An Evidence Based Approach to Advanced Wound Care

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Disclosure

Dr. Regulski serves on the Regenesis Biomedical Speakers Bureau.

Evidence Based Medicine

"Good doctors use both individual clinical expertise and the best available external evidence, and neither alone is enough.

Without clinical expertise, practice risks becoming tyrannised by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient.

Without current best evidence, practice risks becoming rapidly out of date, to the detriment of patients".

Sackett, D.L. et al. (1996) Evidence based medicine: what it is and what it isn't. BMJ 312 (7023), 13 January, (71-72)

Grading the Evidence

- Level I — Evidence obtained from at least one properly designed randomized controlled trial.
- Level II-1 — Evidence obtained from well-designed controlled trials without randomization.
- Level II-2 — Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
- Level II-3 — Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.
- Level III — Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

U.S. Preventive Services Task Force

"Evidence-based medicine is not restricted to randomized trials and meta-analyses.

It involves tracking down the best external evidence with which to answer our clinical questions....

...if no randomized trial has been carried out for our patient's predicament, we follow the trail to the next best external evidence and work from there".

Sackett, D.L. et al. (1996) *Evidence based medicine: what it is and what it isn't.* BMJ 312 (7023), 13 January, (71-72)

Evidence Basis for:

Negative Pressure Wound Therapy

Hyperbaric Oxygen

Living Skin Equivalents

Pulsed Radio Frequency Energy

Negative Pressure Wound Therapy

- Use of controlled sub-atmospheric pressure, applied uniformly to the wound through an open cell foam or other interface dressing in a continuous or intermittent fashion.

Negative Pressure Wound Therapy

Blume, Walters, Payne et al **Diabetes Care 31:631-636, 2008**

- Multicenter RCT comparing NPWT-treated group (n=169) to control group (n=166) treated with advanced moist wound therapy (AMWT), i.e. alginates and hydrogels in patients with diabetes.
- Trial length 112 days, with 3 and 9 month follow up.
- Outcomes: Incidence and Time to Closure
- Intent to treat analysis

Negative Pressure Wound Therapy

Blume, Walters, Payne et al

Outcomes:

- Incidence Complete Closure

NPWT	73/169 (43.2%)	
Control	48/166 (28.9%)	p=0.0007

- Time to 75% Closure:

  Median of 26 days shorter with NPWT (p= 0.014)

- Second amputation necessary in seven (4.1%) NPWT and seventeen (10.2%) AMWT patients. p=0.035

Negative Pressure Wound Therapy

Armstrong and Lavery Lancet 366(1704-1710) 2005

- Multicenter RCT comparing NPWT-treated group (n=77) to control group (n=85) treated with alginates, hydrocolloids, foams or hydrogels in post-partial foot amputation in patients with diabetes.
- Trial length 112 days.
- Outcomes: Incidence of Closure, Time to Complete Closure, Granulation Response
- Intent to treat analysis

Negative Pressure Wound Therapy

Armstrong and Lavery

Outcomes

- Incidence Complete Closure

NPWT	43/77 (56%)	
Control	33/85 (39%)	p=0.040

- Time to Closure:

  Median of 21 days shorter with NPWT ($p < 0.01$)

- Second amputation necessary in two (3%) NPWT and nine (11%) control patients. $P > 0.05$

Hyperbaric Oxygen

- The use of 100% oxygen breathed at increased atmospheric pressure

Hyperbaric Oxygen

Cochrane Review 2004

- Kranke P et al. *Hyperbaric Oxygen Therapy for Chronic Wounds,* The Cochrane Database of Systematic Reviews 2004, Issue 1.
- Four randomized controlled trials in DFUs (147 subjects total)
- Pooled data from 3 RCTs (n=118) showed reduction in risk of Major Amputation with adjunctive HBOT vs alternative therapy:
- Relative Risk 0.31 (95%CI 0.13 to 0.71)
- Number Needed to Treat: 4 (95% CI 3 to 11)

Hyperbaric Oxygen

Faglia et al (1996)

- HBOT (n=35) vs. Standard Wound Care (n=33)
- DFUs, Wagner stage II, III, IV
- 6 week study
- Randomized, Not blinded
- Primary outcome: major amputation rate (BKA, AKA)

Outcomes

- Major Amputation Rate

  HBOT: 3/35 (8.6%)

  Control: 11/33 (33.3%)

  p=0.016

  Relative Risk: 0.26

Faglia E, Favales F et al. Diabetes Care. 19(12): 1338-1343, 1996

Hyperbaric Oxygen

Cochrane Conclusions

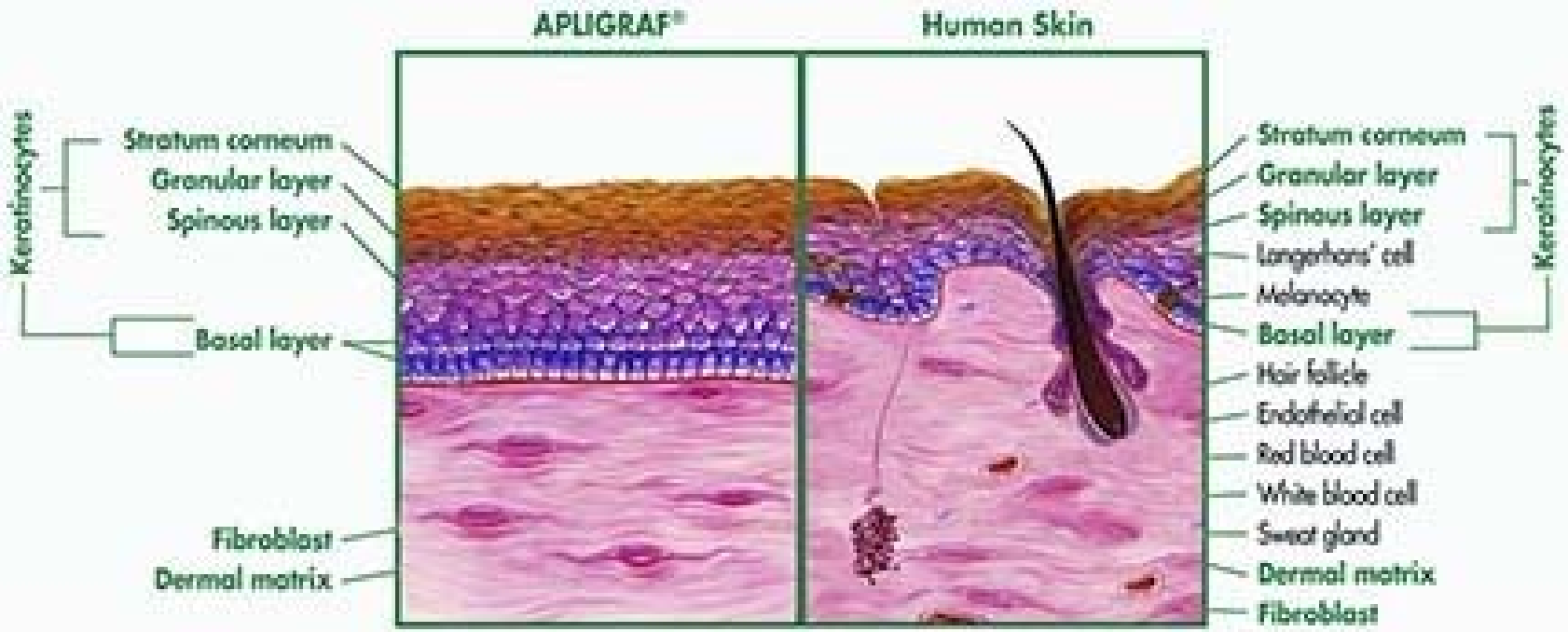
- "In people with foot ulcers due to diabetes, HBOT significantly reduced the risk of major amputation and may improve the chance of healing at 1 year.

- …In view of the modest number of patients, methodological shortcomings and poor reporting, this report should be interpreted cautiously however…"

Living Skin Equivalents

Bilaminate

- Living bi-layer of bovine type 1 collagen and human foreskin fibroblasts and keratinocytes



Parentau NL et al. J Cell Biochem. 1991;45:245-251

Bi-Layer Skin Equivalents

Veves, Falunga, Armstrong et al

- Prospective RCT comparing Apligraf plus saline moistened gauze (SMG) (n=112) to SMG alone (n=96) with ≤5 applications in 4 weeks
- Full thickness neuropathic DFUs
- Standard debridement and off-loading
- 12-week study period
- Outcomes: Incidence and Time to Closure

Diabetes Care 2001; 24(2):290-295

Bi-Layer Skin Equivalents

Veves, Falunga, Armstrong et al

Outcomes

- Mean Ulcer Age: 11.5 months
- Mean Ulcer Area: 2.9 cm^2
- Incidence of Complete Closure

Apligraf + SMG:	63/112 (56.0%)	
SMG Alone:	36/96 (38.0%)	p=0.0042

- Median Time to Closure

Apligraf + SMG:	65 days	
SMG Alone:	90 days	p=0.0026

Living Skin Equivalents

Human Fibroblast Derived Dermal Substitute

Cryopreserved human fibroblast-derived dermal substitute

Composed of fibroblasts, extracellular matrix, and a bioabsorbable scaffold.

Human Fibroblast Derived Dermal Substitute

Marston, Hanft, Norwood et al

- Prospective, single-blind, multicenter RCT evaluating Dermagraft plus standard wound care (n=130)to standard wound care alone (n=115).
- Chronic Plantar DFUs > 6 weeks duration
- 12 Week study period
- Outcomes: Incidence of Complete Wound Closure, Percent Wound Closure at 12 Weeks
- 35 centers

Diabetes Care. 2003;26:1701-1705.

Human Fibroblast Derived Dermal Substitute

Marston, Hanft, Norwood et al

Outcomes

- Mean Ulcer Age: Dermagraft 41 weeks; Control 67 wks
- Mean Ulcer Area: 2.4 cm^2

- Incidence Complete Closure

Dermagraft	39/130 (30%)	
Control	21/115 (18%)	p=0.023

- Median Percent Closure

Dermagraft	91%	
Control	78%	p=0.044

Pulsed Radio Frequency Energy

Radio-frequency electro-magnetic energy applied to wound non-invasively.

Non-thermal, non-ionizing.

Pulsed Radio Frequency Energy

Lavery, Driver, Isenberg et al

- Retrospective analysis of registry data (2005-2008)
- 70+ outpatient US medical centers contributing 490 wounds of various types
- Diabetic foot ulcers n=79
- Multiple prior failed therapies
- PRFE as adjunct to on-going wound care
- 4 week follow up
- Outcomes: Wound Trajectory, Median Reduction in Area, proportion reaching 50% closure in 4 weeks

Manuscript in preparation; data on file Regenesis Biomedical Inc.

Pulsed Radio Frequency Energy

Outcomes

• Median age	61 years
• Median Wound Age	12.5 months
• Median Wound Area	3.7 cm^2
• 50% Closure in 4 weeks	32.2%
• Median Reduction in Area	36.7%
• Wound Healing Velocity	3.6 mm^2/day

Pulsed Radio Frequency Energy

Lower Extremity Wounds: 4-Week Outcomes

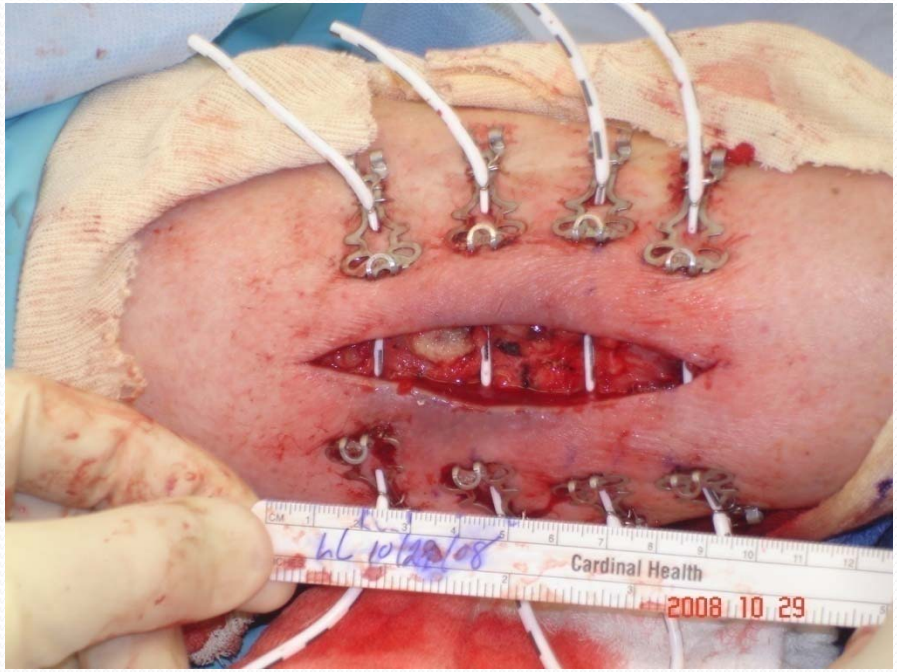
	Diabetic Ulcers	Venous Ulcers	Pressure Ulcers
Wound Area (cm^2)	3.7	17.5	10.8
Wound Age (months)	12.5	12.0	6.0
50% Closure in 4 weeks (%)	32.2	27.1	36.5
Median Reduction in Area (%)	36.7	37.5	46.4
Wound Healing Velocity (mm^2/day)	3.6	19.0	12.5

Canica Wound Compression System

Primary Closure of Chronic Wounds

Lower Leg application currently in US Clinical Trials

Canica Wound Compression System



Canica Wound Compression System

Canica Wound Compression System

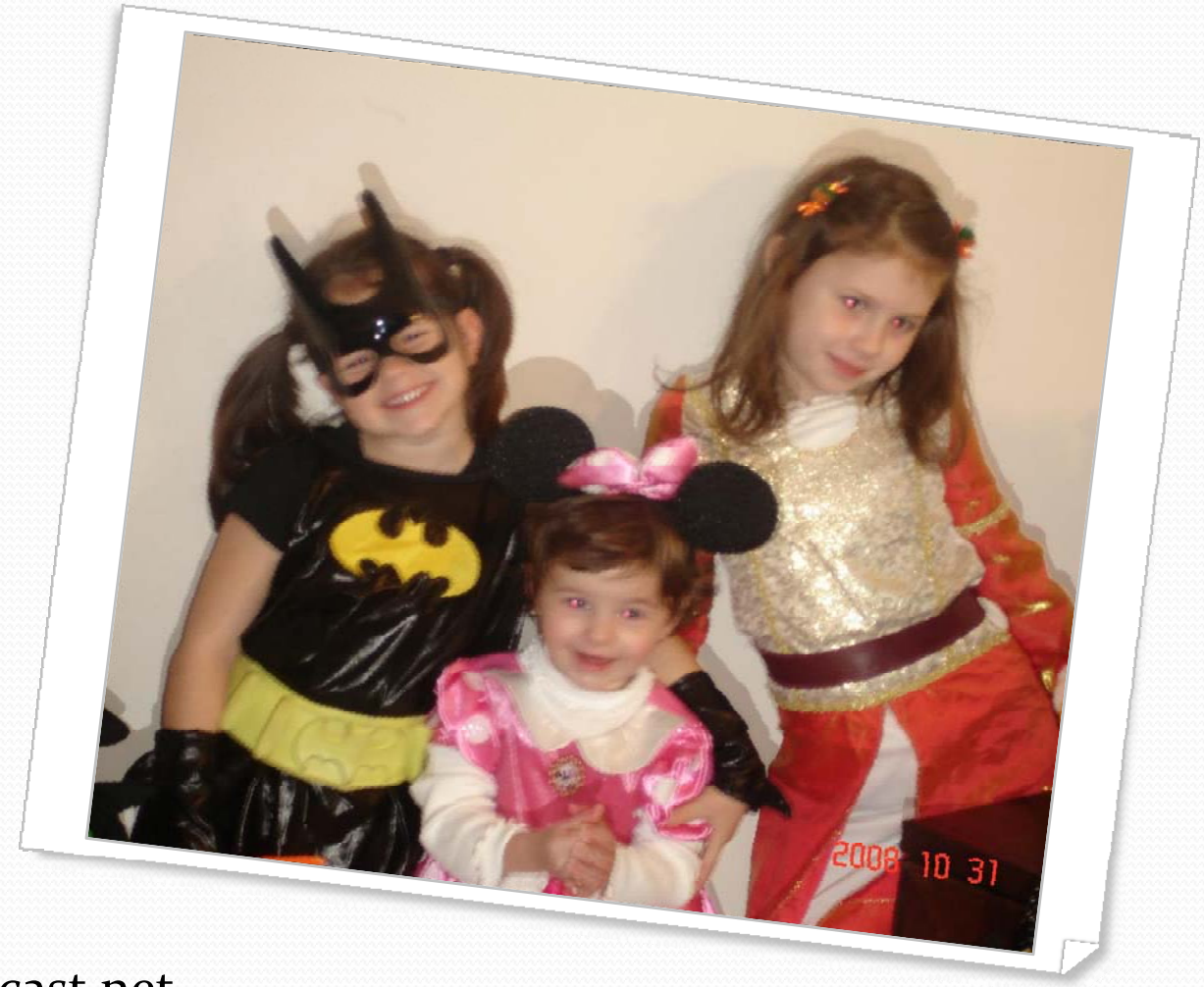
Closure of Post-Amputation Wound

An Evidence Based Approach to Advanced Wound Care

SUMMARY

- Carefully designed multicenter, randomized, controlled trials help the clinician make reasoned decisions about choice of treatments.
- There is high level evidence to support the clinical use of several advanced wound care modalities.
- In the absence of high level evidence, the clinician should base his/her treatment decisions on the best available evidence, including lesser grade studies, committee reports, opinions and/or clinical experience of respected authorities.

Thank you!



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