SSI SUMMIT 4, ADVANCING SURGICAL CARE ACROSS THE OPERATIVE CONTINUUM

Options in Post-Operative Care
William J. Ennis DO,MBA,MMM
Catherine and Francis Burzik Professor of Surgery, Chief Section of Wound Healing and Tissue Repair
University of Illinois Hospital and Health Sciences System
DISCLOSURE

- Chief Science Officer Healogics
- NIH funding
OVERVIEW

• History
• SSI/Wound care
• UIC Department structure/ACWHTR
• Physiology
• Diagnosis/Surveillance
• Advanced technologies
  • Diagnostic
  • Therapeutic
• Prevention
• Rules,Benchmarks, Payment structure
• Summary and Q+A
CHANGE IS DIFFICULT!
HEALING WOUNDED SOLDIERS TO ORDER

BY A REMARKABLE NEW SYSTEM OF IRRIGATING DEEP WOUNDS, DEVISED AT THE FRONT
BY DR. ALEXIS CARREL, OF THE ROCKEFELLER INSTITUTE—AND THE WAY
THE SURGEONS CAN FORETELL TO THE DAY WHEN
A WOUNDED MAN WILL RECOVER

BY

LEWIS R. FREEMAN

William J. Ennis, DO
Principles of Antibiotic Prophylaxis

Preop administration, serum levels adequate throughout procedure with a drug active against expected microorganisms.

- **High Serum Levels**
  1. Preop timing
  2. IV route
  3. Highest dose of drug

- **During Procedure**
  1. Long half-life
  2. Long procedure – redose
  3. Large blood loss – redose

- **Duration**
  1. None after wound closed
  2. 24 hours maximum


William J. Ennis, DO
INFECTIOUS DISEASE AND THE SURGICAL PATIENT

• Community acquired infections
• SSI
• Nosocomial
• Absence of large volume of well designed RCT’s to drive practice
• Wide practice variation
• Adequate risk based evaluations lacking
• Numerous treatment options
• Culture of dogmatic approaches
• Complex patients
• Increased surveillance leads to increased cost and reported frequency
• Are superficial SSI’s really all the same, reported as such, are all wounds the same
SSI = CHRONIC WOUND

• Wound Healing Society Definition of a chronic wound
  • A wound that fails to heal within an anticipated time frame

• Although considered a surgical wound, after the occurrence, the SSI is essentially a chronic non-healing wound and all the principles of modern moist wound care should and do apply
• 20 billion dollar industry
• 5-7 million patient in US
• Increasing age, diabetes, obesity, chronic conditions, surgical procedures
• Simultaneous health care reform, cost containment, pay for performance, increasing complexity of medical technology
• No formal medical education in wound care
• Conflicting certification process and confusion as to representative voice of the field

However, our current medical school curriculums address this epidemic by dedicating only 9.2 hours of training over 4 years. This cannot continue.

6.7 million people are suffering and adding 18.3 billion dollars in cost to the health care system.
*2004 first physician one year fellowship in wound healing, Advocate Christ hospital, Univ. of Illinois teaching facility
*Physician hired into practice
*December 2009, key opinion leaders met in St. Thomas and drafted initial conceptual model
*Launch of SST meeting July 2008
*University of Illinois Hospital and Health Sciences System creates Section of Wound Healing and Tissue Repair
*First fellow accepted to University based program
Research Fellow in Minimally Invasive & Robotic Surgery
Galaxy Shah, MD
2008–2009

Instructor in Advanced Surgical Laparoscopic and Basic
Open Techniques in Resident Training
Francesco Bianco, MD
2008–2009

Presented by Pier C. Giulianotti, MD
Distinguished Lloyd M. Nyhus Chair of Surgery
Professor & Chief, Division of General, Minimally Invasive
and Robotic Surgery

Wound Healing and Tissue Repair Fellow
Małgorzata Anna Plummer, MD
August 1, 2008–July 31, 2009

Presented by Martin Borhani, MD
Chief, Division of Vascular Surgery
PROTOCOL

LCD MODEL
Tissue perfusion
Bioburden/Infection
Immune status/Nutrition
Pressure
Wound bed
Psychosocial/Functional
One-time injury

\[ \downarrow \]

Bleeding/platelet activation/growth factor release

\[ \downarrow \]

PMN influx → secretion of pro-inflammatory cytokines

\[ \rightarrow \] bacterial kill/debridement

\[ \downarrow \]

PMN's recede

Macrophage/fibroblast influx

\[ \downarrow \]

Inflammatory phase ends/Proliferative phase begins

• Metabolically active cells

• Growth factors present

• Appropriate levels of pro-inflammatory cytokines (TNFα, IL-1, etc.)

• Balance between matrix metalloproteinases (MMP's) and tissue inhibitors of metalloproteinases (TIMP's)

• Healing occurs in predictable phases

• Excellent potential to heal despite dressing choice

• Complications are rare

• Good patient compliance
CHRONIC WOUND

- Repeated trauma
- Ischemia
- Bacterial contamination

Prolonged PMN influx and secretion of pro-inflammatory cytokines (TNFα, IL-1, etc.)

↓

Increased MMP/decreased TIMP activity

↓

Degradation of growth factors and target cell receptors

Degradation of extracellular matrix

↓

Impaired healing
TREATMENT MATRIX?

Systemic Inflammation

| High | Systemic therapy in combination with local therapy |
| Systemic therapy | Standard wound care |
| Normal Healing Process | Local wound bed treatments directed towards lowering inflammation |

Local Inflammation

Low → High
INNOCULUM

- SSI
  - Clean
  - Clean contaminated
  - Contaminated
  - Dirty

- Chronic wound
VIRULENCE

- Robson 10 to the 5\textsuperscript{th}
- Robson 10 to the 6\textsuperscript{th}
- Streptococcus
- Biofilm
- Adjuvant effects
  - Cautery
  - Hematoma
  - Seroma
  - Prosthetic
  - Suture
• Genetic variability
• Comorbid conditions
• Hypoxia
• Anemia
• Medications
• Albumen
• Inflammation
SURVEILLANCE AND CLASSIFICATION

- Superficial SSI
- Deep SSI
- Organ/Space SSI
- All categories have an option for the surgeon to make the diagnosis
- Prosthetic involved one year time frame
- Are all superficial SSI's the same
- SENIC
  - Abdominal operations
  - Operations > 2 hours
  - Surgical site: contaminated or dirty
  - More than 2 discharge diagnoses noted
• ACS contaminated or dirty category
• ASA score of $\geq 3$
• Surgery lasting $>75\%$ in duration for type
• Surgical community looking for risk stratification to include patient risk and severity of SSI in one predictive model
ADVANCED TECHNOLOGIES

- Diagnostic and therapeutic
- Can we determine who will get an infection
- Can we direct costly therapy to those at the most risk
- Can we determine who will heal and who will not
- Can we follow our guidelines
Using an Agent-Based Model to Examine the Role of Dynamic Bacterial Virulence Potential in the Pathogenesis of Surgical Site Infection

Vissagan Gopalakrishnan,1 Moses Kim,2 and Gary An2,*

1Department of Biology, Johns Hopkins University, Baltimore, Maryland.
2Department of Surgery, University of Chicago, Chicago, Illinois.
HEALOGICS/STANFORD DATA EFFORT

Wound Repair and Regen2016

1.000 patients
• Age
• Gender
• Insurance
• Zip code
150,177 wounds
• Wound type
• Wound location
• Wound depth
• Wound width
• Wound length
• Wound margin
• Wound color
• Wound texture
• Wound odor
• Other wound qualities

Train model
Model selection
Model evaluation

90,166 training cases
30,065 validation cases
10,054 test cases

a. ROC Curve
b. Precision vs Recall
c. Sensitivity vs Recall

Sensitivity vs Recall

- Sensitivity
- Recall
- Precision
- False Positives
- True Positives
- False Negatives
- True Negatives
- Observed fraction of delayed wound healing

- Predicted probability of delayed wound healing
- Observed fraction of delayed wound healing

Advanced care decisions for wound care specialists
Screening for evidence-based wound care centers

Effort

- 68 Healogics Wound Care Centers in 26 states
- Center Code
- Age
- Gender
- Insurance
- Zip code
- Wound type
- Wound location
- Wound depth
- Wound width
- Wound length
- Wound margin
- Wound color
- Wound texture
- Wound odor
- Other wound qualities

1,015 predictors
**Study period: 1/1/2014-11/2015**

**Table #. Sample identification and healing- excludes no wound, consult, in treatment for one week or less, and missing data**

<table>
<thead>
<tr>
<th></th>
<th>2014-2015</th>
<th>Wounds</th>
<th>Patients*</th>
<th>Wounds per Patient</th>
<th>Wounds</th>
<th>Patients</th>
<th>Wounds per Patient</th>
<th>Wounds</th>
<th>Patients*</th>
<th>Wounds per Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>All wound records w/outcome</td>
<td>907,389</td>
<td>412,687</td>
<td>2.20 (2.10)</td>
<td>1-25</td>
<td>2578</td>
<td>1111</td>
<td>2.32</td>
<td>659</td>
<td>500</td>
<td>1.32</td>
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<tr>
<td>Exclude - No wound</td>
<td>4,080</td>
<td>2,408</td>
<td>63</td>
<td>34</td>
<td>64</td>
<td>64</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>903,309</td>
<td>410,279</td>
<td>2.20 (2.09)</td>
<td>1-25</td>
<td>2515</td>
<td>1077</td>
<td>2.34</td>
<td>580</td>
<td>436</td>
<td>1.33</td>
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<tr>
<td>Exclude - Consult only</td>
<td>44,142</td>
<td>27,806</td>
<td>652</td>
<td>268</td>
<td>114</td>
<td>102</td>
<td></td>
<td></td>
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<tr>
<td><strong>Total</strong></td>
<td>859,167</td>
<td>382,371</td>
<td>2.25 (2.14)</td>
<td>1-25</td>
<td>1863</td>
<td>809</td>
<td>2.30</td>
<td>466</td>
<td>334</td>
<td>1.40</td>
</tr>
<tr>
<td>Exclude - seen once (days first to last &lt;=7)</td>
<td>191,876</td>
<td>87,325</td>
<td>75</td>
<td>46</td>
<td>35</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>667,291</td>
<td>295,046</td>
<td>2.26 (2.14)</td>
<td>1-25</td>
<td>1,788</td>
<td>763</td>
<td>2.34</td>
<td>431</td>
<td>310</td>
<td>1.39</td>
</tr>
<tr>
<td>Exclude - missing wound measurement data</td>
<td>24,042</td>
<td>10,327</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td><strong>Final Total</strong></td>
<td>643,249</td>
<td>284,719</td>
<td>2.24 (2.19)</td>
<td>1-25</td>
<td>1,788</td>
<td>763</td>
<td>2.34</td>
<td>431</td>
<td>310</td>
<td>1.39</td>
</tr>
<tr>
<td>Percent of screened</td>
<td>71.21</td>
<td>69.40</td>
<td>69.40</td>
<td>68.70</td>
<td>65.40</td>
<td>62.00</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>483,652</td>
<td>1,322</td>
<td>319</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completely healed</td>
<td>75.19</td>
<td>73.80</td>
<td>74</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>185,269</td>
<td>471</td>
<td>214</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with all wounds healed</td>
<td>65.07</td>
<td>61.70</td>
<td>69</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Patient admissions

Number of centers= 626

Number of centers=1

Number of centers= 1
ORIGINIAL ARTICLE

Surgical site infection: poor compliance with guidelines and care bundles

David J Leaper¹, Judith Tanner², Martin Kiernan³, Ojan Assadian⁴ & Charles E Edmiston Jr⁵

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2 Clinical Nursing Research, DeMontfort University, Leicester, UK
3 Prevention and Control of Infection, Southport and Ormskirk Hospitals NHS Trust, Southport, UK
4 Department of Hospital Hygiene, Medical University of Vienna, Vienna, Austria
5 Department of Surgery, Medical College of Wisconsin, Milwaukee, WI USA

Key Messages

- surgical site infection rates do not seem to be falling
- national and international guidelines and care bundles exist which are based on level I evidence-based medicine
- compliance to care bundles has to be audited and acted on
Silver-Impregnated Dressings for Sternotomy Incisions to Prevent Surgical Site Infections in Children

Conclusions The evidence did not support the superiority of silver-impregnated dressings for prevention of surgical site infections in children after cardiac surgery. Adherence to a bundle for prevention of surgical site infections may have decreased the incidence of such infections in the study population during the study period. (American Journal of Critical Care. 2016;25:402-408)
Incidence of wound complications in cesarean deliveries following closure with absorbable subcuticular staples versus conventional skin closure techniques

Tabitha L. Schrufer-Poland\textsuperscript{a,1,6}, Maria P. Ruiz\textsuperscript{a,1}, Samuel Kassar\textsuperscript{a}, Christopher Tomassian\textsuperscript{a}, Stacey D. Algren\textsuperscript{b}, John D. Yeast\textsuperscript{c}

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\textsuperscript{b}University of Missouri Kansas City School of Medicine, Department of Obstetrics and Gynecology, and Saint Luke’s Hospital of Kansas City, Kansas City, MO, United States
\textsuperscript{c}University of Missouri Kansas City School of Medicine, Department of Obstetrics and Gynecology, Division of Maternal and Fetal Medicine; Vice President of Medical Education and Research, Saint Luke’s Hospital of Kansas City, Kansas City, MO, United States

Comorbidities. The overall incidence of wound complications at our institution during this study was 5.7%. The incidence of complications among the suture and subcuticular staple closure was not significantly different (3.6% versus 0%, \( p = 0.3 \)), however there were significantly less complications in the suture and subcuticular staple closure groups when compared to traditional staple closure (14.3%) (\( p = 0.03 \) and \( p = 0.01 \), respectively).

\textit{Conclusion:} Herein, we report a decreased incidence of composite wound complications with subcuticular staple closure versus traditional staple closure in patients undergoing cesarean section. Absorbable subcuticular staple closure represents a convenient, safe and cost-effective closure technique.
Efficacy of silver coated surgical sutures on bacterial contamination, cellular response and wound healing

Anna Lucia Gallo a, Federica Paladini a,b, Alessandro Romano b, Tiziano Verri c, Angelo Quattrini b, Alessandro Sannino a, Mauro Pollini a

a Department of Engineering for Innovation, University of Salerno, Via Marinasveglia, 74100 Salerno, Italy
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Original Article

Antimicrobial-coated sutures to decrease surgical site infections: a systematic review and meta-analysis

X. Wu1 · N. Z. Kabilay2 · J. Ren1 · B. Allegrini1 · P. Bischoff1 · B. Zayed1 · D. Pitter2 · J. Li3

Received: 27 June 2016 / Accepted: 22 August 2016
Antibiotic-loaded bone cement reduces risk of infections in primary total knee arthroplasty? A systematic review

A. Schiavone Panni¹ · K. Corona³ · M. Giulianelli³ · G. Mazzitelli³ · C. Del Regno¹ · M. Vasso¹

Received: 14 June 2016 / Accepted: 23 August 2016
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Conclusion

The findings of the present review did not reveal any statistically significant differences in terms of the rate of deep or superficial surgical site infections in patients receiving ALBC versus PBC. Although ALBC is worldwide frequently used, the periprosthetic knee infections continue to verify. However, the rigorous use of perioperative prophylactic systemic antibiotics, efficient antiseptic procedures and improved surgical techniques remain the gold-standard in infection prevention in TKA surgery.
Endoscopic vein harvest in patients at high risk for leg wound complications: A cost–benefit analysis of an initial experience

Heyman Luckraz MD, FRCS a, Prabhjeet Kaur RGN a, Moninder Bhabra MD, FRCS b, Pankaj Kumar Mishra FRCS (CTh), MCh (CTh) a, Kumaresan Nagarajan MRCS a, Nelam Kumari RGN a, Kamran Saleem FCPS a, Alan M. Nevill PhD a

a Cardiothoracic Surgery, Heart & Lung Centre, Wolverhampton, United Kingdom
b Cardiothoracic Surgery, QE Hospital Birmingham, Birmingham, United Kingdom

Conclusions: In patients at high-risk of leg wound complications, EVH was associated with significant cost-savings and less leg wound complications.

Table 2

<table>
<thead>
<tr>
<th>Data variable</th>
<th>Endoscopic vein harvest (n = 50)</th>
<th>Open vein harvest (n = 50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB time (min)</td>
<td>111 ± 46</td>
<td>118 ± 49</td>
<td>.3</td>
</tr>
<tr>
<td>Postoperative ward stay (d)</td>
<td>4 (1-9)</td>
<td>5 (2-38)</td>
<td>.01</td>
</tr>
<tr>
<td>Total wound clinic visits</td>
<td>10</td>
<td>290</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Total district nurse visit</td>
<td>5</td>
<td>462</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Total costs of wound treatment (£)</td>
<td>2,758</td>
<td>78,036</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

NOTE. Values are presented as mean ± standard deviation, median (range), or n.
Antimicrobial peptide elicitors: New hope for the post-antibiotic era

Ernesto Prado Montes de Oca

Effect of an Investigational Vaccine for Preventing Staphylococcus aureus Infections After Cardiothoracic Surgery
A Randomized Trial

Conclusions and Relevance Among patients undergoing cardiothoracic surgery with median sternotomy, the use of a vaccine against S. aureus compared with placebo did not reduce the rate of serious postoperative S. aureus infections and was associated with increased mortality among patients who developed S. aureus infections. These findings do not support the use of the V710 vaccine for patients undergoing surgical interventions.

Trial Registration clinicaltrials.gov Identifier: NCT00518687

International Journal of Nanomedicine

Reducing the risk of infection associated with vascular access devices through nanotechnology: a perspective

This article was published in the following Dove Press journal: International Journal of Nanomedicine
20 November 2013
Number of times this article has been viewed
Results: From May 2015 to December 2015, 71 patients were enrolled in this study, including 33 in the experimental group and 38 in the control group. There were 10 cases of incision complications, all superficial infections, with an incidence of 14.1%. The surgical site infection incidence was statistically different between the experimental and control groups (3.0% vs 23.7%, p = 0.031). Multivariate logistic regression analysis showed that incision length ≥20 cm increased the surgical site infection incidence (odds ratio value of 15.576, p = 0.004) and that the application of negative-pressure wound therapy reduced the surgical site infection incidence (odds ratio value of 0.073, p = 0.029).

Conclusion: Negative-pressure wound therapy can reduce the incidence of surgical site infection in open abdominal surgery.
Negative-Pressure Wound Therapy with Instillation: International Consensus Guidelines

Paul J. Kim, D.P.M., M.S.
Christopher E. Attinger, M.D.
John S. Steinberg, D.P.M.
Karen K. Evans, M.D.
Burghard Lehner, M.D.
Christian Willy, M.D., Ph.D.
Larry Lavery, D.P.M., M.P.H.
Tom Wolvos, M.D., M.S.
Dennis Orgill, M.D., Ph.D.
William Ennis, D.O., M.B.A.
John Lantis, M.D.
Allen Gabriel, M.D.
Gregory Schultz, Ph.D.

Washington, D.C.; Heidelberg and Berlin, Germany; Dallas, Texas;
Scottsdale, Ariz.; Boston, Mass.;
Chicago, Ill.; New York, N.Y.;
Vancouver, Wash.; Gainesville, Fla.

**Background:** Negative-pressure wound therapy with instillation is increasingly utilized as an adjunct therapy for a wide variety of wounds. Despite its growing popularity, there is a paucity of evidence and lack of guidance to provide effective use of this therapy.

**Methods:** A panel of experts was convened to provide guidance regarding the appropriate use of negative-pressure wound therapy with instillation. A face-to-face meeting was held where the available evidence was discussed and individual clinical experience with this therapy was shared. Follow-up communication among the panelists continued until consensus was achieved. The final consensus recommendations were derived through more than 80 percent agreement among the panelists.

**Results:** Nine consensus statements were generated that address the appropriate use of negative-pressure wound therapy with instillation. The question of clinical effectiveness of this therapy was not directly addressed by the consensus panel.

**Conclusion:** This document serves as preliminary guidelines until more robust evidence emerges that will support or modify these consensus recommendations. *(Plast. Reconstr. Surg. 132: 1569, 2013.)*
Prospective, observational registry

N = 32 infected joint implants (22 acute, 10 chronic)

% of patients where joints retained
- 86.6% acute, 80% chronic

Published literature retention rates
- 65% acute, 30% chronic

*off label use in the US
Prospective study: n = 131 patients treated with Veraflo Therapy
- Wounds were either “infected or at risk for infection”
- Soak time 10 minutes, interval at least 4 hours
- Wounds included:
  - Open fracture
  - Infected Hematoma
  - Pressure Ulcers
  - Dehisced Surgical Incisions
  - DFUs
  - Necrotizing Fasciitis
- 35% of wounds were not responding to standard NPWT
- 98% could be closed after debridement
The Impact of Negative-Pressure Wound Therapy with Instillation Compared with Standard Negative-Pressure Wound Therapy: A Retrospective, Historical, Cohort, Controlled Study

• Retrospective chart review, n=142 wounds requiring admission and operative debridement
  6 min dwell time/3.5 hrs VAC: n=34
  20 min dwell time/2 hrs VAC: n=34
  Standard VAC: n=74
• Solution used: Prontosan (Polyhexanide/Betain)
• Single Center, 4 surgeons (2 plastic and 2 podiatric)

The authors found a statistically significant difference in the following:

- Number of OR Visits (6-minute and 20-minute dwell)
- Length of Stay (20-minute dwell)
- Time to Final Surgical Procedure (6-minute and 20-minute min. dwell)
<table>
<thead>
<tr>
<th>Outcome</th>
<th>NPWT (%)</th>
<th>NPWTi –d (6 min dwell) (%)</th>
<th>P-Value *</th>
<th>NPWTi –d (20 min dwell) (%)</th>
<th>P-Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of OR visits</td>
<td>3.0</td>
<td>2.4</td>
<td>0.04</td>
<td>2.6</td>
<td>0.003</td>
</tr>
<tr>
<td>Length of stay</td>
<td>14.9</td>
<td>11.9</td>
<td>0.10</td>
<td>11.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Time to final surgical procedure</td>
<td>9.2</td>
<td>7.8</td>
<td>0.04</td>
<td>7.5</td>
<td>0.002</td>
</tr>
<tr>
<td>Closed at d/c</td>
<td>46</td>
<td>32 (94)</td>
<td>0.0004</td>
<td>27 (80)</td>
<td>0.08</td>
</tr>
<tr>
<td>Remained closed @ 1 month</td>
<td>28 (61)</td>
<td>24 (75)</td>
<td>0.23</td>
<td>14 (52)</td>
<td>0.47</td>
</tr>
<tr>
<td>Culture improvement with Gram-negative</td>
<td>17 (63)</td>
<td>19 (90)</td>
<td>0.0001</td>
<td>13 (65)</td>
<td>0.77</td>
</tr>
</tbody>
</table>

More patients were closed prior to discharge and in fewer days compared to NPWT.

PROTOCOL

• Evaluate patient, understand goals of wound care, maximize modifiable conditions
• Debride the wound, in OR if at all possible, remove all non viable tissue, prosthetic material if possible
• Local wound care includes
  • Moist dressings
  • Pt modalities, UVC light, electrical stimulation, ultrasound, npwt
• Social service involvement
• Sub acute wound unit when possible and indicated
• Follow up in multidisciplinary surgical clinic
Advanced Technologies to Improve Wound Healing: Electrical Stimulation, Vibration Therapy, and Ultrasound

William J. Ennis, DO, MBA
FACOS
Claudia Lee, MPT
Karen Geller, MD
Thomas F. Corbley, BS
Timothy J. Koh, PhD
Chicago, IL

Background: Cellular energy is required for the healing cascade to occur. A combination of cells, cytokines, chemokines, tissue perfusion, an extracellular matrix, and local forces are all required to allow for human tissue repair to proceed. Although there are many examples of treatment options, energy-based therapies are the least understood, appreciated, and employed by practicing wound care physicians. The recent growth of tissue engineering has encouraged researchers to employ both electrical stimulation and therapeutic ultrasound (US) to stimulate cells, induce migration, and modify tissue constructs.

(Plast. Reconstr. Surg. 138: 00, 2016)
### Table 1. Current Levels of Evidence for Ultrasound and Electrical Stimulation

<table>
<thead>
<tr>
<th>Reference</th>
<th>Wound Type</th>
<th>Ultrasound Wavelength Nonspecified</th>
<th>Kilohertz Ultrasound</th>
<th>Megahertz Ultrasound</th>
<th>Electrical Stimulation</th>
<th>Author Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>129</td>
<td>Pressure ulcer</td>
<td>NA</td>
<td>Strength of evidence = C</td>
<td>Strength of evidence = C</td>
<td>Strength of evidence = A</td>
<td>There were no studies focused on pressure ulcers leading the reviewers unable to recommend</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Strength of negative recommendation = neutral</td>
<td>Strength of recommendation = neutral</td>
<td></td>
<td>Only quoted articles accelerated healing but did not increase total healing rate</td>
</tr>
<tr>
<td>130</td>
<td>Pressure ulcer</td>
<td>Quality of evidence = low</td>
<td>NA</td>
<td>NA</td>
<td>Quality of evidence = moderate</td>
<td>Suggest using as an adjunct if conventional therapies fail</td>
</tr>
<tr>
<td></td>
<td>Treatment over comparator = no difference</td>
<td></td>
<td></td>
<td></td>
<td>Treatment over comparator = improved</td>
<td>Different sources of electrical energy used, uncertain why ultrasound studies not included</td>
</tr>
<tr>
<td>5</td>
<td>Pressure ulcer</td>
<td>Not studied</td>
<td>Not studied</td>
<td>Not studied</td>
<td>Level 1 evidence to support</td>
<td>ES is effective in reducing the size of venous ulcers</td>
</tr>
<tr>
<td>131</td>
<td>Diabetic foot ulcer</td>
<td>Not studied</td>
<td>Not studied</td>
<td>Not studied</td>
<td>Level 1 evidence to support</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Arterial ulcer</td>
<td>NA</td>
<td>Level 3 not enough studies</td>
<td>Level 3 recommendation</td>
<td>Not studied</td>
<td>ES is effective in reducing the size of venous ulcers</td>
</tr>
<tr>
<td>4</td>
<td>Venous leg ulcer</td>
<td>NA</td>
<td>Level 3 not enough studies</td>
<td>Level 3 recommendation</td>
<td>Not studied</td>
<td>ES is effective in reducing the size of venous ulcers</td>
</tr>
<tr>
<td>Current authors opinion</td>
<td>Pressure ulcer</td>
<td>2B</td>
<td>NA</td>
<td>NA</td>
<td>1B</td>
<td>ES is effective in reducing the size of venous ulcers</td>
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<tr>
<td>Current authors opinion</td>
<td>Diabetic foot ulcer</td>
<td>NA</td>
<td>1B</td>
<td>NA</td>
<td>1B</td>
<td>ES is effective in reducing the size of venous ulcers</td>
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<tr>
<td>Current authors opinion</td>
<td>Arterial ulcer</td>
<td>NA</td>
<td>2B</td>
<td>NA</td>
<td>2B</td>
<td>ES is effective in reducing the size of venous ulcers</td>
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<tr>
<td>Current authors opinion</td>
<td>Venous ulcer</td>
<td>NA</td>
<td>2B</td>
<td>2C</td>
<td>2B</td>
<td>ES is effective in reducing the size of venous ulcers</td>
</tr>
</tbody>
</table>
INSTILLATION
ADMISSION DATE: April 22, 2015 72 yo s/p massive BCCA resection
*Initiated Veraflo therapy; Instillation of Saline, dwell time of 20 min & NPWT 125mmHg 2hours
* Current view: Posterior shoulder Measurements: 26x27x1.2
Admission Date:
April 22, 2015

Side view of patient’s LEFT shoulder

Measurements: 26x27x1.2
April 24, 2015

Veraflo therapy: 20min dwell, 2hour Soak; 125mmHg
Application of Adaptic Touch over exposed structure

Side view of left shoulder
April 28, 2015

Veraflo therapy: 20min dwell, 2hour NPWT; 125mmHg
Application of Adaptic Touch over exposed structure

Measurements: 25x26x0.8
May 1, 2015: Veraflo therapy cont’d

Back view of left shoulder
Front view of left shoulder
May 4, 2015

Veraflo therapy  20 min dwell; 2-hour Soak; 125 mmHg

Facility switched to Mepitel for contact layer

Back view of left shoulder

Measurements: 25x25x0.5
MAY 6, 2015: Veraflo Therapy discontinued & standard VAC therapy was applied

NOTE: Pressure set to 150 mmHG, Continuous & still applied Mepitel
MAY 6, 2015: Veraflo Therapy discontinued & standard VAC therapy was applied

NOTE: Pressure set to 150 mmHg, Continuous & still applied Mepitel
May 11, 2015

Patient discharged from LTAC;

Application of Promogran Prisma until HHA could apply the ActiVAC

Measurements: 22.5x24x0.2
MAY 19, 2015

VAC therapy; Continuous at 150mmHg

Mepitel as contact layer

Measurements: 18.5x22x0.2

Back view of left shoulder
MAY 19, 2015

VAC therapy; Continuous at 150mmHg

Mepitel as contact layer

Side view of left shoulder
Side & Front views of left shoulder
MAY 25, 2015  : Back view of shoulder  Measurement: 18.0 x 21.0 x 0.1
CASE MAY 26, 2016—STSG

NOTE: VAC therapy was utilized to bolster the graft; 125 mmHg, Continuous
PAYMENT, REGULATIONS, VALUE BASED PURCHASING, AT RISK MODELS
PATIENT EDUCATION PROGRAM WITH AMERICAN COLLEGE OF SURGEONS
RESEARCH (IF TIME PERMITS)
Examining Chemical and Structural Information from Tissues

Molecular and Structural Analysis

Use stains to visualize and identify molecular information

Chemical Imaging
It is Critical to Segment Tissues into Key Cell Types/Components for Tissue Diagnosis

- Vimentin
- SMA
- Masson's Trichrome
- Calponin
- H&E
- CD31
- PR
- ER
- Her2/neu
- Ki67
- P53
- P63
- Cytokeratin
- Collagen Distribution
- Protein Distribution
- Classification e.g. epithelial vs. stromal distribution

Goal: Acquire same information in a label-free approach
Sustained Inflammasome Activity in Macrophages Impairs Wound Healing in Type 2 Diabetic Humans and Mice
Figure 8—Model of the role of the inflammasome/IL-1β pathway in impaired wound healing in type 2 diabetes. Our data indicate that IL-1β can act as an upstream signal (signal 1) for sustaining inflammasome activity in chronic wound Mp and that ROS are involved in the second signal (signal 2) required for inflammasome activity. Since the inflammasome, in turn, activates IL-1β, this cytokine appears to be part of a proinflammatory positive-feedback loop that promotes a bias toward a proinflammatory Mp phenotype and inhibits upregulation of the prohealing phenotype and healing in diabetic wounds. ab, antibody; ko, knockout.
Blocking Interleukin-1β Induces a Healing-Associated Wound Macrophage Phenotype and Improves Healing in Type 2 Diabetes


Rita E. Mirza,1 Milie M. Fang,1 William J. Ennis,2,3 and Timothy J. Koh1,3

[Images and graphs related to the study are shown here.]

[Additional images for IL-1β, CD68, and IL-1β+CD68 are included.]
NEUTRALIZING ANTIBODY IL-1B, IL knock out mice also used
CRITICAL REVIEW

Stem Cells and Healing: Impact on Inflammation

William J. Embleton, Kimberly A. Donohue, and Melanie Bartholomew

Significance: The number of patients with chronic wounds has rapidly increased over the past 10 years in both the United States and worldwide. Some prospective factors at the national level include an aging population, epidemic numbers of obese and diabetic patients, and an increasing number of acquired immunodeficiencies. At the micro level, chronic inflammation is a consistent feature.

Recent Advances: A number of treatment modalities are currently used to accelerate wound healing, including growth factors, cytokines, the use of stem cell transplantation, exosomes, and cell-based therapies. The use of stem cell therapy has been hypothesized as a potentially useful adjunct for methicillin-resistant Staphylococcus aureus (MRSA) cutaneous wound infections.
MSC Treatment and Tensile Strength

**Hypothesis**

Treatment with MSC may reprogram wound healing towards regeneration.

Regeneration can be analyzed by tensile strength of the wound.

Stronger wound may indicate tissue regeneration versus scar formation.

- B6 Mouse
- aMSC
- nMSC
- Fibroblast (3T3)
Association for Academic Surgery

Activated mesenchymal stem cells increase wound tensile strength in aged mouse model via macrophages

Simon Lee, MPH, Erzsebet Szilagyi, MD, PhD, Lin Chen, PhD, Kavitha Premanand, MS, Luisa A. DiPietro, DDS, PhD, William Ennis, DO, and Amelia M. Bartholomew, MD, MPH

a Department of Surgery, University of Illinois, Chicago, Illinois
b College of Dentistry, University of Illinois, Chicago, Illinois
c Cancer Center, University of Illinois, Chicago, Illinois
MSC and Tensile Strength

4 Treatment Groups

- Allogeneic aMSC (activated)
- Allogeneic nMSC (naïve)
- Fibroblast (3T3)
- Control (HBSS)

3 Cell Doses adjusted to standardized volume 200 microliters

- 50,000
- 250,000
- 500,000

Subcutaneous injection into a 3 cm incisional wound on the dorsum of B6 mice and surgically clipped.

Day 7 - wounds excision and tensiometry
Activated MSC provide more powerful anti-inflammatory and pro-angiogenic properties

Tensile Strength vs. Dose Response Following Treatment with aMSC, nMSC, fibroblast

![Bar graph showing tensile strength vs. dose response following treatment with aMSC, nMSC, fibroblast. The x-axis represents cell concentration (50,000, 250,000, 500,000), and the y-axis represents tensile strength (% of control). The graph shows a significant increase at 500,000 cell concentration for nMSC.*]
MSC Treatment and Blood Flow

- Diabetic cynomolgus monkey model (n = 3)

- [Insert chart of different glucose readings to show hyperglycemia]

  - 4 (2 x 1 cm) wounds on lateral and medial side of the anterior femoral region
    1. Autologous aMSC with Integra
    2. Autologous nMSC with Integra
    3. Integra alone
    4. Saline soaked guaze

  - Blood flow measured hourly for first 6 hours with Laser Doppler

A = control excision wound
B = scaffold with MSC
Excised Nonhuman Primate Wound VEGF Content

VEGF (pg/2 microgram wound homogenate)

Wound Treatment

- scaffold alone
- scaffold + aMSC
- scaffold + MSC
- control
Low-Intensity Vibration Improves Angiogenesis and Wound Healing in Diabetic Mice

Eileen M. Weinheimer-Haus, Stefan Judex, William J. Ennis, Timothy J. Koh

1 Department of Kinesiology and Nutrition, University of Illinois at Chicago, Chicago, Illinois, United States of America; 2 Center for Tissue Repair and Regeneration, University of Illinois at Chicago, Chicago, Illinois, United States of America; 3 Department of Surgery, University of Illinois at Chicago, Chicago, Illinois, United States of America; 4 Department of Biomedical Engineering, Stony Brook University, Stony Brook, New York, United States of America

Figure 3: Angiogenesis is enhanced following low-intensity vibration. Wound sections were stained with antibodies against CD31.
QUESTIONS/SUMMARY