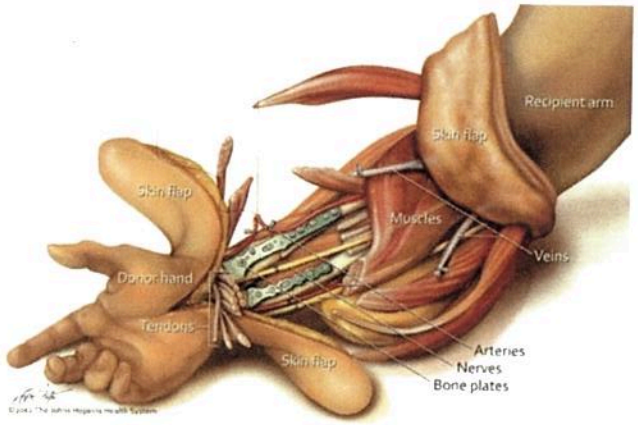
Vascularized composite allotransplantation (VCA)





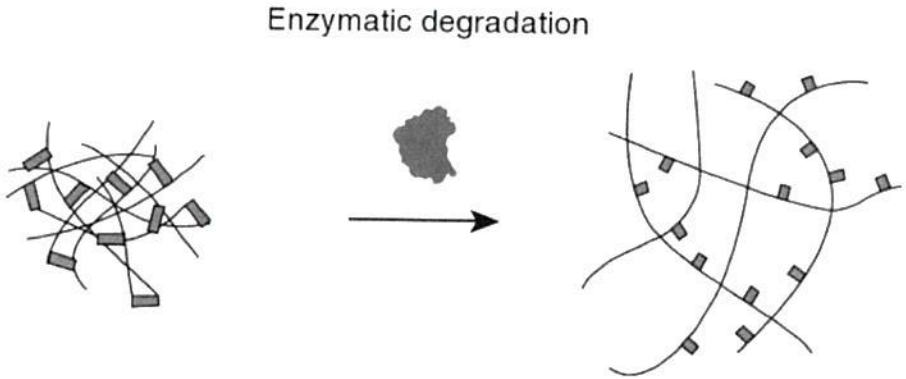


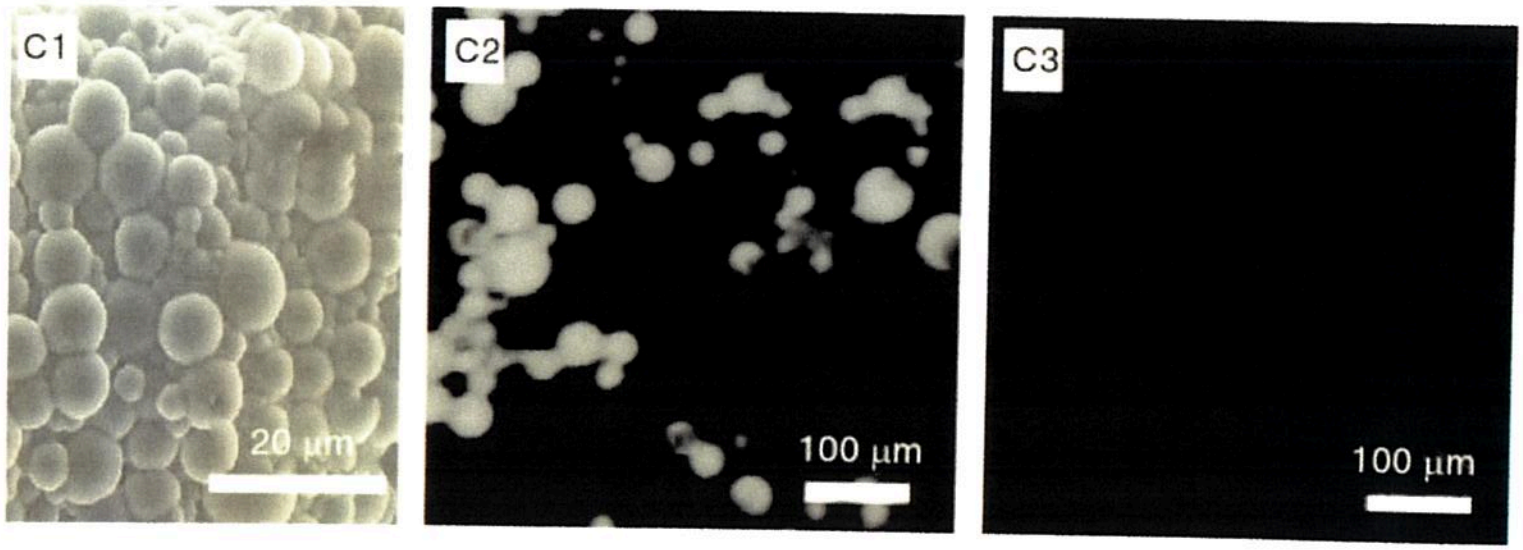
Current limitations to vascularized composite allotransplantation (VCA)



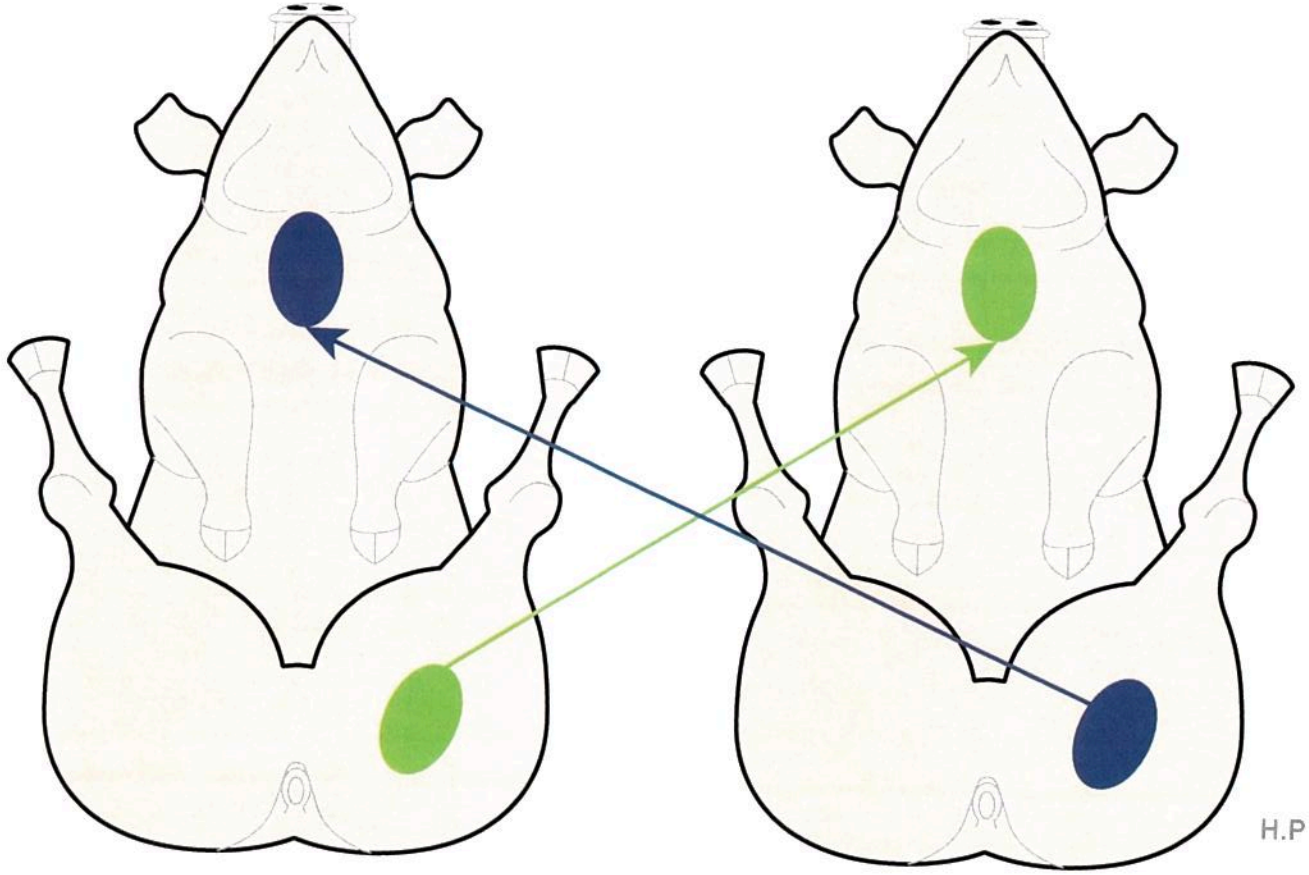
- Requires systemic immunosuppression
- Skin is a primary target for rejection
- Limited donor pool
- Shorter period for ischemia time
- Ischemic reperfusion injury

Enzyme Activated Drug Eluting Hydrogel

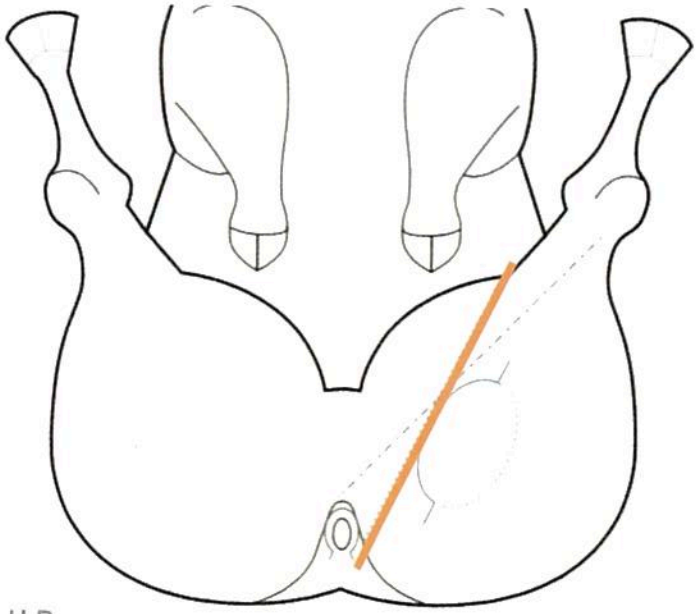




Allotransplantation



Gracilis myocutaneous VCA model



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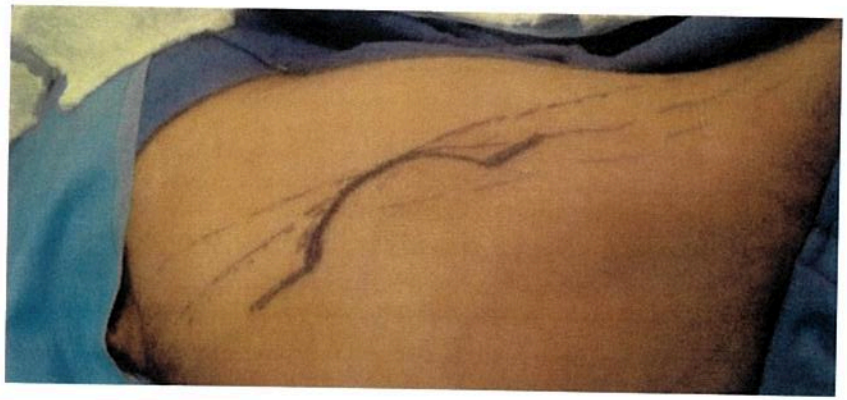
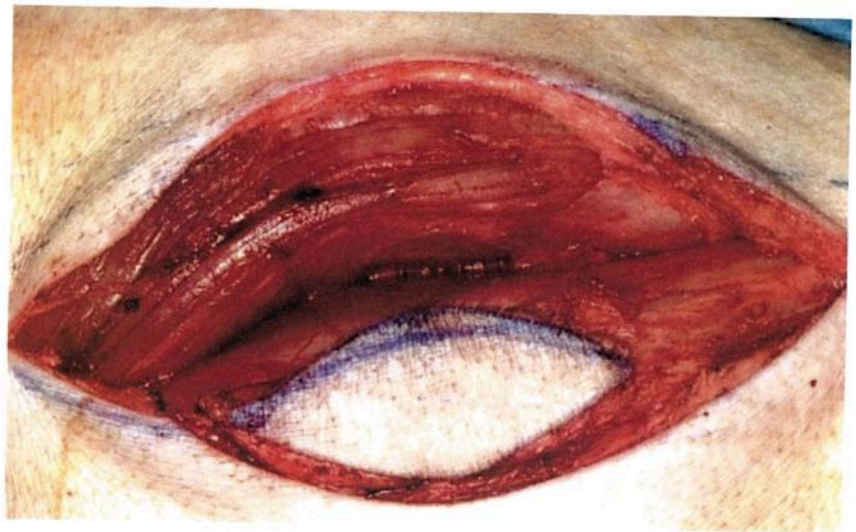
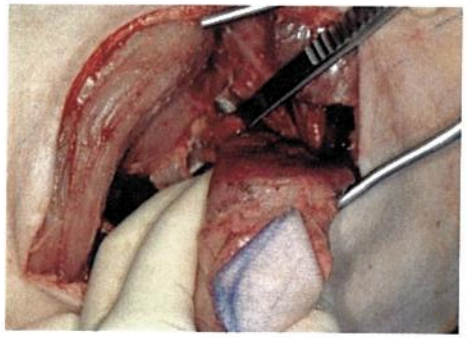
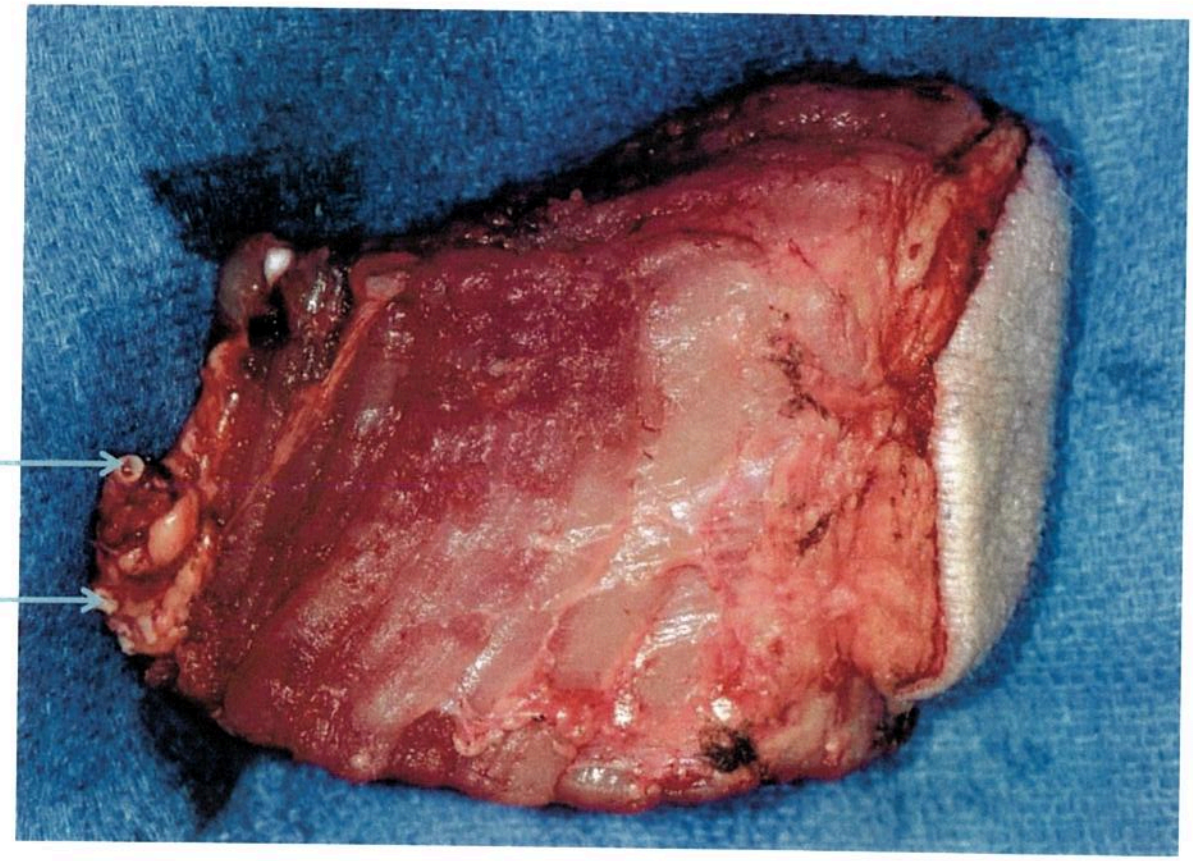


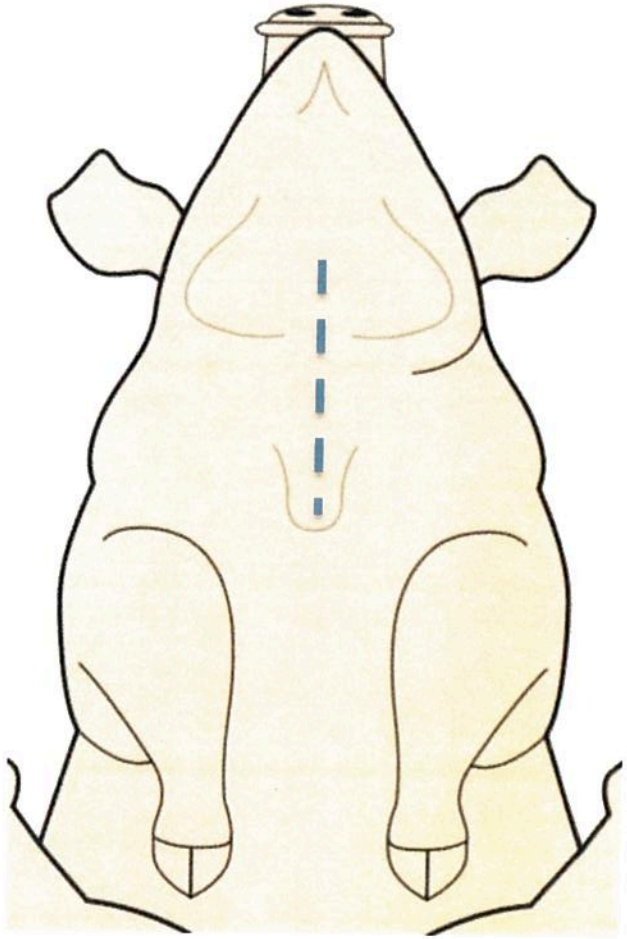


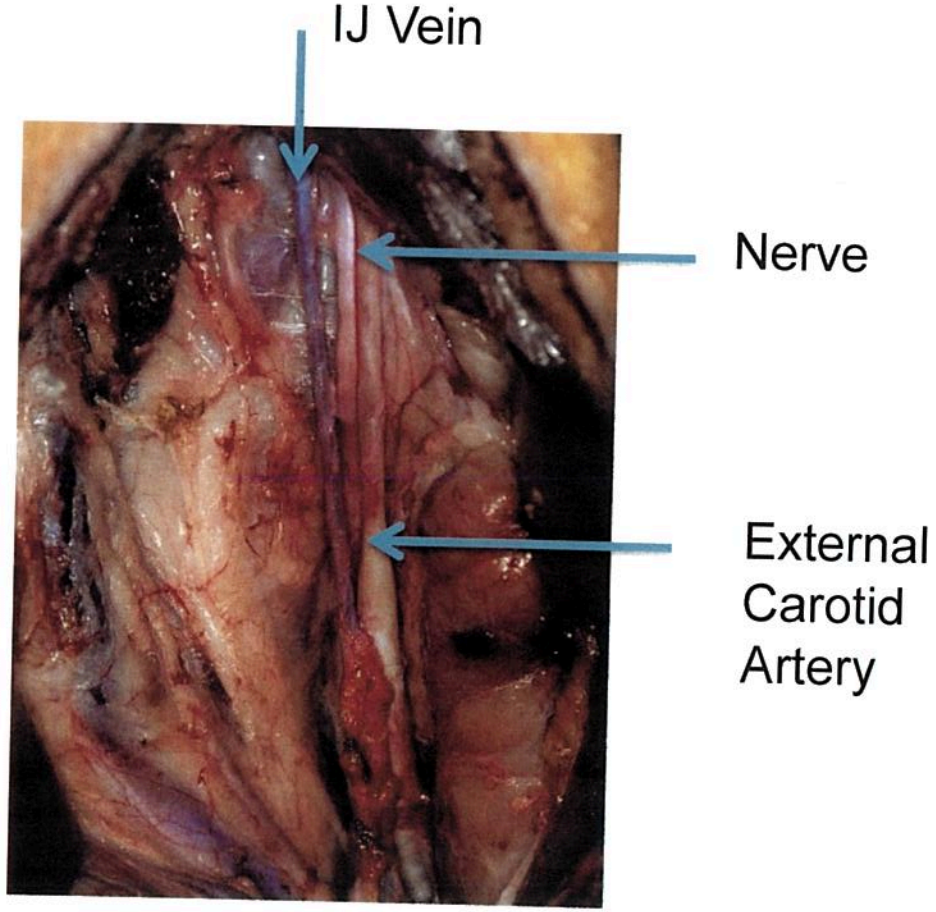
Gracilis myocutaneous VCA model



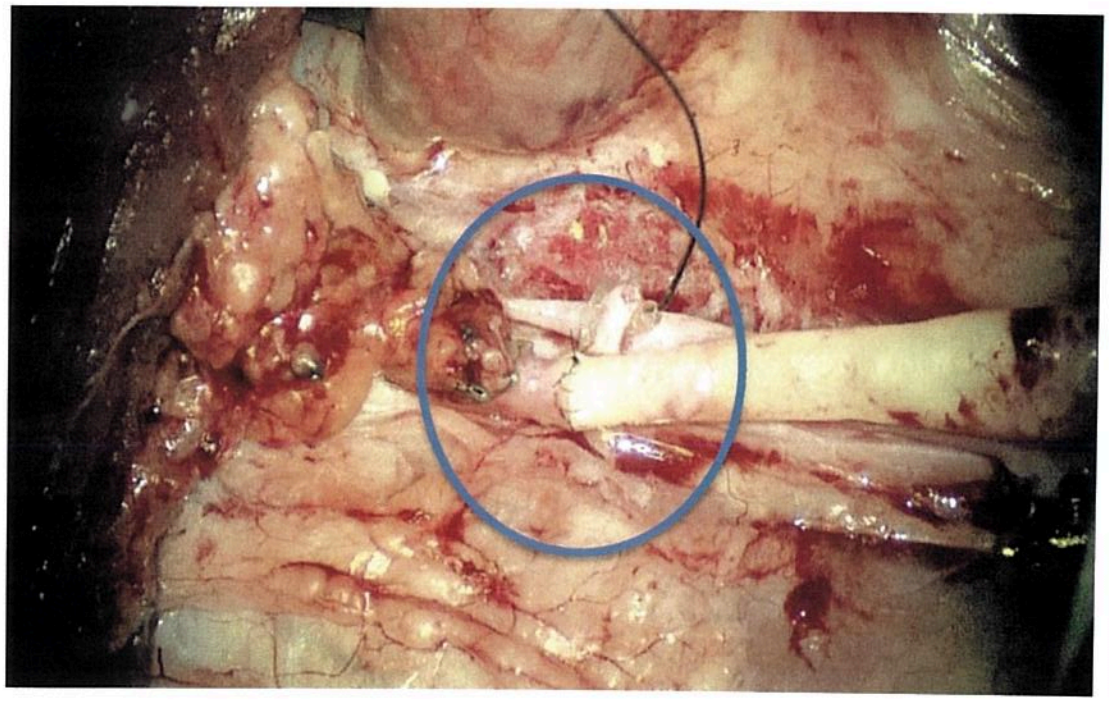


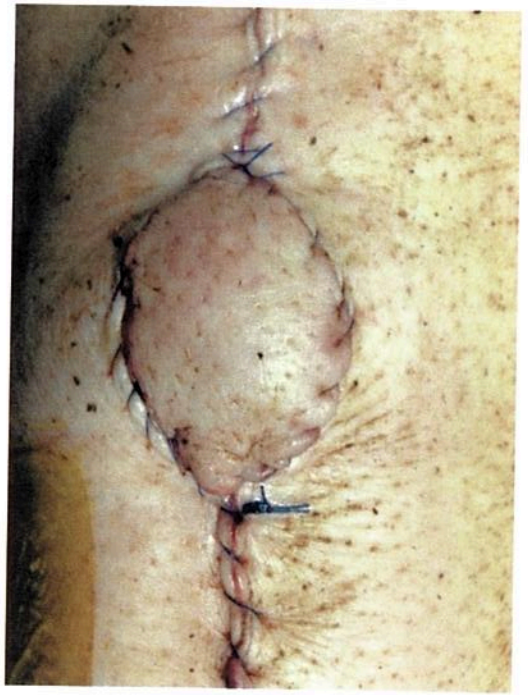
Gracilis myocutaneous VCA model





Gracilis myocutaneous VCA model





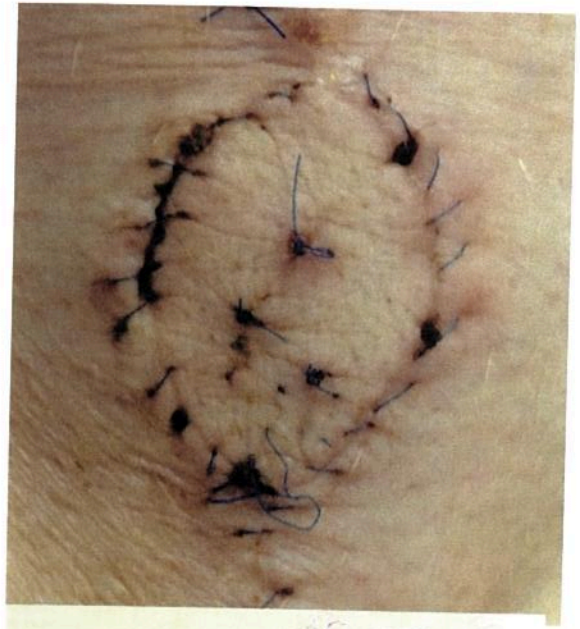
Methods

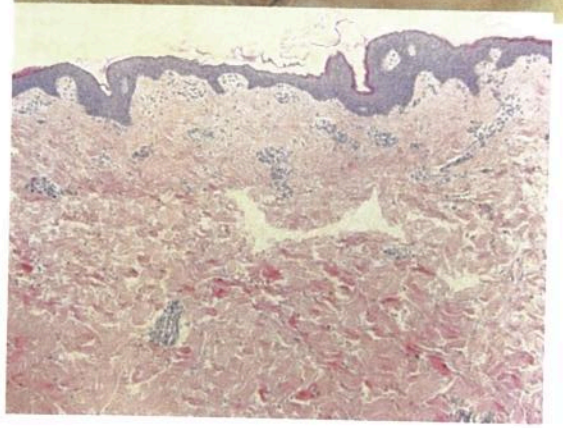
- Heterotopic gracilis myocutaneous flap VCA was performed between swine donor-recipient pairs with a single swine leukocyte antigen (SLA) mismatch.

- 2 Groups
  - Group 1 (controls, n=8) received no drug intervention.
  - Group 2 (experimental, n=3), a tacrolimus-eluting hydrogel (28 mg in 4 cc) was injected subcutaneously into the donor flap immediately before end of ischemia time.

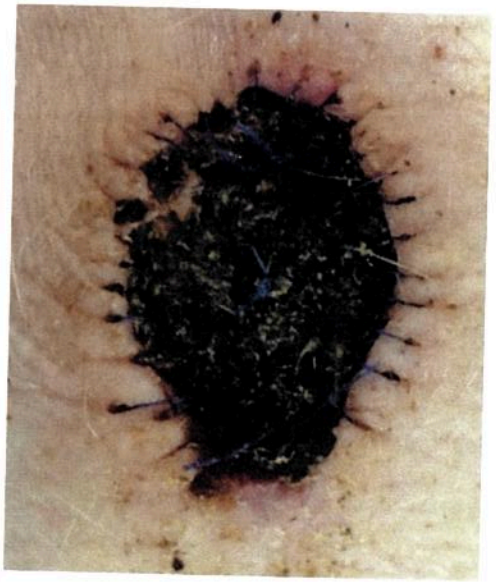
- Post-operative period
  - 4-mm punch biopsy every 1-3 days for 23 days
  - Blinded histologic examination using Banff working classification

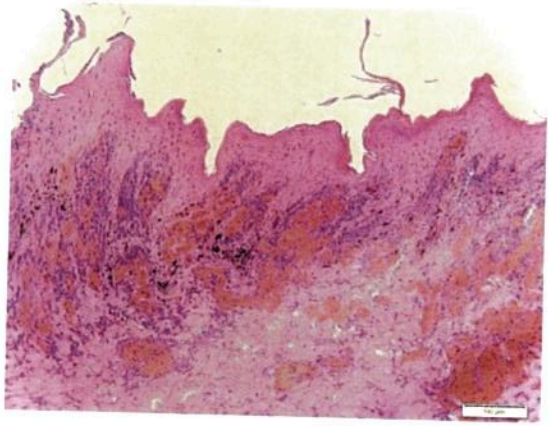
Results





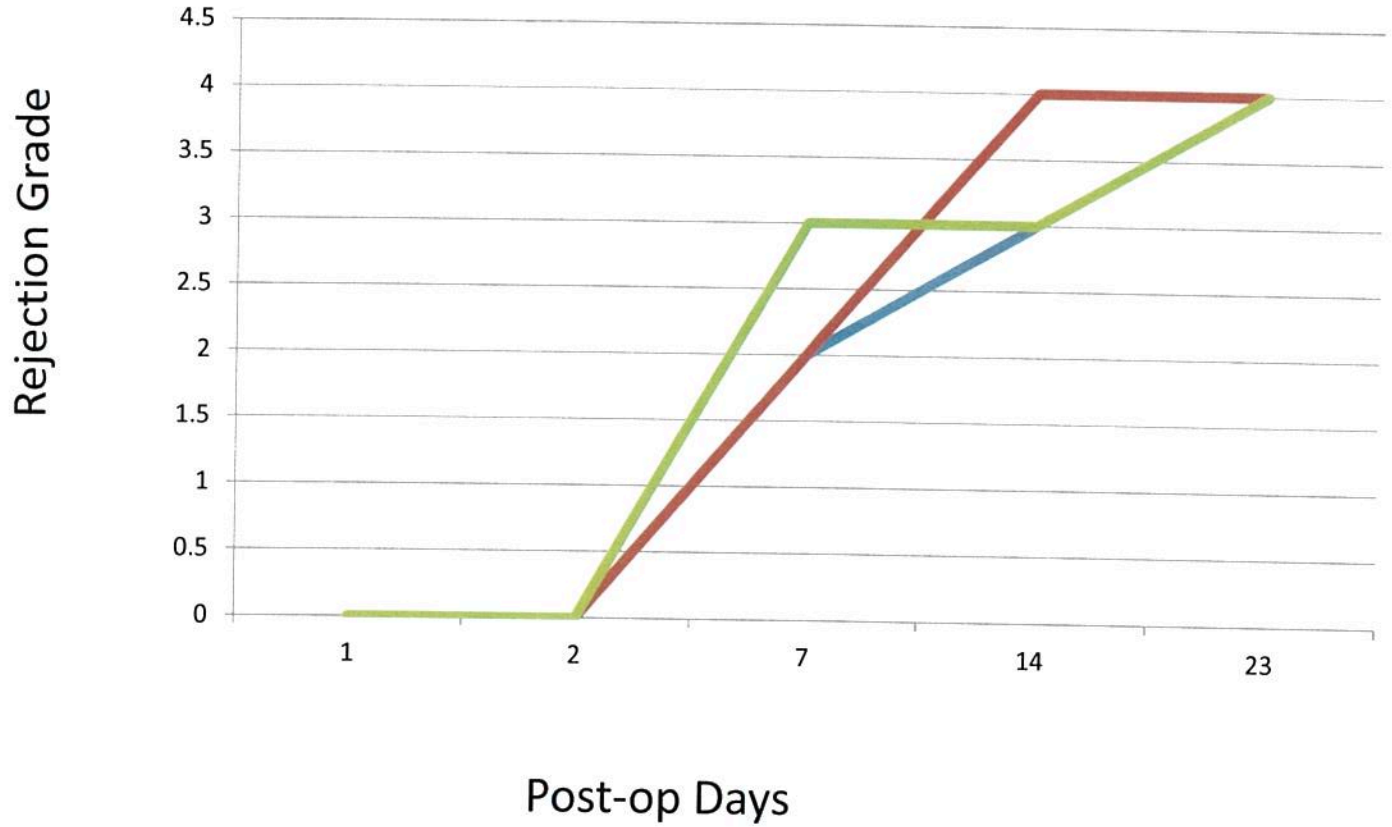
Grade 0



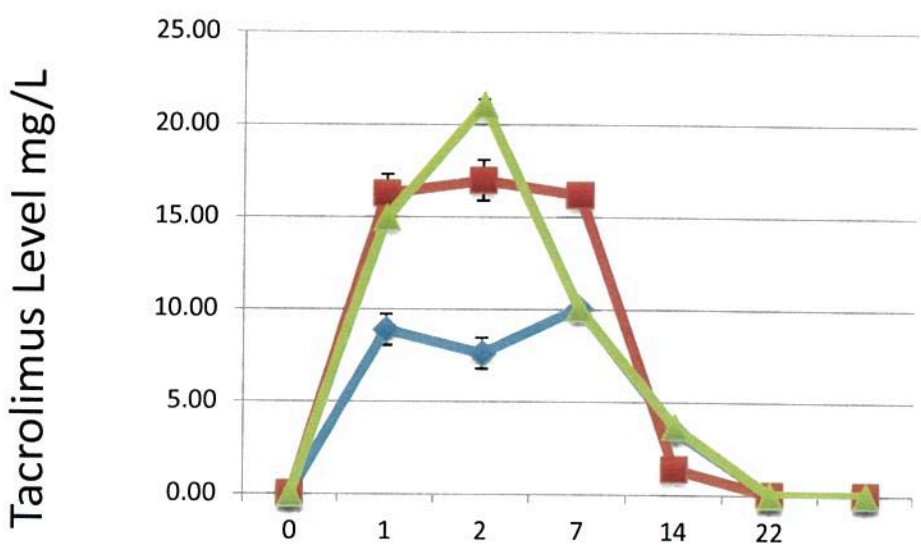


Grade 4

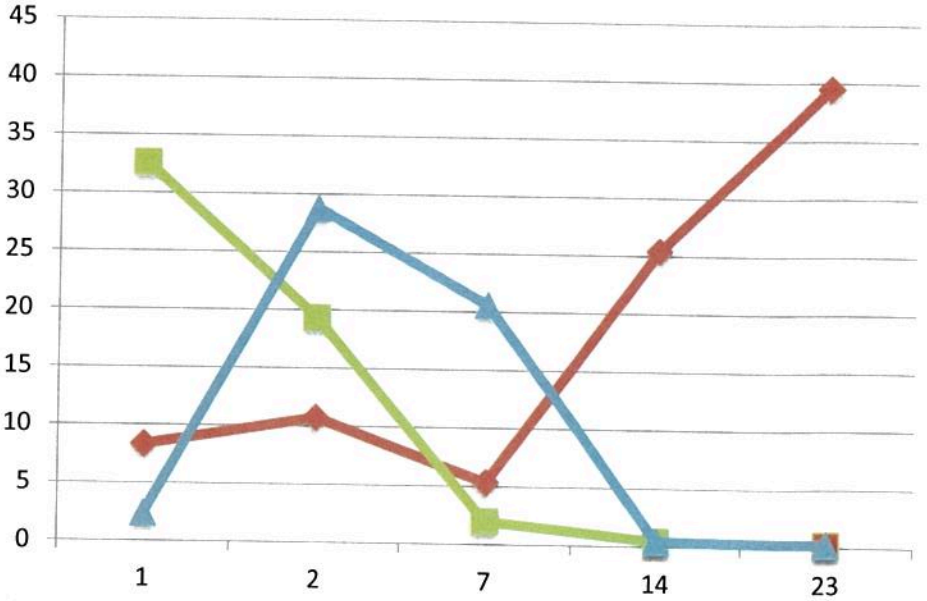
Time to rejection



Tacro Blood Level



Tacro Tissue Level



Post-op Days

Conclusions

- Swine gracilis myocutaneous flap is a reliable and consistent animal model for studying VCA rejection
- Analysis of gel exhaustion related to the inflammatory and acute rejection process aids in timing and dosage of the subsequent reload of the gel
- Hydrogels are able to delay the onset of acute rejection regionally and without clinically detectable systemic levels of tacrolimus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Thank You