A History of Deep Tissue Injury – a Bioengineering perspective

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First recorded evidence in the Egyptian Section of British Museum – Priestess of Amen
Research area has become an international “Hot Topic”
Incidence is a Quality of Care and Safety Issue

PU classification Grades I, II, III, IV and Deep Tissue Injury (DTI)
Grades (or stages) of Pressure Ulcers

- Grade 1
- Grade 2
- Grade 3
- Grade 4
Pressure Ulcers –
A bridge too far for Superman

Christopher Reeves died of septicaemia as a direct result of a deep pressure ulcer in 2004
Categories/Stages of PUs

- **NPUAP Grade/Stage 1 Pressure Ulcer Definition**

  “An observable pressure-related alteration of intact skin whose indicators as compared to the adjacent or opposite areas on the body may include changes in one or more of the following:
  
  Skin temperature (warmness/coolness), **tissue consistency** (firm or boggy feel and/or sensation) (pain/itchy) 
  
  The ulcers appear as a defined areas of persistent redness in lightly pigmented skin whereas in darker skin tones, the ulcers may appear with persistent red, blue or purple hues……”

There are 4/5 such Stages, each
- Defined by anatomical limit of soft-tissue damage
- Requires a complex skill that needs training and time to develop
- Concept of Deep Tissue Injury (NPUAP, 2005)
Pathophysiology of PUs
Tissue response to biomechanical factors

- Localised ischaemia

- Impaired fluid flow and lymphatic drainage
  
  *(Miller and Seale 1981 Lymphology 14, 161-66)*

- Ischaemic/Reperfusion injuries - toxic level of ROSs
  

  - Animal models – related to Pressure Ulcers
    
    *(Peirce et al, 2000; Unal et al., 2001; Saito et al., 2008)*

- Sustained deformation of cell
  
Abnormal Response to Biomechanical Loading - Intrinsic Risk Factors

- Subjects have limited mobility
  - chair bound, sedated, anaesthetized, acute care/ICU

- Subjects have impaired sensitivity
  - paralysis, neuropathy

- Soft tissues are more vulnerable to pressure-induced damage than normal
  - Breakdown and atrophy, lack of muscle tone, dehydrated & malnourished, fragile soft tissues

An inevitable consequence of prolonged surgery? 

Hierarchical Approach to Pressure Ulcers

Analytical Techniques
Gefen et al.

Model systems

Cell mechanics

From Lab to Clinic
Sitting Acquired Pressure Ulcers

- Considerable effort of monitoring patients in bed – 2 hr turning policy
- If judged favourable, patient is moved from bed to a sitting environment and often left for > 6 hrs
- During this period some patients do not move
- This practice is continued in care homes and the community
Are Sitting Acquired PUs Avoidable?

- In 1985, Pam Hibbs said that 95% were avoidable
- Modern technology has the potential
  - to elucidate the aetio-pathogenesis in different tissue layers
  - identify non-reversible tissue injury
  - identify characteristics of susceptible patients
  - Evaluate and optimise pressure-relieving strategies
- Simple screening methods need to be developed
- Experience and knowledge of individual carers remains critical
Critical Bioengineering Research Associated with PU Prevention

- Development of measurement systems to monitor the interface
- The prediction of the interface/interstitial conditions leading to tissue breakdown
- Establishment of objective screening methods
- Early identification of those subjects particularly at risk
- Advanced bioengineering technologies
Critique of Interface Pressure Monitoring

Potential

• Established clinical measure to compare support surfaces and other interventions for individual subjects
• Ideal for feedback for subject posture

Limitations

• Analysis of large data sets (*Bogie et al. 2008*)
• Relevance to interstitial pressures?
• Relevance to location of initial tissue damage?

Pressure measurements alone are not sufficient to alert the clinician to potential areas of tissue breakdown

The effects of pressure and time on tissue viability or status
# Deep Interstitial Pressures versus Interface Pressures

<table>
<thead>
<tr>
<th>Study</th>
<th>Model system</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bader and White 1998</td>
<td>Loaded greater trochanter of surgical patients</td>
<td>0.28 - 0.41</td>
</tr>
<tr>
<td>Lee et al. 1984</td>
<td>Pressure sensors implanted in a pig model</td>
<td>3 - 5</td>
</tr>
<tr>
<td>Ragan et al. 2002</td>
<td>Axisymmetric 3D (FE) model of buttock</td>
<td>3.7</td>
</tr>
<tr>
<td>Oomens et al. 2003</td>
<td>3D FE model – variable properties of muscle, fat and skin</td>
<td>2.4</td>
</tr>
<tr>
<td>Gefen et al. 2005</td>
<td>3D FE model</td>
<td>266</td>
</tr>
<tr>
<td>Sun et al. 2005</td>
<td>FE model based on non-sitting MRI</td>
<td>3.5</td>
</tr>
</tbody>
</table>
Non-Invasive Methods for Monitoring Tissue Viability/Status
Physical Sensors and Biosensors

Laser Doppler fluxmetry


Transcutaneous gas monitoring ($T_c$PO$_2$ and $T_c$PCO$_2$)

*Bader and co-workers 1985 – ; Colin et al. 1995*

Sweat Biochemistry

*Ferguson-Pell 1988 ; Bader, Knight et al.1997-2006*

Early Biochemical Markers – Cytokines and chemokines

*Bronneberg et al. 2007*

Plasma and Urine based markers

*Rodriguez et al. 1988; Loerakker et al. 2012*
Testing Performance of Support Surfaces

Chai and Bader 2012; White and Bader, 1999; Zenhorst et al.
Experimental Protocol with APAMs

• Attach transcutaneous gas electrodes to both the sacrum & scapular
• Healthy Volunteers carefully positioned supine onto the test surface
• Interface pressure measurements at surface
• Continuous measurements of $T_c$PO$_2$ and $T_c$PCO$_2$ over 30 min test period
Distinctive Gas Tension Responses (1-3) to Alternating Support Pressures

Chai and Bader, 2013
Assessing tissue viability in patients at the UK National Spinal Injury Centre

42 SCI subjects
  23 lesions above T6
  19 lesions below T6
Assessments (2 - 6 within 1 year of injury) performed on prescribed support cushions

Transcutaneous gas tensions with time
Study I

Early progressive changes in tissue viability during sitting

*Bogie, Nuseibeh and Bader (1995) Paraplegia 33, 1441-47*

- Paraplegics with flaccid paralysis are at higher risk of tissue breakdown than both tetraplegics & paraplegics with spasticity
- This supported a clinical finding by *Noble et al. 1980*
- *Levine et al. (1990)* – reported Tissue Shape Changes with FES

**TABLE 1: Relative incidences of complete spinal injury** and levels of spinal lesions of 83 patients admitted to Royal Perth Rehabilitation Hospital with pressure sores.

<table>
<thead>
<tr>
<th>Sub-group</th>
<th>Level of Spinal Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C1-C7</td>
</tr>
<tr>
<td>Males (complete lesions)</td>
<td>52%</td>
</tr>
<tr>
<td>Males with sores</td>
<td>25%</td>
</tr>
<tr>
<td>Ratio</td>
<td>0.47</td>
</tr>
<tr>
<td>Females (complete lesions)</td>
<td>23%</td>
</tr>
<tr>
<td>Females with sores</td>
<td>5%</td>
</tr>
<tr>
<td>Ratio</td>
<td>0.20</td>
</tr>
<tr>
<td>All patients (complete lesions)</td>
<td>46%</td>
</tr>
<tr>
<td>All patients with sores</td>
<td>19%</td>
</tr>
<tr>
<td>Ratio</td>
<td>0.42</td>
</tr>
</tbody>
</table>
A specialised seating assessment clinic: changing pressure relief

Coggrave and Rose (2003) Spinal Cord 41, 692-95

- Review of 46 newly injured & chronic SCI subjects, median age 41 y
- Mean duration of pressure relief of 1min 51s (42-210s) required to restore $T_cPO_2$ levels
- Brief pressure lifts of 15-30 seconds are ineffective.
- Other strategies, e.g. forward leaning and tilt back, are more effective
Concept of Early Detection

Preventive measures
Wound treatment

Test

Additional investigations
Biomarkers from Sweat

Polliack et al., 1993, 1997; Knight et al. 2001; Bader et al. 2005

Can we measure tissue metabolites by sweat collected at the skin surface?

Do specific metabolites accumulate during loading?

Are they dispersed in reperfusion phase?

Ideal Characteristics of Biomarker
Easy specimen collection, Non-invasive, stable marker, Simple analysis with good Sensitivity and Specificity
Materials and Methods

- Tests conducted in a controlled room at 35°C
- 31 independent subjects - 19 subjects, mean age 27 (19-41)
- Subjects lay prone on a standard hospital mattress
- Assembly mounted over subject to provide loading at the sacrum for periods up to 60 min.
- Unloaded control site
- Continuous gas monitoring
- Annular sweat pads analysed
- Lactate and urea concentrations
- $T_cPO_2$ and $T_cPCO_2$ monitored
Results from both unloaded and loaded sacrum

Pressures 40-120 mmHg
Time 30-60 min

- Loaded sacrum
- Unloaded sacrum

Median value of TcPO2 / mmHg
Lactate concentration / mmol/L
The relationship between % age reduction in median $T_cPO_2$ with (a) lactate ratio (b) $T_cPCO_2$ parameter

Threshold level established beyond which sweat lactate was elevated

Knight et al. 2001
Skin Biomarkers for Pressure Ulcer Detection

Problem:
Current risk assessment techniques for PU are limited

Objective:
Identify early biochemical markers following skin irritation and damage
Keratinocytes release a number of cyto- and chemokines

Methods
In vitro studies with TE-epidermis
In vivo studies with human skin

Biomarker release from the epidermis:
IL-1α, IL-1RA, IL-8, TNF-α, MCP-1, GRO-α (ELISA)
In Vivo Loading Study

• A total of healthy human volunteers age 23 – 64 years

• Exclusion criteria: eczema or psoriasis

• Room temperature 25° C.

• Loaded site (L) of 100mmHg (13.3 kPa) for a period of 2 hours - NL control site, TS tape stripping

Sebutape
Perkins et al. 2001
Results - Human volunteers
Values normalized to their own control values

AL after loading immediatley and after 10 and 20 mins, respectively; NL adjacent to loaded site; TS after tape stripping

Clinical Study - Test Objectives

- Is there a difference at the site of a grade I ulcer compared to visually intact skin?
- Patients (age 20-80 years) from general surgery, orthopaedics, lung disease
- Medical Ethics approval of Catharina Hospital in Eindhoven

Patients with sacral grade 1 pressure ulcer
Biochemical Changes in skin composition in spinal cord injury: A possible contribution to decubitus ulcer formation

Rodriguez & Claus-Walker 1988 Paraplegia 26, 1208-13

Hypothesis

The established changes in external resistance to external forces post-SCI could be due to breakdown of collagen

• Methods - Measured collagen breakdown products in urine of SCI subjects

• Results - Increased levels of hydroxyllysine & hydroxyproline suggesting a decrease in skin stiffness and strength
Plasma variations of biomarkers for muscle damage in male able-bodied and SCI subjects

Loerakker et al. 2012 J Rehab Res Dev 49(3), 1-12

- Biomarkers measured in blood: creatine kinase (CK), myoglobin (Mb), heart fatty acid binding protein (H-FABP), C-reactive protein (CRP)

- What are the inter- and intra-subject variations levels?

- Do the levels increase with risk of pressure ulcer developing?

- Subject groups
  - Able-bodied controls (n = 7)  -  age range 39-66
  - SCI without ulcers (n = 7)   -  age range 40-68
  - SCI with pressure ulcer (n = 1)  -  age 59
Results

- SCI group divided into active (SCI-A) and non-active (SCI-NA)
- SCI-A group produced larger CK and smaller CRP levels compared with values from SCI-NA group

a) and b) CK; c) and d) MB; e) and f) H-FABP; g) and h) CRP
Discussion

Loerakker et al. 2012 J Rehab Res Dev 49(3), 1-12

- Intra-subject variations smaller than inter-subject variations
  - Individuals exhibit a specific range of marker levels
- Variations in marker levels are small compared to increases
  - after myocardial infarction (Glatz et al. 1998)
  - with pressure ulcers (Hagisawa et al. 1988)
- Significant correlations with pairs of markers e.g. Mb and H-FABP
- CRP levels in SCI larger than in able-bodied subjects
- Within SCI group → CK increases and CRP decreases with activity
- SCI subject with pressure ulcer
  - Larger H-FABP levels → probably within baseline range
    (no muscle damage, no Mb increase)
  - Larger CRP levels → inflammation due to ulcer
Hypothesis: Muscles are more susceptible to mechanical damage than skin.

Deep lesions first develop in the muscle tissue.

Deep Tissue Injury
Could be misdiagnosed as a mild grade 1-2 ulcer, since the extent of tissue damage is not visible until the gross breakdown of the skin surface – NPUAP Consensus meeting 2005, Black et al, 2003.
Bioengineering Techniques

• Past observations have been limited to the depths of the skin layer
  – blood flow and transcutaneous gas measurements
  – time consuming histology of tissue biopsies
• What about Deep Tissue Injury?
• New techniques are able to examine non-invasively the integrity of cells, skin and deeper tissues using
  – Biosensors
  – Computational modelling (FEA)
  – Live cell imaging
  – Ultrasound (Elastography)
  – Magnetic Resonance imaging
• Reparative techniques
  – Functional Electrical Stimulation
Abnormal Response to Biomechanical Loading - Intrinsic Risk Factors

- Subjects have limited mobility
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- Subjects have impaired sensitivity
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- Soft tissues are more vulnerable to pressure-induced damage than normal
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Implanted gluteal NMES system

Rationale:
- Implanted electrodes reliably deliver NMES to target muscles
- Minimal user training required
- Use of an implanted gluteal NMES may provide individuals at risk of tissue breakdown with a method for achieving an independent pressure relief regimen
Implanted gluteal NMES system
Bogie et al. 2003 and 2006

Study Hypotheses:

Long term NMES exercise of paralyzed gluteal muscles improves intrinsic tissue status in individuals with motor paralysis

Dynamic weight shifting produced by the gluteal stimulation system will augment the efficacy of conventional pressure relief/redistribution strategies

Courtesy of: Kath Bogie, D.Phil
Implanted gluteal NMES system

LASR: Longitudinal Analysis with Self-Registration

Long term effects on interface pressures (*Bogie et al, 2006*)

LASR analysis of long-term changes in static seated IP distribution.

*Green area shows significantly decreased IP*

Courtesy of: Kath Bogie, D.Phil
Clinical relevance

- Predict which patients are at risk of developing DTI
- Development of patient-specific sit orthoses
- Estimate the influence of functional electrical stimulation on internal tissue deformations during sitting in SCI patients

Bogie et al., 2006 Long term pressure ulcer prevention with NMES.
Imaging Strategies to determine Local Tissue Deformation

Magnetic Resonance Imaging

Ultrasound

Finite Element Analysis
Ultrasound Elastography (USE)

USE principles (left) and USE of breast metastasis (right colour) with corresponding ultrasonic image (right greyscale)

US system with a high frequency (5-17 MHz) linear probe and 2-5Hz convex for deeper tissues and more obese subjects with RF output
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