Numerical Characterization of Ultrasound Elastography for the Early Detection of Deep Tissue Injuries

by

Kenton David Hamaluik

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Department of Mechanical Engineering
University of Alberta

Abstract

Deep tissue injuries—casually termed “bedsores”—are a type of wound often suffered as secondary injuries in persons with reduced mobility such as those with spinal cord injuries, the elderly, and people with multiple sclerosis. Deep tissue injuries form when excess pressure is applied to tissue for extended periods of time without relief and begin as the necrotic breakdown of deep tissues at the bone-muscle interface. As these wounds progress, they “tunnel” up toward the surface of the skin where they break open into late-stage pressure ulcers and are completely unnoticeable if the patient lacks sensation. There is currently no clinical tool for detecting these injuries as they form and progress and as such these wounds represent a severe burden on both patients and the health care system alike.

The goal of this work was to numerically characterize the use of three modalities of ultrasound elastography—quasi-static ultrasound elastography, acoustic radiation force impulse imaging, and shear wave speed quantification—for the early detection of deep tissue injuries. Ultrasound elastography is an imaging modality capable of imaging the mechanical stiffness of soft tissue which is a key measure of tissue health. Through combinations of k-space pseudo-spectral techniques, finite-element modelling, and image processing methods, the ability of ultrasound elastography to detect and accurately diag-

nose deep tissue injuries was explored. Parametric studies were undertaken to investigate the effect of a wide range of parameters relevant to the detection sensitivity of ultrasound elastography including both device-design parameters and deep tissue injury lesion properties.

Through the numerical characterizations performed in this work, an understanding of the benefits and limitations of using ultrasound elastography to detect deep tissue injuries was achieved. Shear wave speed quantification was found to provide the most accurate measures of tissue health, however its effectiveness may be limited in very deep tissues. The understanding gained from this work may lead to investigating ultrasound elastography as a viable detection modality for early deep tissue injuries in both animal models and human subjects—these real world tests are the next step on the way to clinical adoption of ultrasound elastography for the early detection of deep tissue injuries.

Preface

Chapter 3 of this thesis has been published as K. Hamaluik, W. Moussa, M. Ferguson-Pell, "Numerical Characterization of Quasi-Static Ultrasound Elastography," *IEEE Transactions on Medical Imaging*. I was responsible for the study design, data collection, and manuscript composition. W. Moussa and M. Ferguson-Pell were the supervisory authors and assisted with manuscript composition.

Dedication

This work was written for all those who have lovingly supported me throughout it's creation.

To my mother Meridel, who instilled in me the desire to always better myself and persist through the greatest of difficulties. Even when things got difficult, you gently pushed me to continue on.

To my late father David, who taught me about the world and inspired my combination of creativity, critical analysis, and work ethic. I wasn't able to finish before he left us, but I know he would be proud of what I accomplished in the end.

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I truly stand as a dwarf upon the shoulders of giants.

Table of Contents

1 Introduction **1**

1.1 Motivation 1

1.2 Objective 3

1.3 Methodology 3

1.4 Thesis Outline 4

2 Literature Review **7**

2.1 Deep Tissue Injuries 7

2.1.1 Aetiology and Histology 11

2.1.2 Prevention and Treatment 15

2.1.3 Detection 16

2.2 Ultrasound Elastography 19

2.2.1 Quasi-Static Ultrasound Elastography 20

2.2.2 Acoustic Radiation Force Impulse Imaging 21

2.2.3 Shear Wave Speed Quantification 23

2.3 Conclusion 24

3 Numerical Characterization of Quasi-Static Ultrasound Elastography **27**

3.1 Introduction 27

3.2 Method 28

3.2.1 Formation of B-Mode Ultrasound Images 31

3.2.2 Finite-Element Model of Tissue Deformation Under Surface Distortion 32

3.2.3 Characterizing Quasi-Static Ultrasound Elastography . 33

3.2.4 Model Validation Using a Commercially Available Phantom . . . 35
3.3 Results and Discussion . . . 36
3.3.1 Finite Element Models of Ultrasound and Deformation 36
3.3.2 Resulting Elastograms . . . 39
3.3.3 Numerical Characterizations . . . 40
3.3.4 Physical Phantom Validation . . . 58
3.4 Conclusion . . . 60

4 Numerical Characterization of Acoustic Radiation Force Impulse Imaging 63
4.1 Introduction . . . 63
4.2 Method . . . 64
4.2.1 K-Space Pseudo-spectral Model of Acoustic Fields . . . 64
4.2.2 Derivation of Acoustic Radiation Force . . . 66
4.2.3 Temporal Finite-Element Model of Soft Tissue Deformation . . . 68
4.2.4 Characterizing Acoustic Radiation Force Impulse Imaging 71
4.2.5 Physical Phantom Validation . . . 74
4.3 Results . . . 74
4.3.1 K-Space Pseudospectral Models of Acoustic Radiation Force . . . 75
4.3.2 Temporal Finite-Element Model of Soft Tissue Deformation . . . 82
4.3.3 Numerical Characterization of Acoustic Radiation Force Impulse Imaging . . . 85
4.3.4 Physical Phantom Validation . . . 96
4.4 Conclusion . . . 97

5 Numerical Characterization of Shear Wave Speed Quantification 100
5.1 Introduction . . . 100
5.2 Method . . . 101
5.2.1 Shear Wave Speed . . . 101
5.2.2 Model Set Up . . . 103

5.2.3 Model Validation 106
5.3 Results and Discussion 106
5.3.1 Acoustic Radiation Force Impulse Simulations 107
5.3.2 Sample Shear Wave Speed Measurement 107
5.3.3 Lesion Detection Characterization 112
5.3.4 Physical Phantom Validation 126
5.4 Conclusions 128

6 Conclusion **130**
6.1 Comparisons Between Methods 132
6.2 Recommendations and Future Work 143

References **146**

Appendix A Data Tables **171**
A.1 Quasi-Static Ultrasound Elastography 171
A.2 Acoustic Radiation Force Impulse Imaging 173
A.3 Shear Wave Speed Quantification 177

Appendix B Source Code **178**
B.1 Quasi-Static Ultrasound Elastography 178
B.2 Acoustic Radiation Force Impulse Imaging 184
B.3 Shear Wave Speed Quantification 193

Appendix C Experimental Protocols **195**
C.1 Quasi-Static Ultrasound Elastography 196
C.2 Acoustic Radiation Force Impulse Imaging 196
C.3 Shear Wave Speed Quantification 197

List of Tables

3.1 Quasi-static model investigated parameters 29
3.2 CIRS phantom model mechanical properties 35

4.1 K-Space pseudo-spectral model parameters 66
4.2 ARFI model tissue properties 68
4.3 ARFI Maxwell model tissue properties 69
4.4 ARFI model investigated parameters 73

5.1 Shear wave speed quantification model investigated parameters 104

List of Figures

2.1 NPUAP pressure ulcer staging guidelines 10
2.2 Schematic representation of the time course of tissue stiffness changes in a deep tissue injury 14

3.1 Quasi-static model geometries 30
3.2 Point spread function used for simulating b-mode ultrasound scans 31
3.3 Quasi-static finite-element model boundary conditions 34
3.4 Sample deformation finite-element model results for a hard spherical lesion 38
3.5 Sample strain elastogram for a hard spherical lesion 40
3.6 Detection ability as it is related to true lesion stiffness ratio . . 42
3.7 Error characterization for a hard spherical lesion 43
3.8 Error characterization for: co-located, blurred boundary, clustered, and visible human lesion models 44
3.9 Quasi-static lesion size characterization 45
3.10 Quasi-static lesion depth characterization 46
3.11 Quasi-static lesion altitude characterization 47
3.12 Quasi-static ultrasound probing frequency characterization . . 48
3.13 Quasi-static applied strain characterization 49
3.14 Quasi-static lesion separation distance characterization 50
3.15 Sample elastogram for two co-located lesions 51
3.16 Quasi-static lesion blur radius characterization 52
3.17 Quasi-static lesion density characterization 53
3.18 Sample elastogram for a set of clustered lesions 54
3.19 Quasi-static clustered lesion radius characterization 55

3.20 Quasi-static Visible Human model lesion width characterization 56
3.21 Sample elastogram of a Visible Human model lesion 57
3.22 Quasi-static characterization of lesion depth in a Visible Human model 58
3.23 Experimental validation of quasi-static model results 59

4.1 ARFI finite-element model boundary conditions 70
4.2 ARFI model schematics 72
4.3 Sample acoustic radiation force distribution 76
4.4 Effect of depth and interrogation frequency on magnitude of acoustic body forces 77
4.5 Effect of transducer aperture on the magnitude of acoustic radiation force 78
4.6 Magnitude of developed acoustic radiation force in relation to the number of applied pulse cycles 79
4.7 Strong dependence on source pressure of focal point force . . . 80
4.8 I_{SPPA} safety measures of ARFI pulses 82
4.9 ARFI-induced deformation at various depths and interrogation frequencies 83
4.10 ARFI-induced deformation at various depths and source pressures 84
4.11 ARFI-induced deformation across various interrogation frequencies and source pressures 85
4.12 Numerical characterization of ARFI imaging-acquired stiffness ratio with changing lesion radius 86
4.13 ARFI imaging-acquired lesion stiffness mean squared error related to lesion radius 87
4.14 Numerical characterization of ARFI imaging-acquired stiffness ratio with changing lesion depth 88
4.15 ARFI imaging-acquired lesion stiffness mean squared error related to lesion depth 89
4.16 Numerical characterization of ARFI imaging-acquired stiffness ratio with blurred lesions 90
4.17 ARFI imaging-acquired lesion stiffness mean squared error related to lesion blurring 90

4.18 Numerical characterization of ARFI imaging-acquired stiffness ratio with clustered lesions 91
4.19 ARFI imaging-acquired lesion stiffness mean squared error related to small lesion cluster density 92
4.20 Numerical characterization of ARFI imaging-acquired stiffness ratio with clustered lesions 93
4.21 ARFI imaging-acquired lesion stiffness mean squared error related to small lesion cluster density 94
4.22 Numerical characterization of ARFI imaging-acquired stiffness ratio with changing lesion radii in a visible human model . . . 94
4.23 ARFI imaging-acquired lesion stiffness mean squared error related to MRI-acquired lesion size in a Visible Human model . 95
4.24 Experimental ARFI model results 96
4.25 Experimental validation of ARFI imaging model results 97

5.1 Schematic of shear wave speed quantification-investigated lesions 105
5.2 Sample radiation force distribution in relation to lesion location 108
5.3 Sample shear wave motion through time 109
5.4 Sample continuous surface plot of shear wave induced displacement 110
5.5 Sample continuous surface plot of shear wave induced axial displacement highlighting the shear wave location in time 110
5.6 Sample extracted shear wave position-time trace 111
5.7 Sample trace of shear wave speed through the focal line 112
5.8 Numerical characterization of shear wave speed measured stiffness ratio with changing lesion radius 113
5.9 Shear-wave speed quantified squared error related to lesion radius 114
5.10 Numerical characterization of shear wave speed measured stiffness ratio with changing lesion offsets 115
5.11 Shear-wave speed quantified mean squared error related to lesion offset 116
5.12 Numerical characterization of shear wave speed measured stiffness ratio with changing lesion depth 117

5.13 Shear-wave speed quantified mean squared error related to lesion depth . . . 118
5.14 Numerical characterization of shear wave speed measured stiffness ratio with blurred lesions . . . 119
5.15 Shear-wave speed quantified mean squared error related to lesion blurring . . . 120
5.16 Numerical characterization of shear wave speed measured stiffness ratio with clustered lesions . . . 121
5.17 Shear-wave speed quantified mean squared error related to small lesion cluster density . . . 122
5.18 Numerical characterization of shear wave speed measured stiffness ratio with clustered lesions . . . 123
5.19 Shear-wave speed quantified mean squared error related to small lesion cluster density . . . 124
5.20 Numerical characterization of shear wave speed measured stiffness ratio with changing lesion radii in a visible human model 125
5.21 Shear-wave speed quantified mean squared error related to MRI-acquired lesion size in a Visible Human model . . . 125
5.22 Experimental shear wave speed quantification results . . . 126
5.23 Experimental validation of shear wave speed quantification model results . . . 127

6.1 Detection sensitivities of hard-boundaried spherical lesions using the three investigated imaging modalities . . . 133
6.2 Percent error of measured stiffness ratios for spherical lesions across the three investigated modalities . . . 134
6.3 Detection sensitivities of blurred-boundary spherical lesions using the three investigated imaging modalities . . . 136
6.4 Percent error of measured stiffness ratios for blurred lesions across the three investigated modalities . . . 136
6.5 Detection sensitivities of clustered lesions using the three investigated imaging modalities . . . 137
6.6 Percent error of measured stiffness ratios for clustered lesions across the three investigated modalities . . . 139

6.7 Detection sensitivities of MRI-acquired Visible Human lesions using the three investigated imaging modalities 140
6.8 Percent error of measured stiffness ratios for MRI-acquired Visible Human lesions across the three investigated modalities . . 141
6.9 Experimental results of the three methodologies investigated . 142
6.10 Experimental validation of the simulation results across all three methodologies investigated 143

Nomenclature

Mathematical Symbols

Symbol	Meaning
α	Acoustic absorption coefficient
α_0	Power law prefactor
B/A	Acoustic nonlinearity parameter
b_i	Body force
b_r	Blurred lesion blur radius
b_ρ	Clustered lesion density
C	Elasticity tensor
c_0	Speed of sound
c_T	Shear wave speed
d	Lesion depth
d_f	Focal depth
δ_{sep}	Co-located lesion separation distance
E	Young's modulus
E_{lesion}	Young's modulus of lesion
$E_{rel,meas}$	Lesion stiffness ratio
$E_{rel,nom}$	Nominal lesion stiffness ratio
E_{tissue}	Young's modulus of tissue
ε	Strain
ε_{app}	Transducer-applied strain
ε_{lesion}	Measured lesion strain
ε_p	Percent error
$\varepsilon_{rel,meas}$	Measured lesion strain ratio

Symbol	Meaning
$\varepsilon_{rel,true}$	True lesion strain ratio
ε_{tissue}	Measured tissue strain
F	Applied body forces
f	Ultrasound frequency
f_i	Applied load
G_m	Shear modulus of the m^{th} branch of a Maxwell model
Γ	Boundary domain
h	Lesion altitude
I	Acoustic intensity
I_{SPPA}	Spatial peak pulse average intensity
I_{SPTA}	Spatial peak time average intensity
K	Bulk modulus
k	Wave number
λ_{tissue}	Lamé constant
λ_{wave}	Ultrasound wavelength
MI	Mechanical index
MSE	Mean squared error
μ_{tissue}	Lamé constant (shear modulus)
n_c	Number of acoustic periods
∇	Del operator
P_r	Refractory pressure
P_{source}	Ultrasound transducer source pressure
p	Acoustic pressure
r_{lesion}	Lesion radius
r_{bl}	Clustered lesion radius
ρ	Acoustic density
ρ_0	Equilibrium density
S_M	Acoustic pressure source term
$\varnothing S$	Lesion diameter
$\varnothing L$	Visible Human lesion width
σ	Stress tensor
σ_0	Initial stress distribution
$\sigma_{applied}$	Stress applied to tissue

Symbol	Meaning
t_{inson}	Insonification time
τ_m	Relaxation time of the m^{th} branch of a Maxwell model
$\vec{u}$	Particle displacement
$\vec{v}$	Particle velocity
u_0	Initial displacement
v_{max}	Maximum tissue displacement in the axial direction
w_{active}	Total width of active transducer elements
y	Power law exponent

Abbreviations

Abbreviation	Meaning
ARFI	Acoustic radiation force impulse
DTI	Deep tissue injury
IES	Intermittent electrical stimulation
MRI	Magnetic resonance imaging
NPUAP	National Pressure Ulcer Advisory Panel
PU	Pressure ulcer
SCI	Spinal cord injury
USE	Ultrasound elastography

Chapter 1

Introduction

1.1 Motivation

Pressure ulcers are debilitating wounds often suffered by people with limited mobility such as those undergoing lengthy surgical procedures, the elderly, and those with spinal cord injuries (SCI) [1]—up to 80 percent of people with SCI will develop a pressure ulcer in their lifetime [2]. Pressure ulcers are generally characterized by a deterioration of the skin leading to painful open wounds and while many pressure ulcers may be blamed on excess friction and moisture at the skin surface, many start as "deep tissue injuries" (DTI) which start deep below the skin surface—most often at the bone-muscle interface [3]. DTI are generally thought to be formed due to some combination of excessive deformation and ischemia resulting from sustained loading on localized tissue [4]–[6]. As of the time of writing, there is no clinically feasible method of detecting deep tissue injuries until they begin to damage superficial skin—even the National Pressure Ulcer Advisory Panel's description of them is largely based on their appearance after the fact [7]. With our inability to detect these

forming injuries and subsequently implement deep tissue injury prevention and mitigation protocols, the injuries may eventually progress to form large subcutaneous cavities which eventually break through the surface of the skin and reveal themselves as stage III or IV pressure ulcers [8], [9].

Currently, the only tool capable of readily detecting early deep tissue injuries is T_2^*-weighted MRI [6], [10]. Unfortunately, MRI is not cost-effective for detecting the onset of DTI in a clinical population. Alternately, ultrasound is a much more cost-effective, if less sensitive imaging modality. While it has been shown that some DTI may be discerned using classical b-mode ultrasound imaging [3], [11], the sonographic features of DTI are difficult to separate from regular tissue inhomogeneities. To overcome this, ultrasound elastography may provide more reliable results by imaging the mechanical tissue stiffness rather than its acoustic properties. Ultrasound elastography is an imaging modality which utilizes sonographic techniques to determine the localized mechanical stiffness of tissue and is currently used clinically to detect breast and prostate cancer lesions [12], [13] as well as liver fibrosis [14]. It is known that as DTI form, they undergo mechanical stiffness changes throughout their progression [9], [15], [16], with tissue undergoing significant 1.8 – 3.3-fold mechanical stiffening during injury formation [5]. Initially damaged tissues show signs of increased relative stiffness due to edema-related swelling while eventually showing signs of decreased relative stiffness due to decomposition and necrosis [17]. Since ultrasound elastography is capable of imaging these stiffness changes, it follows that the formation and progression of DTI may be imaged using ultrasound elastography. In fact, ultrasound elastography has shown to be a valid technique for imaging the formation of a DTI in a rat model [18]. Before this technique can be fully understood and used

in human patients, the various parameters involved in performing ultrasound elastography must be characterized with respect to detecting DTI in humans.

1.2 Objective

The broad objective of this work was to numerically characterize the use of ultrasound elastography to detect and monitor formative and progressive deep tissue injuries. Although it has been shown that ultrasound elastography is capable of imaging DTI [18], the degree of suitability of this technique with regard to DTI is not yet understood. When the effects of numerous interrogation parameters on detection sensitivity and ability are known, the technology may be evaluated on its feasibility and usefulness to detect deep tissue injuries. The ultimate goal of this characterization is to be the first stage in the process of allowing ultrasound elastography to be implemented clinically for detecting DTI. It is reasoned that if early detection modalities are implemented clinically, both patients and the health care system may benefit by lowering the incidence and outright cost of treating fully-formed deep tissue injuries.

1.3 Methodology

In order to investigate the use of ultrasound elastography for the detection of deep tissue injuries, the technology must first be characterized and fully understood. While traditional experimentation provides an opportunity to work with physical subjects it can be severely limiting as absolute control over all investigated parameters is relinquished. Further, subject recruitment may present an insurmountable barrier to the execution of such a study. As

such, in this exploratory work, various numerical models of the technology have been utilized to investigate the controlled effect of a broad number of parameters relating to each technology. Specifically, k-space models of ultrasonic wave propagation and finite-element models of tissue deformation have been developed. These models were coupled with tissue strain estimation algorithms to fully simulate ultrasound elastography procedures. Parametric studies on the detection sensitivity and ability of the various ultrasound elastography modalities were carried out with respect to various lesion and technological parameters. Chief parameters of interest included those related to the physical realities of deep tissue injuries such as lesion depth, size, and relative mechanical stiffness as well as parameters related to the design and development of appropriate ultrasonic transducers such as probing frequency, transducer dimensions, etc.

1.4 Thesis Outline

In this work, three methods of ultrasonic elastogram image formation have been investigated: quasi-static ultrasound elastography, acoustic radiation force impulse imaging, and shear wave speed quantification. While all three methods may be used to interrogate tissue stiffness, each does so in a distinctively unique way. The academic background leading to the motivation for this work and the development of the numerical models is presented in Chapter 2.

Quasi-static ultrasound elastography estimates tissue strain by tracking inhomogeneities across pre- and post- compression b-mode scans where the compression is generated by manual indentation of the transducer against the surface of the skin. Naturally, mechanically stiffer regions of tissue will strain

significantly less than the relatively unstiff surrounding tissue. To investigate this technique, two-dimensional b-mode ultrasound scans of simulated pre- and post-compressed tissue were generated. A finite-element model of tissue deformation was utilized to generate the post-compression simulated scans. A published tissue strain estimation algorithm was utilized to then generate elastograms for the parametric study. The models and results pertaining to this technique are presented in Chapter 3.

After performing experiments using quasi-static ultrasound elastography on a phantom model, it became clear that quasi-static methods present significant challenges that acoustic radiation force impulse imaging may overcome. Chief amongst these challenges is the repeatability and inter-operator reliability of the technique as quasi-static elastography is heavily reliant upon manual force generation. Acoustic radiation force impulse imaging estimates tissue strain by applying an acoustic radiation force body load to deep tissue, causing the interrogated tissue region to deform which is then tracked using conventional ultrasound beams fired at a high frame rate. The magnitude of deformation and tissue relaxation time may then be correlated to tissue stiffness. This technique presents an advantage over quasi-static elastography in that the interrogation process is entirely automated, hence more repeatable and reliable. To simulate acoustic radiation force impulse imaging, a k-space pseudo-spectral method was used to generate simulated acoustic body loads which were then combined with a finite-element model of tissue deformation to analyze the sensitivity of ARFI imaging to investigate formative DTI. The models and results for this technique are presented in Chapter 4.

Although acoustic radiaton force impulse imaging has some advantages over quasi-static elastography, it only provides qualitative measures of relative

tissue stiffness which is limited utility. To provide a quantitative measure of tissue stiffness and subsequently, tissue health, shear wave speed quantification may be used. Shear wave speed quantification quantifies tissue stiffness by tracking shear waves generated by an acoustic radiation force impulse and correlating the speed of the relatively slow-moving generated shear waves to the mechanical stiffness of the tissue. To simulate shear wave speed quantification, the k-space pseudo-spectral method of simulating acoustic body loads adopted in Chapter 4 was used in combination with a finite-element model of tissue deformation to investigate the interaction between lesions and shear wave speed. The models and results for this technique are presented in Chapter 5.

Finally, the conclusions derived from this work and their implications along with suggestions for future studies are discussed in Chapter 6. Data tables for all the characterization plots that are presented in this work are given in Appendix A, while the MATLAB® source code for performing the simulations are given in Appendix B. Lastly, experimental protocols used in the acquisition of experimental validation data are given in Appendix C.

Chapter 2

Literature Review

In order to understand the need for a clinical method of detecting deep tissue injuries, the full scope of the issue must be explored. To this end, the current state of the literature regarding deep tissue injuries, how they form, what factors characterize them, and how they are currently treated is explored here. In order to relate this disease to the detection modalities proposed in this work, the mechanics and history of ultrasound elastography are also explored and related back to the problem at hand. The major gaps in the current literature regarding the use of ultrasound elastography for detecting and monitoring deep tissue injuries are presented as this work attempts to partially fill those gaps and bring the technology one step closer to clinical implementation.

2.1 Deep Tissue Injuries

Pressure ulcers, commonly referred to as "bedsores", are an extraordinarily large problem facing the health care system today. At least $11 billion is spent in the United States of America alone treating approximately 500,000 injuries

annually [19], [20] while only a minute fraction of that is spent toward pressure ulcer research [21]. Compared to hospital stays for all other conditions, patients with at least a secondary diagnosis of a pressure ulcer were more often discharged to a long-term care facility and more likely resulted in death [20]. These injuries place an extremely significant burden on the people who suffer from them—pressure ulcers were found to have a profound impact on people's lives including: altering their physical, social, and financial status; changing their body image; losing independence and control; and subjecting them to the grieving process [22], [23]. These debilitating wounds are often suffered by people with limited mobility such as those undergoing lengthy surgical procedures, the elderly, and those with spinal cord injuries (SCI) [1]—approximately 80 percent of people with spinal cord injuries (SCI) will develop at least one pressure ulcer during their lifetime [2] and approximately 19 percent of elderly patients in long-term care facilities will develop one [24]. Pressure ulcers exist throughout the entire health-care system and are often formed when undergoing hospitalization [25]. These injuries have a tendency to become chronic, non-healing wounds and many patients die from complications related to them [26]. Furthermore, patients who have developed at least one pressure ulcer in their life are at a significantly greater risk of developing a second one [27].

Pressure ulcers generally form over boney prominences with approximately 64 % occurring over the ischial tuberosities, trochanter, or sacrum [28] and typically start at the surface of the skin and progress deep in the tissue. Deep tissue injuries—currently defined as a type of pressure ulcer—form in the same regions are pressure ulcers but generally form at the bone-muscle interface deep in the tissue [3]. In general, these injuries are characterized by a some manner of tissue loss through necrosis of the tissue, though there is currently

some debate on the exact nature of these wounds as well as the accuracy of the clinical descriptions attributed to them by the National Pressure Ulcer Advisory Panel (NPUAP).

The NPUAP defines pressure ulcers as a "localized injury to the skin and / or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear and / or friction" and are generally staged according to a tiered system of increasing damage [7]. The various stages of pressure ulcer classifications are depicted in Fig. 2.1 and described as follows [7]:

Suspected Deep Tissue Injury

Purple or maroon localized area of discoloured intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and / or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer or cooler as compared to adjacent tissue.

Stage I

Intact skin with non-blanchable redness of a localized area usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its colour may differ from the surrounding area.

Stage II

Partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. May also present as an intact or open / ruptured serum-filled blister.

Stage III

Full thickness tissue loss. Subcutaneous fat may be visible but bone,