THESIS FOR THE DEGREE OF LICENTIATE OF ENGINEERING IN SOLID AND STRUCTURAL MECHANICS

Calibration and Modelling of Adipose Tissue Under Impact Loading

Application to Vehicle Safety

HOSEIN NASERI

Department of Mechanics and Maritime Sciences
CHALMERS UNIVERSITY OF TECHNOLOGY

Göteborg, Sweden 2017

Calibration and Modelling of Adipose Tissue Under Impact Loading
Application to Vehicle Safety
HOSEIN NASERI

Thesis for the degree of Licentiate of Engineering 2017:09
Department of Mechanics and Maritime Sciences
Chalmers University of Technology
SE-412 96 Göteborg
Sweden
Telephone: +46 (0)31-772 1000

Chalmers Reproservice
Göteborg, Sweden 2017

Calibration and Modelling of Adipose Tissue Under Impact Loading
Application to Vehicle Safety
Thesis for the degree of Licentiate of Engineering in Solid and Structural Mechanics
HOSEIN NASERI
Department of Mechanics and Maritime Sciences
Chalmers University of Technology

Abstract

Vehicular injury is one of the main reasons for traumatic injuries. Finite Element Human Body Models (FEHBM) have become very popular to assess car crashes and the subsequent injuries. It provides the possibility to predict stress and strain values in tissue level by representing anatomical structures in details. An essential requirement for the FEHBM is to exhibit human-life response, i.e. being biofidelic. Obese occupants are one of the vulnerable populations at higher risk of death and severe injuries in car crashes. However, the developed FEHBMs do not, neither in body shape nor the material properties, represent obese population. In particular, there is no appropriate constitutive model for adipose tissue (fat tissue) in FEHBMs. In the interaction between obese occupants and restraint systems both the body shape and the material property of adipose tissue plays an important role.

Therefore the first goal of this research (and the main goal of this thesis) is finding and calibrating a biofidelic constitutive model for adipose tissue. To this end a nonlinear viscoelastic constitutive model was formulated. To have a reliable model calibration at large deformation and a wide range of strain rates (similar to car crash situations), test data of two experiments were used; the frequency-sweep test and the ramp loading-unloading shear test. Prescribing the power-law relation for shear stiffness, which is suggested in the frequency-sweep test, as a constraint in the ramp loading-unloading shear test considerably improved the model prediction for large deformations and high strain rates. To investigate the effect of uncertainties in model parameters and identify important parameters in different experiments, commonly used mechanical testing setups were analyzed. Global sensitivity analysis was used for this purpose. It was found that the amount of compressibility highly affects the behavior of adipose samples in high rates. It is important specially when studying how adipose tissue behavior affects the dynamics of obese occupant responses during crash situations.

Keywords: Finite element human body models, Adipose tissue, Constitutive modelling, Obesity, Global sensitivity analysis

to TiTi

Why repeat the old errors, if there are so many new errors to commit

Bertrand Russell

Preface

The work presented in this thesis has been started on February 2015 to November 2017 at the Division of Dynamics at Chalmers University of Technology. This project is financed through the Swedish Research Council (VR), grant no. 621-2013-3909.

First of all, I would like to thank my main supervisor, Associate Prof. Håkan Johansson for the invaluable guidance, encouragement and support he has provided through these years. I like to thank my co-supervisor Prof. Karin Brolin for her advice, great discussion and positive energy. I like to also thank my colleagues for creating a warm, pleasant and productive environment.

Finally, I am grateful to my parents for their kindness and support. Especially, I like to thank my beloved wife for her love and support and encouragement and my newborn son, Ali, for the much joy and happiness he has brought to my life.

Gothenburg, November 2017
Hosein Naseri

Thesis

This thesis consists of an extended summary and the following appended papers:

Paper A	Naseri H., Johansson H., Brolin K., A Nonlinear Viscoelastic Model for Adipose Tissue Representing Tissue Response at a Wide Range of Strain Rates and High Strain Levels, In press, J Biomech Eng , (2017); doi:10.1115/1.4038200
Paper B	Naseri H. and Johansson H. A Priori Assessment of Adipose Tissue Mechanical Testing by Global Sensitivity Analysis, Submitted for international publication

The appended papers were prepared in collaboration with the co-authors. The author of this thesis was responsible for the major progress of the work in preparing the papers, took part in developing the theory, performed all implementations and numerical calculations, and took part in writing the papers.

Contents

Abstract **i**

Preface **v**

Thesis **vii**

Contents **ix**

I Extended Summary 1

1 Background and Motivation **1**
1.1 Aim 2

2 Adipose Tissue Histology **3**

3 Adipose Tissue Modelling **4**
3.1 The Constitutive Model 4
3.2 Finite Element Modelling of Common Experimental Setups 5

4 Global Sensitivity Analysis **7**

5 Summary of Appended Papers **8**

6 Conclusion and Future Work **9**

II Appended Papers A–B 13

Part I
Extended Summary

1 Background and Motivation

Vehicular injury is one of the main reasons for traumatic injuries. Vehicular crashes and subsequent injuries are studied in physical testing by mechanical models of human, anthropomorphic test devices (ATD) (also called crash test dummies) which are available in three body sizes; large male, midsize male and small female. With the advent of new advanced computers and decreasing cost of computational resources, numerical simulations nowadays are extensively used to study vehicular injuries. More detailed study can be performed if occupants are modelled with numerical human body models. A human body model is a numerical anthropomorphic model with the details of human anatomy. Basically two methods are applied for human body modelling: multi-body methods and finite element methods. In the multi-body method the body is modelled by a system of flexible and rigid bodies connected by kinematic joints. But in the finite element (FE) method anatomical structure is represented in more detail by elements. More internal organs, bones, soft tissues and muscles are included in the FE human body models which enable us to get better understanding of stresses and strains inside organs. Current FE human body models such as THUMS [1] and GHBMC [2] represent adult occupants similar to the same size as ATDs.

Obesity affects the risk of injury in vehicular crashes. A higher risk of fatality are found for obese occupants than non-obese occupants [3]. Also in [4] the increased risk of non-fatal injury such as lower extremity, upper extremity and spine injury was associated with the increased body mass index. How obesity affects the mechanism of injury is not clearly understood. Arbabi et al. [5] reported a 'cushion effect' due to an increase in adipose tissue which protects internal organs during impacts. Kent et al. [6] studied the kinematic of obese occupants. They found an increased body excursion for obese occupants and less torso forward rotation compared to non-obese occupants. Reed et al. [7] found that obesity by changing the routing of the seatbelt relative to the underlying skeletal structure increase the risk of injury. Specially the higher routing of the lap belt can cause submarining in frontal crashes. Forman et al. [8] studied midsize and obese post mortem human surrogates (PMHS) in frontal impact sled tests. They reported more chest compression and greater forward motion of head and shoulder for obese PMHS and higher chest acceleration and more number of rib fractures for midsize PMHS.

Still more studies are needed to understand how obesity affects vehicular injuries in order to improve the restraint system for obese people. But current injury assessment tools, such as ATDs and human body models, do not account the obese population. FE human body models are available only in three adult sizes which do not represent obese individuals. Recently mesh morphing technique has been used to consider geometrical variations in human body models [9, 10, 11]. In [9] a statistical human ribcage geometry model was proposed which has considered different factors including body mass effect on the ribcage geometry. Shi et al. [11] used mesh morphing technique to change the geometry of THUMS version 4 [12] midsize for obese size and presented a parametric FE human model. Then the effect of obesity on occupant response in frontal crashes were studied. The higher injury risk due to obesity was attributed to the increased mass and poor belt fit.

In addition to the shape and size of obese occupants, in the interaction between obese occupants and restraint systems during car crashes, the material properties of adipose tissue (fat tissue) affects the dynamics of response and subsequently injury mechanism. For example in the contact between the belt and body surface (mostly adipose tissue for obese individuals) material behavior of adipose tissue plays an important role to understand how the change of belt routing observed in [7] happens or how impacts are transferred into internal organs (e.g. in submarining). However, based on the best knowledge of author, there is neither an appropriate constitutive model for mechanical behavior of adipose tissue in FE human body models nor any study to investigate the effect of constitutive behavior of adipose tissue on mechanism of injury. And even there are very few reports on mechanical testing on adipose tissue in the literature [13, 14, 15, 16, 17] to accordingly develop a suitable constitutive model. Besides, the intrinsic wide variations in the physical properties of biological materials (including adipose tissue) has made the situation more challenging.

1.1 Aim

The ultimate goal of this research is to add understanding how obesity affects occupants response and subsequent injuries during car crashes. This understanding is essential to design and improve safety measures for obese population in vehicles. According to the literature, obesity will result in changes in different safety related factors among them the kinematic of occupant-restraint interaction, the kinetic energy, severity of counteracted restraint forces, the propagation of impacts into internal organs. Therefore, first, a constitutive model for adipose tissue will be formulated for use in human body simulation in crash situations. Then the effect of obesity on occupant responses will be studied. The following key questions are the center of this research.

- **Research questions at tissue level:**
  - What is the mechanical behavior of adipose tissue samples at different loading rates and large deformations corresponding to vehicular crash situations? (**Paper A,B**)
  - What is a suitable model to predict adipose tissue in vehicle crash situations? How should this model be calibrated? (**Paper A,B**).
  - Considering no adipose tissue experiments with acceptable repeatability of results in large deformation and high stain rates, how should model parameters be identified in this region? (**Paper A**).
  - Which experiment can be representative for adipose tissue behavior in vehicular injuries? Which experiment should be selected for further material parameter identification? What is the effect of uncertainty in model parameters? (**Paper B**)

- **Research questions at human body level:**
  - What is the effect of the newly formulated constitutive model in human body response compared to the current material models? (**Future work**).
  - How does the new constitutive model will affect a morphed FE human body model prediction for obese individuals? How does it change the dynamics of obese occupant responses during crashes? (**Future work**).
  - How should current injury criteria be changed to incorporate obesity effects? (**Future work**)
  - Considering the wide variation in adipose tissue properties and lack of test data, how will this uncertainty be carried over to the human body level? (**Future work**)

2 Adipose Tissue Histology

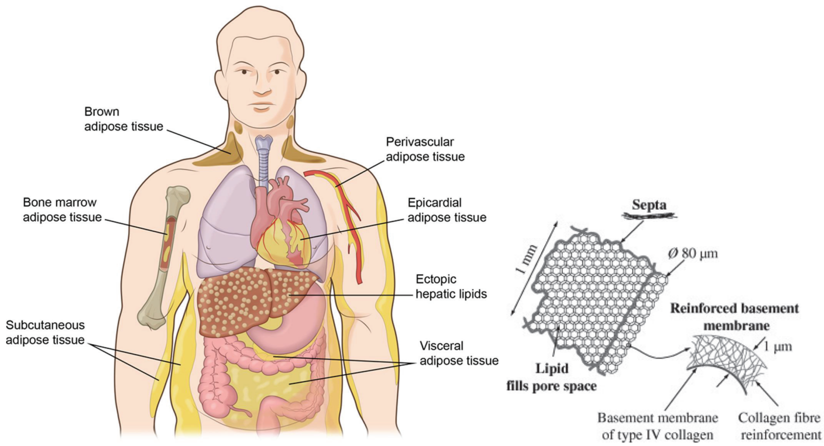

Figure 2.1: *Depot sites of adipose tissue and the anatomy*

The adipose organ constitutes several depots located throughout the human body. These depots are mainly divided into visceral and subcutaneous adipose tissue. 60–80% mass of the adipose tissue is lipid, 5–30% mass is water and the remaining 2–3% mass is composed of proteins (collagen fibers). The tissue structure is a loose association of lipid-filled cells called white adipocytes, held in a framework of collagen fibers. Lipids within the white adipocytes are organized in one droplet. The diameter of the white adipocytes ranges from 30 to 70 μm, depending on the site of deposition. At an higher level there exist an open-cell foam like structure called the interlobular septa which contain adipocyte cells and is about 1 (mm) in size. There is very little interstitial fluid in the tissue to consider it as porous media and lipid droplets in cells are completely confined. The main stiffness of tissue comes from the collagen fibers surrounds adipocyte cells and the volume fraction of interlobular septa is sufficiently low that its contribution to the macroscopic stiffness is negligible [14]. Cross-link collagen fibers and their alignment gives nonlinear properties to the tissue stiffness. Large amount of liquid in the tissue (mostly lipid droplets in cells) gives incompressibility to the tissue [14].

3 Adipose Tissue Modelling

To model adipose tissue at large deformations, a suitable kinematic framework is needed which enable us to consider large perturbations from the elastic equilibrium. This can be done by multiplicative decomposition of the deformation gradient tensor $\mathbf{F}$ into elastic and viscous parts as introduced in [18]. In order to model adipose tissue at wide range of loading rates, the generalized Maxwell model is used as the finite viscoelastic model. It incorporates one elastic chain for equilibrium response in parallel to N chains of Maxwell type for non-equilibrium response. By adding more chains, it is possible to cover wider range of impact rates for adipose tissue.

$$\mathbf{F} = \mathbf{F}_e^{(k)}\mathbf{F}_v^{(k)}, \quad k = 1, 2, ..., N \tag{3.1}$$

$$\Psi(\mathbf{F}, \mathbf{F}_v^{(1)}, \mathbf{F}_v^{(2)} ..., \mathbf{F}_v^{(N)}) = \Psi^{EQ}(\mathbf{F}) + \overbrace{\sum_{k=1}^{N} \Psi^{NEQ(k)}(\mathbf{F}_e^{(k)})}^{=\Psi^{NEQ}} \tag{3.2}$$

3.1 The Constitutive Model

Adipose tissue is usually taken as incompressible material in literatures [14] but here since adipose tissue response under impacts is studied, it is considered as a nearly incompressible material. Therefore the strain energy function Ψ in Eq. (3.2) is split further into volumetric U and deviatoric parts $\hat{\Psi}$.

$$\Psi = \overbrace{\hat{\Psi}^{EQ} + U^{EQ}}^{=\Psi^{EQ}} + \overbrace{\sum_{k=1}^{N} \left(\hat{\Psi}^{NEQ(k)} + U^{NEQ(k)}\right)}^{=\Psi^{NEQ}} \tag{3.3}$$

The neo-Hookean material model is considered for deviatoric parts while a simple function as $U = \frac{\kappa}{2}(J-1)^2$ represents the volumetric strain energy function. Correspondingly, the second Piola-Kirchhoff stress consists of elastic and inelastic (overstress) contributions which are calculated from equilibrium and non-equilibrium parts respectively.

$$\mathbf{S} = 2\frac{\partial \Psi^{EQ}}{\partial \mathbf{C}} + 2\sum_{k=1}^{N} [\mathbf{F}_v^{(k)}]^{-1} \left(\frac{\partial \Psi^{NEQ(k)}}{\partial \mathbf{C}_e^{(k)}}\right) [\mathbf{F}_v^{(k)}]^{-T} = \mathbf{S}^{EQ} + \mathbf{S}^{NEQ} \tag{3.4}$$

As suggested by [18], the evolution rule for any viscous chain is given as:

$$\dot{\mathbf{F}}_v[\mathbf{F}_v]^{-1} = \Lambda \frac{3\bar{\mathbf{M}}_{dev}}{2\tau_{eq}^{NEQ}}, \quad \Lambda = \frac{1}{t_\star}\eta(\tau_{eq}^{NEQ}) \tag{3.5}$$

where $\mathbf{M}_{dev}$ is the deviatoric part of Mandel stress and τ_{eq}^{NEQ} is the von Mises stress of the overstress. To consider nonlinear viscoelasticity and incorporate the softening behavior of adipose tissue [15, 16] the overstress function η is defined as a power-law function of τ_{eq}^{NEQ} in which n_c is the exponent ($n_c > 1$ for nonlinear viscoelasticity) and τ_c is an scaler corresponds to the stress in linear viscoelastic regions.

3.2 Finite Element Modelling of Common Experimental Setups

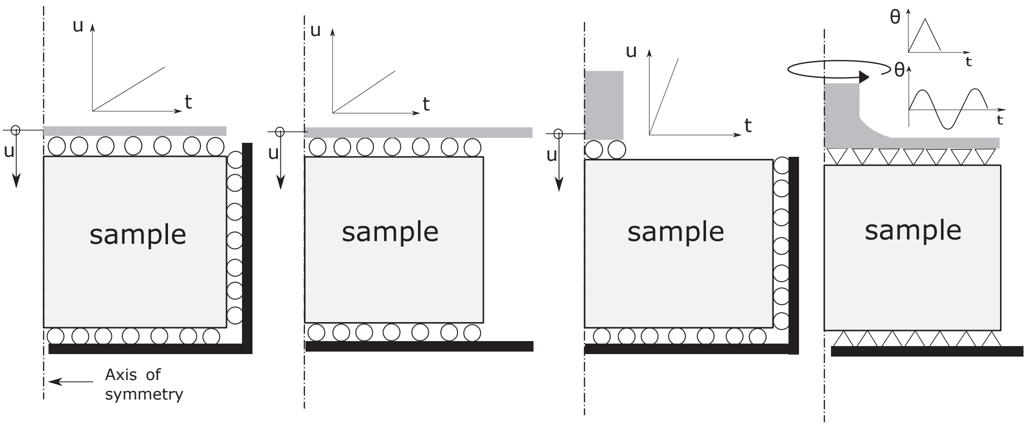

Figure 3.1: *Modelling experimental setups; loadings and boundary conditions. from left to right: confined- and unconfined-compression tests, indentation tests, rheometer tests. circle: frictionless contact, triangle: fully clamped. Black: stationary parts, grey: moving parts.*

Adipose tissue samples are usually tested in one of the following experimental setups: confined- and unconfined-compression tests, indentation tests, rotational rheometer tests. In Fig. 3.1 these setups with some possible loading conditions are shown. For the rheometer test, it can be a simple ramp loading-unloading or a sinusoidal excitation (e.g. frequency sweep test). In frequency sweep tests, a sinusoidal shear strain, $\gamma(t)$, is imposed at one frequency ω. This, in the steady state, results in a sinusoidal shear stress, $\tau(t)$

with a phase angle δ.

$$\begin{aligned}\gamma(t) &= \gamma_0 \sin(\omega t)\\ \tau(t) &= G_d(\omega)\gamma_0 \sin(\omega t + \delta)\\ &= G'\gamma_0 \sin(\omega t) + G''\gamma_0 \cos(\omega t)\\ G_d &= \sqrt{G'^2 + G''^2}, \quad \tan(\delta) = \frac{G''}{G'}\end{aligned} \tag{3.6}$$

where G' and G'' are storage and loss modulus respectively and G_d is frequency-dependent shear stiffness.

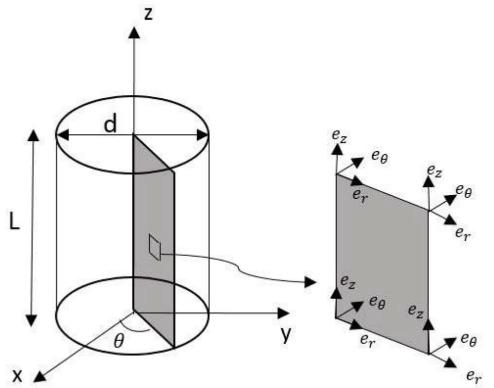

Figure 3.2: *The finite element model for adipose tissue samples and its four node quadrilateral element in cylindrical coordinates.*

The finite element model of these experimental setups is presented in cylindrical coordinates (as the cylindrical shape of samples). The undeformed position vector, $\mathbf{X}$, and the deformation vector, $\mathbf{u}$, and the deformed position vector, $\mathbf{x}$, are defined using unit vectors $\mathbf{e}_R$, $\mathbf{e}_\Theta$ and $\mathbf{e}_Z$ in the radial, circumferential and axial directions respectively.

$$\begin{aligned}&\mathbf{X} = R\mathbf{e}_R + Z\mathbf{e}_Z, \quad \mathbf{u} = u\mathbf{e}_R + v\mathbf{e}_\Theta + w\mathbf{e}_Z\\ &\mathbf{x} = \mathbf{X} + \mathbf{u}\end{aligned} \tag{3.7}$$

where R and Z are the undeformed radial and axial coordinates, and u, v and w are the displacements in the direction of cylindrical coordinate unit vectors.

Looking at all the setups, no change of material parameters is expected in samples with respect to Θ direction, i.e. $\frac{\partial(\bullet)}{\partial(\Theta)} = 0$. This holds even for the rheometer setup with $v \neq 0$. Therefore the 3-D experimental setups can be represented by only considering the $RZ-$plane and by a 2-D finite element model. But still there are 3 displacement-degrees of freedom at each point Fig. 3.2. The corresponding deformation gradient tensor $\mathbf{F}$

becomes:

$$\mathbf{F} = \begin{bmatrix} 1+\frac{\partial u}{\partial R} & -\frac{v}{R} & \frac{\partial u}{\partial Z} \\ \frac{\partial v}{\partial R} & 1+\frac{u}{R} & \frac{\partial v}{\partial Z} \\ \frac{\partial w}{\partial R} & 0 & 1+\frac{\partial w}{\partial Z} \end{bmatrix} \tag{3.8}$$

Introducing the total Lagrangian formulation [19], the momentum balance equation takes the following form after applying the spatial discretization:

$$M\ddot{U} + F_{int}(\dot{U}, U, t) = F_{ext}(t) \tag{3.9}$$

where M is the mass matrix, F_{int} is the nodal forces equivalent to the element stress and F_{ext} is nodal loads correspond to externally applied displacements. A composite implicit time integration procedure [20] is used which has been shown to be more effective for producing stable solution for nonlinear dynamic problem [20, 21]. The subsequent equations after time integration is coded and solved in Matlab R2015b.

4 Global Sensitivity Analysis

A wide individual spread of mechanical properties is an intrinsic characteristic of biological materials including adipose tissue. Therefore, modelling adipose tissue without considering this fact is not complete. Specially noticing the lack of experimental data for adipose tissue, its uncertainty is even higher. In fact since there is a range of mechanical properties for adipose tissue, any prediction and modelling should be reported in probabilistic way.

Global sensitivity analysis is served here as a tool to consider uncertainties. A possible definition of sensitivity is the study on how uncertainty in the output of a model can be apportioned to different sources of uncertainty in the inputs, [22]. This means how each input random variable contributes to the total variance of the output. Here this concept is mentioned briefly. The global sensitivity analysis is based on decomposition of the output variance. If an output variable Y depends on a vector of n independent random variables, $\mathbf{X} = [X_1, X_2, ..., X_n]^T$, via a function as $Y = h(\mathbf{X})$, then the total variance V_Y can be decomposed as:

$$V_Y = \sum_{i=1}^{n} V_i + \sum_{i<j} V_{ij} + \sum_{i<j<k} V_{ijk} + ... \tag{4.1}$$

where V_i is the reduction in V_Y as a result of fixing X_i. The same way V_{ij} considers the effect of both X_i and X_j. Two sensitivity indexes are defined in literatures: primary sensitivity S_i [23] and global sensitivity S_{Ti} [24]. An computationally efficient way for calculating these indexes is proposed in [25] which is called multiplicative dimensional reduction method (M-DRM) in which sensitivity indexes are approximated as

$$\begin{aligned} S_i &= \frac{V_i}{V_Y} \approx \frac{\theta_i/\rho_i^2 - 1}{(\prod_{k=1}^{n} \theta_k/\rho_k^2) - 1} \\ S_{Ti} &\approx \frac{1-\rho_i^2/\theta_i}{1-(\prod_{k=1}^{n} \rho_k^2/\theta_k)} \end{aligned} \tag{4.2}$$

where ρ_i and θ_i are one-dimensional integrals that can be efficiently computed by Gaussian quadrature.

$$
\begin{aligned}
\rho_i &= \int_{X_i} h(X_i, \mathbb{C}_{-i}) f_i(X_i) dX_i \approx \sum_{j=1}^{N_G} w_j h_j(X_i^{(j)}, \mathbb{C}_{-i}) \\
\theta_i &= \int_{X_i} \left[h(X_i, \mathbb{C}_{-i})\right]^2 f_i(X_i) dX_i \approx \sum_{j=1}^{N_G} w_j [h_j(X_i^{(j)}, \mathbb{C}_{-i})]^2
\end{aligned}
\tag{4.3}
$$

$f_i(X_i)$ is the distribution function for X_i, $\mathbb{C}_{-i}$ is the mid-point (also called cut-point) vector for random variables where all variables are fixed at their mid points except X_i which varies and $h(X_i, \mathbb{C}_{-i})$ is the corresponding functional evaluation. Usage of global sensitivity analysis in this research follows as

- Consider the effect of uncertainties in human body level (**Future work**)
- Assess material parameter identifiability from different experiments, **Paper B**.

5 Summary of Appended Papers

- **Paper A:**
  Performing an experiment on soft tissues with a full control and acceptable repeatability of results is practically achievable either for large deformations and low rates or small deformations and high rates. But here the behavior of adipose tissue under large deformations and wide loading rates (as the situation in car crashes) is sought. In **Paper A** the shear behavior of adipose tissue in this region was predicted. For this purpose the results of a frequency sweep test (small shear deformations and wide loading rates) was incorporated into a loading-unloading shear test (large deformations and low rates). A power-law relation for the frequency-dependent shear stiffness of adipose proposed in [15] was used in the simulation of the loading-unloading shear test. It was observed that considering both the experiments together can improve model prediction in large deformation and high rates.

- **Paper B:**
  Compared to other soft tissues, there are very few studies for characterising the mechanical behavior of adipose tissue in literatures. These studies have used different setups and loading conditions for their experiments. Sometimes the reported properties for adipose tissue are not even consistent. In **Paper B** the following fundamental questions are addressed: Which information can be obtained from a specific experiment? Which experiment should be used to identify model parameters? Which experiment can be representative for adipose tissue behavior in car crashes?

  For assessing different experimental setups, global sensitivity analysis was used. In any experiment, model parameters were considered as inputs and a measurable integral quantity from the experiment as an output. A high sensitivity index for a model parameter indicates its potential to be identified through parameter identification. It also has information regarding the mechanism of response of adipose tissue samples in a specific experiment. It is a valuable information specially to know if an experiment can be representative for adipose tissue behavior in car crashes.

6 Conclusion and Future Work

First of all by simulating adipose tissue in different experimental setups and interpreting the results, the computational framework was found reliable for our application domain. Also it was observed in **Paper A** that the shear behavior of adipose tissue at large deformations and a wide range of loading rates can be predicted better by considering its frequency-dependent shear stiffness. But for a more general response, indentation tests seems to be a good representative for adipose tissue behavior under impacts, **Paper B**. Specially it was noted that at high rates, the mechanism of tissue response was highly affected by its compressibility. Considering slightly more compressibility for adipose tissue indicates that it has both shear- and pressure-wave propagation during impacts. While nearly-incompressible material assumption leads to only pressure-wave propagation. This information is important in order to understand how impacts are transferred into internal organs.

The implementation of the new material model into human body models to see how it affects the prediction of THUMS models is for the future work. Specially the effect of material behavior of adipose tissue in the morphed human body model for obese occupants will be of main focus. Also the effect of intrinsic variations in adipose tissue properties will be studied in the human body level.

Finally, after considering the consequent material and anatomic changes due to obesity, the last step of this study will be to investigate current injury criteria and its suitability for obese individuals.

Bibliography

[1] Masami Iwamoto, Yoshikatsu Kisanuki, Isao Watanabe, Katsuya Furusu, Kazuo Miki, and Junji Hasegawa. Development of a finite element model of the total human model for safety (thums) and application to injury reconstruction. *Proceedings of the 2002 International Research Council on Biomechanics of Injury, Munich, Germany*, pages 31–42, 2002.

[2] Jaeho Shin, Neng Yue, and Costin D Untaroiu. A finite element model of the foot and ankle for automotive impact applications. *Annals of biomedical engineering*, 40(12):2519–2531, 2012.

[3] Thomas M Rice and Motao Zhu. Driver obesity and the risk of fatal injury during traffic collisions. *Emerg Med J*, pages emermed–2012, 2013.

[4] Jonathan D Rupp, Carol AC Flannagan, Andrew J Leslie, Carrie N Hoff, Matthew P Reed, and Rebecca M Cunningham. Effects of bmi on the risk and frequency of ais 3+ injuries in motor-vehicle crashes. *Obesity*, 21(1), 2013.

[5] Saman Arbabi, Wendy L Wahl, Mark R Hemmila, Carla Kohoyda-Inglis, Paul A Taheri, and Stewart C Wang. The cushion effect. *Journal of Trauma and Acute Care Surgery*, 54(6):1090–1093, 2003.

[6] Richard W Kent, Jason L Forman, and Ola Bostrom. Is there really a "cushion effect"?: a biomechanical investigation of crash injury mechanisms in the obese. *Obesity*, 18(4):749–753, 2010.

[7] Matthew P Reed, Sheila M Ebert-Hamilton, and Jonathan D Rupp. Effects of obesity on seat belt fit. *Traffic injury prevention*, 13(4):364–372, 2012.

[8] Jason Forman, Francisco J Lopez-Valdes, David Lessley, Matthew Kindig, Richard Kent, and Ola Bostrom. The effect of obesity on the restraint of automobile occupants. In *Annals of Advances in Automotive Medicine/Annual Scientific Conference*, volume 53, page 25. Association for the Advancement of Automotive Medicine, 2009.

[9] Xiangnan Shi, Libo Cao, Matthew P Reed, Jonathan D Rupp, Carrie N Hoff, and Jingwen Hu. A statistical human rib cage geometry model accounting for variations by age, sex, stature and body mass index. *Journal of biomechanics*, 47(10):2277–2285, 2014.

[10] HU Jingwen, Jonathan D Rupp, and Matthew P Reed. Focusing on vulnerable populations in crashes: recent advances in finite element human models for injury biomechanics research. *J. Automot. Saf. Energy*, 3:295–307, 2012.

[11] Xiangnan Shi, Libo Cao, Matthew P Reed, Jonathan D Rupp, and Jingwen Hu. Effects of obesity on occupant responses in frontal crashes: a simulation analysis using human body models. *Computer methods in biomechanics and biomedical engineering*, 18(12):1280–1292, 2015.

[12] Ryosuke Watanabe, Hiroshi Miyazaki, Yuichi Kitagawa, and Tsuyoshi Yasuki. Research of collision speed dependency of pedestrian head and chest injuries using human fe model (thums version 4). In *22nd International Technical Conference on the Enhanced Safety of Vehicles (ESV), WA*, pages 11–0043, 2011.

[13] Kerstyn Comley and Norman Fleck. The compressive response of porcine adipose tissue from low to high strain rate. *International Journal of Impact Engineering*, 46:1 – 10, 2012.

[14] Kerstyn Comley and Norman A Fleck. A micromechanical model for the young's modulus of adipose tissue. *International Journal of Solids and Structures*, 47(21):2982–2990, 2010.

[15] Marion Geerligs, Gerrit WM Peters, Paul AJ Ackermans, Cees WJ Oomens, and Frank Baaijens. Linear viscoelastic behavior of subcutaneous adipose tissue. *Biorheology*, 45(6):677–688, 2008.

[16] Marion Geerligs, Gerrit WM Peters, Paul AJ Ackermans, Cees WJ Oomens, and Frank PT Baaijens. Does subcutaneous adipose tissue behave as an (anti-) thixotropic material? *Journal of biomechanics*, 43(6):1153–1159, 2010.

[17] Amit Gefen and Einat Haberman. Viscoelastic properties of ovine adipose tissue covering the gluteus muscles. *Journal of biomechanical engineering*, 129(6):924–930, 2007.

[18] Stefanie Reese and Sanjay Govindjee. A theory of finite viscoelasticity and numerical aspects. *International journal of solids and structures*, 35(26-27):3455–3482, 1998.

[19] Klaus-Jürgen Bathe. *Finite element procedures.* Klaus-Jurgen Bathe, 2006.

[20] Klaus-Jürgen Bathe and Mirza M Irfan Baig. On a composite implicit time integration procedure for nonlinear dynamics. *Computers & Structures*, 83(31):2513–2524, 2005.

[21] Klaus-Jürgen Bathe and Gunwoo Noh. Insight into an implicit time integration scheme for structural dynamics. *Computers & Structures*, 98:1–6, 2012.

[22] Andrea Saltelli, Stefano Tarantola, Francesca Campolongo, and Marco Ratto. *Sensitivity analysis in practice: a guide to assessing scientific models.* John Wiley & Sons, 2004.

[23] Andrea Saltelli and Ilya M Sobol. About the use of rank transformation in sensitivity analysis of model output. *Reliability Engineering & System Safety*, 50(3):225–239, 1995.

[24] Toshimitsu Homma and Andrea Saltelli. Importance measures in global sensitivity analysis of nonlinear models. *Reliability Engineering & System Safety*, 52(1):1–17, 1996.

[25] Xufang Zhang and Mahesh D Pandey. An effective approximation for variance-based global sensitivity analysis. *Reliability Engineering & System Safety*, 121:164–174, 2014.