PEARLS AND PITFALLS OF TECHNOLOGY

FRIEND OR FOE?

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OBJECTIVES

1. Identify two areas of medicine where technology leaves healing challenges
   a. Battlefield Medicine; How successful battlefield management of wounds leads to life time wound healing challenges
   b. Surviving ICU with a pressure ulcer, then what?
2. Describe the evolution of technology in the world of wound assessment/monitoring
   a. Digital photography
   b. Wearable sensors
   c. Serum biomarkers
3. Describe 2 key technological advances in world of wound healing and describe how they have impacted practices
   a. Negative Pressure Wound therapy (NPWT)
   b. Advanced biologics; from womb to wound
4. Describe 2 technological advances in preventing wounds and/or preventing recurrence
   a. Temperature monitoring for diabetic feet
   b. Human GPS (turn monitors)

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TECHNOLOGICAL ADVANCES IN WOUND PREVENTION AND WOUND HEALING

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THANK YOU * RESEARCH ASSISTANT AND COLLEAGUE

- MANDY PETERSEN WOCN, NP, RN

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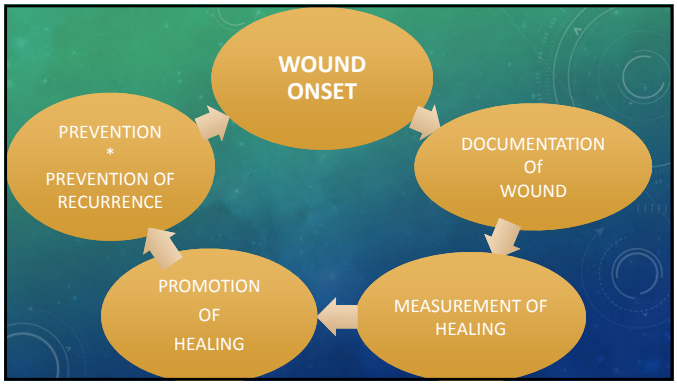

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WOUND ONSET

- HOW SUCCESSFUL BATTLEFIELD (or ICU) MANAGEMENT OF LIFE THREATENING CONDITIONS LEADS TO A LIFETIME OF WOUND HEALING CHALLENGES

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34YO VETERAN (2017)

- IED 6/2013 Afghanistan (Improvised Explosive Device aka road side bombs)
  - Bilateral LE severe trauma-> bilateral transfemoral amputation, bowel and bladder injury , pneumothorax, multiple fractures
  - Medivac to Landstuhl, transferred to San Antonio
  - 2013-2017 >140 surgical procedures
    - Colostomy, ICP for bladder through stoma site,
    - Revision right transfemoral amputation
    - Multiple skin grafts

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PROFILE OF AN 62 YO ICU SURVIVOR

62 yo male w/DM2, Right BKA (2007) on hemodialysis admitted to acute hospital for sepsis

3 mo PTA h/o fall resulting in R hip fx

❖s/p repair in w/THA

❖ADMISSION DIAGNOSIS

❖Sepsis 2/2 to HD-cath infection, PNA, and right hip infection

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HOSPITAL COURSE

❖Procedure: removal of hip prosthesis

❖same side as amputation (BKA)

❖Survived sepsis, PN and right hip infection

❖DISCHARGED : SNF

❖Non-WB on right

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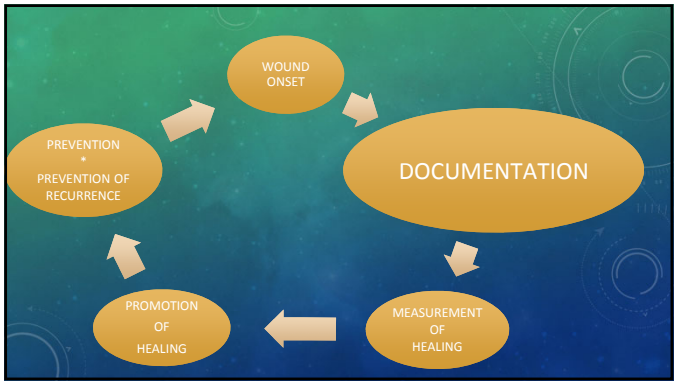

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WOUND ASSESSMENT AND DOCUMENTATION

- **MEASUREMENTS**
- **DIGITAL PHOTOGRAPHY**
- ELECTRONIC MEDICAL RECORD

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TECHNIQUES FOR MEASURING WOUND AREA/VOLUME

MANUEL MEASUREMENTS

- Simple ruler method
- Mathematical model (shortest x longest radii x (VARIABLE) assumes ellipitical or spherical)
- Manual planimetry

PROBLEMS

- Inconsistency, inaccuracy
- Inter-tester reliability
- Time

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WHO CARES HOW RELIABLE OUR MEASUREMENTS ARE?

- INSURORS
- LAWYERS

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TECHNIQUES FOR MEASURING WOUND AREA/VOLUME

- **OPTICAL TECHNOLOGIES**
- *Digital planimetry
  - Requires tracing of the image, then trace overlay on computer to calculate area (planimetric tablet or smart phone)
- ***Digital Imaging + SMART software**
  - **ADVANTAGES**
    - Time, consistency, reproducibility, accuracy
  - **CHALLENGES**
    - Angle of the lens (relationship to the surface, needs to be perpendicular)
    - Tracks and undermining cannot be measured
    - Cost
    - EHR; interface

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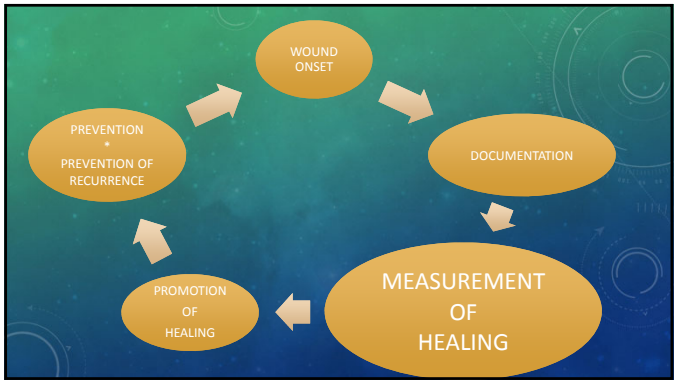

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MEASUREMENT OF HEALING

MEASUREMENT OF THE HEALING PROCESS

*measuring physiology of healing

- DIAGNOSTICS TOOLS/ASSESSMENT TOOLS
  GOALS:
  - IDENTIFY WOUND PARAMETERS THAT MAY BE A BARRIER TO HEALING
  - MONITOR HEALING PROGRESS
    - CHANGES IN WOUND METABOLISM OVER TIME
    - CHANGES IN OXYGENATION/PERFUSION OF THE TISSUE
    - PROGRESS THROUGH THE STAGES OF HEALING

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MEASUREMENT OF HEALING

- ULTIMATE GOAL
  - GUIDE TARGETED INTERVENTIONS
    - IDENTIFY HIGHEST RISK PATIENTS
    - ALLOW FOR BEST USE OF RESOURCES
    - MAXIMIZE HEALING OUTCOMES

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MEASUREMENT OF HEALING PROCESS

- WOUND BASED
  - Wound monitoring
    - IN-SITU physiologic surveillance of the wound
  -
- SYSTEM BASED
  - Serum (blood draw)
  - Tissue analysis

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MEASUREMENT OF HEALING

WOUND BASED

ASSESSMENT/DIAGNOSTIC TOOLS
wearable technology

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MEASUREMENT OF HEALING

WOUND BASED

ASSESSMENT/DIAGNOSTIC TOOLS
Wearable technology

Courtesy of collaborative ; Tufts University, Harvard Medical School and Purdue University

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WEARABLE TECHNOLOGY

BASICS

- Flexible biosensors capable of monitoring physiological information
  - Biosensors for:
    - Oxygen
    - pH
    - bacteria
    - Temperature
    - cytokines
    - Glucose
    - biomarkers

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MEASUREMENT OF HEALING

WOUND BASED

ASSESSMENT/DIAGNOSTIC TOOLS
Wearable technology = SMART dressings

- Biosensors combine a biological component with a physiochemical detector to observe and analyse a chemical substance and its reaction in the body

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SMART BANDAGE HAS 2 PARTS

1) bandage itself with pH and temp sensors w/drug releasing microbeads
2) Electronic module connected to the bandage via a flexible cable = scans what the sensors are measuring and signals for the drug to be released

Courtesy of collaborative ; Tufts University, Harvard Medical School and Purdue University

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WEARABLE TECHNOLOGY

- BENEFITS
  - Avoid/minimize lab testing (delayed information, static, time consuming, costly)
  - Reduce clinic appts
  - Real time, continuous monitoring of wound status and vital biomarkers at the wound site
  - Stimulating the healing process

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MEASUREMENT OF HEALING * BIOASSAYS

WHAT IF A LAB TEST OR TISSUE ANALYSIS COULD TELL US THE STATE OF THE WOUND AND WHAT WAS NEEDED?

THEY CAN!

Serum OR Tissue biomarker analysis

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WHAT IS A BIOMARKER?

BIOMARKER

- A biologic feature which is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacologic responses to a therapeutic intervention.
  - E.g. prostate specific antigen (PSA) is a biomarker for cancer of the prostate

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WHAT IS THE ADVANTAGE OF IDENTIFYING BIOMARKERS?

- Helps identify reason for delayed healing
  - Prolonged inflammation, infection, deregulation of proteases, reduced growth factor activity, stem cell dysfunction, cellular senescence
- Helps to identify which treatments may be beneficial
- Helps identify who will respond to different treatments
- May allow for personalized, efficacious and cost effective treatment

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WHAT TYPE OF (WOUND) BIOMARKERS ARE THERE? WHERE ARE THEY FOUND?

- Biomarkers can be
  - Diagnostic; what is the cause of delayed healing?
  - Predictive; predict outcomes or likelihood of benefit from treatment
  - Indicative; used to monitor disease progression or response to therapy in real time
- Biomarkers can be found in;

blood/serum	wound fluids
tissue specimens	wound swabs

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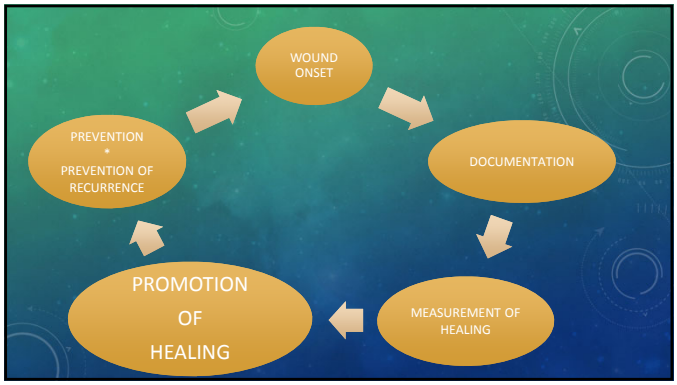

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Wound care technologies

Biophysical

Negative pressure wound therapy

Electrical stimulation, diathermy, pulsed electromagnetic fields, pulsed radiofrequency energy

Low-frequency noncontact ultrasound—MIST/AROBELLA

Growth factors/Cytokines

Acellular matrix tissues

Placental tissues

Bioengineered allogeneic cellular therapies

Bilayered skin equivalent—Apligraf

Dermal replacement therapy—Dermagraft

Stem cell therapies

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Wound care technologies

Biophysical

Negative pressure wound therapy

Electrical stimulation, diathermy, pulsed electromagnetic fields Pulsed radiofrequency energy
Low-frequency noncontact ultrasound—MIST/AROBELLA
Extracorporeal shock wave therapy

Growth factors

Becaplermin—platelet-derived growth factor—Regranex
Platelet-rich plasma

Acellular matrix tissues

Xenograft dermis
Integra—bovine collagen
Xenograft acellular matrices
Oasis—small intestine submucosa
Human dermis
Graftjacket

Placental tissues

Amniotic tissues/amniotic fluid
Umbilical cord
Dehydrated human amnion/chorion membrane (dHACM)

Bioengineered allogeneic cellular therapies

Bilayered skin equivalent—Apligraf
Dermal replacement therapy—Dermagraft

Stem cell therapies

Autogenous—bone marrow-derived stem cells
Allogeneic—amniotic matrix with mesenchymal stem cells—Grafix

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NPWT IN THE 20TH CENTURY

- Many clinicians used NPWT in the 20th century
  - Dr E. Klapp first used a suction pump around 1907
  - Russian doctors first used a canister with NPWT in the 1980s
  - Chariker & Jeter first used a wound bed contact layer in 1989
- Morykwas & Argenta used a foam contact layer in 1997
  - This was patented as a system called vacuum assisted closure
  - This patent prevented other systems from being used
- In 2006 a court ruled that other NPWT systems could be used without patent infringement
  - A wide choice of NPWT systems is now available

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GROWTH FACTORS
OVER 50 CYTOKINES IDENTIFIED

- AUTOLOGOUS PLATELET RELEASATE
  - Platelet rich plasma gel activated by thrombin results in topical application of fibrin and growth factors released from alpha granules
- PDGF (platelet derived growth factor)
  - Regranex/Becaplermin

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BIOENGINEERED TISSUE/ CELL THERAPY/SKIN EQUIVALENTS

- **OrCell**
  - Bilayered bioengineered tissue
  - FDA indications for burns, EB (VLU, DFU)
- **Apligraf**
  - Bilayered bioengineered tissue
  - Bovine collagen
  - FDA indications DFU, VLU, EB
- **Dermagraft**
  - Single layer fibroblasts on biodegradable mesh
  - FDA indications DFU

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STEM CELLS (MESENCHYMAL STEM CELLS/MSC)

- DEFINED characterized by (1) a prolonged self-renewal capacity and (2) the ability to differentiate into mature stages and various different tissue types by asymmetric replication
- PROPERTIES They are undifferentiated cells that renew themselves for the entire life span of an organism through cell division and ii) they have a remarkable capacity to develop from a common precursor into multiple cell types with specialized functions.
- SOURCES
  - Adult stem cells (Bone Marrow, adipose tissue, nerve tissue, umbilical cord blood, dermis, adult hair follicles)
  - Bone marrow
    - Decorticate exposed bone at the base of the ulcer
    - Bone marrow production of MSC decreases with age
  - Embryonic stem cells (ethical and practical issues)
  - Induced pluripotent stem cells (iPS cells) = adult human skin cell reprogramed back to embryonic state

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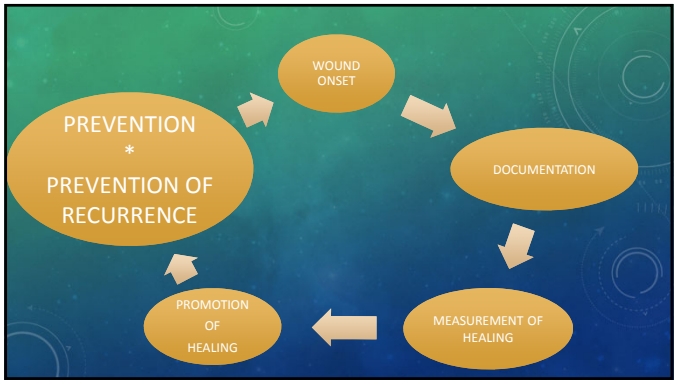

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PREVENTION OF WOUND/RECURRENCE

- PREVENTION
  - HUMAN GPS
- PREVENTION OF RECURRENCE
  - HEAT MAPPING

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Remote Thermometry for the Early Detection of DFU

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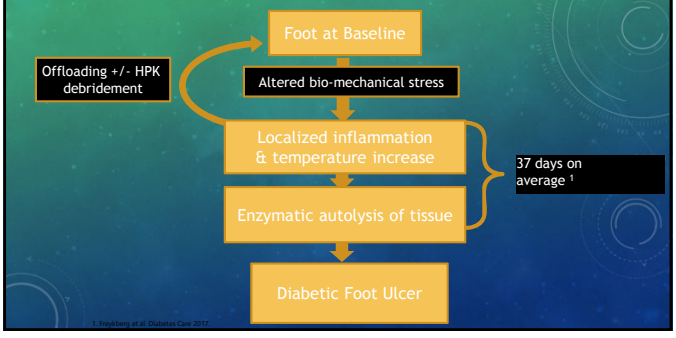
FOOT ULCER PATHOGENESIS



1- Frykberg et al. Diabetes Care 2017

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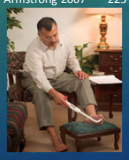
EFFICACY OF TEMPERATURE GUIDED AVOIDANCE THERAPY (TGAT)

Study	N	Follow-up period	Recurrence, SOC	Recurrence, TGAT	p-Value	Relative Reduction
Lavery 2004 [1]	85	6 mos	15.9%	2.4%	0.01	85%
Lavery 2007 [2]	173	15 mos	29.3%	8.5%	0.0046	71%
Armstrong 2007 [3]	225	18 mos	12.2%	4.7%	0.038	61%
					Mean:	72 %



"Based on quality studies in this area, the results of this review have indicated that the use of ***temperature-monitoring is an effective way to predict, and thus prevent, diabetic foot ulceration.***" [4]

1. Lavery et al. Diabetes Care. 2004;27(11):2642-7.
2. Lavery et al. Diabetes Care 2007; 30(1):14-20.
3. Armstrong et al. Am J Med. 2007; (120(12):1042-6.
4. Houghton et al. J Foot Ankle Res. 2013;6(1):31.

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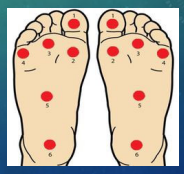
TEMPERATURE GUIDED AVOIDANCE THERAPY

Daily procedure:

1. Record temperatures at the 12 locations indicated in the diagram
2. Calculate the asymmetry (delta-temperature) between each ordered pair.
3. Trend degree of asymmetry over time.
4. If any region's asymmetry exceeds 2.2 °C for two consecutive days, reduce activity until temperatures normalize and contact the clinician.



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PODIMETRICS PREDICTIVE ACCURACY

Diabetes Care Volume 40, July 2017 1

Feasibility and Efficacy of a Smart Mat Technology to Predict Development of Diabetic Plantar Ulcers

Diabetes Care 2017;40:1–8 | https://doi.org/10.2337/dc16-2294

Performance Results:

97% — 30% of DFU developed approximately 5 weeks before ulceration occurred

Adherence Results:

86% — [illegible]

Ease of Use Results:

88% — [illegible]

These data suggest the Podimetrics System may detect up to **97%** of non-traumatic DFU approximately **five weeks** before clinical presentation

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GPS FOR HUMANS

- randomized trial of more than 1,200 patients at a large California academic medical center concluded that the pressure ulcer incidence rate was 74 percent lower among patients monitored by the wearable monitoring system.

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