

AD-A201 453

AD

3

TECHNICAL REPORT 8811

DTIC FILE COPY

USE OF ELECTRICAL IMPEDANCE TO ASSESS
FROSTBITE INJURY SEVERITY IN A SWINE

By

Patricia M. Dubill; Neil W. Ahle, CPT; Mark W. Sharp, SSG;
Rodrigo A. Mariano, SGT; Florence H. Broski; and Stephen J. Engler, VMD

15 September 1988

Final Report for Period Covering January 1987-September 1988

U S ARMY BIOMEDICAL RESEARCH & DEVELOPMENT LABORATORY
Fort Detrick
Frederick, MD 21701-5010

Approved for Public Release; Distribution
is Unlimited.



U S ARMY MEDICAL RESEARCH & DEVELOPMENT COMMAND
Fort Detrick
Frederick, MD 21701-5012

88 11 3 06 9

DISCLAIMER STATEMENT

The views, opinions, and/or findings contained in this report are those of the authors and should not be construed as official Department of the Army position, policy, or decision, unless so designated by other official documentation. In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care," as promulgated by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences, National Research Council.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

| | | | |
|--|--|---|-------------------------------------|
| 1. REPORT SECURITY CLASSIFICATION Unclassified | | 1b. RESTRICTIVE MARKINGS | |
| 2. SECURITY CLASSIFICATION AUTHORITY | | 3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for Public Release; Distribution is Unlimited. | |
| 3. DECLASSIFICATION/DOWNGRADING SCHEDULE | | 5. MONITORING ORGANIZATION REPORT NUMBER(S) | |
| 4. PERFORMING ORGANIZATION REPORT NUMBER(S) 8811 | | 7a. NAME OF MONITORING ORGANIZATION | |
| 5. NAME OF PERFORMING ORGANIZATION J.S. Army Biomedical Research and Development Laboratory | | 6b. OFFICE SYMBOL (if applicable) | |
| 6. ADDRESS (City, State, and ZIP Code) Fort Detrick Frederick, MD 21701-5010 | | 7b. ADDRESS (City, State, and ZIP Code) | |
| 8. NAME OF FUNDING/SPONSORING ORGANIZATION | | 9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER | |
| 8b. OFFICE SYMBOL (if applicable) | | 10. SOURCE OF FUNDING NUMBERS | |
| c. ADDRESS (City, State, and ZIP Code) | | PROGRAM ELEMENT NO. 62787A | PROJECT NO. 3S162787 A874 |
| | | TASK NO. BA | WORK UNIT ACCESSION NO. 225 7740 |

1. TITLE (Includes Security Classification)
(U) Use of Electrical Impedance to Assess Frostbite Injury Severity in a Swine

2. PERSONAL AUTHOR(S) Dubill, Patricia M., Ahle, Neil W., Sharp, Mark W., Mariano, Rodrigo A., Broski, Florence H., Engler, Stephen J.

| | | | |
|-----------------------------|--|--|----------------------|
| 3a. TYPE OF REPORT Final | 13b. TIME COVERED FROM 1/87 TO 9/88 | 14. DATE OF REPORT (Year, Month, Day) 1988 September 15 | 15. PAGE COUNT 22 |
|-----------------------------|--|--|----------------------|

6. SUPPLEMENTARY NOTATION

| | | | |
|-----------------|-------|-----------|--|
| 7. COSATI CODES | | | 18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number) Detector, Necrosis, Debridement, RA II, Lab Animals, Pig |
| FIELD | GROUP | SUB-GROUP | |
| 23 | 01 | | |

8. ABSTRACT (Continue on reverse if necessary and identify by block number)
 Management of frostbite poses a significant problem for the military, because the accepted method of treatment, waiting for demarcation of necrotic tissue, is unsuitable for the combat casualty care environment. A preferable method of frostbite management would be development of an objective indicator of tissue viability that could be used to guide debridement soon after injury, minimizing the hospital stay. Based on previous work on necrotic tissue detection, electrical impedance was studied for its potential in assessing frostbite injury severity. An air jet cooler system was used on one swine to produce 48 lesions of different severities by varying the freeze time. Results from measurements made 1, 2 and 3 days post-freezing indicated a significant difference between mean impedance for controls and second and third degree lesions, but not between mean impedance for second and third degree lesions. The small sample size limits interpretation of the results, and it is possible that significant differences between degrees of frostbite would be seen if additional test animals are used. If further studies are pursued, additional technologies should be considered and the measurement period should be extended beyond three days post-injury.

| | | | |
|--|--|--|----------------------------------|
| 9. DISTRIBUTION/AVAILABILITY OF ABSTRACT <input checked="" type="checkbox"/> UNCLASSIFIED/UNLIMITED <input type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS | | 21. ABSTRACT SECURITY CLASSIFICATION Unclassified | |
| 10. NAME OF RESPONSIBLE INDIVIDUAL Patricia M. Dubill | | 22b. TELEPHONE (Include Area Code) (301) 663-7527 | 22c. OFFICE SYMBOL SGRD-UBE-C |

Technical Report

8811

Use of Electrical Impedance to Assess
Frostbite Injury Severity in a Swine

by

Patricia M. Dubill, Neil W. Ahle CPT, Mark W. Sharp SSG,
Rodrigo A. Mariano SGT, Florence H. Broski, and Stephen J. Engler, VMD

U.S. Army Biomedical Research and Development Laboratory
Frederick, Maryland 21701-5010

TABLE OF CONTENTS

| | Page |
|---------------------------------|------|
| INTRODUCTION | 1 |
| MATERIALS AND METHODS | 3 |
| RESULTS | 7 |
| DISCUSSION | 10 |
| CONCLUSIONS AND RECOMMENDATIONS | 11 |
| REFERENCES | 12 |



| | |
|----------------------------|-------------------------------------|
| | |
| THIS DRAWING | <input checked="" type="checkbox"/> |
| IS TO BE | <input type="checkbox"/> |
| REPRODUCED | <input type="checkbox"/> |
| BY THE DTIC | |
| ON BEHALF OF THE | |
| DEFENSE DEPARTMENT | |
| WASHINGTON, D. C. | |
| OFFICE OF THE | |
| DIRECTOR | |
| OF THE | |
| DEFENSE INFORMATION CENTER | |
| COLUMBIA UNIVERSITY | |
| NEW YORK, N. Y. | |
| A-11 | |

PREFACE

This research was done in conjunction with a study by USARIEM personnel to develop a quantitative, reproducible method for producing first, second, and third degree frostbite. At the time of the experiment, the exact values of freezing parameters to achieve each degree of severity were unknown, so design of a balanced statistical experiment was not possible. The authors wish to acknowledge the assistance of Mr. Darryl Fritz, Dr. Cenzgis Topakoglu, and Dr. Murray Hamlet.

ABSTRACT

Management of frostbite poses a significant problem for the military, because the accepted method of treatment, waiting for demarcation of necrotic tissue, is unsuitable for the combat casualty care environment. A preferable method of frostbite management would be development of an objective indicator of tissue viability that could be used to guide debridement soon after injury, minimizing the hospital stay. Based on previous work on necrotic tissue detection, electrical impedance was studied for its potential in assessing frostbite injury severity. An air jet cooler system was used on one swine to produce 48 lesions of different severities by varying the freeze time. Results from measurements made 1, 2 and 3 days post-freezing indicated a significant difference between mean impedance for controls and second and third degree lesions, but not between mean impedance for second and third degree lesions. The small sample size limits interpretation of the results, and it is possible that significant differences between degrees of frostbite would be seen if additional test animals were used. If further studies are pursued, additional technologies should be considered and the measurement period should be extended beyond three days post-injury.

INTRODUCTION

"Frostbite is by far the number one cold injury in the military and poses the most significant threat to military operations" (Hamlet, 1987). In World War I, for example, British frostbite and trench foot cases exceeded 100,000 (Vaughn, 1980). Compounding the difficulties of treating such large numbers of patients is the low rate of return to duty for cold injury casualties (only 15 percent for the U.S. in World War II), (Vaughn, 1980) indicating a significant problem with management of cold-injured patients.

Frostbite injuries vary considerably in severity, which is characterized in terms of degree, as in thermal burns, or in terms of depth of injury (superficial or deep). In first degree frostbite, there is hyperemia and edema; in second degree--hyperemia and vesicle formation; in third degree--necrosis of the skin and underlying tissues; and in fourth degree--complete necrosis and loss of tissue, including bone (Christenson and Stewart, 1984).

Accepted treatment of the disease is autoamputation--watching and waiting for demarcation and spontaneous detachment of the necrotic tissue, with surgical intervention as required (Vaughn, 1980). Since this process can take months in cases of severe injury, and would result in some patients occupying a bed at every echelon of care, its implementation by the Army could create a considerable burden on the combat casualty care system. A preferable treatment regimen for the military would be the provision of early surgical treatment to remove all tissue that would eventually necrose.

A problem with early surgical intervention of frostbite injury is difficulty in assessing the severity of injury, which if done incorrectly can result in excessive excision of viable tissue or insufficient debridement requiring subsequent surgical revision. The inadequacy of current criteria for wound debridement stems from the methodology's subjectivity and dependence on prior surgical experience (often lacking in the field, particularly for frostbite injury). An improvement over visual evaluation would be the development of an objective methodology involving changes in some tissue property that are correlated with tissue devitalization. Several areas of investigation towards such a development show promise for civilian use, but would be impractical for the field. These include thermography (Lawson, 1961) and radionuclide imaging techniques (Salimi et al., 1986).

Preliminary work towards the development of a more fieldable methodology utilizing tissue impedance measurements has been done (Lambert et al., 1973), and the results indicated that there is a significant reduction in the impedance of non-living tissue, attributed to the loss of non-conductive cellular elements associated with tissue death. Other investigators have also studied the relationship between impedance and quality of tissue (Jaskowski, 1986), but none have examined frostbite injury. This report documents the results of a preliminary study on the use of tissue impedance as an objective indication of injury severity for varying degrees of frostbite.

MATERIALS AND METHODS

To study different degrees of frostbite injury, a realistic, reproducible freezing methodology was needed. Personnel at the U.S. Army Medical Research Institute of Environmental Medicine (USARIEM) developed an apparatus utilizing a packaged air chiller with very precise cooling controls, capable of producing simulated wind chill injuries characteristic of the natural arctic environment (Sharp et al., 1987). The freezing apparatus was comprised of an air compressor, air dryer, air-jet crystal cooler, and temperature controller. Cold air flow was directed to an acrylic tissue chamber that could be placed on an animal's skin to produce a frostbite lesion approximately 2.5 centimeters (cm) in diameter. System temperatures were monitored via thermocouples and a computerized data acquisition system. Frostbite lesions of different severities were produced by varying the freeze time, defined as the time for the intradermal temperature to fall below 0 degrees Centigrade ($^{\circ}\text{C}$) to the time freezing was stopped (Sharp et al., 1987). Air temperature and wind speed were kept constant at -75°C and 13.4 meters per second, respectively.

A pig model was studied because of that species' similarities to humans in skin characteristics and microvasculature (Lane-Petter, 1963). A 32 kilogram, female, Hanford (HMS^R) Miniature Swine (Charles River Breeding Laboratories, Inc., Wilmington, MA) was studied. The animal was restrained by a Panepinto Sling (Model #DL800, Dutton-Laiison Co., Hasting, Nebraska) and was anesthetized with Halothane by mask throughout dermal freezing, impedance measurement and biopsy procedures. Freeze times ranging from 5 seconds to 10

minutes produced a total of 48 lesions, as shown in Figure 1.

Tissue impedance measurements were made using a tetrapolar configuration of electrodes, which minimized errors due to electrode polarization. Four 26-Gauge (0.41 millimeter (mm) diameter), Teflon-coated, stainless steel electrodes (Life-Tech, Inc., Houston, TX) were linearly and symmetrically arranged and housed in a plastic casing (Figure 2). The outer electrodes, used to supply current, were separated by 7 mm, and the inner electrodes, used to record the impedance of the medium under investigation, were separated by 3 mm. The electrodes were terminated at a pin connection enabling easy attachment to a function generator and oscilloscope.

The function generator, a Krohn-Hite Model 5200 (Cambridge, MA) was used to deliver constant current (approximately 75 microamperes) square waves at a frequency of 10 kilohertz and voltage of 10 volts. Use of low amplitude/high frequency values ensured that there was no stimulation of excitable tissue due to the applied signal (Geddes and Baker, 1975). The resulting waveform, representing tissue impedance, was displayed on a Tektronix 5111A Storage Oscilloscope (Beaverton, Oregon), and was photographed using a Tektronix C-50 Oscilloscope Camera. Tissue impedance was calculated from measurements made on the photographs using the method described by Lambert et al., 1973.

Impedance measurements on the lesions were made at 1, 2, and 3 days following the day of freezing, because debridement in the combat casualty care scenario would be performed several days following the time of injury. In addition to the measurements on the lesions, control measurements were made on the untreated tissue between lesions on days 1 and 2 post-freezing. Elliptical biopsy specimens approximately 1-1.5 cm x 1 cm x 1 cm were

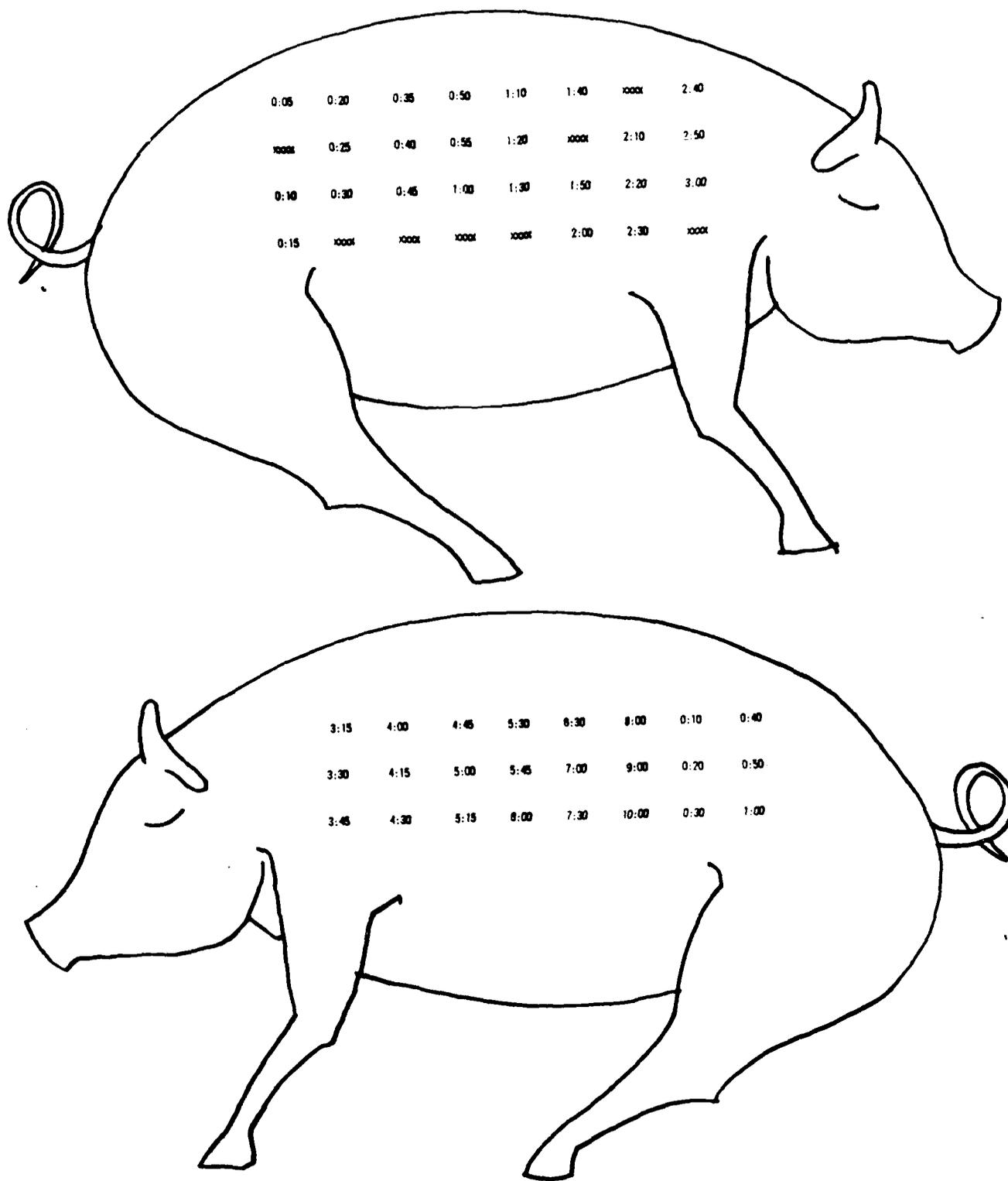


Figure 1. Freeze times (minutes:seconds) used to assess injury severity in impedance studies on a swine frostbite model: 5 seconds = first degree, 10-55 seconds = second degree, 1-10 minutes = third degree, xxx = site not studied, control data taken on top 3 rows between sites

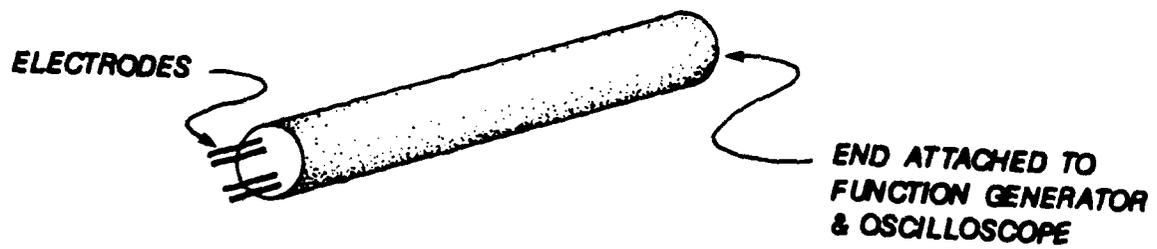


Figure 2. Sketch of probe used to assess injury severity in impedance studies on a swine frostbite model

collected and fixed in 10% buffered neutral formalin on 1, 3, 6, and 9 days post-injury. They were analyzed by a pathologist from Tufts University, Medford, MA and were subjectively categorized as to first, second or third degree injury. Analysis of variance was used to test for effects and interaction using the F-test for pairwise comparisons between means and Scheffe's multiple comparison procedure for comparisons among means. Statistical analyses were done using the general linear models procedure of SAS commercial computer software (SAS, 1985).

RESULTS

The pathology report indicated that only one lesion could be considered first degree frostbite, and that most of the lesions were third degree, making the data very unbalanced. Data for the first degree lesion were excluded from the analysis. Results for the controls and second and third degree lesions are shown in Tables 1 - 3¹. Analysis of variance indicated an overall degree effect, an overall day effect, and marginally insignificant interaction between day and degree ($p = 0.0582$). Therefore, the data were analyzed by day across each level of degree and by degree across each level of day, applying the F-test or Scheffe's multiple comparison procedure (SAS, 1985) as appropriate.

¹Tables 2 and 3 are presented separately due to the lack of control data for day 3, necessitating the use of two different statistical methods for comparing means.

Table 1. Analysis of variance for main effects and interactions for in vivo tissue impedance in controls and second and third degree frostbite lesions in a swine

| Effect | Statistic | |
|---------------------|-----------|--------|
| | F | p |
| Main Effects | | |
| Degree | 51.15 | 0.0001 |
| Day | 17.96 | 0.0001 |
| Degree * Day | 2.54 | 0.0582 |
| By Degree | | |
| Control, Day Effect | 0.08 | 0.7845 |
| 2, Day Effect | 7.40 | 0.0018 |
| 3, Day Effect | 14.08 | 0.0001 |
| By Day | | |
| 1, Degree Effect | 15.64 | 0.0001 |
| 2, Degree Effect | 32.69 | 0.0001 |
| 3, Degree Effect | 0.33 | 0.5709 |

alpha = 0.05

Table 2. Comparisons among mean values of *in vivo* tissue impedance over time in controls and second and third degree frostbite lesions in a swine (Mean in ohms \pm Standard Error)

| Day | Treatment | | | | | | | | |
|-----|----------------|----|----|----------------|----|----|----------------|----|----|
| | Control | | | 2nd Degree | | | 3rd Degree | | |
| | Mean \pm SE | SG | N | Mean \pm SE | SG | N | Mean \pm SE | SG | N |
| 1 | 2941 \pm 124 | ND | 18 | 2234 \pm 137 | A | 15 | 2051 \pm 100 | A | 32 |
| 2 | 2999 \pm 156 | ND | 24 | 1609 \pm 184 | B | 15 | 1554 \pm 115 | B | 32 |
| 3 | | | | 1431 \pm 140 | B | 15 | 1353 \pm 66 | B | 32 |

ND = Not significantly different (F-test, F = 0.08, p = 0.7845)

SG = Scheffe grouping (means with the same letter are not significantly different--comparisons made vertically among days)

Table 3. Comparisons among mean values of *in vivo* tissue impedance by degree in controls and second and third degree frostbite lesions in a swine (Mean in ohms \pm Standard Error)

| Treatment | Day | | | | | | | | |
|------------|----------------|----|----|----------------|----|----|----------------|----|----|
| | 1 | | | 2 | | | 3 | | |
| | Mean \pm SE | SG | N | Mean \pm SE | SG | N | Mean \pm SE | SG | N |
| Control | 2941 \pm 124 | A | 18 | 2999 \pm 156 | A | 24 | | | |
| 2nd Degree | 2234 \pm 137 | B | 15 | 1609 \pm 184 | B | 15 | 1431 \pm 140 | ND | 15 |
| 3rd Degree | 2051 \pm 100 | B | 32 | 1554 \pm 115 | B | 32 | 1353 \pm 66 | ND | 32 |

ND = Not significantly different (F-test, F = 0.33, p = 0.5709)

SG = Scheffe grouping (means with the same letter are not significantly different--comparisons made vertically among degrees)

Analysis by degree showed that there was no day effect for the controls, and for the second and third degree lesions, mean impedance was significantly higher for day 1 than for days 2 and 3, which were not different from each other. Analysis by day indicated that for days 1 and 2, the mean impedances for controls were significantly higher than for the second and third degree lesions, but mean impedances for second and third degree lesions were not different. For day 3, mean impedances for second and third degree lesions were not different from each other. Since no control measurements were taken on day 3, no statistical comparison between lesions and controls for that day can be made.

DISCUSSION

It could not be demonstrated that tissue impedance would be an effective means of distinguishing frostbite injury severity in the pig model studied, although significant differences between the lesions and controls were seen on days one and two. If it can be assumed that the control mean for day 3 would have been approximately equal to the mean for controls on days 1 and 2, then the mean impedance for lesions on day 3 also would presumably be different than the control mean. The reduction in impedance seen in the lesions may have been due to a combination of the osmotic changes associated with the continued development of tissue edema several days following thawing (Mills, 1973, Geddes and Baker, 1975) and the changes associated with the destruction of cells (Lambert, et al., 1973).

Since this study included only one animal, interpretation of the results

is limited. It is possible that if additional test animals were used, impedance would be a reliable discriminant of frostbite injury severity. Also, since there was variation in impedance over time for the lesions, it is possible that the reduction in edema and further tissue changes known to develop subsequent to the three day time period studied (Mills, 1973) would later yield significant differences in impedance among varying degrees of frostbite.

CONCLUSIONS AND RECOMMENDATIONS

Impedance could not be used to differentiate between all degrees of frostbite for the animal studied. The results do not preclude the possibility of using impedance for tissue assessment in other test models or with an increased sample size, and it might be beneficial to study impedance differences over a longer period of time following the time of injury. Therefore, more lengthy, balanced studies are required to ascertain whether (and when) impedance can be effectively used to guide frostbite wound debridement. Additional technologies should be considered for possible use in conjunction with impedance.

REFERENCES

Christenson, Catherine, and Stewart, Charles, "Frostbite." American Family Practice, Vol. 30(6), pp. 111-122, 1984.

Geddes, L. A., and Baker, L. E., Principles of Applied Biomedical Instrumentation, second edition, John Wiley and Sons, Inc., New York, NY, 1975.

Hamlet, Murray, "An Overview of Medically Related Problems in the Cold Environment." Military Medicine, Vol. 152 (8), pp. 393-96, 1988.

Jaskowski, J., "Evaluation of the Healing Process of Skin Wounds by means of Skin Absolute Value of Electrical Impedance." Dermatol Monatsschr, Vol. 172(4), pp. 223-8, 1986.

Lambert, Donald H., Thibeault, Roger D., Salisbury, Lloyd L., Hegyeli, Andrew F., and Mehl, David A., "Detection of Tissue Devitalisation by Square-Wave Analysis." Medical and Biological Engineering, Vol. 11, pp.584-590, 1973.

Lane-Petter, W., Animals for Research: Principles of Breeding and Management, Academic Press, New York, NY, 1963.

Lawson, Ray N., Wlodek, G. D., Webster, D. R., "Thermographic Assessment of Burns and Frostbite." The Canadian Medical Association Journal, Vol. 84, pp. 1129-1131, 1961.

Mills, William J., Jr., "Frostbite: A Discussion of the Problem and a Review of an Alaskan Experience." Alaska Medicine, March, pp. 27-47, 1973.

Salimi, Zarrin, Wolverson, Michael K., Herbold, David R., Vas, Wenzel, "Frostbite: Experimental Assessment of Tissue Damage Using Tc-99m Pyrophosphate." Radiology, Vol. 161(1), pp. 227-31, 1986.

SAS^R User's Guide: Statistics, Version 5 Edition, SAS Institute Inc., Cary, North Carolina, 1985.

Sharp, Mark W., SSG, Ahle, Neil W., CPT, Mariano, Rodrigo A., SGT, and Sawyer, William, SGT, Development of a Tissue Freezing and Rewarming Device that Uses Compressed Air as a Medium, T13-87, U.S. Army Medical Research Institute of Environmental Medicine, Natick, Massachusetts, 4 May 1987.

Vaughn, P. Byon, "Local Cold Injury--Menace to Military Operations: A Review." Military Medicine, Volume 145(5), pp. 305-311, 1980.

DISTRIBUTION LIST

No. of
Copies

- 1 Commander
U.S. Army Medical Research and Development Command
ATTN: SGRD-ZA
Fort Detrick
Frederick, MD 21701-5012
- 1 Commandant
Academy of Health Sciences, U.S. Army
ATTN: HSHA-DCD (Colonel Lombard)
Fort Sam Houston, TX 78234-6100
- 1 Commandant
Academy of Health Sciences, U.S. Army
ATTN: HSHA-DCD (Colonel Warner)
Fort Sam Houston, TX 78234-6100
- 1 Colonel David M. Lam
Deputy EUCOM Surgeon
HQ, USEUCOM (ECMD)
APO, New York 09128
- 1 Commander
U.S. Army Medical Materiel Development Activity
ATTN: SGRD-UMZ
Fort Detrick
Frederick, MD 21701-5009
- 1 Colonel Eily P. Gorman, AN
Nurse Consultant
Room 603, Skyline Five
5111 Leesburg Pike
Fall Church, VA 22041-3258
- 1 Commander
U.S. Army Medical Research and Development Command
ATTN: SGRD-OP (Lieutenant Colonel McMarlin)
Fort Detrick
Frederick, MD 21701-5012
- 1 Cold Regions Research and Engineering Laboratory
72 Lyme Road
Hanover, NH 03755

1 **Commander**
HQ, U.S. Army Medical Department Activity (ALASKA)
Fort Wainwright, AK 99703-7300

1 **Commander**
U.S. Army Research Institute of Environmental Medicine
Natick, MA 01760-5007

1 **Commander**
U.S. Army Medical Research and Development Command
ATTN: SGRD-PLB
Fort Detrick
Frederick, MD 21701-5012

1 **Commander**
U.S. Army Medical Research and Development Command
ATTN: SGRD-PLC
Fort Detrick
Frederick, MD 21701-5012