BIOFIDELIC SOFT COMPOSITES- EXPERIMENTAL AND COMPUTATIONAL
MODELING

by

ARNAB CHANDA

VINU UNNIKRISHNAN, COMMITTEE CHAIR

SAMIT ROY

MARK E. BARKEY

ANWARUL HAQUE

KIM LACKEY

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ABSTRACT

Biofidelic soft composites or tissues form the building blocks of the human body. Understanding the complex mechanics of these soft composites is the key to understanding the genesis and progression of disease. Biomechanically, soft composites exhibit anisotropic mechanical behavior and comprise of multiple fiber layers within a soft matrix. To date, there is a lack of understanding of the anisotropic mechanical behavior of soft composites, primarily due to unavailability of a robust characterization framework. In this dissertation, novel multiscale computational and experimental investigation models are developed to simulate and characterize anisotropic soft composite mechanical behavior.

Soft composite surrogates were first developed to simulate various tissues in the human body namely the skin, brain, artery and vaginal tissues. Novel anisotropic soft composite models were also fabricated taking into consideration the tissue anisotropy and multifunctional properties. Hyperelastic anisotropic constitutive relationships were formulated to precisely characterize the mechanical behavior of soft composite considering varying fiber and matrix contributions, fiber-matrix interactions, fiber orientations and multiple fiber layers.

Coupled with high fidelity experimental and computational models, microscopy, and Digital Image Correlation (DIC) studies, the damage and repair of soft composite surrogates are also discussed in this dissertation, with relevance to soft tissue wounds and suture.

Computational modeling to understand the interaction between multiple soft composite systems and its effect on soft composite damage are also highlighted in this work. Some specific soft composite interaction systems modeled were the female pelvic system under abdominal

loads, whole body impact due to blast, and ulceration in diabetic foot. This dissertation lays the foundation for micro and macro scale anisotropic soft composite modeling and characterization using high fidelity experimental and numerical techniques which will be indispensable for studying tissue mechanics and other soft composite applications in engineering and medicine.

LIST OF ABBREVIATIONS AND SYMBOLS

POP	Pelvic Organ Prolapse
AVW	Anterior Vaginal Wall
PVW	Posterior Vaginal Wall
MRI	Magnetic Resonance Imaging
DIC	Digital Image Correlation
UTS	Ultimate Tensile Strength
$\mathbf{C}$	Cauchy Green Deformation Tensor
$\mathbf{F}$	Deformation Gradient
$\mathbf{J}$	Jacobian
$\text{dev}()$	Deviatory Component
$\text{tr}()$	Trace of a Tensor
$\mathbf{R}^2$	Correlation Index
Ψ	Strain Energy Function
$\mathbf{I}_i$	Invariant of Right-Cauchy Green Tensor
θ	Angle
t	Time
$\mathbf{D}_i$	Displacement

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CHAPTER 1

INTRODUCTION

A Composite material is a material made from two or more constituent materials with significantly different physical or chemical properties that, when combined, produce a material with characteristics different from the individual components [13]. The individual components remain separate and distinct within the composite material. Typical engineered composite materials include mortars, concrete, reinforced plastics, such as fiber-reinforced polymer (Figure 1), metal composites and ceramic composites (with composite ceramic and metal matrices). Composite materials are generally used for buildings, bridges, and structures such as spacecraft and aircraft especially in demanding environments [14]. Naturally occurring composites are soft composites such as tissues, which are composed of one or more layers of collagen fibers embedded within a soft gelatinous matrix. The mechanics of soft composites are more complex than hard composites due to non-linear mechanical behavior and anisotropy due to varying fiber distribution and orientation from one location on the body to another. Tissues make organs, which are the most sophisticated form of soft composites. The study of the soft composite mechanics, its damage and repair, and interactions with the environment or other soft composites is the key to understand tissue malfunction (disease).

1.1 Soft Composites

Animal tissues are one type of naturally occurring soft composites which can have single or multiple layers of fibers running in different directions within a soft collagenous matrix. The most distinct feature of such a soft composite is the material anisotropy, which cannot be

characterized using the currently available models applicable for hard composite materials, such as isotropic hyperelastic models, and the transversely isotropic material models. Additionally, developing biofidelic soft composites experimentally is the key to engineering tissue surrogates for biomedical testing applications ranging from clinical training to biomedical device manufacturing. In the following sections, some of the tissue composites are introduced. These tissues form the building blocks of the organ systems which are the most complex composite systems with anisotropic tissue distribution and varying mechanical properties spatially, and will be discussed in later sections.

Figure 1.1: Schematic of a composite material

1.1.1 Skin Tissue

The skin is the outer covering of the human body which protects it from the environment. Its average thickness is 1-4 mm [15], and is composed of the epidermis (outermost layer), dermis (middle layer) and a subcutaneous layer (innermost layer), shown in Figure 1.2. In literature, the mechanical properties of excised human skin has been studied extensively using uniaxial and biaxial tests [16-25]. Also, the mechanical properties of the the human skin has been studied in-vivo [18, 25-27]. Experiments have shown that human skin exhibits a non-linear mechanical behavior, with a pre-stress in its natural state (due to the natural tension of the skin). Based on these findings, there have been few attempts in the past to develop human

skin surrogates for biomedical testing applications such as sports injuries [28, 29], needle insertion simulations [30], and for testing the penetration resistance of ballistics [31, 32]. Historically, cowhides have been utilized for skin testing, which have mechanical properties very different from natural human skin. Additionally, gelatin and polyurethane based materials have been developed to simulate human skin, but are not an ideal skin model system [28, 29, 31-33].

Figure 1.2: Different layers of the Skin

Skin is a highly anisotropic, viscoelastic and nearly incompressible material. On a typical stress-stretch graph for skin, in the initial loading phase, skin is very compliant and large deformation occurs at a relatively low applied load. At this stage, the fibres are largely unaligned. In the second phase, the stiffness of the skin gradually increases as the fibres align themselves in the direction of the load applied. The third phase is an almost linear phase whereby the stiffness increases rapidly as the collagen fibres are mostly aligned and the overall mechanical response becomes dependent on the mechanical properties of the collagen fibres, which are stiffer than elastin by three grades of magnitude [2].

Skin anisotropy was recognized as far back as the 19th century by [34], who mapped the natural lines of tension which occur within the skin. These lines are identified by puncturing the skin with a circular device. The wounds then assume an elliptical shape and by joining the

major axes of the ellipses, a system of lines can be drawn as shown in Figure 1.3. These lines are known as the Langer lines. While the Langer lines are the best known skin tension lines, many variations on the original lines proposed by Langer have been made. These include the Cox lines [35], Kraissl lines [36] and (RSTL) relaxed skin tension lines [37]. Early tensile tests suggested that the deformation characteristics of skin are dependent upon specimen orientation with respect to the Langer lines [38]. More recent work conducted using optical coherence elastography in-vivo, indicates a large difference between the Young moduli of skin along directions parallel and orthogonal to the Langer lines [39].

Figure 1.3: Figure describing A) 11 different body locations and the B) corresponding stress versus strain response of skin samples from respective locations [2].

1.1.2 Brain Tissue

Even after decades of studies, the brain remains one of the most mysterious parts of the human anatomy. The central operator of the nervous system, the brain, controls every thought and action performed by the body. The principal controlling part of the brain, the cerebrum, is composed of two unique tissues called white matter and grey matter [40] (see Figure 1.4). In addition to dendrites and axons for data collection, synapses for inter-neuron communication, glial cells for support and maintenance, and capillaries for microcirculation of blood, grey

matter houses the majority of neuronal cell bodies in the brain. White matter, on the other hand, is composed primarily of long-range axon tracks for information transport. The color difference between the two arises from the white myelin coating present on the axons in white matter. Generally, the grey matter is responsible for processing stimuli leading to human cognition, while white matter allows for communication throughout the brain to generate a response to the stimuli. Typically, grey matter accounts for 40% of the cerebrum by mass, while white matter composes the remaining 60% [40].

Figure 1.4: Cross-section of a brain showing grey and white matter

White matter tissue appears to be preferentially injured during brain trauma [41], and the mechanics of white matter are important for predicting its deformation and associated injury. Since white matter consists predominantly of aligned axonal fibers and their myelin sheaths, it is hypothesized to be mechanically anisotropic, in contrast to grey matter, which is structurally isotropic [42]. More specifically, where fibers are well-aligned, white matter is expected to be transversely isotropic with the fiber axis normal to the plane of isotropy. The literature largely supports this hypothesis, though estimates of specific parameter vary. Mechanical properties of brain tissue have been studied both *in vivo* and *in vitro*. In one study, brainstem was found to demonstrate an anisotropic (transversely isotropic) response to

oscillatory shear deformation *in vitro* ([43]). Subsequent studies *in vitro* [44] [45] confirmed that grey matter appeared isotropic and that white matter from corona radiata, corpus callosum and brainstem appeared anisotropic when subjected to shear deformation at high strains and strain rates. Hrapko et al. [46] suggested that the anisotropy of corona radiata increases with the magnitude of shear deformation but decreases with increasing frequency during dynamic oscillatory shear tests. In contrast, it was observed that white matter from the corona radiata appeared isotropic in shear under small strain (0.0033%) and high strain rates (0.8 s^{-1}) [47]. When uniaxial tensile tests were performed on strips of porcine corona radiata [48], they appeared almost 3 times stiffer when the fiber axis was aligned with the direction of stretch than when stretched perpendicular to the fiber axis. *In vivo* studies of brain tissue using magnetic resonance elastography (MRE) are promising but still not conclusive on this topic, although recent MRE studies [49, 50] have begun to address anisotropy.

1.1.3 Arterial Tissue

The study of biomechanical properties of the arteries are of interest as the mechanical factors may be important for triggering the onset of atherosclerosis, the major cause of human mortality in the western world. *In vivo*, the artery is a pre-stretched material under an internal pressure load resulting in cyclic finite deformations. In general, arteries are roughly subdivided into two types: elastic and muscular. Elastic arteries have relatively large diameters and are located close to the heart (for example, the aorta and the carotid and iliac arteries), while muscular arteries are located at the periphery (for example, femoral, celiac, cerebral arteries). However, some arteries exhibit morphological structures of both types. The microscopic structure of arterial walls are composed of three distinct layers, the intima (tunica intima), the media (tunica media) and the adventitia (tunica externa).

To date, most of the experimental studies have focused on the mechanical properties of animal coronary arteries [51-55]. In addition to a collagenous adventitia and a medial layer (consisting of smooth muscle, collagen, and some elastin), a coronary arterial wall may consist of a complex intimal layer that develops rapidly in early years and continues to grow gradually throughout life [56]. The intima is a prominent layer with a distinctive organization of layered groups of collagen fibers that condense into a few separate alignment families [57]. The intima has also been observed to mechanically stiffen with age [58].

In literature, very few *in vitro* data on the mechanical properties of human coronary arteries are available [58-63]. Also, accurate constitutive material models for the arterial layers are lacking. Because human coronary arteries with non-atherosclerotic intimal thickening comprise three (thick-walled) layers, a better understanding of their mechanical function at the tissue level requires a layer-specific experimental approach and the design of constitutive descriptions that can be implemented efficiently in numerical computations. It appears that Vito and Demiray [51] were the first to document separate mechanical response data for the media and adventitia from canine aorta, which they obtained from uniaxial strip tests in the axial and circumferential directions. Later, Richardson and Keeny [64] performed mechanical measurements during uniaxial tests of intima segments from the region between the left circumflex and left anterior descending (LAD) coronary arteries. Holzapfel et al. [65] conducted a systematic study of the layer specific mechanical response of human coronary arteries, the properties of which are summarized in Figure 1.5.

Figure 1.5: Literature based [3] stress versus stretch plots for various human coronary arterial layers, along the longitudinal and circumferential directions

1.1.4 Vaginal Tissue

The mechanical properties of vaginal tissue need to be characterized to perform accurate simulations of prolapse and other pelvic disorders that commonly affect women. This is also a fundamental step towards the improvement of therapeutic techniques such as corrective surgeries. When a soft biological specimen in general, and vaginal tissue in particular, is loaded in simple tension from its original state, unloaded and then reloaded, the stress required on reloading is less than that reached in the initial loading for stretches up to the maximum stretch achieved in the previous loading step. This stress softening phenomenon is referred to as Mullins effect. This effect is an important factor after birth, when the vaginal tissue supports high load distribution and the tissue do not recover its original behavior. There is evidence that the vagina undergoes significant changes during women's reproductive life. Events such as pregnancy and menopause play a major role, due to significant changes in hormonal status

(mainly estrogen production). In fact, Alperin et al. [66] concluded that the vagina and its supportive tissues actively remodel in response to different environmental stimuli (pregnancy, menopause, the administration of hormone therapy, and prolapse). Specifically in prolapse, vaginal tissues stiffen progressively [6, 67, 68]. Figure 1.6 shows an example of experimental stress versus stretch data of normal and prolapsed vaginal tissue response in low and intense prolapse conditions.

Figure 1.6: Stress versus strain response of normal vaginal tissues compared to vaginal tissues in case of low and high degrees of vaginal prolapse [6, 67, 68]

Biological soft tissues such as the vaginal tissue when subjected to large deformations with negligible volume changes show an anisotropic mechanical response due to their internal structure. In general, three important softening phenomena associated with these tissues may be distinguished. First, the Mullins effect [69] is observed. Second, preconditioning effect is observed due to continuous softening during the first loading until reaching a certain “saturated” state [70]. Third, the softening behavior resulting from fiber rupture and matrix disruption associated with material damage has been recorded [71].

1.2 Soft Composite Damage and Repair

Soft composite damage can be observed in tissue systems in the form of wounds. Understanding the mechanics of wounds will provide insights into the damage mechanics of

synthetic composites, which has not been studied to date. In this dissertation, a detailed study on soft composite damage will be presented for natural composites such as the skin and muscles, and soft synthetic tissue surrogates. Also, the mechanics of soft composite repair using sutures have not been investigated much to date, which will be studied for natural and synthetic composites.

A wound is a disruption to the normal physiological conditions of body tissues [72], due to a tissue rupture. Most commonly, wounds occur on the skin which is body's first line of physical defense. Under most skin is muscle tissue and it is often wounded along with the skin. Damaged muscle tissue heals slowly, and proper care is essential to ensure restoration of muscle strength [73]. Wounds in other tissues occur less often from injury but are common during surgical procedures involving incisions [74, 75]. There are several types of wounds like incisions, lacerations, punctures and abrasions [76, 77]. Additionally, any wound can be classified as acute or chronic. Acute wounds [78-80] heal on their own or with simple treatment; chronic wounds heal slowly and only with continual care [75, 81, 82]. Wounds can be caused by an accident or inflicted intentionally during surgery. Once injured, the body begins to repair itself through regrowth and remodeling of the tissue [75, 83]. The regrowth scar, is often more fibrous than and does not function like the original tissue [84, 85]. Proper treatment of a wound is essential for minimizing scar formation and also for prevention of infection [86], costing the U.S. economy over \$25 billion each year. Modeling of wound closure mechanics would allow better understanding and improvements in wound care [87-89].

Suturing is the most common method of wound closure. In a suture, fibers are pulled through the intact tissue to displace the edges of the wound together. There are two classes of sutures, interrupted and continuous, each with several types of stitches [90-94]. The number of strands and material of the suture affects the effectiveness of the suture [95]. The materials

employed in suturing include Vicryl, Dexon, Polyester, Silk, Plain gut, Chromic gut, Maxon, PDS (Polydioxanone) nylon, and Prolene (Polypropylene) [72, 96-98]. Suturing practices vary widely depending on the surgeon and type of wound operated, often causing the built up of stress concentrations at the suture knots [99-103], and could lead to infections [104, 105] due to inappropriate suture force application. A high suture tension on one hand may limit blood flow and healing [106]. On the other hand, too little tension can lead to excessive scarring or wound dehiscence [107, 108]. Additionally, the bite distance (gap between adjacent sutures) and the number of sutures may affect the wound healing process [109, 110]. A detailed computational study was conducted in the current work to estimate suture forces in wounds with varying geometries and sizes, and repaired with different suture materials and number of sutures.

1.3 Soft Composite Interactions

Interaction between soft composite systems are observed in organ systems with multiple interacting organs. Each organ can be considered to be a composite itself with a different geometry, fiber property and organization, and subjected to multiple different loads. Understanding such complex mechanics is the key to understanding organ system pathophysiology and disease mechanisms. An example of such a system is the female pelvic system (Figure 1.7) with the pelvic organs namely the urinary bladder, uterus, vaginal canal and rectum, which are soft composites attached to each other with connective tissues, and affect mutual functioning. Experimentally, such systems are difficult to model due to lack of data on the geometry and tissue organization. However, advancement in imaging techniques, mainly with Magnetic Resonance Imaging (MRI) based capabilities have allowed for recording of accurate organ geometries and tissue fiber layers. In this thesis, study of three such systems have been presented namely the female pelvic system and Pelvic Organ Prolapse (POP), impact

of blasts on the human body, the diabetic foot mechanics, which are critical study areas in engineering and medicine.

Figure 1.7: Example of interaction modeling of organs in female pelvic system

CHAPTER 2

BIOFIDELIC SOFT COMPOSITE MODELS¹

2.1 Summary

Development of soft composite models simulating tissues is the key to understanding tissue mechanics and are necessary to device surrogates for experimental testing and surgical training. To date, a plethora of phenomenological tissue models have been developed using polymer materials such as gels and silicones, and animal tissues such as cowhide, porcine skin etc. Such surrogates have mechanical properties vastly different from that of the tissues and also have handling and biosafety issues.

In this chapter, the development of novel biofidelic soft composites simulating some of the major human tissues namely the skin, muscles, brain, artery and vaginal tissues is presented. For each soft composite system, the fabrication methodology, mechanical testing framework and results are discussed in detail. These novel soft composites are the most accurate tissue surrogates to date and precisely simulate the non-linear mechanical behavior of the tissues. Also, a soft composite material system comprising of soft fibers embedded within a softer matrix is developed, and the fiber volume fraction (FVF) and fiber orientation is varied to model tissue anisotropy. Additionally, an advanced multifunctional soft composite system is also developed which is anisotropic and conductive for improved biomechanical testing applications.

¹ A. Chanda, C. Callaway, C. Clifton, and V. Unnikrishnan, "Biofidelic human brain tissue surrogates," *Mechanics of Advanced Materials and Structures*, pp. 1-31, 2016.

2.2 Skin Simulant

Based on the concept of silicone based breast implants [111], and extensive mechanical testing data on human skin from literature [2, 10, 112-114], a novel human skin simulant, which mechanically behaves like the natural human skin, was developed [4]. The manufacturing and fabrication steps, and tensile testing methodology involved are discussed in detail in the following sections. The mechanical behavior of the simulant was compared with the non-linear stress-strain profile, modulus of elasticity and tensile strength of natural skin and additional mechanical testing was conducted on pig skin to validate the material modeling framework.

2.2.1 Materials and Methods

2.2.1.1 Fabrication of Skin Simulant Specimens

Silicone based materials are characterized using the Shore (Durometer) hardness scale, defined as per the American Society for Testing and Materials (ATSM) D2240 testing standard. A two-part extremely soft silicone material with shore hardness of 00-10 was combined with a harder two-part silicone material with shore hardness 30A to fabricate the novel human skin simulant material [4]. A mold was designed (Figure 2.1) in Solidworks CAD software with 30 coupons of 5 cm length, 1 cm width and 1-4 mm depth (10 coupons with 2 mm depth, 10 coupons with 3 mm depth, 5 coupons with 1 mm depth and 5 coupons with 4 mm depth). The overall dimension of the mold was 21 cm x 18 cm x 1 cm. This mold design was exported as an stereolithographic (STL) file and sent for 3D printing at the University of Alabama 3D printing lab. The 3D printer used was Stratasys Dimension SST 1200es and the material used for fabricating the mold was Acrylonitrile butadiene styrene (ABS), a very popular material used in the 3D printing industry which provides a good surface finish and high strength.

Figure 2.1: A) Mold design for test coupons in Solidworks, B) 3D printed mold for test coupons, C) Some specimens with different sizes and colour variation (implying different mix ratios).

To start with the fabrication of silicone test coupons, multiple test specimens (55 specimens) of similar dimension ($49\text{mm} < \text{Length} < 50\text{mm}$, $9\text{mm} < \text{Width} < 11\text{mm}$ and $1\text{mm} < \text{Thickness} < 4\text{mm}$) were prepared with abstract weight percentages of the four-part silicone, mechanically tested on the MTS universal testing machine, and the load response plots were fit into hyperelastic models and compared with the most comprehensive literature data [2, 28, 29], to identify weight percentage ranges of the four parts, which will result in developing test specimens with mechanical properties close to that of natural human skin. The best results were obtained by mixing part A (25-45 wt. % silicone with shore hardness 30A), part B (25-45 wt. % silicone with shore hardness 30A), part A (5-25 wt. % silicone with shore hardness 00-10) and part B (5-25 wt. % silicone with shore hardness 00-10) [4] with a mean curing time of 6.5 hours. The next step was to determine a precise mix ratio which can be used to develop a control specimen for testing. For this purpose, a test specimen, named “90-10”, which is composed of precisely measured (using experimental measuring cups and Ohaus Adventurer Pro precision weight measuring device) 45 wt. % part A silicone with shore hardness 30A, 45 wt. % part B silicone with shore hardness 30A, 5 wt. % part A silicone with shore hardness 00-10, 5 wt. % part B silicone with shore hardness 00-10, was fabricated. This 90-10 specimen was further used for the comparison study with the mechanical properties of the natural human

skin. Various control parameters adopted for the uniaxial testing such as the test specimen sizing and strain rate are discussed in the following section.

2.2.1.2 Mechanical Testing for Measurement of Load Response

Several considerations need to be taken while testing soft materials such as silicone rubber and the skin [115]. First, soft materials slip very easily, thereby special grips coated with any material which provides high friction against slipping needs to be used. Second, strain rate significantly affects the load response of soft materials [116] and this phenomenon has been observed with the skin too [117], which necessitates the use of a specific strain rate, so that results can be precisely compared with literature. Third, the shape and size of the specimen may affect the test results [118]. All these issues have been factored in our experimental framework. Special grips have been used for specimen gripping, and a specific specimen size and strain rate have been used throughout for experiments. Additionally a very small initial load (<0.1 N) is applied on each test specimen to ensure there is no slack in the specimen to start with. A constant strain rate of 0.4 s^{-1} and specimen size of $35\text{mm} \times 10\text{mm} \times 2.5\text{mm}$ (after clamping) has been selected for all the uniaxial tests on silicone based material, based on literature on uniaxial tests on human skin [2, 28, 29, 114]. For each of the tests (see Figure 2.2), the Load (N) versus extension (mm) graphs are plotted.

Figure 2.2: Uniaxial tension test on a silicone specimen captured in the beginning and during a test.

Edible grade fresh pig skin sample (Figure 2.3) was obtained from the supermarket in Tuscaloosa, Alabama and tested in the Advanced Computational and Experimental Mechanics Laboratory (ACEML), University of Alabama (UA) which is Biosafety level 2 facility. All the hair on the skin was carefully trimmed off and the skin sample was hydrated in a water bath at room temperature (75° F) for 2 hours. The hypodermis was carefully removed through blunt dissection, ensuring that no damage was caused to the dermis. The average thickness of the skin was measured as 2 ± 0.5 mm and test samples of width ($9 \text{ mm} < W < 11 \text{ mm}$) and length ($33 \text{ mm} < L < 35 \text{ mm}$) were extracted (10 samples). Each test specimen was positioned, dermis side down on an aluminum foil to prevent skin curling, and subsequently clamped in between the grips of the universal testing machine, and the foil was removed carefully. All samples were uniaxially tested at constant strain rate of 0.4 s^{-1} to obtain the load-extension plots.

Figure 2.3: A) Fresh pig skin, B) Pig skin specimens, C) A pig skin specimen clamped on the uniaxial testing machine.

For post-processing of the raw load-extension curves obtained from the universal testing machine, a well defined protocol was followed comprising of seven major steps. First, any part of the plots which show negative load values were trimmed off (which may arise from the specimen being slack initially). Second, any part of the plots after the yield point was trimmed off, as they are insignificant for our analysis. Third, the calibration errors in the MTS machine were tracked and the graphs were shifted accordingly. Fourth, the engineering stress versus engineering strain plots were replotted as true stress versus true strain plots which are obtained

using equations $\sigma_{true} = \sigma_{eng} (1 + \varepsilon_{eng})$ and $\varepsilon_{true} = \ln (1 + \varepsilon_{eng})$. Fifth, highly accurate 5th degree polynomial trend lines are fit to each of the plots with R² (coefficient of determination) values between 0.99 and 1. Sixth, all the plot strain (X-axis) steps and ranges are standardized ($1 < \varepsilon_{true} < 2$ at 0.01 increment steps), and the respective stress values are calculated using the trend line equations obtained in step 5, and re-plotted. Seventh, each stress versus strain plot is converted to stress versus stretch (λ) plots using the relation $\lambda = 1 + \varepsilon$. Subsequently, the stress versus stretch curves are fit into various hyperelastic material models.

2.2.2 Results and Discussion

2.2.2.1 Mechanical Tests to Develop the Human Skin Simulant

The first batch of mechanical tests were performed on silicone specimens made out of mixing abstract percentages of the four-part silicone material, at a strain rate of 0.4 s⁻¹ consistent with uniaxial tests on human skin in the literature [2]. Figure 2.4 captures 23 test results out of the 55 specimens tested [4] to identify a stress versus stretch range in which the mechanical properties of the human skin lie [2, 28, 29]. The four-part mix ratio corresponding to the silicone test coupons exhibiting stress versus stretch ranges in the stress versus stretch regime of the human skin [2, 28, 29] was found to be part A (25-45 wt. % silicone with shore hardness 30), part B (25-45 wt. % silicone with shore hardness 30), part A (5-25 wt. % silicone with shore hardness 10) and part B (5-25 wt. % silicone with shore hardness 10), after repeated testing [4].

The four-part mix ratios for each of the 23 tests shown in Figure 2.4 are listed in Table 2.1. For each test, the modulus of elasticity at low and high stretches were estimated. The low stretch and high stretch modulus of elasticity for the tests 1 through 23 were found to be in the range of 2-8 MPa and 6-90 MPa respectively [4].

Excellent skin simulants with stress versus stretch responses lying within the bounds of natural human skin [2] were identified (see Figure 2.4). The low stretch and high stretch

modulus for excellent skin simulants were found to be in the range of 4-8 MPa and 34-90 MPa (similar to that of natural human skin [2]) respectively [4].

Figure 2.4: Stress versus stretch plots of 23 out of the 55 silicone specimens tested to fabricate the human skin simulant [4], with the lower and upper bounds of actual human skin test data from Annaidh et al. [2].

Table 2.1. Four-part mix ratio for test specimens 1-23 in Figure 2.4

Sample	Soft Silicone Percentage (%), Shore Hardness 00-10		Hard Silicone Percentage (%), Shore Hardness 30A	
	Part A	Part B	Part A	Part B
1	45	45	5	5
2	45	45	5	5
3	15	15	35	35
4	42	42	8	8
5	42	42	8	8
6	35	35	15	15
7	12.5	12.5	37.5	37.5
8	12.5	12.5	37.5	37.5
9	10	10	40	40
10	15	15	35	35

11	15	15	35	35
12	45	45	5	5
13	42	42	8	8
14	25	25	25	25
15	5	5	45	45
16	3	3	47	47
17	3	3	57	37
18	3	3	47	47
19	5	5	45	45
20	5	5	47	43
21	3	3	54	40
22	3	3	52	42
23	4	4	46	46

Figure 2.5: Stress versus stretch plot of 90-10 silicone specimen under 36 times repeatability tests, with the lower and upper bounds of actual human skin test data from Annaidh et al. [2].

A silicone test coupon made of 45 wt. % part A silicone with shore hardness 30A, 45 wt. % part B silicone with shore hardness 30A, 5 wt. % part A silicone with shore hardness 00-10, 5 wt. % part B silicone with shore hardness 00-10, named as the “90-10 specimen” was chosen [4] for our specific comparison study with respect to the elasticity modulus, ultimate tensile stress (or fracture strength), and hyperelastic material modeling. Figure 2.5 shows the results of the

repeatability tests (36 tests performed) on this silicone specimen, which lies in the stress versus stretch regime of the human skin [2, 28, 29]. To the best of our knowledge, this is the first time, a human skin simulant has been developed with the non-linear material behaviour lying between the upper and lower bounds of the stress versus stretch regime of the natural human skin [39].

2.2.2.2 Comparison of Mechanical Behavior of the Skin Simulant and Human Skin

The novelty of the human skin simulant lies in the degree of precision with which it mimicks the mechanical behaviour of the human skin. The non-linear stress versus stretch response, elasticity modulus (at high and low stretches), and the ultimate tensile stress of the 90-10 control specimen made of 45 wt. % part A silicone with shore hardness 30A, 45 wt. % part B silicone with shore hardness 30A, 5 wt. % part A silicone with shore hardness 00-10, 5 wt. % part B silicone with shore hardness 00-10, was compared with the most comprehensive literature on mechanical properties of the human skin [2, 28, 29, 114], and validated using mechanical testing data on pig skin [4].

Figure 2.6: Stress versus stretch plots of 90-10 human skin simulant specimen and actual human skin test literature data obtained from Annaidh et al. [2].

The Figure 2.6 compares the stress versus stretch profile of the 90-10 control specimen with the literature plots on excised human skin mechanical testing [2]. The thick line plot in Figure 2.6, which is the plot of human skin tissue tested from the left back side of the human body by Annaidh et al. [2], was replotted for comparison with the stress versus stretch plot of the 90-10 specimen (see Figure 2.7). The correlation between the 90-10 specimen stress versus stretch plot and the human skin stress versus stretch translated plot was determined by numerically calculating the square of difference between the stress values of the two plots at different stretch ratio values, and eventually calculating the R^2 correlation index, which gave a result of 0.989 rounded to three significant figures.

Figure 2.7: Stress versus stretch plot of the 90-10 human skin simulant specimen and an actual human skin test literature data plot (from Annaidh et al. [2]).

From the stress versus stretch plot of the selected “90-10” test specimen, the mean elasticity modulus was estimated both at low and high stretch ratios from portions of the plot which are linear, similar to Annaidh et al. [2]. The elasticity modulus value were calculated as shown in Figure 2.8 (through estimation of the slope of the stress versus stretch plot). Table 2.2

presents the result of the elasticity modulus at low stretch and high stretch ratios for the 36 “90-10” specimens tested for repeatability. Also, the ultimate tensile strength (mean value shown in Figure 2.8) at which a test specimen fractures was observed for each of the 36 repeatability tests on the 90-10 specimens. Table 2.2 presents the results of the ultimate tensile stresses observed in our experiments. Both the elasticity modulus and ultimate stress values were found to be in close range of the human skin [2]. It should be further noted that the silicone 90-10 control specimen does not rupture like the human skin, but only compares well with the ultimate tensile stress of the human skin as reported in literature [2].

Table 2.2 Comparison of mechanical properties of Human skin and 90-10 skin simulant

Test Specimen	Elasticity Modulus (E) (Low Stretch Ratio)	Elasticity Modulus (E) (High Stretch Ratio)	Ultimate Tensile Stress (σ_{ULT}) MPa
90-10 Human Skin Simulant	2.163 ± 1.196	29.411 ± 4.261	16.23 ± 1.15
Human Skin [2]	1.18 ± 0.88	83.3 ± 34.9	21.6 ± 8.4

Figure 2.8: Estimation of elasticity modulus of the 90-10 skin simulant at high and low stretch ratios, and specimen fracture at ultimate tensile stress.

2.3 Brain Tissue Surrogates

To date, brain tissues are very difficult to obtain for experimental tests in a clinical and lab setting due to ethical and biosafety issues. Additionally, brain tissues obtained from a cadaver change significantly in mechanical behavior due to tissue dehydration and death [119, 120]. In the current work, a silicone based material system was developed, which can precisely mimic the non-linear mechanical behavior of the human grey and white matter tissues. The fabrication and manufacturing methodology is discussed in the following sections. These novel brain tissue surrogates can be used in the experimental study of Traumatic Brain Injury (TBI), for surgical training and practice.

2.3.1 Materials and Methods

Brain tissues (both white and grey matter) are very soft materials [121], which disintegrate easily with the application of loads over a few hundred kilopascals (kPA). This is one of the principal reasons for brain tissues to be tested in compression more often than in tension in literature [121-126]. Recently, brain tissues (both grey and white matter) were mechanically tested in tension extensively at different strain rates (low and high) [5]. Based on the literature results, biofidelic brain tissues surrogates were fabricated using an extremely soft two-part silicone with Shore (Durometer) hardness (defined as per the American Society for Testing and Materials (ASTM) D2240 testing standard) of 10, procured from Smooth-On Inc. The part A of the silicone material was identified as the hardener, which polymerizes only when added to the part B (which activates a silicone functional group to crosslink). A mold was designed (Figure 2 A) in Solidworks CAD software with 30 coupons of 5 cm length, 1 cm width and 3 mm depth. The overall dimension of the mold was 21 cm x 18 cm x 1 cm. This mold design was exported as an stereolithographic (STL) file and 3D printed at the University of Alabama 3D-printing lab . The 3D printer used was Stratasys Dimension SST 1200es and the

material used for fabricating the mold was Acrylonitrile butadiene styrene (ABS), a very popular material used in the 3D printing industry which provides a good surface finish and high strength. The 3D printed mold is shown in Figure 2.8.

The two silicone parts (A and B) were mixed with different ratios by weight starting at 1:1, precisely measured using measuring cups and Ohaus Adventurer Pro precision weight measuring device. After a uniform mixing of the two parts, the average setting time for coupons was recorded to be between 2.5 and 3 hours. The colorless coupons (see Figure 2.9) were marked appropriately to keep track of their composition during testing. Each coupon was mounted in between grips of a MTS universal testing machine. A small initial load (<0.1 N) was applied on each test specimen to ensure the absence of any initial slack in the specimen. Constant strain rates of 2.5 mm/s (low) and 30 mm/s (high), and specimen size of 35 mm x 10 mm x 2.5 mm (after clamping) were chosen for the tests based on literature [5]. For each of the tests, the load (N) versus extension (mm) graphs were obtained.

Figure 2.9: Brain tissue surrogate samples marked for mechanical testing

A total of 85 test coupons (with different two-part silicone compositions) of similar dimensions after clamping were tested at the constant strain rates. Out of the 85 tests, 30 coupons each were tested at a strain rate of 2.5 mm/s (low) and 30 mm/s (high) respectively.

The other 25 test coupons were chosen as control specimens and tested multiple times to ensure repeatability of the test results.

2.3.2 Results and Discussion

2.3.2.1 Brain Tissue Simulant Tests

The parts A and B of the two-part silicone material was mixed in different ratios by weight as discussed in Section 2 to generate a total of 30 test specimens. 5 specimens with 70% A - 30% B, 5 specimens with 60% A - 40% B, 6 specimens with 50% A - 50% B, 5 specimens with 30% A - 70% B, 5 specimens with 20% A - 80% B, and 4 specimens with 10% A - 90% B compositions were tested three times each at high 2.5 mm/s (low) and 30 mm/s (high) strain rates respectively to obtain the average plots in Figure 2.10. It was observed that the silicone specimens do not show significant variations with testing rates (Figure 2.10) unlike actual human brain tissues. Therby, it was concluded that the mechanical behavior of brain tissues (white and grey matter) at two different strain rates can be characterized only with two different two-part silicone composition.

Figure 2.10: Brain tissue simulant tests and comparison with data from literature [5]

The range of mix ratios within which the literature based white and grey matter tissue properties (at high and low strain rate tests) lie were identified from Figure 2.10, and summarized in Table 2.3. The softest brain tissue simulants developed corresponded to the grey matter both at low and high strain rates. The hardest tissue simulant was for the white matter at a low strain rate.

Table 2.3: Silicone composition ranges for grey and white matter tissues at low and high strain rates

Brain Tissue Type	Two-Part Silicone Composition		Strain Rate (mm/s)
	Part A	Part B	
<i>White Matter (low)</i>	30-60 %	40-70 %	2.5 (low)
<i>White Matter (high)</i>	20-30 %	70-80 %	30 (high)
<i>Grey Matter (low)</i>	0-20 %	20-80 %	2.5 (low)
<i>Grey Matter (high)</i>	0-10 %	10-90 %	30 (high)

2.3.2.2 Control Specimens and Repeatability Results

Three sets of control brain tissue surrogates were identified corresponding to three different two-part silicone compositions (summarized in Table 2). The first control specimen was a 50% A – 50% B composition which closely mimicks the mean white matter mechanical behavior [5] at a low strain rate of 2.5 mm/s. Three sets of tests comprising of 8 test coupons were tested two times each to evaluate the repeatability of test results, the average results of which are presented in Figure 2.11.

Table 2.4: Control test specimen compositions for mimicking mean brain tissue biomechanical properties and for repeatability tests

Controls Tests			
Control Specimen No.	Silicone Composition	Brain Tissue Simulated	Number of Tests
1	50 % A, 50 % B	White Matter (low)	8

2	30 % A, 70 % B	Grey Matter (low)	10
3	10 % A, 90 % B	White Matter (high) Grey matter (high)	7

The second control specimen was a 30% A – 70% B composition simulating the mean grey matter mechanical properties [5] at the low strain rate value of 2.5 mm/s. Similar to the case of control specimen 1, three sets of tests with 10 coupons were tested two times each. The average repeatability results are shown in Figure 2.12.

Figure 2.11: Brain tissue composition (control specimen 1) mimicking mean white matter mechanical behavior [5] at low strain rate testing, tested for repeatability

A third control specimen with 10% A – 70% B composition was used to simulate the mean non-linear mechanical behavior (literature based plots) of both the white and the grey matter at high strain rate (30 mm/s) testing. This was done as the white and grey matter plots at high test rates are reasonably close to each other. Seven test coupons were tested two times each to check for repeatability of test results (see Figure 2.13).

Figure 2.12: Brain tissue composition (control specimen 2) mimicking mean grey matter mechanical behavior [5] at low strain rate testing, tested for repeatability

Figure 2.13: Brain tissue composition (control specimen 3) simulating mean grey and white matter mechanical properties [5] at high strain rate testing (30 mm/s), tested for repeatability

2.4 Human Coronary Artery Surrogates

In the current work, a novel technique to develop MRI based patient-specific coronary artery lumen models was developed. This model was 3D printed and a four-part silicone based material was developed to simulate the precise mechanical behavior of the intima (innermost and the stiffest layer of an artery). Using the 3D printed model as a positive mold, the intimal tissue simulant material was used to initially generate a single layer arterial model. Subsequently, the four-part silicone based simulants were developed to mimic the medial (middle layer) and adventitial (outermost) layers. A 3-layer arterial model was generated with layer-specific mechanical properties, thickness and color (to distinguish between the layers), using a time-controlled dipping technique. To date, such a biofidelic three-layered patient-specific coronary arterial section has not been developed to the best of our knowledge, which would be indispensable to visualize and evaluate arterial blockage conditions, select the right stent and stent implantation technique.

2.4.1 Materials and Methods

A set of 100 live MRI images of a patient's heart are obtained from the National Institutes of Health (NIH) visible human database. An image segmentation software such as Turtleseg [127], ITK-Snap or equivalent is used develop a 3D model of an arterial lumen section as shown in Figure 2.14. The 3D model is refined using an iterative process of surface smoothening. The final model is exported in a stereolithographic file format and 3D printed at the University of Alabama, Tuscaloosa 3D printing lab (See Figure 2.14). The 3D printer used was Stratasys Dimension SST 1200es and the material used for fabricating the mold was Acrylonitrile butadiene styrene (ABS), a very popular material used in the 3D printing industry which provides a good surface finish and high strength.

Figure 2.14: Development of 3D printed arterial model from MRI images of coronary artery

The 3D printed arterial lumen sections were used as positive molds for fabrication of hollow arterial models. Initially, a four-part silicone material was developed which simulates the mechanical behavior of the arterial intimal layer. The 3D printed arterial sections were dipped into the fluid material and left to set for an average of 3-4 hours. The layer thickness and uniformity were found to be functions of the time at which the 3D printed arterial sections were dipped in the fluid silicone mixture. Starting at the time of mixing the four-part silicone, an approximate 32 ± 3 min time lapse before dipping a 3D printed arterial section, was found to generate a single layer arterial model with only the intimal layer at a thickness of 0.28 ± 0.04 mm, similar to the actual intimal thickness reported in literature [3]. With an increase and decrease in the time of dipping, the silicone layer thickness was found to increase and decrease respectively. Beyond 65 ± 5 min, the silicone mixture was found to get so hard that any further dipping was not possible. The single layer arterial models are shown in Figure 2.15.

Three layer artery models were made from three different mix ratios of the four-part silicone material simulating the mechanical properties of the intima, media and adventitia layers respectively. The dipping type was regulated to control the thickness of each layer, and also to ensure none of the layers mix with each other. Table 2.5 lists the dipping time estimated for fabricating arterial layers with thicknesses close to the literature values [3]. Figure 2.16

presents five different three layer arterial sections along with the cross-section of one model. It should be mentioned here that over 20 three layer artery model fabrication were attempted before getting a uniform model like the one shown in Figure 2.16.

Figure 2.15: Fabrication of single layer (intimal) coronary artery models

Table 2.5: Dipping time versus arterial layer thickness for three layer coronary artery model

Arterial Layer	Thickness (mm)	Dipping Time (min)
Intimal (<i>Innermost</i>)	0.4 ± 0.1	33 ± 2.5
Medial (<i>Middle</i>)	0.3 ± 0.05	45 ± 5
Adventitial (<i>Outermost</i>)	0.3 ± 0.1	64 ± 5

Figure 2.16: Three layer arterial models with the zoomed in view of the cross-section

2.4.2 Results and Discussions

18 tests with the four-part silicone coupons were identified which covers the entire range of arterial tissue properties in literature [3] (see Figure 2.17). The stress versus stretch for all the 18 tests (each performed thrice) is presented in Figure 2.17 along with the mix ratios the test coupons were made of. The stress and strain ranges for all these 18 tests were 0-700 kPa and 1-1.4 respectively.

The literature based stress versus stretch plots of the upper and lower bounds of the three arterial layers [3] were superimposed onto the stress versus stretch plots of the 18 four-part silicone based tests in Figure 2.17. It can be clearly seen that all the ranges of arterial tissue properties could be recreated using the four-part silicone system. Based on our comparison studies, the four-part mix ratios were estimated for accurate mimicking of the three arterial layers (both longitudinal and circumferential), as listed in Table 2.6.

Table 2.6: Four-part mix ratios corresponding to the three arterial layer properties

Arterial Layer	Corresponding four-part Mix Ratio
Intimal (<i>Longitudinal</i>)	20-55 % 1 A, 20-35 % 1B, 5-30 % 2A, 5-30 % 2B
Intimal (<i>Circumferential</i>)	15-55 % 1 A, 15-35 % 1B, 5-35 % 2A, 5-35 % 2B
Medial (<i>Longitudinal</i>)	2-10 % 1 A, 2-10 % 1B, 40-48 % 2A, 40-48 % 2B
Medial (<i>Circumferential</i>)	5-20 % 1 A, 5-20 % 1B, 30-45 % 2A, 30-45% 2B
Adventitia (<i>Longitudinal</i>)	15-35 % 1 A, 15-25 % 1B, 20-35 % 2A, 20-35% 2B
Adventitia (<i>Circumferential</i>)	5-35 % 1 A, 5-35 % 1B, 15-45 % 2A, 15-45% 2B

Figure 2.17: Mechanical test results of 18 test coupons compared with literature [3] based plots on arterial tissue properties

2.5 Vaginal Tissue Surrogates

Novel vaginal tissue surrogates were developed to simulate normal and prolapsed (diseased) vaginal tissues. The material used was a four-part silicone based system. Extensive mechanical testing was conducted on the surrogates and their stress versus stretch profile, modulus of elasticity in low and high stretches were compared with the vaginal tissue tests in literature [6]. Also control specimens were developed to ensure repeatability of test results and to compare with literature results. The following sections discusses the details of the fabrication methodology, mechanical tests and the results from the study.

2.5.1 Materials and Methods

Two two-part soft silicone material variants were procured from Smooth-On Inc., and mixed at appropriate ratios to obtain a four-part resulting mixture. Ecoflex 00-10 which is an extremely soft silicone rubber, and with a shore durometer hardness (as per the American Society for Testing and Materials (ATSM) D2240 testing standard) of 10 was chosen as the first two-part silicone rubber. The second two-part silicone rubber was selected as Moldstar 30A, which is a comparatively harder silicone material, with a shore hardness of 30A. The four silicone parts were poured in arbitrary ratios initially, and measured precisely in a weighing balance, followed by a uniform mixing. It should be mentioned here, that from here onwards, throughout the document, Ecoflex 00-10 parts A and B have been called out as 1A and 1 B, and Moldstar 30A parts A and B have been termed as 2A and 2B.

30 test coupons of the size 5 cm X 1 cm X 3 mm were generated, and after curing, uniaxial mechanical tests were performed on test coupons made of arbitrary mix ratios of the four-part silicone. A small initial load (<0.1 N) was applied on each test specimen to ensure there is no slack in the specimen to start with. All tests were performed on a universal testing machine from MTS Corporation, and a dynamic test rate of 0.08 mm/sec based on literature [6], was used for all the tests. Each test was repeated three times and an average value of the raw load (Newtons) data was plotted against the displacement (mm). The insignificant parts of the plots such as with negative load values and beyond the specimen rupture point were trimmed off. All the plots were carefully calibrated to have the stress and stretch values start from zero and one respectively. The load versus displacement plots were converted to true stress versus true strain graphs. Fourth degree polynomial trend lines were fit to each of the plots with high R^2 (coefficient of determination) values close to 1. All the plot strains (X-axis) steps and ranges were standardized ($0 < \epsilon_{true} < 1$ at 0.01 increment steps), and the respective stress values were

calculated using the trend line equations recorded for each plot in the previous step, and re-plotted. Each stress versus strain plot was converted to stress versus stretch (λ).

It should be mentioned that none of the silicone test specimens got ruptured during experiments, which is unlike in actual vaginal tissues which were reported to have ruptured in the end of the test in literature [6]. Thereby, there was no way to compare the ultimate tensile strength of the vaginal tissue surrogate material and the actual fresh vaginal tissues tested in literature [6].

Based on the 20 arbitrary four-part mix ratios tested, and the mean normal vaginal tissue property reported in literature [6], a control specimen was identified comprising of approximately part A (35 wt. % Moldstar 30 (2)), part B (35 wt. % Moldstar 30 (2)), part A (15 wt. % Ecoflex 0010 (1)) and part B (5-10 wt. % Ecoflex 0010 (1)), and named as “30-1-70-2” specimen. Five set of tests, each set comprising of 10 tests were conducted with this control mix ratio, and compared with the mechanical behavior of normal and prolapsed vaginal tissues.

2.5.2 Results and Discussion

2.5.2.1 Uniaxial Tests to Develop the Normal and Prolapsed Vaginal Tissue Surrogates

20 specimens made of arbitrary mix ratios of the four-part silicone system were tested mechanically using an uniaxial test. Figure 2.18 shows the stress versus stretch plots of all the 20 tests along with the various plots from the literature [6]. The four-part mix ratio for each of the 20 tests have been mentioned clearly in the legend in Figure 2.18.

The linear modulus of elasticity was estimated from all the 20 tests at both high and low stretch ratios. Table 2.7 lists all such values of elasticity modulus. The lowest and highest modulus of elasticity value recorded for low stretch ratios were 0.347 MPa and 7.917 MPa respectively. For the high stretch ratios, the lowest and highest values obtained were 3.869 MPa

and 58.889 MPa respectively (see table 2.7). These values were found to be within the range of the elasticity modulus values reported in literature [128-130].

Figure 2.18: Stress versus stretch plots of 20 arbitrary four-part mix ratios tested for development of vaginal tissue surrogates, compared with literature values [6]

Table 2.7: Linear elasticity modulus from 20 tests on four-part silicone mix ratios, at high and low stretch values

Test and their Silicone Mixture Composition	Low Stretch Elasticity Modulus <i>MPa/(mm/mm)</i>	High Stretch Elasticity Modulus <i>MPa/(mm/mm)</i>
Test 1 (15.66%1A-14.25%1B-34.42%2A-35.77%2B)	3.382	12.613
Test 2 (15.25%1A-13.92%1B-34.08%2A-36.75%2B)	3.420	17.906
Test 3 (14.08%1A-13.95%1B-36.15%2A-35.82%2B)	1.951	12.746
Test 4 (14.97%1A-14.96%1B-34.97%2A-	3.061	16.520

35.10%2B)		
Test 5 (15.07%1A-15.06%1B-34.94%2A-34.93%2B)	3.164	14.162
Test 6 (8%1A-8%1B-42%2A-42%2B)	5.078	19.503
Test 7 (30%1A-30%1B-20%2A-20%2B)	1.329	9.097
Test 8 (15%1A-15%1B-35%2A-35%2B)	2.122	11.935
Test 9 (48%1A-32%1B-10%2A-10%2B)	1.134	8.157
Test 10 (25%1A-25%1B-25%2A-25%2B)	1.344	7.408
Test 11 (2%1A-2%1B-47%2A-47%2B)	6.223	46.441
Test 12 (2%1A-2%1B-47%2A-47%2B)	7.917	58.889
Test 13 (10%1A-10%1B-40%2A-40%2B)	4.660	20.620
Test 14 (10%1A-10%1B-40%2A-40%2B)	5.297	29.186
Test 15 (15%1A-15%1B-35%2A-35%2B)	3.232	12.613
Test 16 (42%1A-42%1B-8%2A-8%2B)	0.871	10.353
Test 17 (42%1A-42%1B-8%2A-8%2B)	0.704	7.852
Test 18 (45%1A-45%1B-5%2A-5%2B)	0.667	6.596
Test 19 (45%1A-45%1B-5%2A-5%2B)	2.584	4.541
Test 20 (50%1A-50%1B-0%2A-0%2B)	0.347	3.869

The mean stress versus stretch plot of the normal vaginal tissues reported in literature was replotted in Figure 2.19. A control mix ratio of approximately part A (35 wt. % Moldstar 30 (2)), part B (35 wt. % Moldstar 30 (2)), part A (15 wt. % Ecoflex 0010 (1)) and part B (5-10 wt. % Ecoflex 0010 (1)) was selected based on the initial 20 tests, and 50 test specimens were tested in 5 batches (10 tests each). The mean results of this 5 batch tests are plotted along with the error bars, and the literature based mean normal vaginal mechanical behavior [6] in Figure 2.19. The exact percentages of the four-part mix ratios used for every batch are clearly indicated in the legend in Figure 2.19. It should be mentioned that the control specimen 30-1-70-2 was identified mainly for the purpose of comparing experimental datasets in the upcoming sections with the literature.

Figure 2.19: Five batches of 30-1-70-2 mix ratio tested, and plotted along with the mean literature based normal vaginal tissue mechanical behavior [6]

2.5.2.2 Control Tests Compared with Normal and Prolapsed Vaginal Tissues

The control specimen 30-1-70-2 mean test results for the five batches were compared with the literature values on the mechanical testing of the normal vaginal tissues [6]. As can be seen in the Figure 2.20, the control specimen tests very closely simulate the normal vaginal tissue condition reported in literature [6].

Figure 2.20: Five batch of tests with the 30-1-70-2 control test specimens, compared with the literature based normal vaginal tissue mechanical behavior [6]

The mean stress versus stretch ratios from the five batches of uniaxial mechanical tests on the control specimen 30-1-70-2 were plotted along with the literature results on prolapsed vaginal tissues [6] (see Figure 2.21). Few prolapsed vaginal tissues are closer in mechanical behavior to the control specimens. But most of the prolapsed vaginal tissues are stiffer than the control specimen (as seen in Figure 2.21). Thus, any mix ratio which produces a slightly stiffer silicone based vaginal tissue surrogate could be employed to simulate the specific prolapsed vaginal tissue variant. In future, if a vaginal tissue exhibits an even more stiffer mechanical behavior due to an extreme prolapse case, a silicone based surrogate for that tissue could be easily fabricated based on the four-part material model.

Figure 2.21: Five batch of tests with the 30-1-70-2 control test specimens, compared with the literature based prolapsed vaginal tissue mechanical behavior [6]

2.6 Soft Fiber-Matrix Composites

Experimentally, anisotropy has been measured in skin [2], pelvic [131] and brain tissues [132], however to date, there exists no tissue simulant or phantom material which incorporates tissue anisotropy. A way to physically model anisotropic tissue materials would allow the

validation of the results from the computational models. Also, such a model would be indispensable to generate realistic tissue phantoms with anisotropic effects, for various biomechanical testing and tissue engineering applications. In the current work, soft composite-like materials made of silicone were used to simulate tissue anisotropy. The anisotropic mechanical behavior of the skin, pelvic and brain tissues were compared with the properties of the soft composites. Also, the effect of varying FVF, fiber spacing and orientation were also investigated.

2.6.1 Materials and Methods

2.6.1.1 Preparation of Matrix and Fiber Materials

A two-part extremely soft silicone material with shore hardness of 10 was used for developing the matrix material. Part A and part B were mixed at a 1:1 ratio by weight to generate 20 test coupons (see Figure 2.22 A) with the dimensions 49mm<Length<50mm, 9mm<Width<11mm and 2mm<Thickness<3mm. Each coupon was clamped on a universal tensile testing machine (MTS Criterion 42), and tested at a constant strain rate of 0.4 mm/s [2]. The stress versus strain plots generated from the tests were checked for repeatability (Figure 2.23 A) and also compared with literature [8] to ensure that there are no machine calibration errors.

A two-part hard silicone material with shore hardness of 30 was selected to make the hard fibers (Figure 2.22 B). 30 test coupons were generated using 1:1 ratio of part A and part B of silicone, and tested mechanically on the MTS machine. The combined stresses versus stretch results for the 30 specimens are presented in Figure 2.23 B. Hard silicone sheets of area 210 mm X 297 mm and thicknesses 2 mm and 4 mm respectively were fabricated, and multiple thin fibers were cut with different lengths and widths. The following section discusses fabrication of the composite material using the soft matrix material and the hard fiber material.

(A)

(B)

Figure 2.22: A) Soft silicone matrix, B) Hard silicone fibers used in fabricating the soft tissue composites

2.6.1.2 Soft Tissue Composite Fabrication

Fibers made of the hard silicone material, and of different widths and thicknesses were laid in a rectangular box, and the soft silicone material was poured into it. Test specimens were cut out with dimensions Length 30 ± 3 mm, Width 10 ± 4 mm and Thickness 2 ± 2 mm. The fiber volume fraction for each of the test specimen were calculated. The lowest and highest FVF's were estimated to be 0.17 and 0.78 respectively. Figure 2.24 shows the range of specimens created with different FVF's for further testing.

(A)

(B)

Figure 2.23: Stress versus stretch plots for : A) Four batches of samples (5 in each) with 1:1 ratio of two-part silicone with shore hardness 10, simulating matrix material, and B) 30 coupons with 1:1 ratio of two-part silicone with shore hardness 30, simulating fiber material

Figure 2.24: Composite test specimens with varying fiber volume fractions

Multiple fibers were cut with similar cross-sections (with $2\text{mm} < \text{Width} < 3\text{mm}$ and $2\text{mm} < \text{Thickness} < 3\text{mm}$) and test specimens were fabricated with single, two and three fibers (Figure 2.25). The effect of variations of the fiber spacing and number on soft composite mechanical properties were investigated. The overall dimensions of the specimens with one, two and three fibers were $35\text{mm} \times 10\text{mm} \times 3\text{mm}$, $35\text{mm} \times 15\text{mm} \times 3\text{mm}$ and $35\text{mm} \times 18\text{mm} \times 3\text{mm}$ respectively. Each specimen was tested with the fibers pointing in the longitudinal direction (along the line of the force). Also, it was made sure that the ends of all the fibers in each specimen were gripped in clamps. It should be mentioned that in one of the specimen, a fiber was 4 degrees off from the longitudinal direction, which was assumed to be acceptable for the study.

Figure 2.25: Test specimens with single, two and three similar fibers

In another form, soft composite specimens were cut out with the fibers pointing in the direction transverse to the direction of load application. Also, different variants had one, two and three fibers (Figure 2.26). A total of 10 such specimens with $20\text{mm} < \text{Length} < 25\text{mm}$, $15 < \text{Width} < 18\text{mm}$ and $3\text{mm} < \text{Thickness} < 4\text{mm}$ were fabricated and tested on the mechanical testing machine.

Skewed fibers were placed at ± 45 degrees and 3 specimens with one, two and three fibers respectively were fabricated (Figure 2.26 B). The specimens were not of the same size and the dimension ranges were with $25\text{mm} < \text{Length} < 35\text{mm}$, $15\text{mm} < \text{Width} < 20\text{mm}$ and $2\text{mm} < \text{Thickness} < 3\text{mm}$. Each specimen was clamped in such a way that the fiber direction was at ± 45 degrees relative to the direction of application of the load. All the test specimens were tested at a constant strain rate of 0.4 mm/s , and raw data was obtained from the mechanical testing machine in the form of load versus extension data points.

(A)

(B)

Figure 2.26: Soft composites with A) Transverse fibers and B) Skewed fibers at ± 45 degrees

2.6.2 Results and Discussion

2.6.2.1 Effect of Fiber Volume Fraction (FVF)

The effect of FVF on the mechanical properties of the soft tissue like composite materials was investigated. A baseline stress versus stretch plot of the pure matrix material (composite with no fibers) and a pure fiber material (composite with no matrix) were plotted as shown in

Figure 2.27. The stress versus stretch plots of the soft composite specimens with FVF of 0.17, 0.35, 0.52, 0.61 and 0.78 respectively were plotted along with the baseline plots. Each type of specimen was tested three times to ensure repeatability (see error bars in Figure 2.27). It was found that the mechanical behavior of all the composite specimens are within the bound of the baseline plots. Also, with an increase in FVF, the soft composite material exhibits a stiffening behavior. This is very similar to characteristics of soft tissues where the amount of collagen fiber content determines how soft or stiff a tissue is. Also, experimentally, human skin from various parts of the body (having different FVF's) have been shown earlier by Annaidh et al. [2] to follow a similar trend. Thus, it can be concluded that controlling the FVF in a soft composite framework can allow the fabrication of customized soft tissue surrogates with different mechanical properties.

Figure 2.27: Effect of FVF variations on soft composite material properties

2.6.2.2 Effect of Fiber Spacing and Number of Fibers

Soft composites with one, two and three fibers respectively were tested and their mechanical behavior was compared. The average FVF for the specimens with one, two and

three fibers were estimated to be in the ranges of 0.19-0.23, 0.35-0.41, and 0.52-0.58 respectively. The true stress versus true stretch plots for all these three configurations are presented in Figure 2.28 along with the baseline plots of specimens with only fibers and only matrix material. As expected, the three fiber configuration was found to have the stiffest stress versus stretch plot compared to the configurations with the one and two fibers. It should be emphasized that these findings may seem intuitive, but to date, have not been reported for any soft tissue composite material system.

Figure 2.28: Effect of fiber quantity on soft composite material properties

The effect of spacing between the fibers on the soft composite material properties was investigated. For the two and three fiber configurations, a spacing of 2 mm, 4 mm and 6 mm were incorporated respectively. The results are shown in Figure 2.29, based on which, three main observations could be noted. First, the soft composite material becomes more compliant with increased fiber spacing. Second, two fiber configuration with a small fiber spacing (2 mm) is stiffer than the three fiber configuration with a huge fiber spacing (6 mm). Thus, it can be concluded that fiber spacing can be altered to generate material properties superior (in terms of

stiffness) than in the case of more fibers or a higher FVF as observed in earlier Figures 2.27 and 2.28. Third, the three fiber configuration with the minimum fiber spacing (2 mm) was found to generate the stiffest soft composite material, and the two fiber configuration with the maximum fiber spacing (6 mm) was the most compliant material model. It can be concluded from this observation that the maximum number of fibers with the minimum fiber spacing is the combination to obtain the stiffest soft composite material and the reverse relation is applicable for obtaining a highly compliant soft composite material.

Figure 2.29: Effect of fiber spacing for the two and three fiber configurations on the soft composite mechanical behavior

2.6.2.3 Effect of Fiber Orientation

The effect of fiber orientation on the soft composite mechanical properties was studied for the longitudinal (0 degree), transverse (90 degree) and the ± 45 degree fiber orientations. All the angles were measured relative to the direction of application of load (during the mechanical testing). The main observation (from Figure 2.30) was that the longitudinal fiber orientation with the maximum number of fibers yielded the stiffest composite material. The transverse fiber

orientation was found to generate the weakest soft composite materials. For a particular number of fibers (one, two or three), the ± 45 degree fiber orientation led to composite material properties in between the longitudinal and transverse configurations. The combined effect of the number of fibers and the fiber orientation however indicated some interesting results. First, the ± 45 degree orientation with three fibers was found to be stiffer than the longitudinal configuration with one fiber. Second, increasing the number of fibers minimally affects the mechanical behavior of composites with transverse configurations (as can be observed in Figure 2.30). Also, such observations correlate to the fact that tissues with collagen fibers oriented along the principal direction are the stiffest and the ones with fibers along the transverse direction are the weakest [2], with any other orientation causing material behavior to lie in between that in case of the longitudinal and transverse cases.

Figure 2.30: Effect of fiber orientation for one, two and three fiber configurations on the soft composite material property

2.6.2.4 Combined Effects of FVF and Fiber Orientation

In soft tissues, the main measurable quantities using imaging, dissection and histological techniques are the regional FVF and the fiber orientation. Thus, to capture the combined effect of these two parameters, the modulus of elasticity of the various test specimens were estimated at low stretch values. The way this was implemented was by drawing a tangent to the non-linear stress versus stretch plot of any specimen starting at the origin, and measuring its slope [2]. The trends observed are summarized in the 3D plot in Figure 2.31. It is observed that a high FVF and zero degree fiber orientation generates a soft composite material variant with the highest modulus of elasticity. It should be mentioned here that one of the limitations of our work is that no biaxial or multiaxial tests were conducted to simulate real life tissue load responses, and such studies could be conducted in the future. The 3D plot indicates the options with the FVF and fiber orientation combinations which will generate a certain type of tissue anisotropy model with a specific low stretch modulus of elasticity value.

2.6.2.5 Comparison with Human Tissues

The bounds of the soft composite material properties were compared with that of the material behavior of major human tissues namely the skin, pelvic tissues and brain tissues to emphasize the broad scope of the current work. As seen in Figure 2.32, the pelvic and brain tissues could be easily recreated using the soft composite material model by adjusting the FVF, fiber orientation and fiber spacing individually or in combination as shown in the previous sections. A stiffer composite material model needs to be adopted to simulate the anisotropic human skin tissues though as the stress versus stretch ranges are much higher. In the next chapter, continuum based modeling of soft tissue composites is developed to precisely mimic the anisotropic material properties of these three tissue types and also other tissues which are part of the human body.

Figure 2.31: Combined effects of FVF and fiber orientation on low stretch modulus values of soft composite materials

Figure 2.32: Comparison of the range of soft composite material properties with that of the human skin [2], pelvic [7] and brain tissues [8]

2.7 Functionalized (Electrically Conductive) Fiber-Matrix Composites

In the current work, a novel conductive synthetic skin composite system was developed, which would be indispensable for integration into wearable technologies, and also allow the biomechanical testing of the human skin for different engineering and medical applications. The composite system is composed of short carbon fibers dispersed in a multi part silicone based matrix material (which behaves biomechanically like synthetic skin). The volume fraction of the fibers was varied to control the mechanical and electrical properties of the composite. Uniaxial tensile tests were conducted to generate stress versus strain responses of the synthetic skin composites at different fiber volume fractions, and electrical measurements were recorded at different strains. Optical microscopy was used to understand composite fiber orientations in unstretched and stretched states, and its effects on the electrical conductivity of the material.

2.7.1 Materials and Methods

2.7.1.1 Fabrication and Mechanical Testing

Figure 2.33: Novel synthetic skin materials [9]

To develop the skin like conductive polymers, two-part silicones, with Shore (Durometer) hardness of 30A and 00-10 respectively procured from Smooth-On Inc. and Polytek Inc. was used (See Figure 2.35) [9]. The synthetic skin composition used for the matrix material throughout the study was 45% wt. Shore 30A (part A-hardener), 45% wt. Shore 30A (part B-cross linker), 5% wt. Shore 00-10 (part A-hardener) and 5% wt. Shore 00-10 (part B-cross

linker). From a spool of carbon fibers, fibers bundles were chopped in different lengths (0.5-6 mm) and mixed in different weights fractions (FWF's) with the synthetic skin material to generate the test coupons (see Figure 2.34). A microscope (Serial No. 29AX E250223 from Motic Inc.) was used to capture images of the test coupons with low and high FWF's before mechanical testing. A uniaxial test was conducted (on a MTS universal testing machine) to study the load versus deformation behavior of the test specimens. A constant strain rate of 0.4 s^{-1} and specimen size of $35\text{mm} \times 10\text{mm} \times 3\text{mm}$ (after clamping) was selected for all the uniaxial tests on silicone based material, based on literature on uniaxial tests on human skin [2, 28, 29, 114].

Figure 2.34: Short carbon fibers mixed with synthetic skin material to generate test coupons

2.7.1.2 Variable Strain Testing and Electrical Measurements

Accompanying the complete uniaxial tensile testing of each coupon at varying strains, all test coupons were stretched to 100% elongation (strain of 1) and 200% elongation (strain of 2) and the respective electrical resistances were recorded at 1 cm and 5 cm spacing. Two MANNIX digital multimeters (Sr. no. DMM51FSG) were used which can measure resistances in the range of 200Ω to $200 \text{ M } \Omega$. The power source for the instrument is a 9 volt internal battery. Two multimeters were used to double check the accuracy of the measurements at all times and to calibrate the instrument in cases of possible errors. The resistance changes due to varying FWF's were thoroughly characterized for stretched coupons at unstretched, and at 100% and 200%

elongation states. Also, for different strains, the FWF values which would result in a small resistance value ($<1000\ \Omega$) were identified to understand composite material model requirements for a highly flexible synthetic skin composition with a consistent conducting path. Figure 2.35 shows the resistance measurements being conducted at 5 cm spacing for the coupon at 100% elongation, and a representative microscopic image of the fiber alignment in a section of the coupon. Various considerations were made to collect accurate resistance data points. First, two pins were used to hook the multimeter wires and to obtain a stable resistance reading. Second, the 1 cm and 5 cm spacing resistances were measured at two different locations on the coupon for each test, and the average values of the resistances were reported. Third, the percentage elongation was controlled via the tensile testing machine to ensure accuracy, and the tensile test was stopped temporarily for about a minute to record stable resistance readings.

Figure 2.35: A test coupon at 100% elongation and resistance measurements, with a representative microscopy image of fibers in a section of the coupon

2.7.2 Results and Discussion

2.7.2.1 Fiber Length Optimization for Electrical Conduction

The fiber lengths and FWF were varied initially to understand the fiber requirements for a consistent electrical conduction through the synthetic skin material. At a FWF of 0.15, the

coupons started to show a reasonable amount of conduction (Resistance < 15000 Ω). To understand the optimal fiber length for the highest conduction (lowest resistance) in the composite, 10 coupons were generated with FWF of 0.15 ± 0.05 and different fiber lengths. The resulting resistance at 1 cm spacing were recorded at two different locations on each coupon. The average values of the resistances with error bars for different fiber lengths at 1 cm spacing are presented in Figure 2.36.

Figure 2.36: Resistances recorded at 1 cm spacing for test coupons with FVF=0.15 and different fiber lengths

Microscopy images were captured to look at fiber alignments in the coupons with different fiber lengths. It was found that for fiber lengths in the range of 0.5-3 mm, fiber agglomeration took place forming fiber bundles, and resulting in fewer fiber crosslinks (see Figure 2.37 A for a fiber length of 2 mm). This could possibly explain the high resistances indicated in Figure 2.36 for this range of fiber lengths. For fiber lengths $L > 3$ mm, the fiber agglomeration was observed to be reduced and result in an observable increase in the number of crosslinks (see Figure 2.37 B for a fiber length of 5 mm). At a fiber length of approximately

5±0.5 mm and going from fiber lengths of 5 to 7 mm, the resistance value recorded was consistently in the range of 13536-13578 Ω . Thereby, 5±0.5 mm fiber length was considered as the optimum fiber length for the study. Two limitations of the composite fabrication should be acknowledged here, which could be observed in the microscopy images. First, small sized air pockets were observed in the composite matrix material due to air inclusions during cure. However, such small sized inclusions were tested and found to result in minimal variations in the material property of the composite coupons. Second, one or two small fiber residues were observed in the composite specimens, which were formed due to fiber chipping during the fabrication process. The effect of such small residues were assumed to be negligibly affecting the overall composite material property.

Figure 2.37: Microscopy images of the composite coupons for a constant FWF of 0.15 and fiber lengths: A) 2 mm and B) 5 mm

2.7.2.2 Resistances at Different Fiber Weight Fractions

Keeping the fiber length constant (5±0.5 mm), multiple test coupons (30) were generated with different FWF's. Going from a FWF of 0.15 to 0.9, it was found that for a FWF>0.3, the resistance was less than 1000 Ω which is a reasonable number for a consistent conduction pathway in electronic devices [133]. Figure 2.38 A presents the summary of resistances recorded

for different FWF's at a spacing of 1 cm and 5 cm respectively. Figure 2.38 B shows a zoomed in representation of Figure 2.38A, where only the test coupons which yielded a resistance less than 1000Ω are presented. The sharp drop in resistances can be clearly seen beyond FWF of 0.3.

Figure 2.38: FWF versus resistances recorded at 1 cm and 5 cm spacing for test coupons: A) For high resistances, B) below 1000Ω

2.7.2.3 Composite Mechanical Property at Different Fiber Weight Fractions

To characterize the current anisotropic composite material model developed for conductive synthetic skin, 30 test specimens were fabricated with the same matrix material and varying FWF's. Based on the uniaxial mechanical tests, the stress versus stretch responses of 10 composite compositions with different FWF's (listed in Table 2.8) are presented in Figure 2.39. Figure 2.39 also shows the literature plots on mechanical tests on excised human skin (upper and lower bounds) [2, 28, 29, 114].

Table 2.8: Composite compositions tested (see Figure 2.41) and the corresponding FWF values

Composite Composition No.	FWF
1	0.58
2	0.41
3	0.47
4	0.66

Figure 2.39: Stress versus stretch behavior of anisotropic synthetic skin test coupons with different FWF's, within the bounds of literature based excised skin tissue experiments

2.7.2.4 Varying Strains and Fiber Weight Fractions

All the test coupons with different FWF's were subjected to 100% and 200% elongations and the resistances were measured at 1 cm spacing. It was found that there was an observed overall increase in resistance values due to elongation (Figure 2.40A). Figure 2.40B captures the values of FWF which lead to resistance values $< 1000 \, \Omega$. For $\text{FWF} > 0.65$, a high conduction was recorded (with resistance $< 100 \, \Omega$). This FWF value was much higher than the $\text{FWF} > 0.3$ value reported for high conduction (Resistance $< 100 \, \Omega$) in unstretched coupons.

For the 200% elongation state, there was an observed overall increase in resistance values over the 100% elongation and unstretched states (Figure 2.41). Looking at the FWF values which resulted in resistances $< 1000 \, \Omega$ (Figure 2.41 B), high conduction (resistance values $< 100 \, \Omega$) were recorded for $\text{FWF} > 0.8$, which is much higher than the FWF values required to produce high conduction (resistance values $< 100 \, \Omega$) with the coupons at unstretched state and

at 100% elongation. It can be concluded that stretching of the developed conductive synthetic skin material decreases its conductivity. Therefore, for applications which require minimum elongation, fiber inclusions with a small FWF will suffice. However, for high stretch conditions, a higher FWF is required to allow an unobstructed electrical conduction.

(A)

(B)

Figure 2.40: FWF versus resistances recorded at 1 cm spacing for 100% elongation test on the coupons: A) For high resistances, B) below 1000 Ω

(A)

(B)

Figure 2.41: FWF versus resistances recorded at 1 cm spacing for 200% elongation test on the coupons: A) For high resistances, B) below 1000 Ω

To understand the effect of varying microscale fiber-fiber interactions due to stretching on the soft composite conductivity, optical microscopic imaging was carried out. Figure 2.42A captures the fiber alignment of one of the test coupons with FWF of 0.47 in unstretched state. Figure 2.42B and 2.42C shows the curling of fibers due to 100% and 200% elongations respectively captured after relaxation of the test specimen. Three main observations were recorded. First, strains lead to permanent curling of short carbon fibers within the matrix, giving rise to significant residual stresses within the composite especially at high strains. Second, the mechanical properties of the composite changes minimally due to the fiber curling, which was confirmed by comparison of the stress-strain plots of the test specimen tested multiple times. Third, the electrical properties of the composite material changes not only due to strains (as seen in Figures 2.40 and 2.41) but also after stress relaxation. For the particular specimen with FWF of 0.47, before relaxation, the resistances recorded for unstretched state; at 100% and 200% elongation were 101 Ω , 422 Ω and 1341 Ω respectively. After relaxation, and three repeatability tests, the average values for unstretched state, at 100% and 200% elongation were calculated to be 394 Ω , 513 Ω and 1477 Ω respectively.

Figure 2.42: Microscopy images of test coupon with FWF=0.47 in A) Unstretched state, B) At 100% elongation and C) At 200% elongation, showing fiber curling

CHAPTER 3

SOFT COMPOSITE CHARACTERIZATION²

3.1 Summary

Soft composites are non-linear materials with changes in the modulus of elasticity with increasing strain. Even though this mechanical behavior of the soft composites is recognized, they are very often assumed to have linear elastic and isotropic hyperelastic material properties in most of the computational analyses in literature. Hyperelastic constitutive relations are able to curve fit global soft composite behavior for rubbers and tissues. However, to understand the underlying anisotropic composite mechanics, more advanced material models have to be developed to account for fiber distribution and orientation. In this chapter, isotropic hyperelastic models, and widely used transversely isotropic material models are introduced, followed by the development of a novel anisotropic soft composite model which can model individual fiber and matrix contributions, fiber-matrix interactions, fiber orientation, and the effect of multiple fiber layers. Experimental data from Chapter two are used to fit the novel constitutive relations and the curve fit results were reported.

3.2 Isotropic Material Model

3.2.1 Numerical Model

The nonlinear mechanical behavior of soft materials such as tissues and silicone rubbers have been characterized in literature using isotropic hyperelastic constitutive material models such as

² A. Chanda, and V. Unnikrishnan, "Biomechanical Characterization of Normal and Prolapsed Vaginal Tissue Surrogates," *Journal of Mechanics in Medicine and Biology*, *Accepted*.
A. Chanda, C. Callaway, C. Clifton, and V. Unnikrishnan, "Biofidelic human brain tissue surrogates," *Mechanics of Advanced Materials and Structures*, pp. 1-31, 2016.

Fung, Mooney-Rivlin, Yeoh, Veronda-Westmann, and Humphrey [115]. In this work, the biomechanical behavior of brain tissues (both grey and white matter) are characterized using these isotropic hyperelastic models first.

Hyperelastic curve fit models are based on the definition of material dependent strain-energy function (denoted as Ψ), which is a scalar function of the right Cauchy-Green deformation tensor $\mathbf{C} = \mathbf{F}^T \mathbf{F}$ where $\mathbf{F}$ is the deformation gradient. Ψ can also be written as a function of three invariants of $\mathbf{C}$ namely I_1 , I_2 and I_3 , which are given by equation 3.1 [134-138]. Any hyperelastic model is dependent on either the Cauchy-Green tensor invariants or the principal stretches (λ_1 , λ_2 and λ_3) [115] as shown in equations 3.2-3.4.

Figure 3.1: Schematic of soft composite stretching in an isotropic hyperelastic model formulation

$$\psi = \psi(I_1, I_2, I_3) \quad (3.1)$$

$$I_1 = \sum_{i=1}^3 \lambda_i^2 \quad (3.2)$$

$$I_2 = \sum_{i,j=1}^3 \lambda_i^2 \lambda_j^2 \quad (3.3)$$

$$I_3 = \prod_{i=1}^3 \lambda_i^2 \quad (3.4)$$

$$\sigma_1 = \lambda_1 \frac{\partial \psi}{\partial \lambda_1} - \lambda_3 \frac{\partial \psi}{\partial \lambda_3}, \sigma_2 = \sigma_3 = 0 \quad (3.5)$$

Assuming the Cartesian principal axes (x_1 , x_2 and x_3) and a soft material aligned axially along the x_1 axis (see Figure 3.1). If this material is stretched uniaxially along the x_1 axis in the direction of the arrow (see Figure 3.1), the stress-stretch relationship is given by equation 3.5 (where ψ is the strain-energy function, λ_1 and λ_2 are principal stretches and $\sigma_1, \sigma_2, \sigma_3$ are the principal stresses). Solving equation 3.5 using hyperelastic strain energy functions corresponding to the Fung, Mooney-Rivlin, Yeoh, Veronda-westmann, and Humphrey models, the engineering stress versus stretch responses of the soft composites (experimental data) can be characterized using equations 3.6-3.10 respectively. The parameters μ and b (Fung model), c_1 and c_2 (Mooney-Rivlin, Humphrey and Veronda-Westmann model), c_1 , c_2 and c_3 (Yeoh), are estimated.

$$\sigma_{Fung} = \mu e^b (\lambda^2 + 2\lambda^{-1} - 3)(\lambda - \lambda^{-2}) \quad (3.6)$$

$$\sigma_{Mooney} = 2(\lambda^2 - \frac{1}{\lambda})(c_1 + c_2 \frac{1}{\lambda}) \quad (3.7)$$

$$\sigma_{Veronda-Westmann} = 2(\lambda^2 - \frac{1}{\lambda})c_1c_2 \left(e^{c_2(I_1-3)} - \frac{1}{2\lambda} \right) \quad (3.8)$$

$$\sigma_{Yeoh} = 2(\lambda^2 - \frac{1}{\lambda})(c_1 + 2c_2(I_1 - 3) + 3c_3(I_1 - 3)^2) \quad (3.9)$$

$$\sigma_{Humphrey} = 2(\lambda^2 - \frac{1}{\lambda})c_1c_2 e^{c_2(I_1-3)} \quad (3.10)$$

To evaluate the accuracy of the hyperelastic model chosen in predicting the soft composite material behavior, an average R^2 correlation value calculation has to be performed in

all cases, where R^2 can have a value from 0 through 1, 1 representing the best fit and 0 representing worst fit.

3.2.2 Curve Fit Results

Non-linear hyperelastic curve fit models were used to precisely characterize the stress versus stretch response of brain tissue surrogates (shown in Figure 3.2). The average stress versus strain results of six two-part silicone compositions tested at high and low strain rates were fitted with second degree polynomial trend lines as shown in Figure 3.3. Hyperelastic curve fitting was conducted for these trend lines in Figure 3.3 using the Fung, Mooney-Rivlin, Yeoh, Veronda-Westmann, and Humphrey [115] models, the results of which are summarized in Table 3.1.

Figure 3.2: Tensile test results of brain tissue surrogates

Figure 3.3: Average polynomial trendline fits of the silicone specimens tested at high and low strain rates (based test results) for hyperelastic curve fitting

Table 3.1: Hyperelastic curve fit parameters for the average stress versus stretch plots of silicone specimens (brain tissue simulants) corresponding to Figure 3.3

Hyperelastic Curve Fitting Results											
Average Specimen Composition	<i>Fung</i>		<i>Mooney-Rivlin</i>		<i>Yeoh</i>			<i>Humphrey</i>		<i>Veronda-Westmann</i>	
	μ	b	c_1	c_2	c_1	c_2	c_3	c_1	c_2	c_1	c_2
70 % A, 30 % B	24.0	-0.05	0.00060	0.0110	0.0099	-0.00110	-0.00095	-22.2	-0.46	-0.038	-0.480
60 % A, 40 % B	18.5	0.01	0.00020	0.0090	0.0078	-0.00094	-0.00062	-17.3	-0.46	-0.030	-0.475
50 % A, 50 % B	13.0	-0.20	0.00001	0.0061	0.0054	-0.00090	-0.00060	-9.4	-0.59	-0.020	-0.480
30 % A, 70 % B	8.5	-0.13	0.00020	0.0038	0.0033	0.00001	-0.00060	-7.1	-0.50	-0.016	-0.375
20 % A, 80 % B	6.0	-0.10	0.00020	0.0026	0.0022	0.00030	-0.00070	-5.0	-0.51	-0.010	-0.430
10 % A, 90 % B	3.0	-0.50	0.00015	0.0012	0.0011	0.00020	-0.00040	-3.0	-0.40	-0.005	-0.400

The accuracy of prediction of non-linear behavior of brain tissue simulants was estimated for each hyperelastic model (in Table 3.1) through numerical estimation of average R^2 correlation index in each case. Table 3.2 summarizes the R^2 correlation values which falls within

$0.9 < R^2 < 1$. The highest correlation index of ($R^2=0.997$) was generated by the three parameter Yeoh's hyperelastic model, and the least ($R^2=0.953$) was for the primitive Fung's model. This finding was in line with the known comparative accuracy of the hyperelastic constitutive material models in literature [5].

Table 3.2: Accuracy of hyperelastic curve fitting estimated using an average R^2 correlation value calculation

Accuracy of Hyperelastic Curve Fits	
Hyperelastic Model	R^2 Correlation Index
<i>Fung</i>	0.953
<i>Mooney-Rivlin</i>	0.966
<i>Yeoh</i>	0.997
<i>Humphrey</i>	0.984
<i>Veronda-Westmann</i>	0.989

3.3 Transversely Isotropic Model

3.3.1 Numerical Model

A transversely isotropic model involves material symmetry along an axis normal to a plane of isotropy. In a unidirectional composite model (see Figure 3.4), any plane normal to the fiber direction x_1 can be considered as an isotropic plane. In a transversely isotropic model developed by Martins et al. for skeletal muscles [71, 115, 137, 139-142], a tissue composite block is considered to have unidirectional fibers embedded in a muscle like matrix material, such that an uniaxial tensile test causes active muscle contraction and passive stretching of muscle fibers. It is assumed in this model that fiber contribution, fiber-matrix interaction and fiber orientation effects are not considered. In case of a simplified uniaxial test experiment on such a tissue composite, the strain-energy function takes the form in equation 3.11, in which, ψ_I is the isotropic strain energy stored in the material and $\psi_{passive}$ is the strain energy stored in composite

fibers. λ_f is the stretch in the direction of the fiber, c_2 and c_4 are dimensionless parameters, and c_1 and c_3 are parameters with the dimension of pressure [71, 115, 137, 139-142].

$$\psi = \psi_I + \psi_{passive}; \quad \psi_I = c_1(e^{c_2(I_1-3)} - 1); \quad \psi_{passive} = c_3(e^{c_4(\lambda_f-1)^2} - 1) \quad (3.11)$$

The Cauchy stress tensor is given by equation 3.12, where $dev(f)$ function is given by equation 3.13 and the $tr(f)$ used in equation 3.13 is given by equation 3.14, $[\mathbf{b}]$ refers to the Left-Cauchy Green tensor, $[\mathbf{I}]$ is the Identity matrix [71, 115, 139, 142] and p is a parameter and J is the Jacobian which accounts for the compressibility property of the material. For an incompressible material, J is equal to '1', and for a quasi-incompressible material, J approaches a value of '1'.

$$\sigma = \frac{1}{J} dev \left[2 \frac{\partial \psi_I}{\partial I_1} [\mathbf{b}] + \frac{\partial \psi_{passive}}{\partial \lambda} (\bar{\mathbf{n}} \otimes \bar{\mathbf{n}}) \right] + p[\mathbf{I}] \quad (3.12)$$

$$dev(f) = (f) - \frac{1}{3} tr(f)[\mathbf{I}] \quad (3.13)$$

$$tr(f) = 2 \frac{\partial \psi_I}{\partial I_1} (\lambda^2 + \frac{2}{\lambda}) + \frac{\partial \psi_{passive}}{\partial \lambda} \lambda \quad (3.14)$$

Figure 3.4: Schematic of soft composite stretching in a Transversely Isotropic hyperelastic model formulation

Considering fiber alignment along the uniaxial test direction, equation 3.12 reduces to equation 3.15. Substituting the strain energy function of from equation 3.11 into equation 3.15, equation 3.16 (where $\sigma_{Trans-Iso}$ is the principal Cauchy stress for a simple anisotropic composite model) is obtained which could be directly used for material characterization of uniaxial test data (stress versus stretch) [115, 139, 142].

$$\sigma_1 = 2 \frac{\partial \psi_I}{\partial I_1} \left(\lambda^2 - \frac{1}{\lambda} \right) + \frac{\partial \psi_{passive}}{\partial \lambda} \lambda \quad (3.15)$$

$$\sigma_{Trans-Iso} = 2 \left(\lambda^2 - \frac{1}{\lambda} \right) c_1 c_2 e^{c_1 (I_1 - 3)} + 2 \lambda (\lambda - 1) c_3 c_4 e^{c_3 (\lambda - 1)^2} \quad (3.16)$$

3.3.2 Curve Fit Results

The simple transversely isotropic model was used to curve fit the results from tensile testing of normal and prolapsed vaginal tissues discussed in Chapter 2 (Section 2.5) as shown in Figure 3.5. The results (values of parameters c_1 , c_2 , c_3 and c_4 are presented in Table 3.3)

Figure 3.5: Stress versus stretch plots of 20 arbitrary four-part mix ratios tested for development of vaginal tissue surrogates, compared with literature values [6]

Table 3.3: Transversely Isotropic Model curve fit parameters estimated for vaginal tissues tested in literature and 20 experimental tests

Vaginal Tissue Tested in Literature [6]	Trans-Iso Hyperelastic model coefficients				Experimental Tests	Trans-Iso Hyperelastic model coefficients			
	c ₁	c ₂	c ₃	c ₄		c ₁	c ₂	c ₃	c ₄
NPOP 1	14.2	0.167	4.31	0.161	Test 1	9.77	0.103	2.25	0.162
NPOP 2	12.5	0.178	3.74	0.182	Test 2	6.8	0.171	1.64	0.137
NPOP 3	7.9	0.156	1.89	0.151	Test 3	4.5	0.194	0.94	0.189
NPOP 4	2.1	0.412	0.87	0.427	Test 4	5.8	0.214	1.28	0.236
NPOP 5	9.5	0.152	2.15	0.155	Test 5	5.4	0.183	1.19	0.245
POP 1	14.1	0.227	4.48	0.219	Test 6	11.7	0.148	3.42	0.148
POP 2	2.4	0.254	0.93	0.314	Test 7	3.2	0.177	0.83	0.247
POP 3	0.8	0.417	0.46	0.435	Test 8	3.9	0.185	0.79	0.165
POP 4	0.7	0.374	0.39	0.337	Test 9	2.4	0.225	0.73	0.382
POP 5	5.7	0.193	1.23	0.218	Test 10	2.2	0.215	0.75	0.374
POP 6	9.8	0.252	2.48	0.266	Test 11	8.2	0.275	2.12	0.246
POP 7	8.5	0.258	2.19	0.259	Test 12	9.4	0.3	1.95	0.138
POP 8	11.5	0.181	3.24	0.129	Test 13	12.1	0.218	3.62	0.155
POP 9	5.4	0.193	1.16	0.210	Test 14	8.6	0.271	2.36	0.273
					Test 15	10.2	0.127	2.69	0.264
					Test 16	1.2	0.363	0.48	0.513
					Test 17	0.9	0.294	0.44	0.475
					Test 18	0.9	0.378	0.53	0.511
					Test 19	9.9	0.173	2.66	0.173
					Test 20	0.55	0.3	0.51	0.386

The average R^2 correlation index was calculated for the simple transversely isotropic model to be approximately 0.965, which is close to the isotropic material model prediction accuracy discussed in the previous section.

3.4 Anisotropic Soft Composite Hyperelastic Model

3.4.1 Numerical Model

To include the anisotropic effect of fiber inclusions in a matrix (composite model) with all fibers organized initially in the direction of vector $\mathbf{a}_0$, the energy function takes the form $\psi = \psi(\mathbf{C}, \mathbf{a}_0)$, where $\mathbf{C}$ is the Cauchy-Green deformation tensor introduced in section 3.2. To use the invariant approach for modeling transverse isotropy, two additional invariants related to $\mathbf{a}_0$, are defined as $I_4 = \mathbf{a}_0 \cdot \mathbf{C} \cdot \mathbf{a}_0 = \lambda_F^2$, $I_5 = \mathbf{a}_0 \cdot \mathbf{C}^2 \cdot \mathbf{a}_0$ where λ_F is the fiber stretch [134-138]. The strain energy function is rewritten as $\psi(\mathbf{C}, \mathbf{a}_0) = \psi(I_1, I_2, I_3, I_4, I_5)$. To simplify computations, both the matrix and the fibers are assumed to be incompressible materials. As the stiffness of the matrix and fibers are different, so deformation will be non-uniform in matrix and fibers. We use deformation tensor $\mathbf{C}_m$ in matrix to define the invariants in strain energy function of the matrix given by $\psi^M = C_{10}^m(I_1^m - 3)$ where $I_1^m = \text{tr}(\mathbf{C}_m)$ and the material model is neo-Hookean type [134-138]. C_{10}^m is related to shear modulus of the matrix material. The strain energy stored in the fibers is modeled as a function of I_4 , which is based on the assumption that the strain energy stored in the fibers depends mainly on the fiber elongation, where $\lambda_F = \sqrt{I_4}$ is the actual fiber stretch. To account for nonlinear dependence of strain energy on fiber stretch, and also to account for the three-dimensional aspect of the fiber, the strain energy stored in fibers is written as $\psi^F = C_{10}^m f(I_4)(I_1^f - 3)$ where $I_1^f = \text{tr}(\mathbf{C}_f)$ and the material model is neo-Hookean type, $\mathbf{C}_f$ is the deformation tensor of fibers and $C_{10}^m f(I_4)$ is related to stretch-dependent shear modulus of the fiber [134-138].

Figure 3.6: Schematic of soft composite stretching in the novel anisotropic hyperelastic model formulation

Considering initial fiber direction $\mathbf{a}_0$ along x_1 direction of rectangular Cartesian coordinate system, ie. $\mathbf{a}_0 = \mathbf{e}_1 = [1 \ 0 \ 0]^T$. Assuming second arbitrary perpendicular axis $\mathbf{e}_2$ such that $\mathbf{e}_1 \cdot \mathbf{e}_2 = 0$. Third axis $\mathbf{e}_3 = \mathbf{e}_1 \otimes \mathbf{e}_2 = 0$. With a deformation $\mathbf{F}$, the deformed fiber direction $\mathbf{F}\mathbf{a}_0$ is rotated back to original fiber direction $\mathbf{a}_0 = \mathbf{e}_1$. Let the rotation tensors for this be $\mathbf{R}_1$ which is independent of choice of $\mathbf{e}_2$, and $\mathbf{R}_2$ which depends on the $\mathbf{e}_2$ axis. Using $\mathbf{e}_2$ as the rotation axis, $\mathbf{R}_1\mathbf{F}\mathbf{e}_2$ is rotated back to $\mathbf{e}_1$ - $\mathbf{e}_2$ plane. The new deformation gradient tensor $\mathbf{F}^*$ is written as $\mathbf{F}^* = \mathbf{R}_2\mathbf{R}_1\mathbf{F}$. As $\mathbf{R}_1$ and $\mathbf{R}_2$ are rigid body rotations, $(\mathbf{F}^*)^T \mathbf{F}^*$ is the same as $\mathbf{F}^T \mathbf{F}$. $\mathbf{F}^*$ is used as starting point of the following multiplicative decomposition of deformation gradient [134-138].

From definition of $\mathbf{F}^*$ in the current deformation considered in Figure 3.6, $F_{21}^* = F_{31}^* = F_{32}^* = 0$ and $F_{11}^* = |\mathbf{F}\mathbf{a}_0| = \lambda_F$. $\mathbf{F}^*$ in $\mathbf{e}_1, \mathbf{e}_2, \mathbf{e}_3$ coordinate system is given by equation 3.17 [134-138].

$$\mathbf{F}^* = \begin{bmatrix} \lambda_F & F_{12}^* & F_{13}^* \\ 0 & F_{22}^* & F_{23}^* \\ 0 & 0 & F_{33}^* \end{bmatrix} \quad (3.17)$$

The deformation gradient $\mathbf{F}^*$ is multiplicatively decomposed into uniaxial deformation gradient $\mathbf{F}_f^*$ in the fiber direction and subsequent shear deformation gradient $\mathbf{F}_s^*$ such that $\mathbf{F}^* = \mathbf{F}_s^* \mathbf{F}_f^*$. $\mathbf{F}_f^*$ and $\mathbf{F}_s^*$ are given by equation 3.18 [134-138].

$$\mathbf{F}_f^* = \text{diag} \left[\lambda_F, \lambda_F^{-\frac{1}{2}}, \lambda_F^{-\frac{1}{2}} \right], \mathbf{F}_s^* = \mathbf{F}^* (\mathbf{F}_f^*)^{-1} = \begin{bmatrix} 1 & F_{12}^* \lambda_F^{\frac{1}{2}} & F_{13}^* \lambda_F^{\frac{1}{2}} \\ 0 & F_{22}^* \lambda_F^{\frac{1}{2}} & F_{23}^* \lambda_F^{\frac{1}{2}} \\ 0 & 0 & F_{33}^* \lambda_F^{\frac{1}{2}} \end{bmatrix} \quad (3.18)$$

By suitable choice of $\mathbf{e}_2$ axis, $F_{22}^* \lambda_F^{\frac{1}{2}} = 1$. F_{12}^* and F_{13}^* are along fiber shears, and F_{23}^* is termed as transverse shear. Shear deformations are related to invariants of $\mathbf{C}$ given by equation 3.19 [134-138].

$$\left(F_{12}^*\right)^2 + \left(F_{13}^*\right)^2 = \frac{I_5 - I_4^2}{I_4}, \left(F_{23}^*\right)^2 = I_1 - \frac{I_5 + 2\sqrt{I_4}}{I_4} \quad (3.19)$$

3.4.1.1 Effect of Fiber and Matrix Contributions

Soft tissues have been studied extensively in literature and have been found to exhibit a wide range of stress-strain behavior due to differences in collagen fiber content and fiber distribution [10, 115, 135]. The highest collagen fiber content have been observed in connective tissues making them significantly stronger than other tissues [143]. Additionally, due to diseases such as Pelvic Organ Prolapse (POP), soft (pelvic) tissue changes have been attributed to collagen fiber variations [144]. To model the effect of individual fiber and matrix contribution on a soft composite material property, the matrix volume fraction (MVF) ν_m and fiber volume

fraction (FVF) v_f terms were introduced. The strain energy stored in the whole composite during uniaxial deformation $\mathbf{F}_f^*$ is given by equation 3.20 [134-138], where

$$I_1(\mathbf{F}_f^*) = \lambda_F^2 + \frac{2}{\lambda_F} = I_4 + 2I_4^{-\frac{1}{2}} \text{ is the first invariant of } \mathbf{C}_f^* = (\mathbf{F}_f^*)^T \mathbf{F}_f^*.$$

$$\psi_f = \psi_f^M + \psi_f^F = v_m C_{10}^m (I_1(F_f^*) - 3) + v_f C_{10}^m f(I_4) (I_1(F_f^*) - 3) \quad (3.20)$$

On application of shear deformation $\mathbf{F}_s^*$, fiber stretch and stiffness remains constant. In this step, the composite is treated as neo-Hookean matrix embedded with neo-Hookean fibers where $f(I_4)$ is ratio of the fiber and matrix stiffnesses. The quantity of shear deformation is computed by adding the terms as shown in equation 3.21, where $I_1(\mathbf{F}_f^*) = I_4 + 2I_4^{-\frac{1}{2}}$ [134-138].

$$(F_{12}^*)^2 + (F_{13}^*)^2 + (F_{23}^*)^2 = \frac{I_5 - I_4}{I_4} + I_1 - \frac{I_5 + 2\sqrt{I_4}}{I_4} = I_1 - I_1(\mathbf{F}_f^*) \quad (3.21)$$

The energy stored during deformation $\mathbf{F}_s^*$ of the neo-Hookean composite is given by equation 3.22, where c_3 is the effective neo-Hookean modulus, and $I_1 - I_1(\mathbf{F}_f^*)$ is the portion of I_1 remaining after deformation $\mathbf{F}_s^*$ [134-138].

$$\psi_s = c_3 [I_1 - I_1(\mathbf{F}_f^*)] \quad (3.22)$$

Now strain energy function for the anisotropic composite model is sum of the strain energies of the two steps (equations 3.20 and 3.22), which is given by equation 3.23 [134-138]. In equation 3.23, C_{10}^m and $C_{10}^m f(I_4)$ are substituted with constants c_1 and c_2 respectively.

$$\psi = \psi_f + \psi_s = v_f c_2 [I_1(\mathbf{F}_f^*) - 3] + v_m c_1 [I_1(\mathbf{F}_f^*) - 3] + c_3 [I_1 - I_1(\mathbf{F}_f^*)] \quad (3.23)$$

For Humphrey model fibers and matrix definitions, the modified strain energy functions and the net strain energy functions are given by equations 3.24 and 3.25 [115].

$$\psi^M = c_1 \left[e^{c_2(I_1^m - 3)} - 1 \right], \psi^F = c_3 \left[e^{c_4(I_1^f - 3)} - 1 \right] \quad (3.24)$$

$$\psi = v_m c_1 \left[e^{c_2(I_1(\mathbf{F}_f^*) - 3)} - 1 \right] + v_f c_3 \left[e^{c_4(I_1(\mathbf{F}_f^*) - 3)} - 1 \right] + c_5 \left[I_1 - I_1(\mathbf{F}_f^*) \right] \quad (3.25)$$

In equations 3.23 and 3.25, the term $[I_1 - I_1(\mathbf{F}_f^*)]$ goes to zero with $I_1(\mathbf{F}_f^*) = I_1$ as λ_f (the stretch in the direction of the fiber) in case of a uniaxial tensile test coincides with the applied stretch λ [115, 134-138] for a fiber direction along the direction of stretch. Also, substituting $I_1(\mathbf{F}_f^*) = \lambda^2 + \frac{2}{\lambda}$, equations 3.23 and 3.25 can be rewritten as equations 3.26 and 3.27 respectively.

$$\psi_{Neo-Hookean/Modified} = (v_m c_1 + v_f c_2) \left(\lambda^2 + \frac{2}{\lambda} - 3 \right) \quad (3.26)$$

$$\psi_{Humphrey/Modified} = v_m c_1 \left[e^{c_2(\lambda^2 + \frac{2}{\lambda} - 3)} - 1 \right] + v_f c_3 \left[e^{c_4(\lambda^2 + \frac{2}{\lambda} - 3)} - 1 \right] \quad (3.27)$$

The principal Cauchy stress for a given hyperelastic strain energy function was found using equation 3.28, where $\sigma_2 = \sigma_3 = 0$ are the boundary conditions for the uniaxial tension experiment [115, 134-138]. Here $\lambda_1 = \lambda$ and $\lambda_3 = 0$.

$$\sigma_1 = \lambda_1 \frac{\partial \psi}{\partial \lambda_1} - \lambda_3 \frac{\partial \psi}{\partial \lambda_3}, \sigma_2 = \sigma_3 = 0 \quad (3.28)$$

Substituting the strain energy functions from equations 3.26 and 3.27 into equation 3.28, the stress versus stretch equations are given by equations 3.29 and 3.30.

$$\sigma_{Neo-Hookean/Modified} = 2(v_m c_1 + v_f c_2) \left(\lambda - \frac{1}{\lambda^2} \right) \quad (3.29)$$

$$\sigma_{Humphrey/Modified} = 2v_m c_1 c_2 \left(\lambda - \frac{1}{\lambda^2} \right) \left[e^{c_2(\lambda^2 + \frac{2}{\lambda} - 3)} \right] + 2v_f c_3 c_4 \left(\lambda - \frac{1}{\lambda^2} \right) \left[e^{c_4(\lambda^2 + \frac{2}{\lambda} - 3)} \right] \quad (3.30)$$

The material characterization study is conducted using equations 3.29 and 3.30 by substituting the fiber contribution (v_f) and matrix contribution (v_m) in the stress-stretch equations and estimating the values of the constants c 's.

3.4.1.2 Effect of Fiber Orientation

To account for single layer fiber orientation effect in the soft composites, $\lambda_F = \lambda \cos \theta$ substitution is conducted in equations 3.29 and 3.30, so that

$$I_1(\mathbf{F}_f^*) = \lambda_F^2 + \frac{2}{\lambda_F} = \lambda^2 \cos^2 \theta + \frac{2}{\lambda \cos \theta}, \quad [I_1 - I_1(\mathbf{F}_f^*)] = \left[\lambda^2 (\sin^2 \theta) + \frac{2}{\lambda} (1 - \sec \theta) \right] \quad \text{and}$$

$0 \leq \theta < 90^\circ$. The modified stress-strain relationships corresponding to equations 3.29 and 3.30 are equations 3.31 and 3.32 respectively.

$$\begin{aligned} \sigma_{Neo-Hookean/Modified2} &= 2(v_m c_1 + v_f c_2) \left(\lambda \cos \theta - \frac{1}{\lambda^2 \cos^2 \theta} \right) \\ &+ 2c_3 \left[\lambda (\sin^2 \theta) - \frac{1}{\lambda^2} (1 - \sec \theta) \right] \end{aligned} \quad (3.31)$$

$$\begin{aligned} \sigma_{Humphrey/Modified2} &= 2v_m c_1 c_2 \left(\lambda \cos \theta - \frac{1}{\lambda^2 \cos^2 \theta} \right) \left[e^{c_2(\lambda^2 \cos^2 \theta + \frac{2}{\lambda \cos \theta} - 3)} \right] \\ &+ 2v_f c_3 c_4 \left(\lambda \cos \theta - \frac{1}{\lambda^2 \cos^2 \theta} \right) \left[e^{c_4(\lambda^2 \cos^2 \theta + \frac{2}{\lambda \cos \theta} - 3)} \right] \\ &+ 2c_5 \left[\lambda (\sin^2 \theta) - \frac{1}{\lambda^2} (1 - \sec \theta) \right] \end{aligned} \quad (3.32)$$

3.4.1.3 Effect of Multiple Fiber Layers at Arbitrary Orientations

Figure 3.7: Schematic for novel anisotropic material formulation for soft composites with a single matrix and multiple fiber families

For a soft composite with a single matrix and multiple fiber families embedded within it, the mechanical property depends only on the cumulative effect of fiber directions [134-138]. For a composite with n fiber families where the fibers are oriented at angles $\theta_1, \theta_2, \theta_3, \dots, \theta_i \dots \theta_n$ (where $0 \leq \theta_i < 90^\circ$ and $n > 1$), volume fractions are v_m for the matrix and $v_{f1}, v_{f2}, v_{f3}, \dots, v_{fi} \dots v_{fn}$ for each fiber family respectively, the homogenized strain energy function can be written as equation 3.33 [134-138].

$$\psi_{Composite} = \sum_{i=1}^n \psi^i \quad (3.33)$$

The modified generic stress-strain relationships based on equations 3.31, 3.32 and 3.33 for a soft tissue composite with multiple fiber families are given by equations 3.34 and 3.35.

$$\sigma_{Neo-Hookean/Modified3} = \sum \left\{ \begin{aligned} &2((1-v_f)c_1 + v_f c_2) \left(\lambda \cos \theta_i - \frac{1}{\lambda^2 \cos^2 \theta_i} \right) \\ &+ 2c_3 \left[\lambda (\sin^2 \theta_i) - \frac{1}{\lambda^2} (1 - \sec \theta_i) \right] \end{aligned} \right\}, 1 \leq i \quad (3.34)$$

$$\sigma_{Humphrey/Modified3} = \sum \left\{ \begin{aligned} &2(1-v_{fi})c_1c_2\left(\lambda \cos \theta_i - \frac{1}{\lambda^2 \cos^2 \theta_i}\right) \left[e^{c_2(\lambda^2 \cos^2 \theta_i + \frac{2}{\lambda \cos \theta_i} - 3)} \right] \\ &+ 2v_{fi}c_3c_4\left(\lambda \cos \theta_i - \frac{1}{\lambda^2 \cos^2 \theta_i}\right) \left[e^{c_4(\lambda^2 \cos^2 \theta_i + \frac{2}{\lambda \cos \theta_i} - 3)} \right] \\ &+ 2c_5 \left[\lambda(\sin^2 \theta_i) - \frac{1}{\lambda^2}(1 - \sec \theta_i) \right] \end{aligned} \right\}, 1 \leq i \leq n \quad (3.35)$$

There are several limitations of the novel anisotropic soft composite hyperelastic model developed. First, a fiber family was assumed to not transition or interact with the adjacent fiber families. In a natural soft tissue composite system, fibers run across the layers, the effect of which will be considered in future modeling studies. Second, within a layer, the fiber orientations also change from one location to another in a natural tissue. In the current model, this location-specific change in the orientation of the fiber families was also not considered. Histology and microscopic imaging needs to be conducted to study such fiber orientation changes in different tissue systems. Third, the mechanical effect of the presence of blood vessels, capillaries and fat within tissue layers was neglected. Inclusion of the fat layer specifically in future modeling studies may lead to better tissue simulation in the study of the effect of impact loads. Fourth, effects of strain rates on the response of soft composite layers were also not modeled. Fifth, the novel computational model was developed mainly for uniaxial mechanical test conditions. In reality, soft tissue composite loads are biaxial and multi-axial, the effect of which will be considered as a part of future work.

3.4.2 Curve Fit Results

For the current soft composites with single fiber layer, the material characterization was carried out using equations 3.29 and 3.30 by substituting the fiber contribution (v_f) and matrix

contribution (V_m), and single fiber angle in the stress-stretch equations and estimating the values of the constants c 's.

True stress versus true stretch data obtained from the mechanical tests of soft composites with fiber angle $\theta = 0^\circ$ and varying fiber volume fractions (v_f) were fit into equations 3.29 and 3.30 and the value of the material constants were determined. Also, to incorporate the fiber orientation effect (Figure 3.9), the equations 3.31 and 3.32 was used to estimate the material constants for $\theta = 0^\circ, \pm 45^\circ$ and varying fiber volume fractions (v_f). To evaluate the accuracy of the hyperelastic model chosen in predicting the soft composite material behavior, an R^2 correlation value calculation was performed (where R^2 can have a value from 0 through 1, 1 representing the best fit and 0 representing worst fit). Only the constants generating curve fits with $0.96 < R^2 < 1$ were reported.

Figure 3.8: Effect of FVF variations on soft composite material properties

Figure 3.9: Effect of fiber orientation for one, two and three fiber configurations on the soft composite material property

The stress versus stretch results for the soft composite compositions with varying FVF's (Figure 3.8) were substituted to the newly developed hyperelastic constitutive models, and the curve fit constants were estimated with R^2 values over 0.97 (see Table 3.4). For FVF=1 (only fiber case) and FVF=0 (only matrix case), some curve fit constants are missing due to a part of the corresponding constitutive relation going to zero.

Table 3.4: Hyperelastic curve fit coefficients for the soft composite materials with varying FVF's presented in Figure 3.8

Hyperelastic Curve Fit Coefficients						
Fiber Volume Fraction (FVF)	Neo-Hookean (Modified)		Humphrey (Modified)			
	c_1	c_2	c_1	c_2	c_3	c_4
1.00	-	4.20	-	-	2.30	0.63
0.00	0.12	-	0.21	0.23	-	-
0.17	0.95	1.23	0.53	0.41	0.40	0.61
0.35	1.80	2.18	1.15	0.33	1.20	0.63
0.52	2.65	2.80	0.72	0.44	1.22	0.64
0.61	3.24	3.56	0.73	0.42	1.97	0.65
0.78	3.96	4.15	0.81	0.45	2.31	0.65

For fiber orientations of 0° and $\pm 45^\circ$, the material behavior of soft composites with one, two and three fibers (presented in Figure 3.9) are characterized using modified neo-Hookean and Humphrey material models (see Table 3.5). Table 3.5 also captures the FVF's corresponding to each of the specimen configurations mentioned. The soft composite variants with specifically $\pm 90^\circ$ were avoided as mentioned previously in the material modeling section due to multiple terms in the constitutive model going to infinity. The soft composite with a 90° fiber angle in the current uniaxial test framework is assumed to behave exactly like a composite with FVF=0. However, it should be mentioned that in reality, such a consideration is not true, as loadings are not uniaxial but multiaxial in nature, which will be subject of future studies.

Table 3.5: Hyperelastic curve fit coefficients for the soft composite materials with different number of fibers and orientations presented in Figure 3.9

Hyperelastic Curve Fit Coefficients									
Fiber (Orientation)	Corresponding FVF	Neo-Hookean (Modified)			Humphrey (Modified)				
		c_1	c_2	c_3	c_1	c_2	c_3	c_4	c_5
One Fiber (0°)	0.21	0.05	3.23	-	0.31	0.55	0.75	0.75	-
Two Fiber (0°)	0.38	0.01	2.95	-	0.45	0.65	0.85	0.65	-
Three Fiber (0°)	0.56	0.01	2.37	-	0.55	0.75	1.14	0.61	-
One Fiber ($\pm 45^\circ$)	0.16	-1.16	9.25	0.95	-1.15	4.85	4.87	5.13	1.3
Two Fiber ($\pm 45^\circ$)	0.27	-2.54	9.41	1.33	-1.05	6.14	2.81	6.18	1.3
Three Fiber ($\pm 45^\circ$)	0.41	-5.88	10.63	1.8	-2.13	5.59	2.52	5.84	2.6

CHAPTER 4

SOFT COMPOSITES DAMAGE AND REPAIR³

4.1 Summary

The study of soft composite damage and repair is crucial for the development of robust soft composites for various applications in engineering and medicine. In a natural soft tissue composite system, damage occurs in form of a wound or tear. Soft tissue repair is typically conducted using surgical sutures. Understanding the macro and micro scale mechanics of wound closure and suture will provide valuable insights into tissue failure prediction and allow to devise preventive measures. Such studies would be valuable information for surgical planning.

In this chapter, a high fidelity multi-layer 3D skin tissue composite model is introduced and the mechanics of wound closure with sutures was modeled to understand soft composite damage and repair. Also, a full scale experimental model of soft composite damage and repair is presented which was developed using a biofidelic synthetic skin composite material introduced in chapter 2. Additionally, these two studies are followed with development of novel techniques to understand local strains at the wound using Digital Image Correlation (DIC) techniques. Varying wound geometries and sizes were considered to understand local and global mechanics of soft composite damage and repair.

³ Chanda, Arnab, and Vinu Unnikrishnan. "A realistic 3D computational model of the closure of skin wound with interrupted sutures." *Journal of Mechanics in Medicine and Biology* 17.01 (2017): 1750025. Chanda, Arnab, et al. "Experimental study on tissue phantoms to understand the effect of injury and suturing on human skin mechanical properties." *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine* 231.1 (2017): 80-91.

4.2 Computational Model of Soft Composite Damage and Repair

To date, soft composite damage in tissues have been mainly studied using 2D computational models of wound closure. So far, the effect of multiple tissue layers, natural biaxial tension, and varying wound geometries and sizes have not been studied. In this work, a realistic 3D computational model of a wound with a varying cross-section within a skin block with the two skin layers (epidermis and dermis) was developed. In the presence of skin pre-stress effects, interrupted sutures were modeled, and using a novel suture pulling technique, force requirements for each suture were estimated numerically. The following sections will discuss the geometrical and finite element (FE) modeling techniques used in the study, the loads and boundary conditions and results from the analyses.

4.2.1 Materials and Methods

4.2.1.1 Geometrical Modeling

The geometrical model of the skin wound-suture was developed in two steps. The first step involved the modeling of the skin layers and the wound geometry, which would be computationally viable to work with the interrupted sutures, modeled in step 2. Another reason behind the development of the geometrical models in two steps was to perform a mesh convergence study after the first step to ensure that a numerically efficient mesh is adopted for the further study to compute the suture forces accurately.

The skin was modeled as a 30 mm X 30 mm block with two layers namely the 0.1 mm thick epidermis and 3 mm thick dermis (shown in Figure 4.1). The epidermal and dermal thicknesses were based on the experimental findings in literature [15]. The wound was modeled as a symmetric diamond shape cavity with length 20 mm, width 2 mm at the top surface (or the top of epidermal layer) and at the bottom surface of length 10 mm, 1 mm width (at a 1.5 mm depth within the dermal layer), as shown in Figure 3. Compared to the dimension of the skin

section considered in our work, the 20 mm X 2 mm wound size was considered reasonable (and was also based on literature[145, 146]). It should be mentioned here that our current computational model is not restricted to any specific wound size, and any wound size could be modeled, based on which the estimated suture forces will differ accordingly.

Figure 4.1: Skin and wound geometries adopted for our computational study

The diamond wound shape was chosen specifically; as finite element modeling becomes very challenging when the lateral surfaces of an elliptical or circular shaped wound intersect the curved suture wire surface [147]. A finer mesh would be required in such complex cases (thus requiring higher computation time), which may subsequently lead to mesh failure under large displacements [147]. Also, the diamond shape has been used previously in literature to characterize wound geometry [148] and is the closest derivative of the widely accepted elliptical wound geometry. Furthermore, to study the effect of the diamond shaped wound on the results from our analyses, compared to a realistic elliptical wound, simple two layer skin models with an elliptical and diamond shape wounds were modeled. Both these models were subjected to skin pre-stresses (0.25 kPa along X-direction, and 10-30 kPa along the Y-direction) and the average differences in the generated maximum stresses and displacements were estimated to vary by 2.8% and 4.1 % respectively. Due to only small differences observed in stresses and displacements between the diamond and elliptical wound shapes, further analysis with diamond shaped wound only was considered in this work.

A varying cross-section along the depth of the wound was adopted to model the wound realistically [149-151]. It should be mentioned that a wound depth of 1.5 mm (or halfway down the dermis) used for the study may vary widely and could also go beyond 3 mm (all through the dermis into the subcutaneous layer), in case of which a subcuticular suture is preferred. Such advanced wound-suture models with three layers of skin would be considered in future studies.

An interrupted suture refers to a set of sutures placed independent to each other at certain intervals for closing a wound (shown in Figure 4.2). The first suture is typically placed at the end of the long edge of the wound (Figure 4.2) and the subsequent sutures are placed alternately on either sides of the wound at an interval, which is close to the suture bite distance (or the distance of the point where the suture needle enters the epidermal skin, from the wound edge, shown in Figure 4.2). The order of suture placements in an interrupted suturing technique are clearly shown with numbers in Figure 4.2.

Figure 4.2: Suture placement order in interrupted suturing technique

Commonly used monofilament synthetic type sutures (Maxon or PDS) [152] with 0.1 mm wire cross-section was chosen for our study. A rectangular cross-section was chosen over a circular cross-section for modeling the sutures to simplify the meshing (and reduce computation time), based on previous experience with modeling fibers [147]. Usually with a rectangular cross-section, with advanced mesh sizing control (element edge divisions set to 1), a

limited number of mesh elements could be generated using a hex-mapped meshing technique, unlike a circular cross-section which could be only discretized using tet-free mesh producing a larger number of elements[147].

Applying realistic loads and boundary conditions on a suture wire could be very challenging due to mainly three reasons: 1) A wire doesn't displace the way we want it to in an FE environment compared to real time surgeries. The multi-directional movements, rotations and pulls applied by a surgeon's hand to a suture wire is very difficult to recreate using an FE framework. Also, trying to recreate such motions may not be worth the time and effort, as suturing technique employed by one surgeon may widely vary from another surgeon, 2) Difficulty in defining friction contact between the suture wire and the skin, 3) As often seen in computational models, the epidermal flaps of a wound are pulled together at different points of the wound to estimate the suturing force requirement [145], which is a very idealized and oversimplified concept. The actual force required to be applied to a suture wire to close a wound depends on the pull of the suture wire on the epidermis as well as the dermis[152].

A novel suture pulling technique has been employed in the current work to estimate the suturing force. Seven sutures were modeled using splines and with subsequent extrusion of a 0.1 mm X 0.1 mm rectangular surface along the splines, in seven steps as illustrated in Figure 4.2. All the 7 sutures in our computational model are shown in Figure 4.3. The varying coloured zones in each of the suture wires in Figure 4.3 is because every wire volume was subdivided into multiple volumes to simplify meshing [9]. Each suture wire was completely embedded into the skin layers (and a frictionless surface to surface contact was defined in between the suture and the skin), and only a part was allowed to come out of the epidermal layer mainly for the sake of visualization. All the equally spaced suture wires were placed at a bite distance of 0.3 mm from the wound long edge. The usual practice of having the distance between the sutures

close to the bite distance [152] was not considered initially in our current model, as it was not thought to be very needful from the computational perspective. This aspect has been addressed later, where a mathematical formulation was established to account for extra sutures in between the seven sutures modeled in our work.

Figure 4.3: Suture wires embedded within the skin layers in the computational model

4.2.1.2 Finite Element Modeling

Effective finite element (FE) modeling involves the discretization of the geometries, generation of a computationally viable mesh, and assignment of appropriate loads and boundary conditions. In our current work, a significant amount of effort was put into the development of an optimized mesh for the skin layers and the suture wires, using a detailed mesh convergence study, presented in the following section.

To ensure the accuracy of results generated by our FE model in ANSYS software, a detailed mesh convergence study was conducted. Four meshes of the skin layers (without the suture wires meshed) were developed, namely the very coarse (12036 elements), coarse (18660 elements), fine (64558 elements) , and very fine (147674) mesh, as shown in Figure 4.4. At a constant pre-stress of 0.25 kPa along the long edge (X-direction) of the wound, the Y-direction pre-stress values were varied from 10-30 kPa to determine the maximum displacements in the FE model for each mesh type. Additionally, the sutures were meshed and their ends (on the epidermal side) were constrained (based on the applied boundary conditions explained in the

following sections) to study the effect of mesh convergence on the localized stresses at the sutures. These results are presented in Figures 4.5 and 4.6.

Figure 4.4: Four meshes of the skin layers namely the A) Very coarse (12036 elements), B) Coarse (18660 elements), C) Fine (64558 elements) , and D) Very fine (147674) mesh for mesh convergence study

From the detailed mesh convergence study presented in Figures 4.5 and 4.6, it was found that the maximum displacements and stresses at a certain pre-stress along the Y direction (along wound short edge) doesn't change much going from the fine to the very fine mesh. Thereby, the fine mesh was chosen for our further FE analysis on wound-suture.

Figure 4.5: Number of mesh elements versus maximum displacements in the FE model, at 10 kPa, 30 kPa, and 50 kPa pre-stresses along the Y-direction (wound short edge) for mesh convergence study

Figure 4.6: Number of mesh elements versus maximum von Mises stress in the FE model at sutures, at 10 kPa, 30 kPa, and 50 kPa pre-stresses along the Y-direction (wound short edge) for mesh convergence study

Meshing for our skin wound-suture computational model was performed in three phases. First, the epidermis layer being the thinnest layer, was meshed followed by the dermis. For the suture wires, advanced mesh controls were used to force mapped meshing in order to generate a limited number of elements (as shown in Figure 4.7). A total of 64768 higher order 3D 20-node Solid 186 type quadratic tetrahedral elements were generated due to meshing. This robust element type is used widely in the industry and supports large deflection, creep, large strains, hyperelasticity, plasticity and stress stiffening [153]. The individual and integrated meshes of the skin layers and the sutures are shown in Figure 4.7.

Figure 4.7: The different phases of mesh generation are shown on the left and the integrated mesh of our skin wound-suture computational model is shown on the right

The epidermis and the dermis layers, and the suture wires in the computational model were perfectly bonded (using flexible and always bonded type contact pairs) all through the analysis. The bottom surface of the dermis was constrained in all degrees of freedom to depict its strong attachment with the subcutaneous connective tissues [15]. Skin pre-stress effects due to the natural tension of the skin was considered in both the X direction (along the wound short edge) and Y direction (along the wound long edge). For the further wound-suture study presented in the upcoming sections, a X pre-stress of 25 kPa and Y pre-stress of 0.25 kPa was applied throughout, to both the epidermis and dermis. Due to limited availability of experimental data on skin pre-stress, pre-stress values used in previous computational models in the literature[145, 146] were readily used. In future studies, more complex pre-stress conditions (specific to age, ethnicity etc.) would be incorporated into the computational modeling framework based on in-vivo experiments on human skin from diverse groups of human subjects. The loads and constraints specific to the suture are discussed in the following section.

Simulating suturing process in a 3D FE model is very challenging. This may be one of the major reasons why mostly simplified 2D computational models have been used in the past to estimate suture forces. In this work, a novel suture pulling technique was implemented which is more realistic than the typical 2D skin flap pulling technique employed in most computational analyses to date, for quantifying the skin suture forces.

Figure 4.8: Force and displacements in actual case of suture and in our computational model, for estimating suture forces

A single interrupted suture typically involves a suture wire running from the bite point (where the needle enters the epidermal skin) on one end of the wound to the bite point (where the needle exits the epidermal skin) through the dermis and the open space in wound, back through the dermis and out of the epidermis on the other side (in case of an actual suture as illustrated in Figure 4.8), forming a wire loop. While suturing, a pull force (marked in yellow color in Figure 4.8) is usually applied to the wire ends to force a shrinking of the wire loop size causing a consequent displacement (marked in white color in Figure 9) of the wound flaps towards each other. Subsequently, a knot is tied to retain the shrunk (strained) loop size and thus not allowing the skin flaps to retract back to their original positions. So the overall action is a suture force and the effect is the coming together of the wound flaps to be flushed with each other.

In this computational model, the applied action is the forced coming together or flushing (displacements) of the wound flaps, and the effect is a force on the suture, which is just the opposite of the case in an actual suture (see Figure 4.8). Constraining the suture ends (at the bite locations) coming out of the epidermis, a displacement was applied to the wound flaps to bring them together (or have them flushed), and the resultant von Mises stresses generated at the suture wire ends (specifically in rectangular mapped mesh elements around the suture wire end) were estimated numerically. The average of the generated stresses (in rectangular elements) at a suture end (in MPa) was multiplied with the suture wire cross-sectional area of 0.1 mm X 0.1 mm to obtain the suture force.

4.2.2 Results and Discussion

4.2.2.1 Step-wise Interrupted Suture Placement for Skin Wound Closure

In an interrupted suturing process, each suture is placed in such a way that the wound's epidermal flaps are pulled all the way to touch each other to initiate epithelial healing [152].

Typically, the sutures are placed starting at the end of the wound long edge and then inward alternatively on either sides, finally ending at the center suture. This is done to ensure that the skin and the suture wire are under minimum tension in each step while suturing. With the same idea, seven sutures were placed in the skin wound-suture computational model using the novel suture pulling technique. The displacements applied to ensure effective suturing were calculated numerically for the diamond wound geometry, which are listed in Table 4.1. The results of the seven-step interrupted sutures are presented in Figure 4.9.

Table 4.1: Applied displacements for each suture in our computational model

Suture Number	Applied Displacement (mm)
1(Right End)	0.75
2 (Left End)	0.75
3 (Second from Right End)	1.25
4 (Second from Left End)	1.25
5 (Third from Right End)	2.75
6 (Third from Left End)	2.75
7 (Center)	3.5

It should be emphasized that while interpreting the suture results in Figure 4.9, it should be kept in mind that the dimension of the wound is very small (2 cm along the long edge and 2 mm along the short edge). The small cavities seen after the placement of the seven sutures would not be visible to the eye like it is shown in the zoomed-in image in Figure 4.9. Also, these small cavities could be filled completely if the rule of having the distance between the sutures close to the wound bite distance is followed. In the current computational analysis, the distance between the sutures chosen were approximately five times of the wound bite distance to save computational time and effort. However, in the following section a novel mathematical formulation was developed to estimate force requirements for sutures placed in between the seven sutures in our model, to ensure complete wound closure.

4.2.2.2 Step-Wise Interrupted Suture Force Estimation

The forces on the suture ends at each step of the seven-step interrupted suturing process were estimated using the novel suture pulling technique. Figure 4.10 presents the results of stress distribution in the particular new suture placed at every step of the seven-step interrupted suturing process. The stresses adjacent to the constraint on the free end of each of the sutures at every step were estimated using an FE algorithm to calculate the equivalent suture forces, which are listed in Table 4.2. A 3D bar plot is presented in Figure 4.11, showing the values of each suture force requirement in the presence of other 0-6 sutures, in each of the seven steps of suture placements. Also, an average standard deviation of ± 0.012 N was found in the force requirement for any suture, in presence of other sutures through the seven suture placement steps.

Figure 4.9: Results of seven step suture placement for skin wound closure

Table 4.2: Suture forces estimated for each suture in our computational

Suture Number	Suture Force (N)
1(Right End)	0.9103
2 (Left End)	0.9457
3 (Second from Right End)	2.0768
4 (Second from Left End)	1.8203
5 (Third from Right End)	3.6480
6 (Third from Left End)	3.8147
7 (Center)	3.6953

Figure 4.10: Stresses on new sutures placed at every step in the seven-step interrupted suturing process

The current computational modeling framework could be used to determine the suture forces, given a certain wound geometry, wound depth, skin material properties, skin pre-stress (based on the location of the wound), suture wire material and cross-sectional area. This information would be indispensable for planning automated suturing in robotic surgeries in the future.

Figure 4.11: Suture force versus the suture number for different steps of the suturing process simulated in the study

The applied displacements were plotted against the required suture forces (obtained from the simulations) and a polynomial curve was fitted to the data with a high correlation index (R^2 value) of 0.9947, as shown in Figure 4.12. This curve fit equation 45 could be used to determine the suture forces for placing more sutures in between the seven sutures in our current computational model. For example, if the rule of having the distance between consecutive sutures close to the wound bite distance is followed, four more sutures should be placed in between every two suture in our model. The forces (F_i) to be applied to each of those extra 24 sutures would lie on the plot in Figure 4.12, and could be estimated based on their locations from the wound center (which is equal to the displacement to be applied, D_i) using

equation 4.1. It should also be mentioned that this novel finding is not only limited to interrupted suturing, and can further be applied to any kind of automated skin suturing.

$$F_i = -0.5017(D_i)^2 + 3.1554(D_i) - 1.1774 \quad (4.1)$$

Figure 4.12: Applied displacement versus the required suture force estimation using curve fitting

4.3 Experimental Model of Soft Composite Damage and Repair

In the current work, a novel biofidelic human skin phantom was developed using a two-part silicone material. Different wound geometries were created on a set of test specimens and tested on a uniaxial tensile testing machine. Subsequently, continuous suturing was performed to close each of the wounds, and the specimens were tested again under uniaxial loading. The average biomechanical behavior of the human skin phantom in the presence of a wound and subsequent suture was characterized using hyperelastic constitutive material models. Also, the effect of varying wound size, quantity, location, with and without sutures were studied.

4.3.1 Materials and Methods

4.3.1.1 Manufacturing of human skin phantom

Based on previous work in literature in testing of human skin [2, 10, 154], two-part silicone material with a shore hardness of 30 A was procured from Smooth-On Inc., and mixed

in a 1:1 ratio by weight, using a high precision weighing balance (Adventurer Pro, Ohaus Inc., NJ, U.S.). The mixture was used to generate 20 test coupons with the size 50 mm X 10 mm X 3 mm. (Figure 4.13).

Figure 4.13: 20 skin phantom test specimens with wounds used in this study

Uniaxial mechanical tests were performed on each of the test coupons using a universal testing machine (from MTS Systems Corporation). A strain rate of 0.4 mm/s was employed for all the tests, to compare the generated stress-strain response with the literature [10]. Also based on the range of human skin pre-stress values reported in the literature [145], a 0-500 kPa stress range was chosen to test all the coupons.

The stress-strain results of the 20 coupons tested were found to be within the bounds of the human skin test data reported in literature [145]. The Results and discussion section presents these results in detail.

4.3.1.2 Wound creation and suturing

Wound geometries varying in shape, size, depth, and location on the coupon were created using a scalpel and regular scissors. Additionally, multiple wounds were created in 4 out of 20 coupons to study the effect of multiple wounds on human skin biomechanics. All wound geometries were captured under a regular lab microscope (Serial No. 29AX E250223

from Motic Inc.) at a magnification of 75. The wound dimensions were estimated precisely through multiple post-processing steps. The results are listed in the Results and Discussion section. Microscopic imaging was used to study wound morphology for possible size, shape, or placement effects on the biomechanical behavior of the human skin phantom.

A continuous suturing technique was employed in suturing of all the wounds similar to Figure 4.14. A 2-0 size Prolene polypropylene suture (from Ethicon Inc., procured from DCH medical center, Tuscaloosa, Alabama) and a size 13 sewing needle was chosen for the suturing. Figure 4.14 captures the image of the top and bottom surfaces of the 20 test coupons with suture.

Figure 4.14: Continuous suturing technique and a look at the final suture envelope

The distance between the consecutive suture loops were kept similar (estimated through crude eye observation), and thus the number and size of suture loops varied with the wound size and geometry among all the test coupons. It should also be mentioned that in two cases (coupon 1 and 17), the coupons were sutured even though they were completely torn apart during the uniaxial tests on wounded specimens. This was done to check whether the stress-strain profile would drastically vary in case of extreme wounds. The results of the uniaxial tests of both the wounded and sutured specimens are presented in the Results and Discussion section.

Figure 4.15: Test specimens after suture, viewed from the A) Top and B) Bottom

4.3.1.3 Uniaxial mechanical testing

Uniaxial tensile tests were conducted for all test specimens at a constant strain rate of 0.4 s⁻¹ selected based on studies of uniaxial tests on human skin [2, 10, 28, 29, 155]. For each of the tests, the load (Newtons) versus extension (mm) graphs were plotted and postprocessed to obtain stress versus stretch plots, which were used for further analyses. Figure 4.16 captures an ongoing uniaxial test on a coupon in presence of a wound and suture.

Figure 4.16: Uniaxial test on a tissue phantoms with wound and sutures

It should be mentioned here that silicones simulating skin tissues typically exhibit a high cut-out or breaking strengths in the range of 15-25 MPa [4, 154, 156], while other tissues such as pelvic tissues (Ultimate tensile strength of 1-6 MPa) [7, 9, 144, 157] and brain tissues (Ultimate tensile strength of 300-900 kPa) [1, 158, 159] may have lower cut-out strengths. Sutures on the

other hand have extremely high cut-out strengths in the range of 100-500 MPa [95]. These cut-out strengths were not investigated for the current experimental model to focus mainly on natural skin stresses (0-500 kPa) and the effect of wound and suturing in such realistic conditions.

4.3.2 Results and Discussion

4.3.2.1 Uniaxial mechanical tests to develop human skin phantom

Uniaxial mechanical tests were performed on 20 two-part silicone based human skin phantom specimens for a stress range of 0-500 kPa. For each specimen, two tests were performed and then an average value was considered for the analyses. Figure 4.17 presents the stress-strain results of the 20 tests, all of which lie within the upper and lower bounds of the human skin stress-strain values reported in the literature [10]. Also, in the figure, the human skin phantoms were compared with silicones, gels and polyurethanes traditionally used to mimic skin.

Figure 4.17: Stress-strain plots of uniaxial tests on 20 human skin phantom specimens, within the bounds of human skin mechanical properties [10], compared with silicones, gels and polyurethanes traditionally used to mimick skin

An average and standard deviation was estimated for the 20 stress-strain response plots of the human skin phantom developed. This mean stress-strain plot with the error bars (equal to the standard deviations) were used for further analyses and comparison studies.

4.3.2.2 Wound Characterization

One of the major goals in the current work was to understand the effect of wound size on the human skin mechanical properties. Single wounds were created on 16 out of the 20 human skin phantom specimens, two wounds were created on the 17th and 18th specimens, and three wounds on the 19th and 20th specimens. All the wounds were observed under a microscope (as discussed earlier in the Materials and methods section) and the wound dimensions were estimated, as shown in Figure 4.18 and presented in Table 4.3. Also, the wound orientations based on whether it was longer along the length of the specimen (axial, specimens 13-16) or along the width (transverse, Specimens 1-12 and 17-20) were recorded. Additionally, for a particular orientation (axial or transverse to the specimen), the wounds were classified based on their lengths recorded along the long edge (between end points, see the long line in Figure 4.18 pictures) as short ($L \leq 4$ mm) or long ($L > 4$ mm) wounds [156, 160, 161] (presented in Table 4.4). The wound position along the length of the test specimen, categorized as top, bottom or center, based on if it lied within the first, second or third $1/3^{\text{rd}}$ length respectively (see Table 4.5), was also considered for specimens 1-16. Additionally, letters A, B and C refer to the number of wounds in specimens 17 through 20, from left to right respectively. For the length of a wounds listed in Table 4.3, the maximum length was chosen between the wound end points. The only exception was specimen 13 (see Figure 4.18) which was measured in two steps as it had a significant bending compared to the other specimens. For the wound thickness estimation, the thickness was measured in multiple locations (shown with short lines in Figure 4.18 pictures) and the average value is reported in Table 4.3.

Figure 4.18: Wound geometry and dimensions estimated on 20 human skin phantom specimen microscopy images

Table 4.3: Wound dimensions for each test specimen

Test Sample No.	Wound Length, L (mm)	Average Wound Thickness, T (mm)
1	9	0.6
2	5	0.01
3	7	0.01
4	4.75	1
5	3.2	1
6	3	1.75
7	4.2	1.3
8	3.6	1
9	3.5	2
10	3.8	1.5
11	4.5	1.1
12	3.2	1.5

13	11	0.01
14	5.7	1.1
15	10	3.2
16	24	0.02
17 A	10	1
17 B	3.85	1.3
18 A	5.8	0.01
18 B	6	0.01
19 A	5.5	0.5
19 B	5	0.01
19 C	5	0.01
20 A	3.5	1.6
20 B	3	2
20 C	4	1.5

Table 4.4: Wound lengths L for specimens 1-20 grouped as long and short based on their length recorded along the long edge from Table 4.3

Wound Length (<i>Long/Short</i>)	Specimen Number
Long ($L > 4$)	1-4, , 7, 13-16, 17 A, 18 A and B, 19 A-C
Short ($L \leq 4$)	5, 6, 8-10, 12, 17 B, 20 A-C

Table 4.5: Wounds 1-16 grouped based on their occurrence along the length of the specimen, based on Table 4.3

Wound Location (<i>Top, Bottom or Center</i>)	Specimen Number
Top (<i>Within 1/3rd length from top</i>)	10-12 (3 Specimen)
Center (<i>Within 1/3rd – 2/3rd length from top</i>)	1-5, 13-16 (9 specimen)
Bottom (<i>Within 2/3rd length from top to bottom</i>)	6-9 (4 specimen)

4.3.2.3 Mechanical testing of human skin phantoms with wounds

The stress-strain response of the test specimens with wounds were found to be inferior to the original human skin phantom specimens with no wounds, as shown in Figure 4.19. This observation was intuitively expected as any wounded skin would be weaker and undergo more strain under the same applied stress, compared to unwounded skin.

Figure 4.19: Stress-strain plots of unwounded and wounded human skin phantom specimens

To understand the effect of wound length on skin mechanical properties, the average of the stress-strain values for all long and short wounds (categorised as per Table 4.4) were plotted, as shown in Figure 4.20 A. No significant change was observed besides the smaller stress-strain error bars for the test specimens with large wounds compared to the ones with small wounds.

The average mechanical behavior of the test specimens (see Table 4.5) with the wound located at the center, top and bottom parts were compared (Figure 4.20 B). The average stress-strain response for the test specimens with center wounds were found to be stiffer than the ones with wounds located on the top or bottom parts. The trends observed in these tests are low because of the very small stress range of 0-500 kPa (based on the in-vivo human skin pre-stress range [145]) used for the mechanical tests. However, the effects would intensify significantly as testing is performed in the stress ranges of 1-20 MPa [2, 10, 28, 29, 155] for in-vitro skin testing. This claim is based on our experiments performed at higher stress ranges.

Figure 4.20: Comparison of the average stress-strain response of test specimens with: A) Long and short wounds, B) Wound location at the center, bottom and top parts

The stress-strain response of the test specimens (Table 4.3) with one wound (specimens 1-16), two wounds (specimens 17 and 18, each tested thrice) and three wounds (specimens 19 and 20, each tested thrice) were compared, as shown in Figure 4.21. As expected, the average stress-strain plot of the tests with three wounds was found to be more compliant than with two or one wound. Moreover, the two wound test results were found to lie in between the three and one wound test results. It was concluded that, in general the skin becomes weaker in the presence of multiple wounds (which is a common occurrence in major accidents or blast injuries [162]).

Figure 4.21: Average stress-strain plots of test specimens with one, two and three wounds

4.3.2.4 Mechanical testing of human skin phantoms with sutured wounds

Sutures were placed on all the wounds in the human skin phantom test specimens as discussed earlier in the Materials and Methods section. The average stress-strain behavior of the sutured test specimens were plotted along with the non-sutured wounded specimens and original non-wounded specimens, as shown in Figure 4.22. The non-linear mechanical response of the sutured test specimens were found to lie in between that of the unwounded and wounded test specimens, with a much closer proximity to the unwounded tests than the wounded tests (as can be interpreted from the standard deviation error bars in Figure 4.22). It was found that suturing improves the mechanical properties of the wounded skin. Also, the non-linear stress-strain response of the sutured specimens were found to overlap precisely with that of the unwounded specimens for low strains of 0-0.2, but show some deviations at higher strain values (as seen in Figure 4.23). These are very significant clinical findings, which to our knowledge, have not been reported previously in the literature. In future, experiments with

better suture material and suturing technique may potentially allow medical practitioners to adjust the mechanical behavior of the skin after an injury back to normal conditions.

Figure 4.22: Comparison of stress-strain response of unwounded, wounded and sutured human skin phantom specimens

The effect of suturing on the mechanical behavior of human skin phantom specimens with long and short wounds (based on the sizing convention in Table 4.4), were compared (see Figure 4.23). No significant trends were observed besides the shrinking of the stress-strain error bars of the specimens with long wounds, with suturing (observed from comparing Figure 4.19 and Figure 4.23). This may indicate that long wounds are more sensitive to suturing and their mechanical properties converge significantly towards an average, compared to the short wounds.

Suturing was found to have a re-orientation effect on the stress-strain response plots of the test specimens with center, top and bottom wounds, when Figure 4.20 and Figure 4.23 were compared. The human skin phantom, which was more compliant for top and bottom wounds compared to the center wounds earlier (see Figure 4.20), became stiffer for the top wound case

compared to the center wound case, with suturing. However, the test specimen was still compliant for the bottom wound case after suturing, as before in Figure 4.20. This finding could be partly attributed to the load application method in the uniaxial test (where the bottom clamp is stationary and the top clamp displaces at a certain speed applying the load). In case of a specimen with top sutured wound, a greater load is applied by the top clamp of the testing machine on the stiff sutures, compared to in the case of a specimen with sutured bottom wound (where greater load is applied to the skin tissue phantom and lesser on the stiff suture which is at a greater distance from the point of load application or the top clamp).

Figure 4.23: Comparison of the effect of suture on the mechanical behavior of skin with: A) Long and short wounds, B) Location (top, center and bottom)

The effect of sutures on the average stress-strain response of test specimens with one, two and three wounds were investigated further. The stress-strain plots were found to be overlapping for the test specimens with one and two wound sutures. However, with three wounds, the skin phantom specimen showed a stiffening behavior greater than the original skin phantom property (see Figure 4.24). This could be attributed to the over-stiffening of the skin

with the suture materials and reduced mobility of the skin phantom material within the test region. Further tests need to be conducted in the future studies with three or more wounds to see if the number of wound sutures could actually stiffen the skin more, which could be clinically relevant information for deciding suture materials and practices.

Figure 4.24: Investigation of suturing effect on test specimens with one, two and three wounds

4.4 Soft Composite Damage Analysis using Digital Image Correlation (DIC)

Digital image correlation (DIC) techniques have been used especially in micro and nano scale mechanical testing applications to understand the localization of strains in a material under varying loading conditions [163]. Especially, DIC techniques have been used to understand crack initiation and propagation in hard composite materials [164]. Recently, DIC was used to understand anisotropic local skin tissue deformation [2]. However, to date, DIC has not been used to study soft tissue composite under damage conditions, studying which would be valuable to understand soft composite failure mechanics.

In this work, five irregular wound geometries were created on human skin phantoms and tested in tension to study localized strains at the wounds. Standard size test specimens were fabricated and their surface sprayed with paint based irregular speckle patterns. These patterns were recorded during the tension test and post processed to estimate local strains. Besides the strain field observed over the entire surface, markers were placed at different locations around the wound surface to evaluate the change in strains accurately. The average stress versus strain was plotted for each specimen and compared with the local strain values to draw inferences. The following sections discuss the materials and methods and key results.

4.4.1 Materials and Methods

Two-part silicone material with a shore hardness of 30 A was mixed in a 1:1 ratio by weight to fabricate skin tissue surrogates discussed in the previous section. 10 test coupons were generated with 50 mm length, 9 mm width and 2.5 mm depth. Wound geometries varying in shape, size, depth, and location on the coupon were created using a scalpel and regular scissors on 5 out of 10 coupons (Figure 4.25 A). The direction along the length of the coupon was considered as the Y-axis and the orthogonal direction along the width of the coupon was considered X-axis. The wounds were classified based on their aspect ratios (AR, Ratio of width along X direction and length along Y direction, see Figure 4.25 A) along the axes as Wound 1 (Medium X, Medium Y), Wound 2 (Medium X, Short Y), Wound 3 (Medium X, Long Y), Wound 4 (Medium X, Long Y), and Wound 5 (Short X, Medium Y) respectively to study the effect of wound lengths on the strain fields. The Short, Medium and Long designations were selected based on comparative wound observations and not based on a particular set of benchmark lengths.

Figure 4.25: A) Synthetic skin phantoms with wounds. AR is the aspect ratio in each case, B) Irregular speckle pattern used for DIC

Spray paint was dispersed on the test coupon surface in such a way that the speckle patterns are fine, dissimilar, and densely populates the surface to be studied (Figure 4.25 B). This process was repeated six times to obtain the desired speckle pattern [163]. A high quality camera (20.1 Mega Pixel Sony DSC-H400 Single-Lens Reflex (SLR) camera) was used on a tripod to record the tensile tests. The videos were run through a video-to-image conversion software also to obtain 20 images from each test. The average length of the videos recorded was 48 seconds. Each test was conducted and recorded three times to ensure repeatability.

Visual Image Correlation (VIC) 2D software (from Correlated Solutions Inc., SC, USA) [163] was used for postprocessing of the image sets from the tensile tests. Visual image correlation VIC-2D analyses subtle differences between two images taken before and after the deformation by a solid-state digital camera. Then the strain variation of both images are found using comparative analysis using the statistical functions of VIC. In Bruck's study of Newton-Raphson method [163], it is mentioned that deformation of image speckles could be demonstrated by vertical distance and horizontal distance of two speckles after displacement, which is commonly known as strain (see Figure 4.26)

Figure 4.26: Vertical and horizontal strain calculations using DIC for a tension test

Uniaxial mechanical tests were performed on each of the test coupons using a universal testing machine (from MTS Systems Corporation). A strain rate of 0.4 mm/s was employed for all the tests, to compare the generated stress-strain response with the literature [10]. Five coupons with no wounds were tested first to calibrate the VIC 2D measurements with the MTS test machine displacement measurements. After machine calibration, tensile tests were conducted on each test specimen with wounds multiple times and average results of strain changes with time were obtained using VIC 2D analysis, which are discussed in the following section.

4.4.2 Results and Discussion

4.4.2.1 Strain Measurements for Skin Phantoms with No Wounds

Skin phantom specimens with no wounds were tested in tension and analyzed using DIC to calibrate the strain calculations for further analyses. Figure 4.27 shows the strain fields postprocessed using DIC during the times 0, 2, 23 and 40 seconds. A total of 14 frames were extracted from the 40 second long video of the tensile test. Markers were placed at 6 different

locations to obtain the average strain versus frames (Figure 4.28) for five coupons each tested twice. Figure 4.29 captures the average experimental result (strain versus time) obtained from the MTS tensile testing machine for the 10 tests with error bars. An R^2 correlation calculation was performed to compare the average strain versus time (frame) plots in Figure 4.28 and 4.29. and the R^2 value calculated was 0.966. Therefore, the setup was considered to be reasonably accurate for further analyses.

Figure 4.27: Strain results from a tensile test on the synthetic skin specimen with no wound using DIC technique

Figure 4.28: strain (Y-axis) versus time frame (X-axis) measured using DIC from tensile test on the synthetic skin specimen with no wound

Figure 4.29: Average strain versus time plot from tensile test of coupons with no wounds, measured from the MTS machine for comparing with DIC measurements

4.4.2.2 Strain Measurements for Skin Phantoms with Wounds

Tensile tests were conducted on specimens with wounds of varying geometries and DIC was used to study the local strains around the wound perimeter. Wound 1 was tested first and significant strain build up was observed along the long Y edge of the wound (Figure 4.30).

Markers were placed at the different locations around the wound periphery and the specific strain values were estimated. One key observation was that the average strain value for the test specimen was lower than that at the points of strain build up. The maximum strain recorded was approximately 31% greater than the average strain. The strain values recorded at the top and bottom points of the wound were lower than that of the average strain observed for the specimen. Also, the strain values recorded on the left and right side of the wound (at points P4 and P5 in the Figure) were almost similar, which could be due to the approximately symmetric elliptical geometry of the wound.

Figure 4.30: Average strain (Y-axis) versus time frame (X-axis) measured using DIC from tensile test on the synthetic skin specimen 1 with wound

The second specimen with the wound geometry was subjected to tensile test for 57 seconds and 12 frames were extracted to conduct DIC measurements. The observation in this case was a symmetric strain build up on the left and right side of the wound to start with, followed by a localized high strain build up on the left side of the wound circumference, finally leading to tearing in that direction (see frame 12 of the Figure 4.31). Four markers were placed along the wound periphery to quantify the strain changes. Point P1 at the left hand corner had a steep rise in strain followed by the point P3 on the right side, P0 on the top P2 at the bottom. The average strain was found to be higher than the strains at the bottom point P2.

Figure 4.31: Average strain (Y-axis) versus time frame (X-axis) measured using DIC from tensile test on the synthetic skin specimen 2 with wound

The third wounded test specimen was tensile tested for 42 seconds and 14 frames were extracted for DIC measurements. A high stress buildup was observed initially on the left hand side of the wound which shifted eventually to the right hand side (see Figure 4.32). On quantification of the the strains along the circumference of the long wound with 7 markers, the strain fields were found to be close to each other all around the wound with the peak at point P2 which is on the left hand side. The lowest strains were observed at the top and bottom of the wound similar to other wounds.

Figure 4.32: Average strain (Y-axis) versus time frame (X-axis) measured using DIC from tensile test on the synthetic skin specimen 3 with wound

The fourth specimen with wound was subjected to tensile test and 14 frames were extracted from 49 seconds length of visual data. A high stress build up was observed on the left and right side of the wound to start with, which shifted dominantly to the right side with increasing strains. Using 6 markers along the circumference of the wound, the lowest strains were estimated at the top and bottom of the wound. All the markers along the left side of the wound (P1, P3 and P4) resulted in similar strain changes as seen in the Figure 4.33. The highest strains were recorded for the marker P2 on the right side of the wound.

Figure 4.33: Average strain (Y-axis) versus time frame (X-axis) measured using DIC from tensile test on the synthetic skin specimen 4 with wound

Specimen with wound 5 (Short X, Medium Y) was subjected to the tensile test for 41 seconds and 14 frames were captured. 8 markers were placed around the wound circumference and the strains were tracked (Figure 4.34). High strain buildups were observed at the top (P0 and P1), left side (P3) and bottom right (P5) locations along the wound periphery. The lowest strain was observed for the bottom most point of the wound. Strains estimated at the other locations were observed to be very similar.

Figure 4.34: Average strain (Y-axis) versus time frame (X-axis) measured using DIC from tensile test on the synthetic skin specimen 5 with wound

Figure 4.35: Average strain versus time plots of the specimens with and without wounds

Four key conclusions can be drawn from the DIC based localized strain analyses on the tensile tests of specimens with five different wound geometries. First, the strain at the bottom most point of the wound is always the lowest and its value is lower than that of the average strains measured for the specimen throughout. Second, for long wounds with the long edge along the Y axis (direction of tension), the maximum strains are observed at the left and right sides of the wound with similar strain values. The wider this long wound was, the greater was the difference between the values of strains on the left and right side. Third, for a short wound, the strain distribution is similar at the top, left and right due to the comparable aspect ratio ($AR \sim 1$) of the wound length (along Y axis) and width (along X axis). However, the geometry of the wound in case of short wounds have been observed to play a significant role in deciding the superior strain build up locations with tension, which may drive soft composite rupture (as seen in case with wound 2). Fourth, for narrow and long wounds (wound geometry 5), a high

strain build up was observed on the top of the wound which may lead to rupture and increase in the length of the wound. All these findings are not only novel but provide valuable insights into the damage process in soft composites, specifically with relevance to soft tissues. The results of this study would be beneficial in robotic surgeries to devise appropriate methods for wound treatment and suture based on the geometry and size of the wound.

The average strain versus time plots of the specimens with no wound and the ones with the different wound were compared as seen in Figure 4.35. As expected from the study of the mechanics of wound [165], the strains quantified for the specimens with wounds are lower than those without wounds. The lowest strains were observed for the specimen with the smallest size and the most symmetric wound (specimen 2). The strains were found to increase with decreasing aspect ratio. The strains for the wound with lowest aspect ratios (Wound 5, $AR=0.07$) was found to be the closest to the strains observed in the specimens with no wounds. It should be mentioned here that the aspect ratios of the wounds in the current work was estimated by calculating length and widths of the wounds using Vernier calipers, which have to be more accurately obtained using microscopy in the future work. Also, in reality, skin tissue undergoes biaxial stretching with an inferior X-axis tension, which if incorporated into the current framework may improve the accuracy of the results. An additional limitation of the current work is the use of hypothetical wound geometries for the study. In future, more realistic wound geometries obtained from patient specific measurements may improve the quality of results for clinical knowledge and consideration.

4.5 Combined Experimental-Computational-DIC Based Model

An arbitrary wound geometry was selected for computational modeling from the human skin phantoms tested in uniaxial tension in the previous sections. Constant strain rates from experiments were applied computationally on the test coupon and the results were

compared with the uniaxial tensile experiments and DIC measurements. The effects of sutures were also simulated similar to the experiments and the result were compared.

4.5.1 Materials and Methods

The coupon size selected for the computational study was 50 mm length, 9 mm width and 2.5 mm depth from experiments. Figure 4.36 shows the wound geometry observed under a microscope. The direction along the length of the coupon was considered to be the Y-axis and along the width to be the X-axis. The wound location and geometry was replicated in the finite element software ANSYS. Also, sutures were modeled to run through the thickness of the coupon (Figure 4.37). Both the coupon and suture geometries were meshed using the higher order 3-D 20-node Solid 186 element which account for large deflections, hyperelasticity, and large strain deformations [153]. A flexible and bonded contact pair was defined to connect the sutures with the human skin phantom material.

Figure 4.36: A) Coupon with wound dimensions observed under a microscope, B) Finite element model of the coupon with a wound

The computational simulation was conducted in two steps. In the first step, sutures were placed similar to the experimental test specimen (see Figure 4.37), followed by the application of tensile displacements in the second step. The first suture was placed at the left side (suture 1) of

the wound followed by the right side (suture 2) and center (suture 3). Three suture placements were simulated as shown in Figure 4.37 using a novel suture pulling technique introduced in the previous section 4.2.

Figure 4.37: Coupon with sutures used to model the suturing process in 3 steps in the finite element model

Non-linear material properties for the human skin phantom was adopted from the isotropic Veronda-Westmann hyperelastic curve fitting parameters obtained from the experiments discussed in section 4.3 (see Table 4.6).

Table 4.6: Average hyperelastic curve fitting parameters for human skin phantoms

Veronda-Westmann Model	C_1 (MPa)	C_2 (MPa)
Human Skin Phantom	0.737	0.338

The test specimen was constrained in all degrees of freedom at the bottom end, and pulled from the top end. Tensile test with a strain rate of 0.4 mm/sec was simulated by transferring the Displacement-Time data points from the experimental measurements into ANSYS dynamic FE solver. The stress-strain plots obtained from experiments were compared

with the computational analysis for wound with and without sutures. Also, the local strains were analyzed and the results were compared with the DIC based measurements.

4.5.2 Results and Discussions

4.5.2.1 Tensile Tests in the presence of Wound with and without Sutures

The stress versus strain was estimated from the tensile test simulation of the coupon with the wound geometry. Figure 4.38 captures the snapshot of the coupon deformation at the times 2 sec, 24 sec and 57 sec from the start of the test. The stress-strain plot of the coupon with no wound recorded during the experiments was compared with the stress-strain plots of the coupon with wound (obtained from the experiment and computational analyses). The stress-strain plot was observed to be more compliant for the coupon with wound compared to without wound, both in the computational model and experiments. The computational and experimental stress-strain plots in Figure 4.38 were found to have an R^2 correlation index of 0.976. The computational stress-strain plot was observed to become stiffer compared to the experimental values after a strain of about 0.4. This observation can be attributed to the skin phantom tearing which was observed during the experiments. However, the tearing was not simulated in the computational model, resulting in higher stress values after a strain of 0.4.

Figure 4.38: Computational results of skin phantom straining compared with experiments

After suture placements in the computational model, tensile strain was applied at a constant rate. The stress-strain plots were compared for the no-wound, with wound and with sutures cases. The stiffness of the sutured specimen was observed to be higher than the wounded specimen and close to the non-wounded specimen. Comparing the experimental and computational stress-strain plots of the sutured coupon, the R^2 correlation index was estimated to be 0.982. In future, the mechanical differences in an actual suture with knots needs to be quantified and compared to in the case of ideal sutures modeled computationally. Additionally, on a closer look into the sutures during the tensile test, wound re-opening was observed at the center suture both in the computation and experiments as shown in Figure 4.39. This finding could be mainly attributed to the excessive stress build-up at the center suture during the soft tissue straining.

Figure 4.39: A) Stress-Strain plots of skin phantoms compared due to the no wound, wound and suture cases, B) Wound re-opening due to application of high strains on sutured skin

4.5.2.2 Local Strains at the Wound compared with DIC measurements

The local strains were now obtained from the computational analysis of the coupon with wound, and were compared with DIC measurements (that was discussed in the previous

section). Figure 4.40 captures the strain distribution around the wound for a constant strain rate of 0.4 mm/sec at 2 sec, 24 sec and 57 sec. The maximum strain was observed at the left side of the wound in both the computational and DIC measurements. This localized strain build-up could be attributed to the geometry of the wound. Another common observation is the occurrence of minimum strains at the top and bottom of the wound. After 24 sec, strain reduction was observed around the wound due to tearing in the DIC measurements, which was not captured by the computational model.

Figure 4.40: Local strains around the wound compared at different times in the computational model and DIC measurements

The maximum local strain variation with time around the wound from the computational model was compared with the experimental data obtained using DIC measurements (see Figure 4.41). It can be seen that there is a good agreement between the computational data and the experimentally measured maximum strain.

Figure 4.41: Maximum local strains measured around the wound under tensile stretching in the computational model and compared with DIC measurements

CHAPTER 5

SOFT COMPOSITE INTERACTIONS⁴

5.1 Summary

In this chapter, soft composite interactions are studied using computational modeling of complex organ systems, where tissue composites interact under multiple loads and boundary conditions. Soft composite models especially for tissues serve as the building blocks for the study of macro level composite system interactions. Understanding, soft composite interactions will lead to the understanding of the genesis and progression of soft composite damages, which is the key to the investigation of tissue based diseases (damage) in the human body such as in case of a heart attack, organ failure, tissue rupture in an accident or due to various pathophysiological outcomes. In this chapter the normal and high level damage mechanics of three critical physiological systems will be covered namely the Female Pelvic System, Whole Body Injury in blast impacts, and diabetic foot ulceration management. All these systems were

⁴ Chanda, Arnab, et al. "Computational modeling of the female pelvic support structures and organs to understand the mechanism of pelvic organ prolapse: a review." *Applied Mechanics Reviews* 67.4 (2015): 040801.

Chanda, Arnab, et al. "A biofidelic computational model of the female pelvic system to understand effect of bladder fill and progressive vaginal tissue stiffening due to prolapse on anterior vaginal wall." *International journal for numerical methods in biomedical engineering* 32.11 (2016).

Chanda, A., Unnikrishnan, V., Richter, H. E., & Lockhart, M. E. "Vaginal Changes Due to Varying Degrees of Rectocele Prolapse: A Computational Study." *Journal of Biomechanical Engineering*, Accepted.

Chanda, Arnab, and Vinu Unnikrishnan. "Effect of Bladder and Rectal Loads on the Vaginal Canal and Levator Ani in Varying Pelvic Floor Conditions." *Mechanics of Advanced Materials and Structures* just-accepted (2017).

Chanda, Arnab, Rebecca Graeter, and Vinu Unnikrishnan. "Effect of blasts on subject-specific computational models of skin and bone sections at various locations on the human body." *AIMS Mater Sci* 2.4 (2015): 425-447.

modeled computationally using high fidelity numerical models of the geometries, Finite Element (FE) meshes, loads and boundary conditions.

5.2 Female Pelvic System Mechanics

The female pelvic floor is a complex system, in which the pelvic organs interact in different ways over the course of a women's life. To date, the pelvic floor mechanics is poorly understood by doctors and medical practitioners, which is the key to understanding the various pelvic floor defects such as child birth complications and Pelvic Organ Prolapse (POP). Currently, millions of women suffer from child birth trauma and POP in the U.S. and across the globe. While experimental studies are being performed on human subjects to understand the various qualitative trends in pelvic floor defects, recently, computational modeling has allowed researchers to better understand the mechanics of the pelvis. Based on a recent review on the state of the art knowledge on numerical modeling of pelvic floor mechanics by Chanda et al. [144], a lack of computational study on the interaction between the pelvic organs and the muscles were highlighted. In the current work, the mechanics of progression of anterior and posterior vaginal prolapse (POP) were modeled to understand the effect of bladder fill and posterior vaginal stresses using computational approaches. A realistic and full-scale female pelvic system model, comprised of the urinary bladder, vaginal canal, uterus, rectum, pelvic floor muscles and fascial connective tissue, was developed using image segmentation methods. All of the relevant loads and boundary conditions were applied based on a comprehensive study of the anatomy and functional morphology of the female pelvis. Hyperelastic material models were adopted to characterize all pelvic tissues, and a non-linear analysis was invoked. In the first part of this work, the interactive effect of the urinary bladder and the rectum on the vaginal canal in normal and prolapsed conditions was investigated without considering the

effect of the pelvic floor muscles. In the second part, the effect of pelvic floor muscles on the interactive mechanics was studied for different pelvic floor conditions (normal and weak).

5.2.1 Materials and Methods

5.2.1.1 Geometrical Modeling and Meshing

The geometrical modeling of the various pelvic organs namely the urinary bladder, vaginal canal (uterus), rectum and the pelvic floor muscle (Levator Ani) were conducted in five steps. First, Magnetic Resonance (MR) Images were obtained from the visible Korean female database [166-168] and TurtleSeg image segmentation software [127] was used to create the initial outer surfaces (see Figure 5.1). Secondly, Meshlab [169] was used to smooth the surface mesh, and to reduce the overall number of elements forming each of the surfaces. Third, Hypermesh (Altair Inc.) was used to iteratively refine the 2D mesh by correcting all surface penetrations and overlaps, and converting the 2D mesh into a 3D solid mesh. The Solid 186 element was chosen for meshing of all the pelvic organs, as it can account for large deflections, hyperelasticity, and large strain deformations [153].

Based on previous studies on mesh convergence and optimization of the female pelvic floor by the authors [170, 171], a semi-fine mesh was chosen for all the pelvic organs with a total of 34,282 tetrahedral elements. Figure 5.2 shows the meshes of the pelvic organs and muscles in four different colors. Appropriate mesh refinement was conducted to prevent any penetrations/overlaps between the meshes. Multiple contact relations (discussed in the upcoming section) were defined numerically to simulate attachments between the pelvic organs.

Figure 5.1: Surface geometries of the various pelvic organs (Urinary bladder, vaginal canal, rectum and pelvic floor muscles) in the female pelvic system model

Figure 5.2: FE meshes of the pelvic organs in the female pelvic system model

5.2.1.2 Boundary Conditions

In the female pelvis FE model, multiple constraints were placed on the pelvic organs based on the anatomical findings by DeLancey et al. [172]. The uterus was assumed to be

connected to the pelvic floor muscles through connective tissues, which provides support when the pelvic floor muscles are intact. If these muscles weaken greatly, the uterus may no longer be supported above the pelvic floor [172]. In the current work, the fundus of the uterus was constrained in all degrees of freedom (Figure 5.3) and the pelvic floor muscles were simulated in normal and diseased (weakened) conditions [170, 171]. The urethra, rectal hiatus (anus) and the vaginal hiatus, which are strongly attached to the ligaments of the pelvic floor, were assumed to be constrained in all degrees of freedom, and does not undergo any change in shape or size over the course of our analyses (Figure 5.3). The top of the rectal canal (which is connected to the intestine) is assumed to not play a role in our analysis, and thus was restricted to movement in all directions.

Figure 5.3: Various constraints corresponding to different pelvic organs in the current pelvic system FE model

The levator ani was constrained to its surroundings in an attempt to recreate the enveloped structure of the pelvic floor muscle and connective ligaments. It was assumed to attach posteriorly to the coccyx (Figure 5.4), bilaterally anterior to the arcus tendinous connective tissues and posteriorly to cardinal ligament and uterosacral ligament (Figure 5.4),

and anteriorly to the pubic bones (Figure 5.4). These fixed constraints were used based on previous experimental studies of the female pelvic floor [172, 173]. In reality, multiple layers of the pelvic floor muscle form the complex levator ani structure, which is difficult to model due to insufficiently known anatomical information.

Figure 5.4: Various levator ani constraints due to ligament attachments, used in the current pelvic system FE model

Multiple fascial contact pairs were used to connect the various pelvic organs. An endopelvic fascial contact pair was defined to capture the attachment of the urinary bladder and the anterior vaginal wall (AVW) (Figure 5.5). Another fascial contact was defined to show the attachment of the anterior rectal wall (ARW) with the posterior vaginal wall (PVW) (Figure 5.5). Based on the anatomical studies by DeLancey et al. [172], the levator ani was attached to the posterior rectal wall (PRW) with an additional contact pair (Figure 5.5). All contact pairs defined in the study were chosen as flexible with a normal penalty stiffness factor of 1 with a penetration tolerance factor of 0.1 and based on the augmented Lagrangian method. The contact surface was considered as fully bonded with null initial penetration and surface offset. An automatic contact adjustment for gap closure and penetration reduction was adopted for the fascial contact representation.

Figure 5.5: Various fascial contacts between the pelvic organs used in the current pelvic system FE model

5.2.1.3 Loading Definitions

A novel forced volume expansion method [9, 170, 171] was used to simulate the bladder and rectal loading conditions. Both the bladder and the rectum geometries were forced to bulge to 1%, 10% and 100% sizes, and the induced stresses and displacements at the vaginal walls and levator ani were estimated. In this method, a hypothetical material independent thermal expansion coefficient (k) of 10^{-4} was specified for the bladder and rectal FE mesh elements. All of the mesh elements were assigned an initial temperature (T_o) of 0 K, and a final temperature (T) of 100 K, 1000 K, and 10,000 K, to force a 1%, 10%, and 100% volume expansions (

$$\text{Percentage Bladder / Rectal Bulge} = \frac{\Delta V}{V} \times 100 = k \Delta T \times 100; \quad (\Delta T = T - T_o) \text{ respectively. It}$$

should be mentioned that a simple forced thermal expansion applied on an organ volume is only based on the hypothetical thermal expansion coefficient and applied temperature, and is independent of the material property of the tissue. The internal stresses which are generated within the bladder and rectum due to this expansion and the stresses generated due to its material property are not considered.

Figure 5.6: Numerical study set 1: A) Novel forced volume expansion technique used to simulate urine filling in the bladder and B) Vaginal tissue stiffening material model with upper and lower bounds used in our analyses

For the first set of simulations, the stresses induced due to bladder filling (Figure 5.6A) on the AVW were estimated. Also, a novel vaginal stiffening material model was developed to look at the AVW changes due to vaginal tissue stiffening secondary to prolapse. The model was comprised of defining vaginal tissue properties in normal, low and high degrees of prolapse (Figure 5.6B). Eight cases were simulated within the upper and lower bounds of prolapsed vaginal tissue conditions, in different bladder fill conditions (empty through full), to look at the combined effects of bladder filling and vaginal tissue stiffening

In the second part of the work, different degrees of rectal prolapse were simulated. Based on literature [174] on functional anatomy of rectal prolapse, the degree of prolapse was quantified based on the maximum distance estimated from the anorectal axis (line passing through the centroidal axis of rectal hiatus or the anus in Figure 5.7A) to the farthest point of the prolapsed rectum [174]. The vaginal length was divided into four equal sections in the Y-Z plane as shown in Figure 5.7B. The average cross-sections of the vaginal canal (along the Y

direction) were estimated in the four sections. An average abdominal pressure of 30 cm H₂O (or 2.94 kPa) was applied in the Y-direction, and the changes in the vaginal cross-sections in the four regions were tracked for different cases of rectal prolapse.

Figure 5.7: Numerical study set 2: A) Example of posterior vaginal wall prolapse simulation and quantification, and B) Vaginal length divided into four equal sections for analyses

The third part of the work is focused on estimating the displacements and stresses generated on the vaginal walls and levator ani, induced due to varying bladder and rectal loads. Experimental tests in literature have revealed that pelvic floor muscles weaken with prolapse [144]. However, to date, no experimental studies have been conducted to study the progressive pelvic floor muscle weakening at different degrees of prolapse. Due to unavailability of such experimental test data, in our current work, five hypothetical but reasonable cases of pelvic floor muscle (Levator ani) weakening are simulated (Figure 5.8) to study their effect on pelvic organ interactions. The Yeoh's curve fit equation was used to characterize all such stress-stretch plots. Also, this equation was used to curve fit the mechanical behavior of pelvic organ tissues reported in literature [11]. Table 5.1 lists the Yeoh's model curve fit coefficients C_{10} , C_{20} , and C_{30} for normal bladder, rectal, vaginal and levator ani tissues, and diseased levator ani tissues simulated using the five pelvic floor weakening cases.

Figure 5.8: Stress versus stretch behavior of pelvic tissues simulated in normal condition (based on literature [11]) and in diseased conditions (levator ani weakening model)

Table 5.1: Yeoh's hyperelastic material model parameters adopted for the pelvic tissues in normal [11] and diseased condition (simulated in Figure 5.8) in current work

	Yeoh Parameters	C_{10} (MPa)	C_{20} (MPa)	C_{30} (MPa)
Normal	Levator Ani	0.018	0.03	0.5
	Vaginal Tissue	0.005	0.018	0.73
	Rectal Tissue	0.003	0.0015	0.50
	Bladder Tissue	0.001	0.005	0.21
Diseased/Weakened	Levator Ani Weak 1	0.01	0.025	0.65
	Levator Ani Weak 2	0.006	0.020	0.70
	Levator Ani Weak 3	0.004	0.015	0.68
	Levator Ani Weak 4	0.003	0.014	0.65
	Levator Ani Weak 5	0.005	0.001	0.30

5.2.2 Results and Discussion

5.2.2.1 Effect of Bladder Fill and Vaginal Stiffening on Vaginal Canal

The urinary bladder volume was forced to expand from 0 through 100 percent (based on assignment of different final temperatures T), to simulate varying degrees of bladder fill. Figure 5.9 shows the effects of an empty bladder and fully filled bladder conditions respectively on the AVW. Three main observations were recorded. First, bladder filling was found to cause a more uniform stress distribution at the AVW. Second, despite a more uniform stress redistribution, at high bladder fills, some small areas developed high stress concentrations, which may potentially cause vaginal discomfort. Third, compared to a maximum stress value of 0.12 MPa at an empty bladder condition, a very high maximum stress build-up of 5.16 MPa was observed at the AVW fully filled bladder condition. Additionally, it was found that the maximum displacement was induced on the AVW in the negative Y direction (pushing the AVW towards the vaginal hiatus). At a fully filled bladder condition, a 7.98 mm maximum negative Y displacement was estimated. Also, a reasonably high [6, 129] mechanical strain of 0.27 was found for the vaginal tissues at fully filled bladder condition, which was almost four times that in case of an empty bladder condition.

Figure 5.9: Stresses (MPa) induced at the AVW due to an empty and fully filled bladder

Figure 5.10: Stress (MPa) induced on AVW for a 50% bladder fill and varying vaginal stiffening conditions

Eight cases of vaginal tissue stiffening were simulated for different bladder fill conditions. At a particular bladder fill condition (Figure 5.10 shows a 50% bladder fill situation), the stress distribution at AVW was observed to be uniform with a small zone of high stress concentration at the mid-vagina. With increasing vaginal tissue stiffening, the size of this high stress concentration zone was found to increase without any significant change in the stress value (1.98 ± 0.05 MPa), which may represent an etiology for progressive vaginal discomfort [175]. A 3D plot was generated for four of the ten bladder fill cases simulated (Figure 5.11), and five of the eight prolapse cases to study the combined effect of bladder fill and vaginal tissue stiffening due to prolapse on the maximum stress build-up at the AVW. Until a 60% bladder fill, the maximum stress at the AVW was found to gradually intensify without any significant effect of vaginal tissue stiffening. However, beyond 60% fill, a more rapid intensification of the maximum induced stresses at the AVW was observed. The maximum stress build-up due to the combined effect of bladder fill and vaginal tissue stiffening was estimated to occur for the upper bound prolapse case with a fully filled bladder. Therefore, it was concluded that clinical examinations of prolapse may be carried out with at least 60 % bladder fill to quantify vaginal discomfort appropriately.

Figure 5.11: Induced maximum stresses (MPa) at the AVW at different percentages of bladder fill and prolapse cases

5.2.2.2 Effect of Rectal Prolapse on Vaginal Canal

In the second set of simulations, a constrained expansion of the rectum (0-100%) was invoked in the presence of an average abdominal pressure on the AVW, and its effects on the vaginal walls were quantified. The 0% rectum expansion was considered to refer to a normal vaginal case (with no prolapse), and the 10% and 100% rectum expansions leading to low and high posterior prolapse cases respectively (Figure 5.12). Assuming as per Figure 5.7, all the positive displacements occur in positive Y direction (a posterior displacement) and the negative displacements occur in negative Y direction (an anterior displacement), a negative Y (or anterior displacement) of the PVW was seen (Figure 5.12) in all cases of rectocele at sections 3 and 4 (as per Figure 5.7), indicating that rectocele has more intense effect on the sections 3 and 4 compared to sections 1 and 2. In sections 1 and 2, the abdominal pressure on the AVW was seen to have a more pronounced effect on the Y displacement causing it to stay positive (a posterior displacement of vaginal wall) unless the case of rectocele was fairly intense (with over 60% bulge). Beyond the case with 60% rectal bulge into the vagina, the rectocele effect dominated

over the abdominal pressure causing the AVW to displace towards the negative Y direction. The maximum PVW displacements (up to 24 mm) were observed in section 3 and 4, which may be the “possible” regions causing vaginal discomfort. The most positive (posterior-anterior) vaginal wall displacement was in section 1 (along positive Y direction), mainly due to the significant effect of abdominal pressure.

A maximum of 4.6 mm (or 8.3 %), 0.6 mm (or 1.6 %), 9.0 mm (or 39.6%), and 5.0 mm (or 32 %) decrease in vaginal cross-section (along the Y direction) were estimated for sections 1 through 4, respectively for a 100 % (high prolapse) rectocele bulge condition (see Table 5.2 based on Figures 5.7 and 5.12) compared to the normal vaginal case with no prolapse (in Table 5.2). Thus, section 3 of the vaginal canal was noted as the most deformed region due to rectocele prolapse, followed by section 4, section 1 and section 2. The maximum PVW displacement reported at the high prolapse case (with 100% rectocele bulge) was approximately 23 mm in the negative Y direction. Additionally, a resultant “kneeling” effect was observed at the PVW, which involved the negative Y displacement of PVW (mainly at the deep blue colored region in Figure 5.12) accompanied with its downward displacement (along Z direction with a maximum value of 7 mm). This effect has been reported previously in literature [176, 177] due to the simulation of the impairment of pelvic floor muscles and connective tissues in PVP cases.

Table 5.2: Changes in cross-sectional dimensions of the four vaginal sections from normal pelvis condition to prolapse

Rectocele Case	Section 1 Cross-section (mm)	Section 2 Cross-section (mm)	Section 3 Cross-section (mm)	Section 4 Cross-section (mm)
Normal Case	55.20	36.90	22.70	15.50
Low Posterior Prolapse Case	54.05	36.28	20.20	13.50
High Posterior Prolapse Case	50.63	36.65	13.70	10.50

Anterior Vaginal Wall (AVW)

Posterior Vaginal Wall (PVW)

Low Posterior Prolapse

High Posterior Prolapse

Figure 5.12: Y Displacements (mm) (along the vaginal cross-section) for the AVW and PVW in low and high degrees of rectal prolapse

5.2.2.3 Effect of Pelvic Loading on Vaginal Canal and Levator Ani in Normal and Diseased Pelvic Floor Conditions

The effect of pelvic loads such as the bladder filling and rectal bulging on the vaginal walls were quantified under normal pelvic floor conditions. The bladder and rectal loading conditions simulated are 1%, 10% and 100% using the novel forced expansion technique. The von Mises stresses (Figure 5.13) and displacements (Figure 5.14) were found to increase significantly at the AVW with an increase in bladder loading. Also, the stresses and displacements were found to distribute uniformly with increase in bladder loading. The maximum stress value recorded at a 100% bladder loading was 5.08 MPa and the maximum

displacement value recorded was 12.92 mm at the midvaginal section on the AVW. Compared to literature [170], the maximum vaginal stress and displacement values were found to be similar with a marginal decrease, which could be mainly attributed to the effect of the presence of the pelvic floor muscles. In the earlier works [170], the effect of pelvic floor muscles were simulated using fixed constraints, as opposed to modeling the flexible pelvic floor muscles in the current work, which led to an induced stress and strain relaxation at the vaginal walls. To date, such quantitative results are for the first time being reported for a full scale female pelvic system model with the pelvic floor muscles, which has significant clinical implications. First, high bladder loads may lead to the development of significant stresses and deformations at the AVW in normal pelvic conditions, which should be factored in by urogynecologists while evaluating prolapse conditions and conducting anatomical measurements. Secondly, low bladder loads (see 10% case in Figures 5.13 and 5.14) may lead to low maximum induced stresses (approx. 28 times less than in 100% bladder fill case) compared to the displacements (approx. 5.5 times less than in 100% bladder fill case) on the AVW leading to underestimation of a prolapse conditions due to low induced stresses on the vaginal wall (or vaginal discomfort [170]). Third, high stresses and displacements were recorded on the neck region (below the uterus) of the vaginal canal, which may lead to prolapse of the vaginal vault [172] when unsupported with connective tissues, like in a post hysterectomy condition where the vaginal vault has no support due to surgical removal of the uterus.

Figure 5.13: Induced von Mises Stress map of anterior vaginal wall (AVW) in bladder loadings: A) 1%, B) 10% and C) 100%, with the combined effect of pelvic floor muscles

Figure 5.14: Induced net displacements of AVW in bladder loadings: A) 1%, B) 10% and C) 100%, with the combined effect of pelvic floor muscles

Figure 5.15: Induced von Mises stress map of posterior vaginal wall (PVW) in rectal loadings: A) 1%, B) 10% and C) 100%

Figure 5.16: induced displacements of AVW in rectal loadings: A) 1%, B) 10% and C) 100%

With increased rectal loading, the stress concentration zone was observed to be consistently located at the central mid vaginal region on the PVW for different degrees of rectal loading (Figure 5.15). The induced displacements were observed to be uniform at low rectal loading conditions (1% loading in Figure 5.16) and develop a concentration zone at the central mid vaginal region with increase in the rectal loading. The induced stresses (Figure 5.15) and displacements (Figure 5.16) recorded at the vaginal walls due to high rectal loads were found to be significantly lower compared to high bladder loading conditions. At 100% rectal loading, a maximum induced stress value of 0.006 MPa and displacement of 3.34 mm were recorded at the PVW. A further look at the displacements along the principal directions also revealed the “kneeling effect” at high rectal loads. This clinical phenomenon is attributed to the displacement of the PVW mid vaginal section inwardly towards the AVW and transversely downward towards the vaginal hiatus [144]. Compared to literature [171], in which the pelvic floor muscles were modeled as fixed constraints, the vaginal stresses and displacements were found to be similar, with a negligible decrease, which could be attributed to the effect of modeling the flexible pelvic floor muscles.

The effect of diseased levator ani (which was modeled using a progressively weakening material model), on the induced stresses and displacements at the vaginal walls, was studied in varying loading conditions. The induced peak stresses and displacements due to levator ani weakening were estimated at the vaginal walls for four loading conditions namely: 1) 10% Bladder, 100% rectum, 2) 100% Bladder, 10% rectum, 3) 10% Bladder, 10% rectum, and 4) 100% Bladder, 100% rectum. At high bladder loads, the weakening of the levator ani was found to lead to a gradual increase in peak stresses as shown in the plot in Figure 5.17 A, with 0 indicating normal levator ani condition and 1-5 corresponding to the five degrees of weakening, mainly at the AVW. At low bladder loads and high rectal loads, the induced peak stresses were estimated to be low, but showed an increasing trend with levator ani weakening. At low pelvic loads (10% Bladder and 10% rectum), there was no observable change in the induced peak stress values with varying degrees of levator ani weakening.

The results from the novel pelvic floor weakening model provide valuable information to the urogynecologist on the interactive effect of the pelvic floor muscles on the vaginal canal in diseased conditions. Some of the key findings are: 1) The rectal loading has an insignificant effect on the vaginal canal due to pelvic floor weakening (in prolapse) 2) At high bladder fills (100% in Figure 5.17 A), increase in the rectal loading conditions lead to a maximum induced displacement increase of 2.2 mm and stress increase of 0.26 MPa. 3) At low bladder loads, the rectal loads affected the maximum induced vaginal displacements at different degrees of levator ani weakening. Going from a normal (0 in Figure 5.17 B) to a very weak levator ani condition (5 in Figure 5.17 B), at a 10% bladder and 10% rectal load, the change in maximum induced displacement at the vaginal walls were estimated to be 2.85 mm. Also for 10% bladder load and rectal load increasing from 10% to 100%, the maximum induced vaginal displacements were almost the same up to a levator ani weakening condition 2, and then decreased for

conditions 3 through 5 with high rectal loads. The exact reason for this finding could not be deduced from the computational analysis, and will be investigated in future work.

Figure 5.17: Induced vaginal wall A) Peak stresses and B) Max. displacements at varying bladder and rectal loads, and varying levator ani weakening conditions (0-Normal, 1-Least weak, 5-Most weak)

The effect of bladder and rectal loads were studied for the pelvic floor muscle (levator ani) in normal pelvic floor conditions. With increased bladder loading and no rectal loading, the stress concentration and displacements on the levator ani (Figure 5.18) were found to increase with maximum displacement going up from 0.22 mm to 0.49 mm. The maximum displacement concentration zone was observed to be close to the posterior attachment of the levator ani at the coccyx. This finding indicated that in severe bladder loading conditions due to prolapse, there might be a high chance of pelvic floor failure initiating at the coccyx region. Also, a high stress and displacement region observed close to the anterior puborectalis section of the levator ani (which supports the urethra, vaginal and rectal hiatus) may indicate high induced obstructions at the bladder, vaginal and rectal hiatus regions leading to pressure and hence difficulty emptying the bladder and stress urinary incontinence (SUI) [144].

Figure 5.18: Induced displacements (mm) of the levator ani due to increasing bladder and rectal expansions (1%, 10% and 100% respectively)

With increase in rectal loading, the peak levator ani displacements increased significantly compared to increasing bladder loading. This could be mainly attributed to the large amount of rectum and levator ani surface interaction compared to bladder and levator ani surface interaction as indicated in the previous modeling section. Another observation was that

at high rectal loading, the effect of bladder loading on the induced maximum displacements on the levator ani were negligible. Additionally, at low bladder loading, increased rectal loading led to a significant change in the shape of the levator ani, with an observable upward curl. The overall stress and displacement concentrations were found to diminish with increased rectal loading in all cases of bladder loading. It was thus concluded that rectal bulging (or prolapse) may affect the levator ani significantly, consequently affecting the overall pelvic system mechanics.

Analyses were carried out to understand the effect of the levator ani weakening on its vertical displacements (along the Z direction) at a 50% bladder and 50% rectal loading condition. The material weakening model introduced in Section 2 was used to simulate the five stages of levator ani weakening. Figure 5.19 captures the levator ani shape changes and displacements along the Z-direction. Three main observations can be made. First, going from a normal to a weak levator ani material representation, the maximum Z-displacement increased from 0.88 mm to 17.60 mm. Second, from a normal to the weakest material model, the levator ani shape changed from a flat surface to a concave up surface with the maximum displacement at the center. Third, with respect to the pelvic organs, the levator ani was observed to undergo a twist (anterior to posterior clockwise), because of the weakening. Such a progressive levator ani tissue weakening model would allow the simulation and quantification of shape changes in the levator ani due to different degrees of prolapse in patient specific conditions.

Figure 5.19: Levator ani displacements (Z direction) at different degrees of weakening

5.3 Whole Body Injury from Blasts and Impacts

To date, soft tissue damage due to blasts and impact loads have been modeled mainly for the human head and lower extremities. In most of such computational models, the soft tissue is usually treated as a bulk isotropic material. A soft composite based tissue analysis for

the different locations of the body under impact loads is necessary to obtain accurate quantitative results for the stresses experienced at the skin, bone, and muscle tissues.

In this work, subject-specific 3D computational models of the skin (with the three layers namely the epidermis, dermis and the hypodermis (muscles)) and bone sections from various parts of the human body (such as the elbow, finger, wrist, cheek bone, forehead, shin etc.) have been developed to study the effect of blast loading. Non-linear material properties have been adopted for the skin and stress impulses at the different skin layers and bone sections are estimated. To date, such an extensive study on the effect of blast loading on the human skin and bone has not been attempted. The results of this study would be indispensable for medical practitioners to understand the effect of blast trauma and plan effective post-traumatic surgical strategies, and also for developing better PPE designs for the military in the future.

5.3.1 Materials and Methods

5.3.1.1 Geometrical Modeling

For our study, skin and bone sections from six locations of the body namely the elbow, finger, wrist, cheek bone, forehead and shin, were chosen and modelled based on the knowledge of human anatomy [178] and eye estimation of three subjects (one Caucasian, and two Asians) [178, 179] representing an average age group of 19-27 years. A 3D circular section with the various skin layers namely the epidermis, dermis, hypodermis (muscles), and bone were modelled in finite element software ANSYS. Locations such as the finger, elbow and the wrist which have a significant curvature were modelled as curved spherical surfaces, and the rest of the sections were modelled as flat cylindrical stacks of skin layers and bone, as shown in Figure 5.20. The thickness of the different skin layers were chosen based on the extensive human skin thickness data available in literature [180-193]. The approximate dimensions of the skin and bone section geometries used in our work are presented in Figure 5.20, and the

thickness values adopted for different skin and bone section layers are listed in Table 5.3. It should be mentioned that the thickness for the bone is assumed only for a small section of the bone and not the entire bone.

Contact pairs were placed numerically to ensure contact between the various skin and bone section layers. The type of contact pair chosen was “bonded always”, with negligible friction. The various constraints and loading conditions adopted for our study are discussed in the upcoming finite element modelling section.

Figure 5.20: Subject-Specific geometrical models of skin and bone sections, based on anatomical locations on the human body

Table 5.3: Subject and body location specific thicknesses of various skin and bone section layers adopted for developing the geometrical models

Thickness (mm)	Elbow (Curved)	Finger (Curved)	Wrist (Curved)	Cheek bone (Flat)	Forehead (flat)	Shin (flat)
Subject 1 (Caucasian)						
Epidermis	0.09	0.22	0.14	0.13	0.11	0.14
Dermis	1.23	0.98	1.15	1.12	0.85	0.97
Hypodermis (Muscles)	0.11	1.22	1.56	1.17	0.08	0.08
Bone section	6.25 (Radius)	4.78 (Radius)	8.77 (Radius)	5.45	5.12	5.30
Subject 2 (Asian)						
Epidermis	0.08	0.19	0.1	0.09	0.09	0.09
Dermis	1.03	0.93	1.0	1.07	0.78	0.92
Hypodermis	0.08	1.2	1.53	1.0	0.07	0.07

(Muscles)						
Bone section	5.66 (<i>Radius</i>)	3.28 (<i>Radius</i>)	8.48 (<i>Radius</i>)	5.0	5.25	4.80
Subject 3 (Asian)						
Epidermis	0.13	0.25	0.15	0.16	0.11	0.13
Dermis	1.20	1.23	1.45	1.27	0.92	0.96
Hypodermis (Muscles)	0.12	1.16	1.74	1.10	0.08	0.07
Bone section	5.45 (<i>Radius</i>)	3.65 (<i>Radius</i>)	8.20 (<i>Radius</i>)	5.68	5.94	4.5

5.3.1.2 Finite Element Modeling

Development of a finite element (FE) model of a biomechanical system comprises of the various steps of geometrical discretization using viable meshing techniques, assignment of appropriate boundary conditions and loads, and the right interpretation of results, which are clinically relevant [9, 144]. For our work, a non-linear transient FE analysis capturing the various phases (or time frames) of blast loading was adopted.

Higher order 3D 20-node Solid 186 type quadratic tetrahedral elements were chosen in ANSYS software for meshing of all the skin and bone section layers. A detailed mesh convergence study was conducted to ensure accuracy of results from our analyses. Figure 5.21A shows the four meshes namely a coarse, semi-coarse, fine and very fine, which were subjected to blast loadings with three different amplitudes as shown in Figure 5.21B. Figure 5.21C presents the results of the mesh convergence study, from which, it was concluded that semi-fine mesh for the curved section with 37885 elements was a stable mesh for our further analyses. Appropriate mesh sizing controls (with a global element edge length of 0.1 mm was applied on the epidermal layer to obtain the semi-fine mesh in Figure 5.21A, followed by a continuum mesh generation for the dermis, hypodermis and the bone section in order) were used to ensure a smooth mesh transition from one layer to another, and also to optimize the number of elements generated [9]. For the current analyses, the bottom surface of the bone and skin layers were constrained in all

degrees of freedom to simulate the strong attachment of the skin layers to the bone [194]. The constraints for a typical flat circular section and curved section models are shown in Figure 5.22. Blast loading (pressure) was applied to the flat circular and curved skin and bone section models as shown in Figure 5.21B with red contour lines. The blast load steps were characterized using the Friedlander equation 5.1, where P_s is the peak pressure and t^* is the time at which the pressure crosses the horizontal X -axis for the first time (before the negative phase). Assuming P_s as 0.375 MPa from 0.5 to 0.6 ms, and -0.5 MPa from 0.6 to 1 ms, a t^* value of 0.826 ms was estimated numerically. Table 5.4 lists the four load steps applied sequentially to simulate the Friedlander blast wave in our analyses.

(A)

(B)

(C)

Figure 5.21: A) Meshes of a typical curved skin and bone section model for mesh convergence (MC) study, and flat circular model B) Blasts waves of varying amplitudes used in MC study, C) MC study results

Figure 5.22: A) Displacement constraints and B) Blast pressure applied (indicated by red contours), on the flat circular and curved section skin and bone computational models

Regarding the boundary conditions employed in our work (Figure 5.22), it should be mentioned that a pressure-time history usually doesn't apply directly on a structure in a blast scenario. However, under the assumption of close proximity of a subject to the blast and the consequent incidence of an uniform blast pressure from all directions, such an application of a time varying pressure on a model directly is reasonable. Additionally, a sudden change in the moment of inertia (or motions) of skin (over less than a millisecond) with respect to a relatively stationary bone structure of an individual has been assumed to reasonably constrain the bottom of the bone section in all degrees of freedom.

Table 5.4: Pressure loads applied at different times (load steps) to simulate blast loading [1] in our computational models

Load Step	Time (ms)	Load/Pressure (MPa)
1	0-0.5	0
2	0.5-0.6	0.375
3	0.6-1	-0.05
4	1-3	0

$$P(t) = P_s e^{-\frac{t}{t^*}} \left[1 - \frac{t}{t^*} \right] \quad (5.1)$$

In the current work, based on the literature on the mechanical testing of the dermis [2], Yeoh's model parameters were determined (listed in Table 5.5) using curve fitting techniques. The reason why Yeoh's model was chosen specifically over any other non-linear material model was because it has been used recently to accurately predict the mechanical properties of the skin [147], brain [195] and breast tissues [196].

Table 5.5: Material model parameters adopted for the skin and bone computational models

Non-Linear Material Property for Dermis				
Yeoh Model Parameters	C ₁₀ (MPa)	C ₂₀ (MPa)	C ₃₀ (MPa)	d ₁ , d ₂ and d ₃
Subject 1, 2 and 3	0.948	4.946	0.01	0.222
Linear Material Properties for Epidermis				
Linear Elastic Parameters	Modulus of Elasticity (MPa)		Poisson's Ratio	
Subject 1	5.0		0.46	
Subject 2	5.25		0.45	
Subject 3	5.75		0.47	
Linear Material Properties for Hypodermis/Muscles				
Linear Elastic Parameters	Modulus of Elasticity (MPa)		Poisson's Ratio	
Subject 1, 2 and 3	100		0.45	
Linear Material Properties for Bone Section				
Linear Elastic Parameters	Modulus of Elasticity (MPa)		Poisson's Ratio	
Subject 1, 2 and 3	15000		0.23	

The epidermal mechanical properties of the Caucasian skin (Subject 1) was obtained (listed in Table 5.5) from the literature [197]. Also, in literature, the elasticity of the epidermal skin layer was reported to be about 26% higher for an African-American person compared to a Caucasian person [198-201]. The reason behind such a variation was found to be because of the amount of melanin (the pigment which gives human skin their color) content in the skin. As the skin color for Asian skin (subjects 2 and 3) would lie between that of Caucasian and African-American skin, a 5% and 15% higher modulus of elasticity was assumed for the subject 2 and subject 3 respectively, compared to the case of Subject 1 [198-201] (listed in Table 5.5). Linear elastic mechanical properties were adopted for the hypodermis (muscles) and bone section [202], which are also listed in Table 5.5. The reason behind choosing a linear material model for the epidermis and hypodermis was mainly the non-availability of non-linear experimental studies unlike in case of the dermis. Such a partly non-linear model is an improvement over most of the completely linear material models adopted in literature for skin related computational studies.

5.3.2 Results and Discussions

The average von Mises stress profiles observed typically at the flat circular and curved skin and bone section models were captured. Figure 5.23 shows the effect of the applied blast load observed on the entire bone and the skin section model for load step 2 (peak pressure), for one of the flat circular (forehead) and curved (wrist) models. Figure 5.24 captures the same, but for the load step 3 (negative pressure).

To further study the effect of blast on the bone section and the various skin layers, the stresses at each of these layers were quantified numerically over time. The following sections present the snapshots and plots for the same.

Besides studying whole body injury computationally, the current work can be extended to study blast-induced traumatic brain injury (TBI) by measurement of the subject-specific curvature of the skull and by incorporating the skin layer thicknesses and material properties from literature.

Figure 5.23: Blast loading effects at load step 2 (peak pressure) for computational models of A) Forehead of subject 3, and B) Wrist of subject 2

Figure 5.24: Blast loading effects at load step 3 (negative pressure) for computational models of A) Forehead of subject 3, and B) Wrist of subject 2

5.3.2.1 Bone Stresses

The average stresses on the bone section were estimated over time. Figure 5.25 captures the stress profile of the bone sections for a flat circular (forehead) and curved (wrist) model at load step 2 (peak pressure). Higher maximum stresses were observed for the flat circular bone section compared to the curved bone section. Also the maximum bone stress developed at the flat circular bone section (1.21 MPa) and curved bone section (0.427 MPa) were greater than the applied blast peak pressure (0.375 MPa), which can be seen in Figure 5.25 B. It can be concluded

that flat circular bone sections (like forehead and shin) are much more vulnerable to blast stresses (and consequent fracture) than curved bone sections (such as fingers, wrists and elbow). At load step 3 (negative pressure), the stresses observed at the flat circular bone section was higher than at the curved bone section (see Figure 5.26). Also, the maximum bone stress observed at both the flat circular bone section (0.173 MPa) and curved bone section (0.061 MPa) were much higher than the negative pressure (-0.05 MPa) applied at load step 3. It can be concluded that the flat circular bone sections are much more prone to blast damage due to negative pressure compared to curved bone sections.

Stress versus time has been plotted for the bone sections in all subject-specific computational models (See Figure 5.27). The main observations are: 1) The peak stress values are higher in flat circular skin and bone models compared to the curved ones, 2) For the curved models (mainly in the forehead), the subject-specific variations in bone stresses are minimal. This could be attributed to the minimal “thickness” changes in skin and bone layers in forehead, which may be an important regulator of stress than the subject-specific variation due to material properties.

Figure 5.25: Blast loading effects at load step 2 (peak pressure) for bone section of A) Forehead of subject 3, and B) Wrist of subject 2

Figure 5.26: Blast loading effects at load step 3 (negative pressure) for bone section of A) Forehead of subject 3, and B) Wrist of subject 2

Figure 5.27: Subject-Specific bone stresses over time for various skin and bone models

5.3.2.2 Hypodermal (muscle) stresses

Blast-induced hypodermal (muscle) stresses are captured for a flat circular section (forehead) and curved section (wrist) skin and bone models. The flat circular model looks thin as the hypodermal (or muscle) layer is very thin on the forehead. The maximum stress for the flat circular section (0.93 MPa) was observed to be higher than the peak blast pressure (0.375 MPa) applied at the load step 2. Compared to the maximum bone stresses discussed in the previous section, the hypodermal stresses were found to be lower in average. Also, the stress distribution was found to be much more uniform in Figure 5.29 for the curved hypodermal section compared to the curved bone section (discussed earlier). There were no sudden maximum stress build-ups (in Figure 5.29 B) unlike in bone sections.

At load step 3 (see Figure 5.30), the maximum stress at the curved surface (0.03 MPa) was found to be less than the applied negative blast pressure (-0.05 MPa). However, for the flat circular section, the maximum stress developed (0.132 MPa) was found to be higher than the applied negative blast pressure.

Figure 5.28: Subject-Specific hypodermal (muscle) stresses over time for various skin and bone models

Figure 5.29: Blast loading effects at load step 2 (peak pressure) for hypodermal skin layer of A) Forehead of subject 3, and B) Wrist of subject 2

Figure 5.30: Blast loading effects at load step 3 (negative pressure) for hypodermal skin layer of A) Forehead of subject 3, and B) Wrist of subject 2

From the stress versus time plots at the hypodermal (muscle) sections of the subject-specific computational models (see Figure 5.28), minimal variations in the stress versus time profile were observed among the three subjects in the case of forehead, shin, and also elbow. However, for the wrist, cheekbone and the finger sections, huge subject-specific variations were observed. This finding could be mainly attributed to the minimal thickness of the hypodermal (muscle) section at the elbow, forehead and the shin, compared to a reasonable muscle thickness at the wrist, cheekbone and the finger sections. Additionally for finger and wrist hypodermal sections, the subject 3 was found to experience the maximum peak stresses at both the load steps 2 and 3. The main reason behind this observation was found to be the geometrical thickness differences among the subjects. Also an inferior dependence on the subject-specific epidermal material property (see Table 5.5) was observed.

In subject 3, for the case of the cheekbone, the hypodermal stress peak at load steps 2 and 3 were observed to be the minimum. On further investigation, the subject-specific geometrical difference was found to be the major reason behind the finding, with an inferior effect of the subject-specific material property variations, which needs further investigation in the future.

5.3.2.3 *Dermal stresses*

Dermis is the thickest layer of skin where the blood vessels end. Thus any bleeding due to injury such as in blasts could be mainly attributed to the rupture of the dermis. Figure 5.31 captures the effect of blast peak pressure at load step 2 on a flat circular dermal section (from the forehead) and a curved section (from the wrist). The maximum stress at the flat circular dermis section (0.49 MPa) in Figure 5.31A was found to be greater than the applied peak blast pressure (0.375 MPa) at load step 2. However for the curved dermis section, the maximum stress was lower than the peak blast pressure. A similar finding was observed in case of load step 3 (negative blast pressure), where the applied negative blast pressure was less than the maximum stress at the flat circular dermal section, but greater than the maximum stress at the curved dermal section (See Figure 5.32). It was concluded that: 1) The curvature of the skin and bone section model indeed reduces the stress at each of the skin and bone sections, and 2) For soft materials such as the skin layers and muscles, the stress has a tendency to go below the applied blast pressure both at the peak and trough (negative pressure state).

From the blast-induced subject-specific stress versus time plots of the dermis (see Figure 5.33), a minimal change in the stress-time profile was observed for the elbow, forehead, and also the shin sections. This finding may be attributed to the extremely thin dermal layers present in all these locations. For the wrist, finger and cheekbone sections, reasonable subject-specific variations were observed in the dermal stresses with time, which however were found to be more of a sectional geometry effect than the effect of varying skin material properties.

In case of the cheekbone, similar to what was observed in the previous section, the huge variation in subject-specific dermal stresses were found (see Figure 5.33) to be due to the high sensitivity of the stresses in relation to the sectional geometrical parameters. Also, the variations in the subject-specific epidermal material properties were confirmed from our simulations to

have an inferior effect on the stresses. The cheekbone section may be studied in the future specifically for further investigating the observed subject-specific trends.

Figure 5.31: Blast loading effects at load step 2 (peak pressure) for dermal skin layer of A) Forehead of subject 3, and B) Wrist of subject 2

Figure 5.32: Blast loading effects at load step 3 (negative pressure) for dermal skin layer of A) Forehead of subject 3, and B) Wrist of subject 2

Figure 5.33: Subject-Specific dermal stresses over time for various skin and bone models

5.3.2.4 Epidermal stresses

Epidermis, which is the outermost layer of the skin, and the most elastic (or weak) was found to develop low stresses compared to the applied blast pressures for both load step 2 (peak pressure condition, shown in Figure 5.34) and 3 (negative pressure condition, shown in Figure 5.35). The stress reduction effect of the curvature was also observed with the epidermal section, like we saw with the dermis, hypodermis and the bone section in earlier sections. Figure 5.36 presents the stress versus time variations in epidermis of the various subject-specific skin and bone models. Like in case of dermis, minimal variations were observed in the stress versus time plots of the elbow, forehead, and shin. Also, for the wrist and finger, a limited subject-specific variation in the epidermal stress profile was observed over time. These observations may be because of the very small thickness of the epidermal layer in all body locations and subjects. The cheekbone epidermal section however showed significant subject-specific variations in the stress profiles. The reason behind this trend with the cheekbone is consistent with the trends observed earlier in case of the dermis, hypodermis and the bone section, due to a high influence of geometrical variations and an inferior effect of material property variations.

Figure 5.34: Blast loading effects at load step 2 (peak pressure) for epidermal skin layer of A) Forehead of subject 3, and B) Wrist of subject 2

Figure 5.35: Blast loading effects at load step 3 (negative pressure) for epidermal skin layer of A) Forehead of subject 3, and B) Wrist of subject 2

Figure 5.36: Subject-Specific epidermal stresses over time for various skin and bone models

5.4 Diabetic Foot Mechanics and Interaction with Insoles

In the current work, a novel custom insole design with arch support and ulcer isolations was tested for effective stress reduction in a diabetic foot with ulcers using Finite Element Modeling (FEM). A full scale model of the foot was developed with ulcers of different geometries and sizes at the ball and metatarsal regions of the foot. The stresses at the ulcer locations were quantified for standing and walking with and without the novel custom insole model. The effect of material properties of the insole on the ulcer stress reduction was quantified extensively. Also, the effectivity of a novel synthetic skin material was tested for offloading at the ulcers and the rest of the foot. From the analyses, significant peak stress reductions were observed at the ulcers and other foot regions due to the ulcer isolation in the novel custom insole design and the skin like material. Based on the results of the study, a working prototype of the custom insole was developed with custom ulcer isolations for effective stress reduction at the ulcers, and a skin like material which could be tailor made to a subject's foot skin mechanical property to prevent stress buildup and further ulceration.

5.4.1 Materials and Methods

A full-scale foot model was developed and ulcers were created numerically at two different locations (heel and ball of the foot). A custom insole was modeled with ulcer isolations [12] and appropriate contacts were defined between the foot and insole. Loads and constraints were assigned to the FE model to simulate standing. The following sections present the various steps in the FE modeling of the foot, ulcers and the novel custom insole model.

5.4.1.1 Geometrical Modeling

A realistic foot model was created based foot measurements from an adult male. A cardboard box with 3 measurement scales along the X, Y and Z directions was constructed to record the 3D coordinates at 850 different locations on the foot (schematic shown in Figure

5.37). Figure 5.38A shows the point cloud manually plotted using the data recorded from the measurements.

Figure 5.37: Schematic of the cardboard box constructed with measurement scales along the X, Y and Z directions to record 850 points on the foot in 3D

Out of the 850 points obtained from the measurements, 325 were connected with lines and splines to obtain the wire mesh in Figure 5.38B. Adopting a bottoms-up modeling approach, areas were obtained from lines and volumes were obtained from areas to obtain Figure 5.39A using manual operation. A custom orthotic insole model was developed (see Figure 5.39B) underneath the foot model, which conforms to the specific foot shape and follows the curves (and arch) in the model. The insole modeling process consisted of three main steps. First, all the points at the bottom side of the foot were projected on a plane 10 mm below the lowest point on the foot to construct the insole base (bottom) and to be able to have a minimum insole thickness of 10 mm (which has been shown in literature to be able to effectively relieve foot stresses [203, 204]). Second, all the points on the bottom surface of the foot were used to construct the top of the insole. Third, a bottoms-up modeling approach was employed again to develop the volume model of the insole from the points.

Figure 5.38: Foot measurement plotting in ANSYS FE software: A) Point cloud (850 points), B) Wire mesh based on lines and splines connecting points

Figure 5.39: A) Volume model of the foot, B) Volume model of the custom insole

Initial studies were conducted with the basic foot-custom-insole model, to determine the optimum meshing criteria, loading conditions and constraints (discussed in the upcoming sections). The second stage of modeling involved the creation of two circular ulcers with the diameter 15 mm and depth 5 mm [205-207], at the heel and the ball of the foot respectively (see Figure 5.40). Another foot model was developed with two ulcers with different and arbitrary geometries (and depth 5 mm) to simulate realistic ulcer shapes at the heel and ball locations (See Figure 5.40), and to also study the effect of sharp corners in ulcer geometry. Besides quantifying the induced stresses at the ulcer locations, a material sensitive study was conducted

to understand the effect of insole material property on ulcer stresses, which is discussed in detail in the upcoming section.

Figure 5.40: Ulcers isolations in the custom insoles for the ulcers simulated on the foot at the heel and ball locations: (a) Circular and same size, (b) Irregular geometries

The third stage in the analyses involved the modeling of ulcer isolations (or cut-out's) [12] in the custom insole corresponding to the ulcer geometries (Figure 5.40) and subsequent simulations to understand the stress reduction at the ulcers.

5.4.1.2 Finite Element Modeling

Meshing of the foot and custom orthotic models involved the discretization of volumes into tetrahedral elements and subsequently conducting a mesh convergence study to select the most accurate and time efficient meshes. A 20-node Solid 186 higher order quadratic tetrahedral element was used for all meshing. The Solid 186 element type was chosen specifically to account for large deflections (strains) and hyperelasticity [153]. The meshed foot model (Figure 5.41A) was connected to the meshed orthotic model (Figure 5.41B) via contact pairs which are discussed in detail in the upcoming sections. The base (bottom) of the orthotic was constrained in all degrees of freedom and uniform pressures of 0.1 MPa, 0.2 MPa and 0.3 MPa were applied to the foot model as shown in Figure 5.41 (Red colored area) to simulate standing [208-210]. The induced von Mises stresses generated at the bottom of the foot was used for the mesh convergence study. Four meshes namely coarse (2756 elements), semi-coarse (7565 elements),

fine (9843 elements) and very fine (23547 elements) were developed (see Figure 5.42) and the maximum values of the von Mises stresses on the foot were compared (Figure 5.43).

Figure 5.41: A) Meshed model of the foot with the applied pressure (red colored area), and B) Meshed model of the orthotic insole

Figure 5.42: Foot and insole meshes: A) Coarse (2756 elements), B) Semi-coarse (7565 elements), C) Fine (9843 elements) and D) Very fine (23547 elements)

From the mesh convergence study (Figure 5.43), it was observed that the maximum von Mises stress on the foot (for a particular applied foot pressure) was different going from a coarse mesh with few thousand elements through the fine mesh with approximately 10,000 elements. However, going from the fine mesh to super fine mesh, negligible difference in the maximum von Mises stress on the foot was recorded. Based on these findings, the fine mesh (with 9843 elements) was considered to be computationally suitable for further analyses.

Figure 5.43: Mesh convergence study results for different meshes

The foot loads and boundary conditions vary widely from one person to another (due to body weight, height, foot dimensions etc.) and based on the daily physical activities [211]. However, for the diabetic community, mobility is hindered due to neuropathy and incidences of foot skin cracking and ulcer formations [207, 212]. Hence, in the current work, only foot pressures in cases of standing or walking were simulated [208-210]. The main load applied was on the area indicated in Figure 5.41A. The base of the custom insole was constrained in all degrees of freedom to simulate stationary ground, and a contact pair was created between the bottom surface of the foot and top surface of the custom insole to allow effective load transfer and simulate the interaction between the foot and insole models. The contact pair chosen was flexible with a normal penalty stiffness of 1 and penetration tolerance of 0.1. The algorithm for the contact pair was based on the augmented Lagrangian method [213]. The surfaces in contact were considered fully bonded with negligible initial surface offset and penetration. Also, an automatic contact adjustment for penetration reduction and gap closure was adopted for effective representation of the contact surfaces.

The human foot structure is composed of the phalanges (distal, middle and proximal), metatarsals, the cuboid bone, talus, calcaneus, and transitions into the tibia and fibula [214]. In literature, detailed models of the foot have been developed along with the skin tissue representations to extensively understand foot mechanics [208, 215-217]. In the current work, the main focus is to study the effect of a novel custom insole design with ulcer isolations on the diabetic foot with ulcers, and hence a simple foot model has been used which includes the geometrical and material effects of all the bones and the skin tissue covering in a diabetic foot condition [208, 215-217]. The material model assumed is based on literature values of the modulus of elasticity and Poisson's ratio of the bones, cartilages, ligaments and muscles in a diabetic foot condition [218, 219] (Table 5.6). To validate the chosen material model for diabetic foot condition, standing posture was simulated with the foot FE model, and the resulting stresses were estimated. From the analysis, the peak stress on the foot model was quantified to be 0.232 MPa, which lied reasonably within the values of peak stresses (0.2-0.25 MPa) reported in literature for diabetic foot [208, 215-217].

Table 5.6. Linear elastic material properties used for the foot model to optimize the material property based on literature [208, 215-217] for a diabetic patient

Linear Elastic Parameters	Modulus of Elasticity (MPa)	Poisson's Ratio
Foot Bones [208, 215-217]	7300	0.3
Cartilage [208, 215-217]	1	0.4
Ligaments [208, 215-217]	300	0.3
Muscles [202]	100	0.45
Diabetic Foot Model	483	0.4

In the current work, commonly used custom insole materials [208, 215-217] were adopted followed by a novel human skin like material designed by Chanda and Unnikrishnan et al [4]. Figure 5.44 shows the stress versus stretch plots of ten different materials used in the study for the custom insoles with the upper and lower bounds of skin properties in literature

[2]. The skin material was used specifically because it could be tailor made to any specific diabetic condition (such as varying degrees of diabetes), any person or location of the body. The advantage it offers over traditional insole materials are twofold. First, an insole material similar to the foot skin of the diabetic patient would enhance comfort and alleviate stresses to prevent skin cracking and ulceration. Second, the soft skin like material would reduce generation of insole induced stresses transfer to the ulcer, which may accelerate wound healing. Each of the material samples in Figure 5.44 were characterized by curve fitting with different parameters of the Veronda-Westmann's hyperelastic model. For each curve fit, an R^2 correlation value calculation was performed (where R^2 can have a value from 0 through 1, 1 representing the best fit and 0 representing worst fit) to estimate the accuracy.

Figure 5.44. Ten Material systems adopted for the custom insole for the current analyses

5.4.2 Results and Discussions

The major focus of the current work was to understand the effect of a novel custom insole designed to isolate diabetic ulcers, on the ulcer and the rest of the foot. The following

sections will discuss the various results of the numerical analyses for different ulcer shapes (regular and irregular), in presence and absence of the custom insole with the ulcer isolations. Also, the effect of material property of the custom insole on the stresses induced at the ulcers were evaluated to fully understand the insole performance.

5.4.2.1 Diabetic Foot Stresses with Custom Insole with No Isolations

Standing was simulated initially with the foot in contact with a hard flat ground, and with the diabetic foot material properties estimated in materials and methods section. The resulting von Mises stress profile on the bottom of the foot is shown in Figure 5.45A. With the custom insole (with material property 3 in Figure 5.44) with no isolations, and same loads and constraints, the induced stresses were mapped at the bottom of the foot again (Figure 5.45B). There was a uniform redistribution of the stresses on the foot due to the custom insole, which is in agreement with the literature [208, 215-217]. Secondly, the peak stress went down from 0.232 MPa to 0.175 MPa and finally, the area of major stress concentration moved from the heel region towards the midfoot, which may possibly reduce the incidences of localized heel ulcers.

Figure 5.45: Foot stresses for standing: A) On hard ground, B) Custom insole

5.4.2.2 Stress Distribution with Circular Ulcers and Insole Ulcer Isolation

Circular foot ulcers were created on the heel and ball regions of the foot as explained in materials and methods section, and standing with the custom insole with no ulcer isolation was simulated. Increased stress concentrations were observed at the ulcer locations (see Figure 5.46A) compared to a foot without ulcers. Peak stresses of approximately 0.393 MPa were observed at the wall of the ulcer (Figure 5.46B), which are almost two times more intense than in a diabetic foot without ulcers (see Figure 5.45) and may not allow the ulcer to heal normally and also possibly spread out and grow in size over time [220]. In future, further studies would be conducted to understand diabetic ulcer propagation with stress. Additionally, the high stress zone around the ulcer may indicate the possible direction of ulcer growth in the X-Y plane, which could be validated with the commonly observed findings in cohort studies involving diabetic patients with ulcers [221, 222]. If proper care is not given, chronic non-healing ulcers usually leads to amputations in diabetic patients.

Figure 5.46: Foot stresses for standing with circular ulcers on custom insole without ulcer isolations: A) Bottom of the foot, B) Peak stress at the heel ulcer

The novel custom insole with the ulcer isolations [12] was simulated for the foot model with circular ulcers and standing was simulated to estimate resultant stresses. Figure 5.47A

shows the stress profile on the bottom of the foot with this insole design. Five major observations were recorded. First, the peak stress induced at the ulcer dropped to 0.133 MPa from 0.393 MPa by approximately 66 percent. Second, compared to the previous case of standing on the custom insole with no ulcer isolations (Figure 5.46A), there was a stress relief at the heel due to the ulcer isolation design. Third, zooming into the heel ulcer (Figure 5.47B), the stress was observed to be uniformly distributed along the wall of the ulcer compared to the stresses observed in the custom insole without ulcer isolation (Figure 5.46B). This finding implies that the chances of ulcer spreading over time was minimized due to the ulcer isolation design. Fourth, the stress concentration zone around the ulcer was circular and symmetric, indicating lower possibilities of ulcer growth (in Figure 5.47B) [220]. Finally, a reduction in the average stress on the foot arch section (Figure 5.47B) was observed, the cause of which is not very clearly known, and could possibly be a pressure relief effect of the ulcer isolation design in the custom insole.

Figure 5.47: Foot stresses for standing with circular ulcers on custom insole with ulcer isolations: A) Bottom of the foot, B) Peak stress at the heel ulcer

5.4.2.3 Stress Distribution with Irregular Ulcer Geometries and Insole Ulcer Isolation

In a diabetic foot condition, the foot is prone to ulceration at high stress points due to skin cracking [205-207]. Naturally occurring ulcers are not circular in geometry (as simulated in the previous section) but in different shapes and sizes. To understand the effectiveness of the novel ulcer isolation design in reducing stresses at ulcers of irregular shapes and at arbitrary locations Figure 5.48A, two ulcers were created at the heel and ball regions of the foot as discussed in the materials and methods section. The primary reason for choosing the specific ulcer geometries was to study the effect of smooth and sharp corners on the ulcer stresses. The first set of simulation was run to model standing on a custom insole with no ulcer isolations. The stress profile at the bottom of the foot in this scenario is presented in Figure 5.48A. The maximum stresses recorded were extremely high at the wall of the heel ulcer (0.93 MPa), which may be the effect of sharp corners, and possibly may result in a rapid growth of the ulcer. The maximum stress recorded at the ulcer in the ball of the foot region was 0.66 MPa, which was significantly higher than in case of circular ulcers, but lower than the heel ulcer with sharp corners. Figure 5.49A and 5.49C indicates the stress distribution at the two ulcers corresponding to Figure 5.48A.

Next the custom insole with the custom ulcer isolation [12] for the irregular ulcer shapes was simulated. From the analyses, this novel ulcer isolation design was found to phenomenally reduce the stresses (by 91.5 percent) at the ulcers (see Figure 5.48B and Figure 5.49B and 5.49D). Also, an overall stress relief was recorded with these insole isolations, making the peak stress value go way below in the case of foot without ulcers. The zoomed in views (Figure 5.49) highlights the stress distributions at the ulcer locations with no specific noticeable trends. Thereby, it was concluded that the insole ulcer isolations lead to massive stress reductions at the ulcers with no discernable patterns in the case of irregularly shaped ulcers.

Figure 5.48: Foot stresses generated due to standing with irregular ulcers on: A) Custom insole without ulcer isolations and B) Custom insole with ulcer isolations

Figure 5.49: Stress distribution at ulcers without (A, C) and with ulcer isolations (B, D)

5.4.2.4 Effect of Custom Insole Material Property on Foot Stress

The effect of material on the effectiveness of the novel custom insole design (with ulcer isolations) in reducing foot stresses was investigated. Ten different material systems introduced in materials and methods section were assigned to the custom insole model to estimate the peak stresses in the foot while standing. The Veronda-Westmann's hyperelastic coefficients for each

one of the material models were quantified using curve fitting techniques (see Table 5.7), with an average correlation index (R^2) of over 0.96. Also, in Table 5.7, the linear elastic material properties used for the diabetic foot model are indicated.

Table 5.7: Material properties adopted for foot and custom insole in the analyses

Non-Linear Material Property for Custom Insole		
Veronda-Westmann Model Parameters	C_1 (MPa)	C_2 (MPa)
Material 1	1.3	0.25
Material 2	2.5	0.21
Material 3	3.2	0.28
Material 4	7.3	0.25
Material 5	9.5	0.23
Material 6	14.2	0.29
Material 7	16.7	0.27
Material 8	21.4	0.21
Material 9	24.6	0.18
Material 10	25.4	0.22
Linear Material Property for Foot Model		
Linear Elastic Parameters	Modulus of Elasticity (MPa)	Poisson's Ratio
Foot Model	483	0.4

All the results are summarized in Figure 5.50. From the analyses, the maximum peak stresses were obtained for all material systems in the case of irregular ulcers with no ulcer isolation (see Figure 5.50). The minimum peak stresses were obtained for irregular ulcers with insole ulcer isolations. Even with circular ulcers, a considerable amount of peak stress reduction was observed with insole ulcer isolations and all insole materials. Also, with hard insole materials close to the upper bound of skin (Materials 5-10), the peak stress was found to be sensitive to the custom insole material property. However, for soft insole material configurations (Materials 1-5), the change in peak stresses with the insole material was found to

be negligible. These findings imply that excessive softening of custom insole material may not lead to any valuable peak stress reduction on the foot in all cases (no ulcers, ulcers, and with insole ulcer isolations). This is a clinically valuable finding for designing of custom insoles in the future. It can be concluded from the material study that a material system close to the material 5 would be ideal to allow effective stress reduction at the foot for all kinds of custom insoles. Additionally, the novel ulcer isolation has been found to drastically reduce stress at the ulcers (regular or irregular at any location), which validates the significance of this custom insole design [12].

Figure 5.50: Foot peak stresses for different cases with ulcers and ulcer isolation insoles, for ten different custom insole material systems

There are several limitations to the current work. First, the effect of footwear was neglected, which will have to be incorporated to obtain realistic peak stress values. Second, only circular and two irregular ulcer geometries at the heel and toe locations were studied. Realistic ulcers may have varying geometries which have to be obtained from clinical measurements in the future to obtain accurate quantitative results from the analyses. Third, a linear elastic material model was adopted for the foot and hyperelastic material properties may improve the

accuracy of the results. Also, based on the FE study, the working prototype of the custom insole developed, needs to undergo a series of mechanical tests and cohort studies before their use in patients with diabetic ulcers.

5.4.2.5 Novel Custom Insole Prototyping

Based on the results of the finite element analyses, the skin simulant material was used to develop a prototype of a novel custom insole [12] using CAD designing and then molding to a person's foot (see Figure 5.51). This custom insole model can have an isolation for one or more ulcers of any size and shape, and occurring in any section of the foot for effective stress reduction at these locations and to potentially expedite ulcer healing. The skin like material employed in fabrication of the custom insole can be tuned to match the properties of the skin of a subject specific diabetic foot to reduce chances of stress buildup on the foot and avoid further ulceration. Also, a thick side layer was retained in the insole to provide a cushion around the foot and prevent its rubbing against any footwear. Additionally, the insole size and thickness can be adjusted based on subject-specific requirements.

Figure 5.51: A) Novel custom insole CAD design and B) Prototypes insoles with different skin-simulant materials and cosmetic colors [12]

The skin simulant material used in the novel custom insoles can be molded easily into any shape or size, making the insole manufacturing process simple and cost effective. Also this material has been observed to undergo negligible deformation after cyclic mechanical tests,

which allows the insole not to wear due to prolong use [223]. The isolations in the insole also provide a location for integrating Vacuum Assisted Closure (V.A.C) technology [224] which helps in application of a negative pressure on ulcers to drain fluids and expedite healing. Other peripheral technologies such as pressure monitoring sensors, antimicrobial layer, and sweat absorbent layer could be added to the insole design during its fabrication, due to the ease of molding the skin like manufacturing material.

CHAPTER 6

SUMMARY AND FUTURE WORK

Naturally occurring soft composites or tissues form the building blocks of the human body and their multiscale mechanics affects the functioning of the body. Understanding the biomechanics of soft composite systems is the key to understand the genesis and progression of diseases. This dissertation presents a robust experimental and computational framework developed to study and characterize the mechanics of soft composite systems, soft composite damage and repair, and soft composite interactions. In this work, novel biofidelic soft composites simulating human tissues were developed and a novel experimental model was created to simulate and characterize complex biofidelic soft composites. Experimental and computational modeling was conducted using the biofidelic soft composites developed to understand soft composite damage mechanics and repair strategies. Macro scale interactions studies were conducted using high fidelity numerical techniques to understand how soft bio composites (tissues and organ systems) interact due to multi axial loadings and complex boundary conditions under normal and diseased conditions.

Chapter 2 presents a discussion on the development of isotropic biofidelic soft composites simulating the human skin, brain, arterial and vaginal tissues in normal and diseased conditions. To incorporate tissue anisotropy into the soft composite model, anisotropic soft fiber-matrix composite models were developed. Extensive mechanical tests were conducted on the anisotropic soft composites to study the effect of fiber contribution and distribution in tissues. Additionally, a multifunctional anisotropic soft composite system was introduced to

simulate skin tissue and conduct electricity, which would be valuable for improved biomechanical testing of soft composites in the future.

Chapter 3 introduces the existing soft composite characterization methods, especially the isotropic hyperelastic constitutive relations and the transversely isotropic material formulations. A novel characterization framework for anisotropic soft composites with multiple fiber families embedded in a matrix material is presented. This material model considers both the matrix and fibers as hyperelastic materials, and takes into account the matrix contribution and the individual fiber contributions, the fiber-matrix interaction, and fiber orientations for each fiber family within the soft composite. Using the novel anisotropic soft tissue characterization model, stress-strain relationships were formulated for uniaxial tension tests and the results from mechanical tests of biofidelic soft composites were curve-fitted using these novel constitutive relationships.

Chapter 4 investigates the damage and repair mechanics of soft composites using computational, experimental and imaging studies. A multi-layer skin composite model was developed numerically to understand the effect of damage (wounds) on the skin mechanics under the natural tension of the skin. Sutures were placed computationally to repair the damage and the mechanics of these sutures under varying loading conditions were studied. A robust experimental framework was developed to investigate the average stress-strain changes under tension in soft composite (skin) due to damage. The effect of damage (wound) geometry, location, size and quantity on the mechanical behavior of the soft composite was studied in detail. Digital Image Correlation (DIC) based studies were conducted to understand local strain fields around a damage (wound) in tension. The local strain changes due to varying damage (wound) geometry and size were quantified and the experimental results were validated using the imaging study.

Chapter 5 presents studies to understand the complex interactions of soft composites under multiaxial loads and boundary conditions. Three computational studies were covered which investigated the soft composite (tissue) mechanics in organ systems in normal condition and its progression to damage states (diseased conditions). The first system studied was the female pelvic system in bladder and rectal prolapse conditions, and due its interaction with a progressively weakening pelvic floor muscle composite material model. The second system studied was the effect of blasts and impacts on subject and location specific skin-muscle-bone composite models. The third system presented was a diabetic foot with ulcers and its interaction of a diabetic orthotic insole under varying loads. All the three systems studied are critical areas of studies in engineering and medicine, and provides valuable insights into macro scale soft composite interactions.

Future work will be conducted mainly in 3 areas. First, multi-layer anisotropic soft composite experimental models will be developed to more precisely simulate tissue properties. Second, soft composite damage will be studied with single and multi-layer anisotropic soft composite models using experiments and DIC techniques. Third, the novel anisotropic soft composite characterization framework will be used to model tissue properties in computational models of soft composite interactions (especially in the study of Pelvic Organ Prolapse (POP)) for accurate multiscale quantitative analyses. A robust framework will be developed to model soft tissue damage using the characterization model, and its effect on macro scale interaction of organs will be studied. These investigations would be indispensable for understanding tissue composite mechanics and its role in various diseases.

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