A clinical investigation into the relationship between increased periwound skin temperature and localized wound infection

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Many studies relate the presence of chronic wound infection to reduced strength of healing tissue and delayed healing. Although failure to heal may be the result of many coexisting factors, infection is often found to be a significant contributor.

Increased local temperature is a classic sign of wound infection and its accurate measurement may have the potential to aid in diagnosis of chronic wound infection at the bedside. Although infrared thermometry is currently utilized for this purpose in some chronic wound care practice settings, research evidence to support reliability of the infrared thermometer utilized for this study (Pearson’s Correlation r = .939). Analysis of data collected from participants with chronic, non-arterial, leg ulcers (n = 40) is supportive of a statistically significant relationship between increased periwound skin temperatures and wound infection (P = 0.000).

Participants were enrolled from within the population of a chronic wound healing clinic. Data collected from non-wounded participants (n = 20) using a test-retest method support reliability of the infrared thermometer utilized for this study (Pearson’s Correlation r = .939). Analysis of data collected from participants with chronic, non-arterial, leg ulcers (n = 40) is supportive of a statistically significant relationship between increased periwound skin temperatures and wound infection (P = 0.000).

Does infrared light therapy improve sensation in diabetics?

Lawrence A. Lavery; Douglas P. Murdoch; Jayme Williams; David C. Lavery; Scott & White Memorial Hospital

Objective: To determine the efficacy of monochromatic infrared photo energy (Anodyne) in-home treatments over a 90-day period to improve peripheral sensation and self-reported quality of life in persons with diabetes mellitus.

Methods: This was a double-blinded randomized, sham-controlled clinical trial. We randomized 69 patients with diabetes with sensory neuropathy demonstrated by vibration perception threshold between 20–45 V on the great toe and fifth metatarsal
head on both feet into two treatment groups. Sixty patients (120 limbs) completed the study. Patients were randomly assigned to an active or sham treatment group. Anodyne units were used at home every day for 40 minutes for 90 days. We evaluated nerve conduction velocities, vibration perception threshold, Semmes Weinstein Monofilaments (SWM) (4-, 10-, 26-, and 60-g monofilaments), the Michigan Neuropathy Screening Instrument (MNSI), 10-cm visual analog pain scale, and the Neuropathy Quality of Life Instrument.

Results: Sixty-nine subjects were enrolled and 60 subjects completed the study. No differences were noted in measures for quality of life, Neuropathy Disability Score, Michigan Neuropathy Screening Instrument, VPT, SWM, or NCVs in active or sham treatment groups ($P > 0.05$).

Summary: Anodyne therapy was no more effective than sham therapy in the treatment of sensory neuropathy in persons with diabetes.

**Effects in diabetic midfoot Charcot deformity with wounds after posterior tibial tendon reconstruction using acellular regenerative tissue matrix**

*Daniel Lee, DPM; Gerit Mulder, DPM, MS, University of California, San Diego*

A diabetic midfoot wound is a challenging condition in the presence of Charcot midfoot deformity. Severe collapse of the midfoot due to Charcot arthropathy can increase abnormal peak pressures; thus, preventing normal wound healing process. One of the deforming factors in a flexible and semi-rigid deformity has been the dysfunction of the posterior tibial (PT) tendon in stabilizing the midfoot. Despite proper offloading of the extremity and tissue grafting to the wound, recurrence and complications occur when this deformity is not addressed. We present a series of 10 patients with chronic midfoot wounds who failed with advanced wound healing modalities and underwent PT tendon reconstruction surgery with acellular regenerative tissue matrix (ARTM) to rebuild and stabilize the midfoot and obtained wound healing.

**Methods:** We followed 10 patients with diabetes with recalcitrant wounds with collapsed midfoot and failed local wound care. Only patients with medical clearance for surgery, normal non-invasive vascular studies, and biomechanical abnormality were included. Evaluations of wound, radiographic, and clinical biomechanic measurements of the collapsed midfoot were performed. All patients underwent PT tendon reconstruction with ARTM, then were treated with continuous wound care and followed for 1 year to assess for ulceration, clinical biomechanics, and radiographic collapse recurrence.

**Results:** All 10 patients progressed to full healing along the midfoot without any recurrence of the wounds after a minimum of 1-year follow up. The average time to wound healing was 3 months (2 to 6). The midfoot alignment between the bisection of the talus and metatarsal remained nearly parallel without any signs of collapse (mean 5 degrees, range 0 to 15). Increased stability and strength of PT tendon was noted in all patients, compared to the contralateral uninvolved limb (normal heel rise test). No complications from the procedure were noted and all patients tolerated the postoperative course well.

**Conclusion:** Our preliminary study suggests that midfoot wounds can be successfully treated with reconstructive surgery addressing the PT tendon deficiency using ARTM technology. Early identification and intervention of this condition can prevent further morbidity and progression to rigid, nonreducible arthropathic deformity. Further research in a large patient scale is needed.

**Shear force Initiative**

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**Objective:** To report on the progress and activities of the Shear Force Initiative. This initiative was established to increase the field’s awareness of the role of “shear” in tissue damage and improve methods of its characterization and measurement.

**Methods:** Members of the initiative designated five areas of interest and assigned subcommittees to address definitions and education, devices that measure shear, measurement of the effect of shear on the patient, clinical guidance to meet the patients’ needs, and support surface/tissue interaction.

**Discussion:** Although shear is widely accepted as a major contributing factor in the development of
pressure ulcers, the Shear Force Initiative’s comprehensive approach is beginning to accumulate the body of knowledge to characterize and measure shear and prepare methods of disseminating the information to the industry. The effort is worldwide with corroboration between labs in Europe, Japan, US, and Israel.

The subcommittees have met twice per year and laid the foundation for the balance of the work to be built upon. This foundation includes:

- Creation of a Shear Reference Collection, which attempts to be comprehensive
- Circulation of a questionnaire to gather information on shear measurement methods and devices
- Creation of a list of shear-related definitions and points requiring industry education
- An analysis of what is known about shear and what remains to be elucidated
- Creation of a method of characterizing and validating devices to measure shear.

**Conclusion:** This work has provided a forum for exchange and accumulation of knowledge that allows the field to properly identify insufficiencies in the knowledge base and direct future work in a coordinated effort to provide the groundwork for clinical practice and device interventions that can allow the research and management of shear.

**Separation of components in re-amputation surgery: applying basic surgical tenants to maximize outcome**

_J.C. Lantis, MD; C. Gendics, RN; G. Todd, MD; St. Luke’s, Roosevelt Hospital Center, New York, NY_

**Introduction:** Patient seek below-the-knee re-amputation for poor function, pain, and/or poor match to prosthesis. We believe the best technical outcomes require identification of all the constituent portions of the limb before reconstruction; we identify and separate the tibia and fibula, muscles, and neurovascular bundles of the four compartments of the lower leg and the subcutaneous skin and nerve tissue of the envelope.

**Methods:** Ten patients over a 30-month period underwent re-amputation. Pre- and postoperative pain, time to return to function, narcotic requirement, and quality of life were assessed. The patients all had undergone unilateral traumatic lower extremity injuries and were younger than 50 years old, eight men and two women, and had undergone initial amputation 17 (± 31) days after their injury. All patients underwent complete preoperative trigger point mapping, x-ray evaluation, and physical exam. They then underwent surgical revision consisting of complete separation of components, and resection of all scar noted not to be identifiable as one of the components, including bone remodeling and primary closure. Four of 10 had Ertl procedures, 60% had (I)mmediate (P)ost (O)perative (P)rosthetic placement, and three of the 10 underwent immediate postoperative radiation therapy to the surgical site.

**Results:** The average return to independent ambulation with crutches was 30 days; without crutches, 48 days. The patients’ pain scale decreased from an 8 to a 2 and 90% of patients stopped all narcotics within 45 days. An average or four neuromas were identified and removed per patient.

**Discussion:** The complete separation of components before revision of the lower limb amputation appears to facilitate fast recovery with identification of previously unrecognized technical problems as the primary reason for the techniques effectiveness. In addition, adjuncts such as IPOP and radiation appear to have a positive effect on outcomes.

**Vacuum-assisted closure** instill as a method of sterilizing massive venous stasis wounds prior to split-thickness skin graft placement

_J.C. Lantis, MD; L. Tyrie, MD; C. Gendics, MD; G. Todd, MD; St. Luke’s, Roosevelt Hospital, New York, NY_

**Introduction:** Patients with massive venous stasis ulcers that have high bacterial burden represent some of the most difficult wounds to manage. The vacuum-assisted closure* (VAC) device is known to optimize blood flow, decrease local tissue edema, and facilitate the removal of bacteria from the wound bed. However, these patients have too high a bacterial burden for simple VAC application to facilitate all these functions. We present the application of the VAC with instillation of dilute Dakin’s solution as a way to eradicate bacteria in these patients’ wounds.
**Methods:** Over 2 years, five patients with venous stasis ulcers >200 cm² that were colonized with greater than 10⁵ bacteria were treated with the V.A.C. Instill. Two patients had multidrug resistant Pseudomonas, three with MRSA. All patients were treated for 10 days with V.A.C. Instill therapy with 12.5% Dakin’s instilled for 10 minutes every hour. At 10 days, all five patients underwent quantitative culture before undergoing STSG, which was matured under a V.A.C.

**Results:** All five patients had negative quantitative cultures after 10 days of therapy. All five of the STSGs had 100% take with complete healing still evident at 1 year.

**Discussion:** Adequate delivery of bactericidal agents to the infected tissue can be difficult, especially while promoting tissue growth. By providing a single delivery system for a bactericidal agent for a short period of time followed by growth-stimulating therapy, the V.A.C. Instill provides a unique combination that appears to maximize wound bed preparation.

*V.A.C. Instill, KCI, San Antonio, Tex*

**Advanced foot surveillance with skin temperature monitoring reduces the risk for diabetic foot ulceration in high-risk patients**

*David G. Armstrong; Katherine Holtz-Neiderer; Christopher Wendel; M. Jane Mohler; Heather R. Kimbriel; Lawrence A. Lavery; Dr. William M. Scholl College of Podiatric Medicine*

**Background:** Diabetic foot ulcers are preceded by inflammation, making their occurrence or recurrence potentially detectable and preventable by empowering the patient. Therefore, the purpose of this study was to evaluate the effectiveness of home temperature monitoring to reduce the incidence of foot ulcers in high-risk persons with diabetes.

**Methods:** In this physician-blinded, 18-month, randomized controlled trial, 225 subjects with diabetes at high risk for ulceration were assigned to standard therapy (ST) or dermal thermometry (DT) groups. Both groups received therapeutic footwear, diabetic foot education, and regular foot care and performed a structured foot inspection daily. DT subjects used an infrared skin thermometer to measure temperatures on six foot sites, twice daily. Temperature differences >4°F between left and right corresponding sites triggered patients to contact the study nurse and reduce activity until temperatures normalized.

**Results:** A total of 8.4% (n = 19) subjects ulcerated over the study period. Subjects were three times less likely to ulcerate in the DT group compared to ST group (12.2% versus 4.7%, OR = 3.0, CI 1.0 – 8.5, *P* = 0.038). Proportional hazards regression analysis suggested that thermometry intervention was associated with a significantly shorter time to ulceration (*P* = 0.045), adjusted for elevated foot ulcer classification (International Working Group Risk Factor 3), age, and minority status. Persons that ulcerated had a temperature difference that was 4.8 times greater at the site of ulceration in the week before ulceration than did a random seven consecutive day sample of 50 other subjects that did not ulcerate (3.50 ± 1.0 versus 0.74 ± 0.05; *P* = 0.001).

**Conclusions:** These results suggest that high temperature gradients between feet may predict the onset of neuropathic ulceration and that temperature monitoring reduces the risk of ulceration.

**Diabetic foot ulcer and VAC resource utilization and economic cost based on a randomized trial**

*Jan Apelqvist; David G. Armstrong; Lawrence A. Lavery; Andrew JM. Boulton, Dr. William M. Scholl College of Podiatric Medicine*

**Objective:** To evaluate resource utilization and direct economic costs of care for patients treated with negative pressure wound therapy (NPWT) vacuum-assisted closure system (VAC) compared to standard moist wound therapy (MWT) in the treatment of partial diabetic foot amputation wounds.

**Methods:** 162 patients with diabetes with post-amputation ulcers (up to the transmetatarsal level) entered a 16-week, randomized clinical trial. Patients randomized to VAC (n = 77) received therapy with dressing changes every 48 hours. Control patients (n = 85) received standard MWT. Resource utilization and costs for inpatient hospital care, surgical procedures, re-amputations, post-baseline debridements, antibiotics, outpatient treatment visits, dressing changes, and dressing materials were calculated and analyzed in this post-hoc retrospective study.
**Results:** No difference was found between groups for inpatient hospital stay (number of admissions or length of stay). More surgical procedures (including debridement) were performed in the MWT group (120 versus 43 NPWT, *P* < 0.001). The average number of dressing changes performed per patient was 118.0 (range 12 to 226) for MWT versus 41 (6 to 140) for NPWT (*P* = 0.0001). The MWT group had 11 (range 0 to 106) outpatient treatment visits during the study versus four (range 0 to 47) in the NPWT group (*P* < 0.05). The average direct cost per patient treated for 8 weeks or longer (independent of clinical outcome) was $27,270 and $36,096 in the NPWT and MWT groups, respectively, yielding an incremental cost difference in favor of NPWT of $8,826. Proportionally, the highest costs were related to inpatient hospital stay, antibiotics, and wound dressing treatment. The average total cost to achieve healing was $25,954 for patients treated.

**Novel palliative wound dressing promotes healing**

*Aletha Tippett, MD*

**Introduction:** Wounds are a tragic problem at the end of life, with little expectation that wounds will heal. A novel wound dressing was developed for palliative treatment of wounds to reduce pain and prevent infection. Palliation was achieved, and surprisingly, nearly all of wounds treated healed or were healing.

**Methods:** Retrospective case study review of 323 wounds in hospice patients treated over a 30-month period. Wounds treated included pressure (44%), neuropathic (10%), and arterial (10%). 231 wounds were treated with the novel dressing, 92 received other treatments.

**Results:** Median age of patients was 82 years. Average length of time that patients lived after treatment started was <90 days, with a majority of patients living <30 days. No new wound infections were reported. Pain relief was significant, as assessed by nurse and physician observation. Despite short treatment times, nearly 50% of wounds in the novel treatment group were healed or healing, compared to 20% in the other treatment group.

**Conclusion:** Using a novel dressing designed for palliation not only reduced pain and prevented infection, but also resulted in wound healing more than double that of wounds treated with other methods.

*Proprietary mixture containing liquid hydrogel, lidocaine, and antibiotic on gauze*

**The impact of pressure ulcers on patient quality of life: validation of the Cardiff wound impact questionnaire**

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**Purpose:** The purpose of this study was to validate the Cardiff Wound Impact Questionnaire (CWIQ) for patients living with pressure ulcers.

**Study Design:** Patients with pressure ulcers (PPUs) were recruited from hospitalized and community population associated with an urban 600-bed tertiary center in Toronto, Canada. Consenting subjects completed both the CWIQ and SF-36, a gold standard generic HRQL tool. Construct validity was assessed by comparing the CWIQ scores to specific domains of the SF-36 and evaluating the responsiveness of the tool to differing health states and wound types.

**Results:** Eighteen (18) patients were enrolled in the study. The mean age was 46 years. The CWIQ’s Social Life domain was correlated with both Social Functioning (SF-36) (*r* = 0.514, *P* < 0.05) and Physical Role Limitation (SF-36) (*r* = 0.569, *P* < 0.05). Physical Symptoms and Daily Living (CWIQ) correlated with Bodily Pain (SF-36) (*r* = 0.640, *P* < 0.01). PPUs had lower CWIQ scores in Social Life and Physical Symptoms and Daily Living domains compared to mean scores from patients with healed leg and diabetic ulcers (67.5 versus 76.1, *P* < 0.05; 63.3 versus 71.1, *P* < 0.01). No significant difference was found between CWIQ mean scores of PPUs and a sample of patients with other chronic wounds. However, trends toward lower mean scores in the PPU group were observed. Similarly, a trend toward lower scores among those with chronic medical conditions was observed. No significant correlation was found between wound severity and CWIQ means for PPUs.

**Conclusions:** The results of this study provide the first evidence for the validation of the CWIQ in PPUs. Modest correlations of two CWIQ domains with the...
SF-36 were documented. Two domains of the CWIQ were able to discriminate between PPUs and patients with healed venous and diabetic ulcers. In order to illustrate the tool’s ability to discriminate between PPUs and other types of non-healed chronic wounds, a larger sample size is required. Wound severity does not appear to correlate with CWIQ scores.

**Methicillin-resistant Staphylococcus aureus (MRSA): evidence of silver-resistant genes**

Steven L. Percival, PhD; Christine A. Cochrane, PhD; Jia V. Loh, BSc; Emma J. Woods, PhD; ConvaTec Wound Therapeutics GDC

MRSA is an increasing healthcare problem and is particularly problematic in wounds. Methods available to treat infections colonized with MRSA rely on the use of topical antiseptics such as ionic silver. Despite the recent evidence of silver resistant genes being present in Enterobacter cloacae, presence of silver-resistant genes in methicillin-resistant Staphylococcus aureus (MRSA) has not been investigated. Subsequently, our initial studies were to determine the prevalence of silver-resistant genes in MRSA isolated from wounds in both humans and animals. Polymerase chain reaction (PCR) and agarose gel electrophoresis (AGE) were utilized to determine the frequency of 3 sil genes, silE, silS and silP in 52 MRSA’s. Analysis of all MRSAs confirmed absence of the silP and silS genes. However, 5% of MRSA strains were found to contain the silE gene. To determine whether the MRSA strains, containing the silE gene, were sensitive to a silver-containing Hydrofiber™ dressing, confocal laser microscopy was employed. Results confirmed that the silver-containing Hydrofiber™ dressing was effective in killing all MRSA with and without the silE gene.

**Assessing the efficacy of silver-containing wound dressings on silver resistant wound isolates using rapid confocal laser scanning microscopy (RCLSM)**

Steven Percival, PhD; Emma Woods, PhD; ConvaTec Wound Therapeutics GDC

Despite evidence of silver-resistance genes being documented in bacteria isolated from chronic wounds, the efficacy of silver-containing dressings on these isolates has not be investigated. For this study, we investigated whether four silver-resistant Enterobacter cloacae, known to contain the silE, silS and silP genes, were killed in silver-containing wound dressings. Fluorescent dyes (BacLight, Live/Dead Kit) were added to fresh cultures (inoculum 108 cfu/mL) of all silver-resistant wound isolates and used to visualize their viability over time using rapid confocal laser scanning microscopy (RCLSM —Leica UK). Live bacteria stained green and dead/dying bacteria turned red. When inoculated into samples of all dressings, the viability of the bacteria could be effectively monitored after 3, 24, 48, and 72 hours using RCLSM. All silver-resistant isolates were observed to turn progressively red (ie, died) within 24 hours; the majority of bacteria were shown to be killed in all dressings after 48 hours. In conclusion, this study has shown that evidence of silver-resistant genes to silver in bacteria does not necessarily translate into phenotypic resistance.

**Electrical stimulation therapy to promote wound closure: a meta-analysis**

Pamela E. Houghton, BScPT, PhD; M. Gail Woodbury, PhD; University of Western Ontario

The objective of this study was to search, appraise, and summarize the evidence for electrical stimulation therapy (EST to accelerate the closure of chronic ulcers.) Electronic databases and bibliography searches were used to find articles published before October 2006. Inclusion criteria consisted of controlled clinical trials that had a between-group statistical comparison, a study population of adult humans, with chronic skin ulcer(s) who underwent EST treatment using surface electrodes; wound size was assessed objectively before and after treatment. Consensus between four independent reviewers was required to reject articles. Of 2,265 articles that were reviewed, 19 studies were included in this review that involved a total subject number of 888 (EST group = 522; Control = 366). 12 of the studies had data to support that EST accelerated wound healing while seven studies found no differences between EST and control groups. Data were pooled from five studies that assessed the proportion of completely healed ulcers. Overall effect size in favor of EST treatment was 3.93; P < 0.0006. Studies that tended to show the better responses to EST included
those that used randomization, large sample sizes (n = 25), had similar subject characteristics at baseline, pressure ulcers, or using EST parameters including a monophasic pulsed current, negative or alternating polarity, a relatively high pulse frequency (64 Hz). This evidence provides strong support that EST can significantly improve the proportion of chronic wounds healed.

Pressure ulcer awareness program
Heather Orsted; Sue Rosenthal; Gail Woodbury; Robert Ketchen; and the CAWC PUAP Task Force

In 2003, the Canadian Association of Wound Care funded a study to determine the extent of pressure ulcers in Canada; it indicated prevalence rates of 25% in acute care, 30% in nonacute care, 22% in mixed healthcare settings, and 15% in community care. The mean prevalence overall was 26%.

Recognizing this as a huge health-related problem, in 2006 CAWC funded and created a quality improvement program that in a pilot demonstrated:
- Increased awareness about pressure ulcer prevention
- Improvements in clinical practice toward a best practice approach
- Changes in policy relating to pressure ulcer prevention within facilities
- Reduction in prevalence of pressure ulcers by 35% (according to preliminary data).

The CAWC Pressure Ulcer Awareness Program (PUAP) has been designed to provide the education, processes, and tools necessary to reduce the number of pressure ulcers in all types of settings across Canada. The ultimate goal of the PUAP is to create a culture shift from treating pressure ulcers to preventing pressure ulcers.

Rehydration of a human acellular dermal regenerative tissue matrix in a heparin-blood saline solution for the treatment of chronic diabetic lower extremity wounds
Brock A. Liden, DPM; Melitta Simmons, DPM; Jodi F. Hartman, MS; Michelle L. Wright, BS; Circleville Foot & Ankle, Berger Health System

Rehydration of a human acellular dermal regenerative tissue matrix for wound management traditionally occurs in a saline solution. This study presents an alternative method of rehydration in a heparin-blood saline solution. Twenty-eight chronic, full-thickness wounds of the lower extremity were evaluated in 19 patients with diabetes for whom a standardized application and postoperative management protocol involving the use of this matrix was used. Rehydration was achieved in a solution of 10 cc of the patient’s blood collected at the time of patient preparation, 1,000 units of heparin, and enough sterile saline to cover the matrix. University of Texas Wound classifications included: 1 (3.6%) 1B, 1 (3.6%) 1C, 2 (7.1%), 1D, 3 (10.7%) 2C, 1 (3.6%) 2D, 1 (3.6%) 3B, 2 (7.1%) 3C, and 16 (57.1%) 3D. Mean time to graft incorporation, 100% granulation, and complete healing was 1.1 weeks (0.43–3.6), 5.3 weeks (0.43–16.7), and 15.9 weeks (1.7–38.0), respectively. Overall graft success rate was 89.3%. One failed wound subsequently healed approximately 7 weeks after graft reapplication. The healing rate was 92.9%, as 26 of the 28 wounds healed. Absence of graft-related complications and high rates of closure in a wide array of diabetic wounds support the use of this graft for the treatment of complex lower extremity wounds. The use of a heparin-blood saline solution for rehydration may enhance graft incorporation by stopping coagulation at the graft edges, permitting immediate blood flow across the graft, and enabling the host cells to begin utilization of the matrix as quickly as possible.

Improved pain control at dressing changes with topical lidocaine and morphine as part of a multidisciplinary team for comprehensive wound pain management
Janet Loitman; Cassandra Ward; Linda Stamm; Laurel Wiersema-Bryant; Pat Dulle; Katie Baella; John P. Kirby; Washington University School of Medicine

Introduction: Wounds often have a pathophysiologic pain component that we believe should be addressed. We report herein our regimen of local viscous lidocaine and oral morphine applied topically for pain control at dressing changes as part of our overall pain management program. Although many regimens exist, relatively little data exist for a topical pain regimen in concert with more conventional pain medications.
Materials and Methods: Members of our multidisciplinary team rounded on patients with acute and chronic wounds. Although a variety of techniques were applied as needed by the patient’s specific medical status and pain complaints, topical agents are often used and detailed herein. Patients needing additional pain control at their dressing changes received a local application of oral morphine sulfate (20 mg/mL) mixed in equal parts with viscous lidocaine over their open wounds. Patients underwent dressing changes with monitoring of pain complaints along an established pain scale and response to treatment as part of our best practice habits.

Results: Over the course of the last 6 months, approximately 20 patients whose charts were available for review underwent treatment. During and after the dressing changes, both patients and staff offered favorable responses for ease of execution, acceptance of the therapy, and pain reduction response. Patients subjectively reported increase ease of dressings and less anxiety associated with dressing changes. No complications were reported in association with this technique.

Conclusion: Adequate attention to pain management is a central tenet to advanced wound care. Our practice habits demonstrate one method of achieving that goal, utilizing easily available medications topically. Our data suggest that our pain management regimen augmented by topical lidocaine and morphine is a safe and effective strategy that needs further clinical study to better define its quantitative effects on patient pain and wound healing.

Effect of vibration on skin blood flow; an in-vivo experimental study in a microcirculatory model
Gojiiro Nakagami; Manabu Takano; Hiromi Sanada; Atsuko Kitagawa; Shigeru Ichikawa; Junko Sugama; Hideki Yokokawa; Naomi Sekiya, The University of Tokyo

We studied the effects of vibration on skin microcirculation to investigate the applicability of vibration to clinical use for prevention and treatment of ischemic wounds. A vibration applicator with a 47 Hz frequency and 600, 800, 1,000 mVpp of vibrational intensity was applied horizontally to the ear auricle of male hairless mice (n = 6 in each group) for 10 minutes under inhalation anesthesia. A control group (n = 6) received no vibration. Venular blood flow was measured using an intravital videomicroscope at baseline and at 0, 5, and 15 minutes after stopping the vibration. Significant increases were observed in the 600 mVpp group at 5 and 15 minutes after starting vibrations compared to controls (P = .002, and P = .046, respectively). We also detected increased blood flow in the 800 mVpp group (P = .028) and 1,000 (P = .012) at 5 minutes after stopping the vibration; however, these increases were attenuated at 15 minutes after. These results indicated that direct skin vibration at 47 Hz frequency improves the skin blood flow. Nitric oxide production induced by the mechanical stresses of vibration including shear stress, compression, and cell stretching on to the endothelial cells via mechanotransduction was a possible mechanism to explain the vasodilation of venules. Negative feedback was considered to have occurred in the 800 and 1,000 mVpp, indicating that caution needs to be exercised in respect to vibrational intensity for its clinical use.

Limb salvage through a combination Achilles tendon and ulcer repair using an acellular human dermal matrix: a case study
Brock Liden, DPM; Berger Wound Care Center

Creative techniques combined with safe and effective products provide surgical flexibility and expanded clinical options. This case demonstrated how powerful the combination of current treatment modalities with traditional surgical practice can be in saving limbs that would historically have been amputated. A 64-year-old woman with diabetes who had previously failed conservative treatment for a large skin wound with exposed Achilles tendon presented a 7-cm deficit and complete loss of Achilles tendon structure interoperatively. In attempt to salvage the limb, the gastrocnemius was sectioned and flipped to provide a bridge for the Achilles tendon. The mop ends of the Achilles tendon were resected and covered with an acellular human dermal matrix, GRAFTJACKET® Matrix 5 cm x 10 cm (Wright Medical Technology Inc, Arlington, Tenn). The graft was wrapped “burrito” style around the construct and anchored to the gastrocnemius proximally and the calcaneus periosteum distally. The remaining open ulcer area was closed with another acellular human dermal matrix. Throughout
the tendon healing process, the patient was kept non-weight bearing. Additional treatment modalities were employed post-operatively to promote wound granulation and soft tissue coverage of the tendon. The Achilles tendon and diabetic foot ulcer had completely healed by 29.7 weeks, allowing the patient’s full return to normal activities.

The temporary “intra-wound” use of nanocrystalline silver* to aid primary closure of infected arteriovenous graft wounds in patients with end-stage renal disease
Gregory K. Patterson, MD, FACS, CWS; Erkan Alci, MSIII, BS; Derren Harrison, PA-C; South Georgia Surgical Associates

Infected wounds with foreign body such as vascular graft material are extremely difficult to deal with, especially in patients with end-stage renal disease. We report a series of three patients over a recent period who presented with infected arteriovenous (AV) graft utilized in hemodialysis. With a graft infection such as these, the patients often undergo removal of the foreign material and the wounds are many times left open to close in a secondary fashion or even with delayed primary closure some 5 to 7 days later. This often delays further vascular access while the wound is closing and can lead to contamination of other temporary vascular access devices.

Three patients presented with obvious infection of these grafts. Two patients had infected pseudoaneurysms and one patient had swelling and epidermolysis. One patient was frankly septic. One patient had undergone removal of an infected graft several weeks prior and had a small remnant of graft material left on the brachial artery as a patch repair. Two patients underwent repair of the brachial artery utilizing a reverse saphenous vein bypass directly in the infected field for distal upper extremity salvage. The other patient had a salvageable portion of the graft remaining.

In all three cases, primary loose closure was performed after removal of the infected foreign graft material, debridement, and washout of the wounds were performed. In all three patients, nanocrystalline silver-based dressings were utilized by cutting these into 0.5- to 1.0-cm wide strips. These were placed into the wound between the skin suture material. These classic external dressings acted as internal wicks, removing wound exudate and delivering silver for antimicrobial treatment in to the depth of the wounds. The wicks were removed between post-operative Day 5 to 7. In all three cases, wound healing was achieved without further intervention. One patient died approximately 30 days later from complications from multiple myeloma.

*Nanocrystalline silver dressings – Acticoat™, Smith & Nephew Wound Management, Largo, Fla

Analysis of wound exudate matrix metalloproteinase (MMP) reduction in human chronic wounds following treatment with a novel MMP-inhibiting dressing
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Dysregulated MMP activity leading to excessive tissue destruction is a characteristic feature of chronic wounds. To address this problem, a novel MMP-inhibiting wound dressing* was developed that selectively binds and removes active MMPs from the wound environment.

Dressing efficacy, determined by reduction in wound exudate MMP activity, was evaluated in a 32-subject study with various chronic wound types. After 2 weeks of baseline treatment with practitioner’s standard of care (SOC), patients were randomized to 4 weeks of treatment with either the MMP-inhibiting dressing or SOC. Dressings were collected weekly and exudate extracted for analysis. MMP activity was determined using a broad-spectrum chromogenic substrate assay, while MMP-8 concentration (by ELISA) was measured as a marker of inflammation. All measurements were normalized for sampled exudate mass and protein concentration.

Global treatment efficacy was evaluated using regression analysis on the weekly MMP activity versus MMP-8 concentration data. At baseline, these two parameters were strongly correlated. Following treatment with the MMP-inhibiting dressing, regression line slopes were significantly reduced compared to baseline and control data ($P < 0.0005$), indicating a reduction in the active MMP fraction within the treated wounds.
To correct for changes in inflammatory status, patient MMP activity profiles were expressed relative to MMP-8 concentrations using an “equivalence factor” calculated at baseline. Significant reductions in adjusted MMP activities versus baseline were observed for treated wounds, while controls remained unchanged. These results correlated well with histological improvements in wound bed quality, validating the effectiveness of active MMP targeting for the treatment of chronic wounds.

*MI-Sorb Dressing™, Rimon Therapeutics Ltd, Toronto, Canada

Study of laminin-10 extracellular matrix in keratinocyte attachment and migration using small interfering RNA
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Purpose: Laminin proteins are major extracellular matrix present in various basement membranes and play important roles in mediating cell functions. Laminin-10, a new member of laminin family, is a major component of epithelial basement membrane. However, its function in epithelial cells is not clear. To understand the role of laminin-10 in wound healing, we evaluated the effects of laminin-10 on epithelial keratinocyte attachment and migration by gene knockdown using laminin-10 specific small interfering RNA (Lama5 siRNA).

Methods: Lama5 siRNA was used to transfect normal human keratinocyte NIK cells, 100,000 cells/well in 12-well plate, with final siRNA concentration of 30 nM in keratinocyte growth medium EpiLife. After 72 hours of transfection, cells were tested for their abilities of attachment and migration. Cell attachment assay was performed with 60,000 cells/well, incubated for 45 minutes and analyzed with colorimetric method at OD 570 nm. For migration study, 200,000 cells/well were placed on the top of migration chamber membrane (with 8 micron pores) for 6 hours, cells migrated through the pores and attached to the bottom of the membrane were stained and observed under microscope.

Results: Attachment assay: Cells transfected with Lama5 siRNA showed a reduced attachment by 11.5% at 45 minutes compared with control cells. Chamber migration assay: Lama5 siRNA transfected cells migrated at markedly reduced rate at 6 hours, 90.5% less than control cells.

Conclusion: Our data suggest that laminin-10 may play an important role in wound healing through promoting keratinocyte attachment and migration.

A multisite, transdisciplinary initiative to address pressure ulcers in New Jersey
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Pressure ulcers continue to be an important healthcare concern across care settings. In 2005, New Jersey became the first state to require reporting of Stage III or IV pressure ulcers acquired in the acute care setting. In response to this regulation, the New Jersey Hospital Association (NJHA) Pressure Ulcer Collaborative was started. This quality improvement initiative was designed to focus on patient safety and the quality of care provided in all healthcare settings where the elderly might develop pressure ulcers. Participating hospitals, nursing homes, and home health agencies have been working with national faculty and leading experts in pressure ulcers and patient safety and with each other, focusing on several dimensions of care including assessment, prevention, staging, pressure-relieving devices, and nutrition. The collaborative components include a 2-day educational program on pressure ulcers, monthly conference calls, and a listserv for collaborative partners to pose questions and get answers from the national faculty, NJHA staff, and other participants. Collaborative partners are responsible for submitting data on quality indicators to NJHA on a regular basis.

After months of sharing and implementing assessment strategies, preventive interventions identified as best practices by expert faculty and nursing/medical literature and improved coordination of care between settings, the NJHA Quality Institute was able to demonstrate a 30% reduction in pressure ulcer incidence across the reporting organizations.
The educational programs and conference calls raised the knowledge level for all nurses in the collaborative. Results demonstrate that education can make a difference in outcomes of care. The model of education, collaboration, and participation demonstrates a reduction in pressure ulcer incidence can be achieved. This model is appropriate for individual facilities and other quality initiatives.

**Use of an enzyme-enhanced antifungal* to treat damaged and contaminated perineal skin**

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Although incontinence-induced perineal skin damage is painful and preventable, it is prevalent. ICU patients have complex health issues and skin care is often overlooked. To further complicate matters, little research is available documenting extrinsic factors affecting the skin and optimal treatment in adults.

Seven ICU and medical/surgical patients with urofetal incontinence were evaluated for treatment and management in addition to previous catheterization. Polymicrobial cultures of Candida albicans and Clostridium difficile, VRE, or MRSA were documented for each person. At the first evaluation, the skin was extremely painful, erythematous, and partially denuded. Patients required various potent analgesics before cleaning. After each incontinence episode, foam cleanser was used, followed by an application of enzyme-enhanced antifungal*.

Dramatic improvement in skin inflammation, erythema, edema, and pain was seen within 12 to 24 hours of the initial application of enzyme enhanced antifungal*. Analgesic use quickly decreased and patient cooperation increased. Photos show marked improvement in skin condition. Given the tremendous amount of tissue damage, rapid resolution of inflammation was unexpected and unprecedented. Once the skin healed, a barrier product was used for prevention.

These impressive observations may be partially explained by the enzymes inactivating inflammatory mediators, thereby resolving inflammation. Further research comparing the use of enzyme-enhanced antifungal to antifungal is warranted to document the clinical differences including time to resolution as well as analgesic type and usage.

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**The advantages of a unit dose saline irrigation delivery device in the management of open wounds**

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In the current confusing state of regulatory and certifying agencies, it is difficult to know how to handle medications and solutions to comply with all rules. Saline may or may not be classified as a medication dependent on its packaging and intended use. A unit dose saline*, which is classified as a device, has the advantage of not falling under medication regulations. All solutions fall under National Patient Safety Goals labeling requirements once they are drawn up or transferred from their original containers. The ability to effectively use the product directly from its original packaging resolves any labeling issues. Unit dosing also has the advantage of supporting improved infection control practices by eliminating the use of single bottles of saline for multiple procedures. This unit dose saline provides 30 mL of sterile preservative-free normal saline in a single-use container that irrigates at 6 to 8 PSI with a manual squeeze. While still providing a noncytotoxic wound cleanser with surfactant to our Emergency Department and Urgent Care Center for use when indicated, we have successfully converted our entire system of acute, subacute, and rehab hospitals, nursing homes, and home health and hospice facilities to this unit dose saline device for performing basic wound irrigation.

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**Treprostinil sodium for management of wounds refractory to standard therapy secondary to critical limb ischemia**

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Background: Refractory critical limb ischemia (CLI) can lead to amputation regardless of underlying etiology. Prostacyclin (PGI2) and its analogs have been proposed as a pharmacologic therapy, due to their vasodilatory effects. The prostacyclin analog treprostinil sodium has demonstrated blood flow improvement in severe vascular disease.

Methods: Adults with CLI, who have failed previous therapies (medical wound care, hyperbaric treatment, surgical intervention, endovascular intervention), were invited to participate in a 12-week, open-label study assessing the safety and efficacy of continuous subcutaneous infusion of treprostinil sodium in wound healing, relief of ischemic pain, and limb salvage.

Results: Twenty-two patients (nine males/13 females) were evaluated. Vascular disease etiologies included connective tissue disease (nine), Buerger’s disease (four), PAD (four) and Raynaud’s (three). Four subjects demonstrated complete wound closure. Marked improvement by objective and subjective measures occurred in 12 subjects (two with osteomyelitis). At the completion of week 12, one patient with extensive gangrenous ulceration required modified amputation. The average visual pain score decreased from 4.6 (2 to 8) at baseline to 0.8 (0–6) at week 12. Eleven patients reported pain resolution by Week 4. The mean peak treprostinil dose was 20 ng/kg/min (6 to 60). No serious adverse events were reported. Side effects included subcutaneous infusion site pain, headache, and diarrhea.

Conclusions: Treprostinil sodium was safe and appears to contribute to wound healing, ischemic pain relief and limb salvage in patients with CLI.

Treprostinil sodium for management of wounds refractory to standard therapy secondary to critical limb ischemia: an extension study

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Background: Refractory critical limb ischemia (CLI) results in loss of limbs and digits regardless of etiology. Prostacyclin (PGI2) and its analogs have been proposed as a pharmacologic therapy. Treatment with the prostacyclin analog treprostinil sodium has been shown to improve blood flow in severe vascular disease.

Methods: Twelve weeks of treatment with treprostinil (continuous subcutaneous infusion) in an open-label trial showed encouraging results in ischemic pain (visual analog scale and medication usage) and wound healing in 17 adults with CLI. Nine of these subjects have entered into a 12-week extension study to determine whether additional treatment would be beneficial; both trials are ongoing.

Results: Further wound healing occurred with additional treatment and continued escalation of the treprostinil dose. Four of five subjects completed an additional 12 weeks of treprostinil therapy had complete healing. All subjects reported continued pain relief (three patients discontinued all narcotics). One subject went on to a modified amputation (scheduled). Side effects of treprostinil were manageable and included subcutaneous infusion site pain, headache, and diarrhea.

Conclusions: Treprostinil sodium appears to significantly contribute to wound healing and pain relief in the presence of CLI. Previous studies have limited the duration of therapy to 12 weeks and doses were limited to 15 ng/kg/min. The preliminary results of this extension study suggest that treatment with higher doses and longer durations may increase the benefit of treprostinil in management of patients with CLI.

VEGF enhances angiogenic response in experimental wounds as measured by tensile properties of the wound, increased epithelialization, and decreased time to closure

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Vascular endothelial growth factor (VEGF) is a local stimulator of angiogenesis. In this study, we hypothesized that local sustained-release of VEGF using adenoviral vector mediated gene transfer could reverse the reduced angiogenic response observed in diabetic wounds and accelerate wound healing. This hypothesis was tested by determining the specific effects of VEGF165 application on components of the wound healing process: epithelialization, skin biomechanical properties, histology, and time to 100% wound closure. To determine the effects of VEGF on wound healing in vivo, ADV/VEGF165 and controls (vehicle and saline) were injected into excisional and incisional wounds created on dorsum of BKS.Cg-m+/+Leprdb and NOD mice and mechanical properties and histological evaluations were performed 10, 14, or 21 days post injury. Wounds treated with ADV/VEGF165, healed 6.6 days faster than controls. Treated wounds healed in 27.25 ± 1.4 days. Saline-treated wounds healed in 34.2 ± 7.0 days, while wounds administered with vehicle control alone healed in 33.5 ± 6.5 days. Additionally, analysis of stiffness (N/mm) indicated that skin excised from wound sites of animals treated with VEGF165 had a stronger wound breaking strength than skin excised from control animals’ wound sites. Furthermore, histological analysis revealed accelerated epithelialization at wound sites treated with VEGF165 as measured by analysis of the thickness of the epithelial layer. These results suggest that VEGF accelerates closure of wounds and provide evidence for a new mechanism to increase epithelialization at wound sites.

**Intermittent, gradient, pneumatic compression plus standard compression for hard-to-heal venous ulcers in subjects with secondary lymphedema and chronic venous insufficiency: analysis of a prospective, randomized clinical trial**

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Thirty-four subjects with secondary lymphedema, chronic venous insufficiency, and hard-to-heal lower leg ulceration (> 1-year-old and > 20 cm² surface area) were treated with either intermittent, gradient, pneumatic compression (IPC* n = 17) plus standard care or standard care alone (control). Standard care consisted of a nonadherent primary wound dressing plus a four-layer compression bandage (4-LB† n = 17). The mean age and size of the ulcers were 1.8 years and 34 cm², respectively, and did not differ significantly between groups. IPC was performed using a four-chamber pneumatic leg sleeve and gradient, sequential pump. All pumps were calibrated to a pressure setting of 40 to 50 mm Hg on each subject and treatments were for 1 hour twice daily. Evaluations were performed weekly to measure edema, local pain, degree of wound granulation, and wound healing (incidence of complete closure and rate of healing from wound surface area measurements). The median time to wound closure by 8 months was 135 days for the IPC-treated group and 198 days for the control group (P = 0.039). The rate of healing was 1.1 ± 0.4 mm/day for the control group and 2.3 ± 0.7 mm/day for the group treated with IPC (P = 0.026). When compared to subjects treated with standard care, the group treated with IPC reported less pain at each evaluation point for the first 6 weeks of the trial. At weeks 1, 2, and 3 the visual analog pain scores were significantly lower for the IPC-treated group (P <0.05). During the first 8 weeks, the IPC-treated group had an 8.9% mean decrease in leg edema compared to 4.5% for the group treated with compression bandages alone. These results suggest that IPC is a valuable adjunct to standard care in the management of chronic, difficult to heal, large, or painful venous ulcers.

†Profore Compression Bandage System, Smith and Nephew Inc., Largo, Fla

**Improved healing and down-regulation of gelatinase in neuropathic foot ulcers treated with a primary wound dressing containing Ca, K, Rb, and Zn and total contact cast**

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April 2007 Vol. 53 Issue 4

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Background: One element contributing to wound chronicity is the imbalance of matrix metallo-proteases (MMPs) and their specific inhibitors (TIMP) in the wound bed, resulting in the premature degradation of the provisional matrix. Both, in vitro and in vivo studies have shown that a formulation of polyhydrated ionogens (PHI) may down-regulate the over expression of gelatinases A & B (MMP-2 and MMP-9) in chronic wounds.

Design: A parallel, uncontrolled evaluation (feasibility study) comparing the rate of wound healing and gelatinase content in neuropathic foot ulcers treated with a new PHI-impregnated primary wound dressing (PHI-WD*). PHI-WD is a primary wound dressing containing the trace elements Ca, K, Rb, and Zn, formulated with petrolatum and citric acid and impregnated onto an ethylene vinyl acetate mesh screen.

Methods: Nine subjects with neuropathic plantar foot ulcers were treated once weekly with PHI-WD and total contact cast (TCC). Wound tissue for MMP-2, MMP-9, and TIMP-2 analysis were obtained at baseline (before initial treatment), at week 3 and at week 6 (post-treatment). The concentrations of MMP-2, MMP-9, and TIMP-2 were measured in extracts of ulcer tissue homogenates using ELISA and gelatin-zymography. Wound assessments were performed once weekly and the rate of healing was calculated by digital photo planimetry.

Results: Treatment with PHI-WD for 6 weeks resulted in four-fold decrease of MMP-2, a six-fold decrease of MMP-9 (P < 0.05) and a 45% increase in TIMP-2. The rate of wound healing was 20% greater when compared to historical controls treated with nonadherent dressing and TCC.

Interim results of a randomized, controlled multicenter trial of vacuum-assisted closure therapy* in the treatment and blinded evaluation of diabetic foot ulcers

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Background: Diabetic foot ulcers are a menacing ramification endured by many affected with the disease. The research objective was to evaluate the clinical effectiveness and safety of negative pressure wound therapy (V.A.C.* Therapy*) versus standard moist wound therapy (MWT) in the treatment of diabetic foot ulcer patients.

Methods: This study enrolled 342 patients from 37 centers. Inclusion criteria were patients with diabetes with adequate nutritional status and a foot ulcer 2 cm² located on the dorsal, plantar, or calcaneal region with adequate perfusion. Patients were randomized in a blinded fashion to either V.A.C. Therapy or MWT (eg, alginates, collagen, foam, hydrogels, hydrocolloids, gauze). Ulcers were treated until healed or day 112 and patients were followed 38 weeks post closure. An interim intent-to-treat analysis was conducted after the enrollment of 275 patients.

Results: The interim analysis included 256 patients. The median time to ulcer closure with V.A.C. Therapy was 107 days and was not reached for MWT (P = 0.03). The median time for 76% to 100% granulation tissue formation, from 0% to 10%, was 56 days for V.A.C. Therapy and 114 days for MWT (P = 0.009). Secondary amputations occurred in 14 V.A.C. Therapy-treated patients compared with 34 MWT patients (P = 0.002). Final data from the acute treatment phase will be incorporated and updated results depicted.

Conclusion: V.A.C. Therapy was associated with a significant difference in granulation tissue formation and wound closure attainment. The interim analysis is promising and suggests that patients with diabetic ulcers experience improved wound healing outcomes when treated with V.A.C. Therapy.

*V.A.C.* Therapy, KCI USA, San Antonio, Tex