Negative Pressure Wound Therapy (NPWT): Unsolved Mysteries

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Conceptual Framework

- Disease awareness to disease management
- Wound care to wound healing
- Wound environment to cellular activity
- Passive to active wound bed preparation
- Focus on time to healing
- We are all involved
  - Providers
  - "Influencers"
Normal Healing Process

**Damage to Tissue**
- Platelets
- Neutrophils/Macrophages
- Macrophages/Fibroblasts/Endothelial Cells
- Epithelial Cells
- Fibroblasts

**Healing / Repair**

Acute Wounds

- Sequence of healing is continuous and within expected time frame
- Usually achieved with few or no complications
- Overreaction in healing:
  - Hypertrophic scars
  - Keloids

Chronic Wound: Definition

Has failed to proceed through an orderly and timely process to produce anatomic and functional integrity, or proceeded through the repair process without establishing a sustained anatomic and functional result.\(^1\),\(^2\)

2. Robson MC, Bach 
"The process of healing is powerfully programmed and very difficult to obstruct, but it has its enemies."


Imbalanced Molecular Environments Of Healing And Chronic Wounds

Healing Wounds:
- Low levels of bacteria
- Low inflammatory cytokines
- Low proteases, ROS, RNS
- Intact functional matrix
- High mitogenic activity
- Mitotically competent cells

Chronic Wounds:
- High levels of bacteria
- High inflammatory cytokines
- High proteases, ROS, RNS
- Degraded nonfunctional matrix
- Low mitogenic activity
- Senescent cells

Acute Wound Healing

- Hemostasis
- Proliferation
- Inflammation
- Remodeling
- Compression
Venous Ulcers X 2 Left Leg Present for 14 Months

Clearly something is missing.....

Carpe Diem

“Healing is a matter of time, but also a matter of opportunity”

Hippocrates

Negative Pressure Wound Therapy

An active wound management system that utilizes controlled negative (subatmospheric) pressure which is applied uniformly to the wound through an open cell foam or other interface dressing in a constant or intermittent fashion
NPWT: Over 60 Years of Progress

1952: Raffel A.


The Russian Experience

Pioneered NPWT use post-operatively in the 1980’s
Utilized nonpatented suction device and gauze medium
Published series of 5 case studies ("Kremlin Papers")

Conclusions:
1. TNP therapy is an effective adjunctive treatment in combination with surgical debridement
2. TNP therapy significantly reduced healing times, reduced bacterial burden and normalized the immunological profile
3. TNP therapy resulted in a shorter inflammatory process, lower bacterial levels and faster wound closure
4. The authors highlight the multifaceted effect of TNP therapy on all aspects of the wound healing continuum and how its usage can guarantee successful wound closure

NPWT: Over 60 Years of Progress

1985-1989: M. Chariker and K. Jeter
- Develop negative pressure technique to treat abdominal wounds complicated by fistulae
- Utilized gauze-wrapped drain tube and wall suction
- Evolved into the current form of gauze-based NP for wound healing known as the Chariker-Jeter technique


1993: First investigative study using foam as a wound interface layer

1997: Argenta and Morykwas publish experimental data applying controlled suction topically to an open wound using polyurethane foam; patented technique led to the development of first commercialized system


2002-2009: Further advances in NPWT delivery including more portable devices, instillation and compartment syndrome specialty devices

2009: Patent on foam dressing expires

2009: FDA clearance of a new, ultra-portable, mechanically powered NPWT (MPNPWT) system developed in the Biodesign Innovation Program at Stanford University in Palo Alto, California; RCT completed 2010

Requirements for Wound Healing

- Debridement
- Bioburden Management
- Moisture Balance/Tissue Edema reduction
- Manage Inflammation

Wound Healing

- Promotes Granulation/Contraction
- Removes wastes
- Maintains moisture, reduces periwound edema
- Promotes perfusion

NPWT

- NPWT

- NPWT

- NPWT

- NPWT
Negative Pressure Wound Therapy: Improved Quality of Life

Mechanically Powered vs. Non-Mechanically Powered

- Only Prospective Multicenter RCT Study comparing effectiveness of NPWT devices and meeting the AHRQ call for such studies (6/2009 report)
- 17 Participating Centers, 132 patients enrolled in study
- Demonstrated same wound healing rates (non-inferiority) with better patient quality of life

Key Study Results: Comparative Evidence

Mechanically Powered vs. Non-Mechanically Powered


A Comparison of Powered versus Mechanically Powered NPWT

Venous Leg Ulcer Data
NPWT versus MPNPWT

- Lower Extremity VLUs < 100 cm²
- 13 sites that enrolled VLUs
- 40 subjects


<table>
<thead>
<tr>
<th></th>
<th>NPWT Mean (%) [SD]</th>
<th>MPNPWT Mean (%) [SD]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 weeks</td>
<td>-9.87 (-106.04)</td>
<td>-35.35 (-69.23)</td>
<td>0.0546*</td>
</tr>
<tr>
<td>8 weeks</td>
<td>-30.20 (-116.49)</td>
<td>-47.46 (-110.99)</td>
<td>0.0005</td>
</tr>
<tr>
<td>12 weeks</td>
<td>-38.98 (-118.26)</td>
<td>-56.29 (-112.89)</td>
<td>0.0079*</td>
</tr>
<tr>
<td>16 weeks</td>
<td>-42.00 (-119.20)</td>
<td>-57.80 (-113.00)</td>
<td>0.0082*</td>
</tr>
</tbody>
</table>

*p-values adjusted for baseline wound size
*Statistically significant (*p<0.05)

<table>
<thead>
<tr>
<th></th>
<th>NPWT Prop. Healed (%)</th>
<th>MPNPWT Prop. Healed (%)</th>
<th>Odds Ratio 95% CI [Min, Max]</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>23.80% (5/21)</td>
<td>52.63% (10/19)</td>
<td>3.56 [0.923, 13.699]</td>
</tr>
</tbody>
</table>

Percentage of Patients who... | MPNPWT | NPWT
---|---|---
Felt that their NPWT device was “never” or “rarely” noticed in social situations | 100% | 25%
Felt that noise from their NPWT device “never” bothered them | 100% | 33%
Felt that their NPWT did not interfere with their daily activities | 92% | 42%
“Agreed” that their NPWT was “comfortable to wear” | 85% | 33%

RCT Exit Data: Improved Quality of Life

Clinical Benefits of NPWT
- Increases local blood flow
- Reduces edema
- Stimulates granulation tissue formation
- Stimulates cell proliferation
- Removes soluble healing inhibitors from the wound
- Reduces bacterial load
- Draws the wound edges closer together
- Controls exudate, odor (↓ clothes soiling, ↑ patient comfort)
- Reduces dressing changes
- Reduces treatment costs

Mechanisms of Action
- Negative Pressure Wound Therapy
- Tissue Decompression
- Macro-Deformation
- Micro-Deformation
- Removal of Wastes
- Increased Perfusion

Removal of Wound Exudate/Waste

- Reduction in surface and surrounding tissue exudates
- Reduction in surface bacteria


Edema Reduction/Tissue Decompression

- Tissue is at minimum, perfusion is ideal
- Tissue volume ↑, vascular density ↓, perfusion distance ↑, and blood flow decreases

- Normal Tissue

- Edematous Tissue

- Tissue volume ↑, vascular density ↓, perfusion distance ↑, and blood flow decreases
**Increase in Perfusion**

- 31% increase in perfusion to the wound and 15% increase to surrounding tissue
- Increased neo-angiogenesis to venous and arterial wounds


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**V.A.C.® Therapy System: Family of Reticulated Open-Cell Foam Dressings**

The Essential Component for Effective NPWT

- **V.A.C.® GranuFoam® Dressing - Black**
  - Hydrophobic
  - Open pore nature (400-600 microns) provides uniform distribution of negative pressure at the wound site
  - Aids wound contraction

- **V.A.C.® WhiteFoam Dressing - White**
  - Hydrophilic, pre-moistened with sterile water
  - Denser foam with greater pore size distribution
  - Requires higher pressure (125-175 mmHg) to provide adequate negative pressure therapy distribution

- **V.A.C.® GranuFoam Silver® Dressing - Silver**
  - Hydrophobic
  - Direct and complete contact with wound bed delivers silver
  - Open pore nature (400-600 microns) provides uniform distribution of negative pressure at the wound site

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**NPWT Interface Dressings**

- Reticulated Open Cell Foam
- Gauze
+ Macrodeformation (Macrostrain)

- Wound contraction; the effects on the bulk tissue
- Dependent upon laxity or compliance of the tissue
- Visible alteration of form or shape
- When negative pressure contracts the foam, it draws the wound edges together and removes fluid
- Shown to be the same with foam and gauze
- 5 cm wounds on backs of pigs
- When negative pressure was applied, wound filler hardened, wound surface area decreased instantaneously
- Wound remained contracted for 72 hours, only slight increase when NP removed


+ Microdeformation

- Interaction of tissue and a dressing at a microscopic level
- Though cellular changes/response occurring at microscopic level, visual changes noted on the wound bed
- Tissue blebs, mushrooming, surface undulations
- “Footprint”
+ Microdeformation

- Stretching of tissue into pores of the interface dressing
- Affects the cytoskeleton and initiates a further cascade of biologic effects
- Edema removal
- Angiogenesis and blood flow
- Reduction of bacterial colony counts
- Promotion of granulation tissue formation


+ Foam-Tissue Interaction is Key to Inducing Macrostrain and Microstrain

Microstrain
- Induces tissue deformation at a cellular level leading to cell stretch
- Induces cell proliferation and angiogenesis\(^1\) which is thought to promote wound healing

\(^1\) Huang S, et al. Mol Biol Cell 1998; 9:3176
\(^2\) Chen CS, et al., Science, 1997; 276:1425

The V.A.C.\textsuperscript{®} GranuFoam\textsuperscript{®} Dressing Retains its Open-Cell Structure During Therapy

- 95%
- >80%

Facilitating Removal of Exudate and/or Infectious Materials

Microstrain can be translated to the interior of the cell through integrins (cell surface receptors linked to extracellular matrix).

Chen et al., JBC. 274:18393-400, 1999

Microstrain induces generation of secondary messengers involved in proliferation.

*Finite Element Model

Greene AK, Ann Plast Surg. 2006 Apr;56(4):418-422.

Wounds subjected to treatment had increased microvessel density.

Effect of V.A.C. Therapy with and without V.A.C. GranuFoam® contact on MMP-2 and MMP-9 activity

MMP-2 active
MMP-9/neutrophil gelatinase Associated lipocalin

N = 3 patients

Before therapy
1 week
2 weeks

1.6% ± 0.1
4.5% ± 0.8
1.3% ± 0.1
2.7% ± 0.3
1.5% ± 0.3

N=3

V.A.C.® GranuFoam® Dressing Promotes Granulation Tissue Formation

V.A.C.® Therapy with GranuFoam® contact
V.A.C.® Therapy without GranuFoam® contact

Harvard/MIT Demonstrated That Microstrain Induced by the Foam Dressing Promotes Granulation Tissue Formation

Finite element analysis predicts the effects of the reticulated open-cell foam as demonstrated by granulation tissue formation.
Foam “Footprint”

Gauze “Footprint”

What about Contact Layers?
**Finite Element Model**

- Study comparing foam to a gauze dressing using a 3-dimensional model which supported the Saxena work.
- Simulated tissue microdeformations were generated using foam and standard USP gauze dressing models at equivalent negative pressures.
- Distribution of the microdeformations and strain appear as repeating mosaic beneath foam, and appeared to produce irregular distribution of strains in wound surface with gauze.
- Gauze is an open weave of twisted cotton fiber strands free to move within the constraints of the weave.
- Felt it is likely that the fibers within the strands provide flexible, smooth contact points and minimize contact area.


**Microdeformation in a Pig Model**

- In vivo porcine wound model was used; 5 cm circular subcutaneous wounds were created.
- NPWT was applied at atmospheric pressure (0 mm Hg) and subatmospheric pressures (-75 and -125 mm Hg) to both foam and AMS gauze.
- Aim was to examine the effect on macro- and microdeformation by measuring wound surface area and tissue biopsies.
- Histologic analysis revealed a repeating pattern of surface undulation (blebs).
- This study concluded that NPWT using gauze did result in microdeformation in the wound bed similar to that induced by foam.


**How Do We Make This Practical?**

- Realities:
  - Loyalty in NPWT tends to run deep
  - Interface dressings
  - Sales and service
  - Contracts
- Acute wounds have very specific needs
- Case reports abound with positive outcomes using various NPWT devices/interfaces with chronic wounds.
- Used properly, delivering NPWT via interface of choice should net desired results.
- Now additional consideration can be given to patient needs and quality of life.
**Case in Point**

- 74-year-old female residing in a LTC facility
- Bed- or chair-bound
- Frail, nutrition and other assessments adequate
- Initial consultation contracted wound 2.5 cm deep
- OR excision performed
- 15 days post-op with NPWT

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**Challenge Lies with the Technique, Not the Device**

- Drain tube on top of dressing
- Exudate traveling up tubing on outside mixing with pectin strips on skin as well as into canister
- Minimal contact with drain, though contraction of the dressing evident
- Contact layer bunched up at base of wound
- Despite excellent visual instructions packaged with the dressing kit
- Reapplied according to directions, consulted with treatment nurse at facility

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What Should We See?

Two Weeks

Case in Point

- 61 year old female
- History of venous disease, no other significant PMH
- Trauma to RLE 3 weeks prior to initial visit
- Largest ulcerated lesion with dry eschar
- Initial debridement minimal due to pain
- Eschar unroofed; ordered collagenase changed daily
- Order placed for NPWT

Further Debridement, NPWT Initiated
One month of NPWT
Apligraf applied

One week later

Ulcera closed....

Summary

- NPWT is an effective way to rapidly fill wound space, improve wound bed
- Evidence relating to the interface dressings in use
  - Macro- and micro-deformation
  - Drainage, removal of exudate
  - Key is in appropriate and proper use
- Education is sorely needed
- Clinicians must order and use NPWT with safety in mind
- Start and stop the therapy at the appropriate time
  - Move on to other closure products/therapies
QOL...Driven home

Closed after a 6 weeks; 2 weeks powered, 3 weeks non-powered

Safety Issues
- Bleeding
- Foam adherence
- Dressing retention
- Toxic Shock Syndrome
- Tripping hazard
- Patient non-compliance

WE ARE THE STEWARDS OF SAFETY WITH NPWT!
Thank You!