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The Development And Application Of A Statistical Shape Model Of The Human Craniofacial Skeleton

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Abstract

Biomechanical investigations involving the characterization of biomaterials or improvement of implant design often employ finite element (FE) analysis. However, the contemporary method of developing a FE mesh from computed tomography scans involves much manual intervention and can be a tedious process. Researchers will often focus their efforts on creating a single highly validated FE model at the expense of incorporating variability of anatomical geometry and material properties, thus limiting the applicability of their findings. The goal of this thesis was to address this issue through the use of a statistical shape model (SSM).

A SSM is a probabilistic description of the variation in the shape of a given class of object. (Additional scalar data, such as an elastic constant, can also be incorporated into the model.) By discretizing a sample (i.e. training set) of unique objects of the same class using a set of corresponding nodes, the main modes of shape variation within that shape class are discovered via principal component analysis. By combining the principal components using different linear combinations, new shape instances are created, each with its own unique geometry while retaining the characteristics of its shape class.

In this thesis, FE models of the human craniofacial skeleton (CFS) were first validated to establish their viability. A mesh morphing procedure was then developed to map one mesh onto the geometry of 21 other CFS models forming a training set for a SSM of the CFS. After verifying that FE results derived from morphed meshes were no different from those obtained using meshes created with contemporary methods, a SSM of the human CFS was created, and 1000 unique CFS FE meshes produced. It was found that these meshes accurately described the geometric variation in human population, and were used in a Monte Carlo analysis of facial fracture, which found that past studies attempting to characterize the fracture probability of the zygomatic bone are overly conservative.
Keywords

Biomechanics, Finite Element Analysis, Statistical Shape Model, Monte Carlo Analysis, Probabilistic Finite Element Analysis, Craniofacial, Fracture, Anthropomorphic Testing Device, Principal Component Analysis
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“God only knows what I’d be without you.”

-Bryan Wilson & Tony Asher
Table of Contents

1 A Proposal to use Statistical Shape Modeling to Implement a Combined Monte Carlo and Finite Element Analysis of the Human Craniofacial Skeleton................. 1

1.1 Motivation and Objectives................................................................. 1

1.2 Background....................................................................................... 2

1.2.1 The Skull..................................................................................... 2

1.2.2 Finite Element Modeling (FEA)....................................................... 5

1.2.3 Probabilistic Methods and FEA in Biomechanics......................... 7

1.2.4 Statistical Shape Modeling (SSM).................................................. 10

1.3 Outline of Research Performed........................................................ 17

1.3.1 Validation of a FE Model of Facial Impact .................................... 17
1.3.2 Creation of a Mesh Morphing Algorithm for the Human CFS ................. 18
1.3.3 SSM of the human CFS ............................................................................ 19
1.3.4 Monte Carlo Analysis of Zygoma Fracture .............................................. 20
1.4 Significance ........................................................................................................... 21
1.5 References ............................................................................................................. 22

2 Validation of a Finite Element Model of the Human Craniofacial Skeleton Through
Modal Analysis ............................................................................................................ 26

2.1 Introduction ........................................................................................................... 26
2.2 Methods ................................................................................................................. 28

2.2.1 Experimental Resonant Frequency Acquisition ........................................ 28
2.2.2 Model Creation .......................................................................................... 29
2.2.3 Mesh Evaluation ....................................................................................... 29
2.2.4 Materials Assignment ............................................................................... 30
2.2.5 Boundary Conditions ................................................................................ 31
2.2.6 Data Analysis ............................................................................................ 31

2.3 Results ................................................................................................................... 32

2.3.1 Rigid Body Motion ................................................................................... 32
2.3.2 Mesh Evaluation ....................................................................................... 32
2.3.3 Resonant Frequencies ............................................................................... 35
2.3.4 Mode Shapes ............................................................................................. 39
2.4 Discussion ................................................................................................................................. 41
2.5 Conclusion ................................................................................................................................. 44
2.6 References .................................................................................................................................. 45

3 Development of a Mesh Morphing Algorithm Applied to the Craniofacial Skeleton. 48
   3.1 Introduction .............................................................................................................................. 48
   3.2 Methods .................................................................................................................................... 51
      3.2.1 Mesh Morphing Algorithm .............................................................................................. 51
      3.2.2 Morphed Mesh Quality and Performance ........................................................................ 58
   3.3 Results ........................................................................................................................................ 60
      3.3.1 Mesh Morphing .................................................................................................................. 60
      3.3.2 Model Validation ............................................................................................................... 62
   3.4 Discussion .................................................................................................................................. 65
   3.5 Conclusion .................................................................................................................................. 69
   3.6 References ................................................................................................................................. 70

4 Validation of a Statistical Shape Model of the Human Craniofacial Skeleton ............ 73
   4.1 Introduction .............................................................................................................................. 73
   4.2 Methods .................................................................................................................................... 75
      4.2.1 Statistical Shape Model ...................................................................................................... 75
      4.2.2 Validation of SSM Generated Geometry ........................................................................... 80
   4.3 Results ........................................................................................................................................ 85
6.2 Summary of Research Performed ................................................................. 124

6.3 Significance .................................................................................................. 128

6.4 Future Directions .......................................................................................... 129

6.5 References ..................................................................................................... 132

Appendix A – Reprinting Permissions ................................................................. 133

Bryan et al. ............................................................................................................ 133

Cootes et al. .......................................................................................................... 134

Li et al. .................................................................................................................. 135

Willing et al. ......................................................................................................... 136

Yoganandan et al. ................................................................................................. 137

Zingg et al. .......................................................................................................... 138

Appendix B – Detailed Specimen Information .................................................... 139

Appendix C – Mesh Morphing and Natural Frequency Results for Non-Experimental Craniofacial Specimens ................................................................. 140

Appendix D – Pseudocode for the Morphing Algorithm .................................... 143

Curriculum Vitae .................................................................................................. 149
List of Tables

Table 2-1 - Percent change in numerically derived resonant frequency values across different mesh densities for each specimen. ................................................................. 33

Table 2-2 – Difference between experimental and calculated resonant frequency values for each specimen in terms of root mean square error, average percent error, and absolute % error .................................................................................................................. 35

Table 2-3 – Intra-class correlations between experimental and calculated resonant frequencies. ........................................................................................................ 35

Table 2-4 – Average deviation and standard deviation values of frequency pairs corresponding to Bland-Altman plots. ................................................................. 39

Table 3-1 – Difference between resonant frequency values calculated using manually created and morphed meshes in terms of root mean square error, average percent error, and absolute % error. ........................................................................................................ 63

Table 3-2 – Intra-class correlations calculated for resonant frequency values as calculated using manually created and morphed meshes ......................................................................................................... 63

Table 3-3 – Average deviation and standard deviation values of frequency pairs corresponding to Bland-Altman plots. ................................................................. 65

Table 4-1 – List of craniometric measures used in the geometric validation of SSM produced skull sample................................................................................................. 84

Table 4-2– Howells (sub-populations) and SSM correlation matrices. All off-diagonal correlations were significant at p < 0.01 .................................................................................. 90

Table 4-3 – 95% confidence intervals with Cohen’s d and p-values calculated from t-tests conducted between Howells and SSM generated skull populations.......................... 91
Table 4-4 – Comparison of craniometric measurements between Howells populations and SSM generated models using average error (±σ) in mm. ................................................................. 92

Table 4-5 – ICC values comparing automated and manual CFS metric measurements... 92

Table 5-1 – Summary of results from multivariate multiple linear regression analysis. Significant effects are bolded. The Model Significance row lists each independent variable’s p-value for the entire linear model. The Between-Subjects Effects row lists each independent variable’s p-value for a corresponding dependent variable, with beta values underneath in brackets. ......................................................................................................................... 114

Table 5-2 - Comparison of fracture classification proportions between the Monte Carlo analysis and previous clinical investigations. ................................................................. 120
List of Figures

Figure 1-1 – The bones of the Cranium and Skull. Figure from Human Anatomy ©2012, Benjamin Cummings, p. 141 ......................................................................................................................... 3

Figure 1-2 – Fracture classification system as described by Zingg et al.23 .......................... 5

Figure 1-3 – Discretization of a skull from 3-D geometry into a finite element mesh...... 6

Figure 1-4 – Pareto Curve points from Willing et al.26 Traveling along the pareto solution points, optimizing for kinematics (decreasing the value J\textsubscript{kin}) necessitates a less optimal solution for durability (increasing the value of J\textsubscript{dur}) ........................................................... 8

Figure 1-5 – 5-95% knee force-displacement corridors in the anterior-posterior direction. The curves were generated in a Monte Carlo analysis where 200 unique FE models using unique ligament parameters, such as insertion points and stiffness29 ........................................... 9

Figure 1-6 – Studies employing FE analysis of skull biomechanics. Each only used a single craniofacial geometry, focusing on parametric analyses of other parameters, such as suture formation or material properties. Figure adapted from Li et al.41 ................................................. 10

Figure 1-7 – Shape instances $\mathbf{x}_i$ within an allowable shape space, along with the average shape $\mathbf{x}$. The shape space in this figure is represented by a 3-D ellipsoid volume for illustrative purposes, however, in reality, shape domains are commonly of many more dimensions. ................................................................................................................................. 12

Figure 1-8 – a) A training set of electrical resistors, taken from Cootes et al. 199542, with a set of 32 landmarks used to define each resistor in the training set. b) The average shape of the resistors showing the spread of selected individual landmarks. ............................. 12

Figure 1-9 – The modes of variation of points within the shape space are defined by three principal components in this simplified 3-dimentional example. Since the thickness of the space in the direction of PC3 is small (the 3-D volume is squished into a thin disk) compared to PCs 1 and 2, most of the variation of the data occurs with respect to PCs 1
and 2, and the 3-D shape space can be approximated as a 2-D circle without sacrificing much information of the total variability in the shape space. ........................................... 14

Figure 1-10 – The impact of varying the weighting of the largest and most influential eigenmode on resistor shape from the example in Cootes 1995\textsuperscript{42}. Note how each resistor is still of the same class (\textit{i.e.} is still resistor-shaped), but has a unique geometry. ............ 15

Figure 1-11 – The influence on shape and material distribution due to varying the weighting of the first and most influential eigenmode between $-\lambda_1 \leq b_1 \leq \lambda_1$ in a statistical shape model of the femur\textsuperscript{10}. It is apparent that this eigenmode mostly scales the femur axially, with some effect on cortical thickness. ................................................................. 16

Figure 2-1 - Resonant frequency values for specimen 1641 using mesh densities with 1) no restriction on maximum edge length 2) maximum edge length restricted to 2 mm 3) maximum edge length restricted to 1 mm................................................................. 33

Figure 2-2 - Mesh element distributions for a) radius ratio ($\rho$), b) mean ratio ($\eta$), and c) element condition ($\kappa$) number. ................................................................................................................. 34

Figure 2-3 – Comparison of numerically and experimentally derived resonant frequency values for each CFS specimen. .................................................................................................................. 36

Figure 2-4 - Bland-Altman plot comparing experimental (gold standard) and calculated values for all resonant frequencies of all specimens. The average error is $-206$ Hz with a standard deviation of 296 Hz. The blue line is the average deviation and the red lines represent a 95% confidence interval ($\pm 1.96\sigma$). ................................................................. 37

Figure 2-5 – Bland-Altman plots comparing experimental (gold standard) and calculated values for all resonant frequencies for individual specimens. The blue line is the average deviation and the red lines represent a 95% confidence interval ($\pm 1.96\sigma$). ...................... 38

Figure 2-6 – Mode shape visualizations and descriptions for Specimen 1652 ................ 40
Figure 3-1 - Visualization of the determination of two distance vectors \( DS_i \) and \( DS_i + 1 \) corresponding to nodes \( n_i \) and \( n_i + 1 \) in the mesh morphing algorithm. Note that once all the \( DS_i \) are determined going from \( SS \) to \( ST \), \( DS_j \) will be determined for \( ST \) to \( SS \)...... 53

Figure 3-2 – 2-D illustration of mesh untangling process. a) Tangled elements (red) are identified, and their connected nodes (light blue) grouped into a sub-set. b) Proceeding serially through the node sub-set, a sub-mesh is created (green and red) by selecting all elements connected to the current node (dark blue). c) The untangling algorithm operates on the sub-mesh by minimizing the sum of the inverse element scores of the submesh, simultaneously untangling elements and improving element quality. d) The algorithm moves to the next node in the sub-set (dark blue). If the submesh produced by this node is already untangled, the algorithm proceeds to the next node............................................ 57

Figure 3-3 – Averaged cumulative distribution curves of \( \rho \), \( \kappa \), and \( \eta \) for morphed (red) and manually created (black) meshes. For all measures, maximum corridor width was 0.02 for manual meshes and 0.05 for morphed meshes................................................................. 61

Figure 3-4 – Comparison of resonant frequency values as calculated using manually created and morphed meshes................................................................. 62

Figure 3-5 – Pooled Bland-Altman plot comparing the resonant frequencies using manually created (gold standard) and morphed meshes. The blue line represents the average deviation with red lines representing a 95% confidence interval.............................................. 64

Figure 3-6 – Bland-Altman plots of FE calculated resonant frequencies using manually created (gold standard) and morphed meshes. The blue line represents the average deviation with red lines representing a 95% confidence interval.............................................. 64

Figure 3-7 – Mesh morphing iteration number versus mean distance of all nodes on CFS specimen source meshes to their targets (mm). All specimens were morphed for 20 even if the cutoff of 0.05 mm before all iterations were completed.................................................. 68
Figure 4-1 – Common coordinate system defined for CFS specimens in the SSM Training Set. The Frankfurt Plane is illustrated, and the porions and orbitales used in its definition highlighted. ................................................................. 77

Figure 4-2 – Representation of the average skull shape from the training set. ................. 82

Figure 4-3 – Eigenvalue decay representing the accumulated percentage of shape and stiffness variation inherent in the SSM training set. ................................................................. 85

Figure 4-4 – Visualizations of +/-2σ (green/red) of the first 9 (E1-E9) eigenvectors for CFS geometry ................................................................................................................. 86

Figure 4-5 – Visualizations of +/-2σ of the first 9 (E1-E9) eigenvectors for CFS stiffness distribution .................................................................................................................. 87

Figure 4-6 – Comparison of symmetry scores between SSM produced CFS models and a population of 32 specimens from Willing et al using a whisker plot. The red line represents the median, the lower and upper blue boundaries represent the 25th and 75th percentiles respectively, and the whiskers extend to the most extreme values. ........................................ 88

Figure 4-7 – Scatterplots of the relationship between cranial breadth (XCB) and a) facial breadth (ZYB), facial height (NPH), and cranial length (GOL). ............................................. 89

Figure 4-8 – Comparison of normalized craniometric measurement distributions using a) all Howells data and b) Howells specimens of European descent. Measurement values (mm) are on the x-axis, with proportion of total population on the y-axis. ...................... 91

Figure 4-9 – Bland-Altman plots comparing CFS dimensions measured using manual and automated methods (mm). ......................................................................................... 93

Figure 5-1 –a) Loading node set and b) load direction axis used for the FE simulations. ................................................................................................................................. 106

Figure 5-2 - Nodes set to pinned boundary conditions for the Monte Carlo finite element simulations. ............................................................................................................. 107
Figure 5-3 - Regions of interest used in FE model fracture classification system ....... 108

Figure 5-4 – Inferior view of the craniofacial skeleton showing craniometric measurements investigated for association with craniofacial fractures.................................................. 110

Figure 5-5 - Proportion of finite element simulation resulting in at least one ROI experiencing fracture. ..................................................................................................... 111

Figure 5-6 – Breakdown of fracture types as predicted by finite element simulations. . 112

Figure 5-7 - Representative examples of FE simulations resulting in fractures of types A1, A2, A3, and B/C.............................................................................................................. 112

Figure C-1 - Averaged cumulative distribution element quality curves of $\rho$, $\kappa$, and $\eta$ for morphed (red) and manually created (black) meshes. For all measures, maximum corridor width was 0.02 for manual and 0.05 for morphed meshes. ............................................. 141

Figure C-2 – Bland-Altman plot comparing the FE calculated free vibration natural frequency values using manually created (the gold standard reference) and morphed meshes. ............................................................................................................................ 142

Figure D-1 – Pseudocode for Morph .......................................................................................................................... 144

Figure D-2 – Pseudocode for calc_def_field_subset.......................................................... 145

Figure D-3 – Pseudocode for calc_disp_field.............................................................. 146

Figure D-4 – Pseudocode for diffusion_main ................................................................. 147

Figure D-5 – Pseudocode for untangle_main................................................................. 148
List of Abbreviations

CFS – Craniofacial skeleton.

EUL/EUR – Location of the left/right euryons, the most extremely lateral points on the cranial braincase.

FE – Finite element (as in Finite Element Mesh).

G – Location of the glabella, a smooth, raised region on the frontal bone just above the nasion and between the eyebrows.

GOL – Cranial length (Gonion-Opisthocranion distance).

Hz – Hertz, unit of measure for frequency.

MC – Monte Carlo (as in Monte Carlo Analysis).

N – Location of the nasion, the point in the midline of the face where the nasal and frontal bones intersect.

NPH – Facial height (nasion-prosthion distance).

O – Location of opisthocranion, the most extremely posterior point on the cranium in the SSM – Statistical shape model.

P – Location of prosthion, the most anterior point on the maxillary alveolar process in the sagittal plane.

XCB – Cranial breadth (distance between the euryons).

ZYB – Facial breadth (distance between the zygions).

ZYL/ZYR – Location of the left/right zygions, the most extremely lateral points on the zygomas.
A Proposal to use Statistical Shape Modeling to Implement a Combined Monte Carlo and Finite Element Analysis of the Human Craniofacial Skeleton

1.1 Motivation and Objectives

The human craniofacial skeleton (skull) is the primary structure protecting the brain from external trauma. There is growing evidence that facial fractures are associated with both minor and major brain damage\(^1\), and considering that in 2007, the management of skull fractures topped $1 billion in the United States alone\(^2\), the importance of understanding the mechanics of skull impact and fracture has never been more apparent.

Through various modes of instrumentation, researchers have attempted to measure the forces, strains, and accelerations characterizing skull fracture\(^3^-^9\); however, many of these studies are necessarily destructive, making it difficult and expensive to explore different combinations of fracture conditions. Furthermore, the amount of detail that can be acquired from physical experiments is limited, as transducers such as strain gauges only collect data at discrete locations.

Finite element (FE) methods offer an attractive alternative to *in-vitro* biomechanical investigations since they are implemented via computer hardware and thus non-destructive. Furthermore, they allow for the calculation of field variables (such as strain) throughout the volume of the object of interest instead of at discrete points. Still, the extraction of accurate anatomical geometry from medical images to build the required FE mesh is a slow, tedious process. As a result, FE analyses in biomechanics tend to use small sample sizes, limiting the applicability of any conclusions to the general population\(^10\).
To address this issue, probabilistic methods have been used to incorporate geometric variability in FE analysis. Statistical shape modeling (SSM) quantifies the primary modes of shape variation in a sample (or “training set”) of a given class of object (e.g. the skull) using principal component analysis (PCA). By exploring the shape space as defined by the space’s principal components, a unique shape instance can be created. Applied to FE analysis, SSM can automate the generation of an arbitrary number of FE meshes, each with a unique size and shape. This approach has already been used in analyses of the femur\textsuperscript{10–12}, shoulder\textsuperscript{13}, and knee\textsuperscript{14}. The objective of and motivation behind this thesis is to use SSM as a tool to incorporate the geometric and material variability in FE analysis of the craniofacial skeleton (CFS), and to demonstrate the utility of such a model to improve real-world biomechanical surrogates.

1.2 Background

1.2.1 The Skull

1.2.1.1 Anatomy & Structure

The bones of the skull can be divided into two groups: those of the cranium, and those of the face (Figure 1-1). In the cranium, the large occipital, parietal, frontal, and temporal bones are made of thick plates of cortical bone. They form the braincase, supporting and protecting the brain from injury. These bones are also fairly flat and broad, providing large attachment areas for muscles of the face and cervical spine. The butterfly-shaped sphenoid bone, situated approximately at the center of the skull in the sagittal plane, acts as a kind of keystone, articulating with every other cranial bone. The ethmoidal bone blends into the structures of the face, forming parts of the orbital walls, cranial floor, and roof of the nasal cavity.
The bones of the face provide additional attachment points for facial muscles, and support features of the digestive and respiratory tracts. These include the maxillae, palatine bones, nasal bones, inferior nasal conchae, lacrimal bones, the vomer, mandible, and the zygomatic bones.  

1.2.1.2 Fracture of the Zygoma  

The zygoma forms the prominent structure on the upper check, just inferior and lateral to the orbit. It forms one of the main buttress structures of the face, transmitting force from the dentition to the cranial base, and as such, it is made of dense cortical bone.

The Zygoma is of particular interest in terms of facial fracture because it accounts for 13% of all facial fractures. Zygomatic fractures are also the most frequent facial fracture where only one bone is involved, and second only to nasal bone fractures in overall frequency.
This is primarily due to its exposed position on the side of the face, making it particularly vulnerable in cases of assault or sporting incidents. The zygoma is also commonly fractured as a result of the face impacting the steering wheel due to vehicular collisions, an occurrence which persists despite the development of safety design features such as energy-absorbing wheels and airbags\textsuperscript{17}.

Despite several attempts to classify fractures of the zygoma\textsuperscript{18–21}, no single classification system that has been widely adopted due to the many ways in which fractures can present\textsuperscript{22}. The most favored system is that developed by Zingg \textit{et al}, which accounts for the three-dimensional nature of zygomatic fracture (which often includes dislocation), and describes fracture with respect to the zygoma’s articulations with other major bones of the face\textsuperscript{23,24}.

In this system, fractures are split into one of three major groups. The first is type A, which is divided into three sub-categories: fracture of the zygoma at one of its three articulations with either the maxilla at the infraorbital rim, the frontal bone at the lateral orbital rim, or with the zygomatic process of the temporal bone at the zygomatic arch. (It is noted that Zingg specifies that the zygoma also articulates with the greater wing of the sphenoid bone, but does not include this articulation in the fracture classification system.) Fracture at all of these articulations concurrently, resulting in displacement of the zygoma, is classified as a Type B fracture. Type C fractures are a special case of Type B where comminution of the zygomatic bone occurs in addition to dislocation.
1.2.2 Finite Element Modeling (FEA)

1.2.2.1 What Is FEA?

Finite element (FE) modeling is a mathematical framework that describes objects as being composed of many smaller elements of finite size, as opposed to being continuous (Figure 1-3). Elements connect with one another at nodes, and collectively form a FE mesh. In a FE model, the response of a physical system is the result of the combined responses of each element, which are described by closed-form equations that can be solved numerically. This offers an alternative to a continuous model when object geometry becomes overly complex, but is more calculation-intensive since the number of equations increases with
mesh fineness. In general, a fine mesh (i.e., many small elements) is more accurate than a coarse mesh (i.e., fewer large elements), creating a trade-off between model accuracy and computation time; however, computer hardware has developed to the point where FE meshes composed of millions of elements can be solved in a matter of hours.

![Figure 1-3 – Discretization of a skull from 3-D geometry into a finite element mesh.](image)

### 1.2.2.2 FEA in Biomechanics

Being an approximation of physical reality, a FE model is built on assumptions that require validation against experimental data before it can be used to make predictions about the physical world. In biomechanics, this is often performed through the static loading of bones, and correlating surface strains recorded from strain gauges with FE strains calculated at the corresponding location on the FE model\(^7\).\(^{25}\).
Once a FE model is validated, input parameters can be changed relatively easily (and cheaply) in computer software. This sort of flexibility facilitates parametric analysis, where model inputs are varied, or perturbed, to quantify their effects on corresponding outputs\textsuperscript{25}.

Parametric analysis has been quite fruitful in the field of biomechanics, yielding a valuable tool in the characterization of design objectives in orthopaedic implants\textsuperscript{26}, improving the understanding of the elastic properties of bone\textsuperscript{27}, and predicting the response of bone to different implant designs\textsuperscript{28}, to name just a few applications.

1.2.3 Probabilistic Methods and FEA in Biomechanics

The existence of variability in biomechanical parameters such as anatomic geometry, material properties, and the insertion points of ligaments and tendons, is a pervasive issue in biomechanical research. It is important to acknowledge that this variability has a large effect on the outcomes of patient interventions such as orthopaedic joint replacement or reconstructive surgery. As a result, biomechanical studies that don’t account for the full spectrum of parameter values may be limited in their application.

The ability to automatically vary key parameters of interest through numerical experiments has afforded biomechanical researchers a powerful means of efficiently exploring the design space of orthopaedic implants using parametric studies in combination with FE analysis. This enables a deeper understanding of which variables are of importance to a particular outcome of interest. For example, Willing et al. used parametric analysis to vary 14 design parameters of the tibial and femoral components of an orthopaedic knee implant\textsuperscript{26}. The study was able to quantify the competing goals of kinematics and durability
in a Pareto Curve (Figure 1-4), which describes the limit where changing design parameters to improve one design objective necessarily reduces performance in a competing objective.

Parametric analyses of biomechanical systems reveal how outcomes might change with respect to inputs, which can yield very useful information. However, just as important is the determination of the likelihood of any particular outcome. An FE analysis is a deterministic model, however the inputs exist as probabilistic distributions, which need to be accounted for when considering whether or not a specific combination of variables, and thus a specific outcome, is likely to occur.

Figure 1-4 – Pareto Curve points from Willing et al.\textsuperscript{26} Traveling along the pareto solution points, optimizing for kinematics (decreasing the value $J_{\text{kin}}$) necessitates a less optimal solution for durability (increasing the value of $J_{\text{dur}}$)
Figure 1-5 – 5-95% knee force-displacement corridors in the anterior-posterior direction. The curves were generated in a Monte Carlo analysis where 200 unique FE models using unique ligament parameters, such as insertion points and stiffness\(^29\).

The Monte Carlo (MC) method is one approach researchers have taken to incorporate parameter probability. In MC analysis, input parameters are sampled randomly from their respective probabilistic distributions, with the resulting distribution of the output variable(s) characterizing the likelihood of a given result. For example, Baldwin et al. performed 200 FE analyses of the knee joint while randomly varying ligament stiffness, reference strain, and attachment point locations to generate 5-95 percentile corridors describing the force-displacement behavior of anterior-posterior and internal-external laxity in the knee joint (Figure 1-5)\(^29\). MC analysis has also been applied to study the influence of material properties in cervical spine on disc annulus stress\(^30\), as well as activation levels of lower limb muscles on knee loading\(^31\), and other examples involving bone material properties, joint axes, and gait mechanics\(^32–34\).
1.2.4 Statistical Shape Modeling (SSM)

Variation of mesh-independent inputs, such as insertion points or material properties, can be incorporated into a FE model simply by specifying a configuration vector in a programming script. However, accounting for variation in anatomical shape is a much more challenging problem because making an individual FE mesh from a CT scan is a tedious procedure. While commercial software packages provide sophisticated algorithms for extracting and meshing geometry from medical images, bone shapes are highly irregular, and a quality mesh requires much manual intervention. Thus, many FE investigations of the skull use small samples (some as few as one), putting more effort into increasing the accuracy and fidelity of a single model at the expense of the ability to generalize due to under-representation of geometric variability\textsuperscript{35–40} (Figure 1-6).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{skull_images.png}
\caption{Studies employing FE analysis of skull biomechanics. Each only used a single craniofacial geometry, focusing on parametric analyses of other parameters, such as suture formation or material properties. Figure adapted from Li \textit{et al.}\textsuperscript{41}.}
\end{figure}
While much can be gained from a single, thoroughly validated model, there is great potential in creating tools that would allow FE analyses to incorporate geometric variability. Recently, researchers have turned to Statistical Shape Modeling to achieve this. Statistical Shape Modeling (SSM) is a procedure originally developed in image processing that has been used to describe shape variation inherent in a particular class of object. By training a single mesh topology to a set of training objects that are of the same class, a SSM can automatically produce new unique geometries within that shape class.

1.2.4.1 Implementation of SSM

In SSM, \( m \) objects of the same class (e.g. m skulls) form a training set, or representative sample, and are subsequently discretized using a set of corresponding landmarks. After first describing all instances in a common coordinate system (hence eliminating variation in position among training set instances, which is rarely of interest), each instance is recorded as a unique point, \( \mathbf{x}_i \) in a domain called an allowable shape space. The shape space consists of \( d \times n \) dimensions, where \( n \) is the number of landmarks used to discretize a shape and \( d \) is the number of degrees of freedom required to define each landmark:

\[
\mathbf{x}_i = \begin{bmatrix} x_{i1}, x_{i2}, x_{i3}, \ldots, x_{ij}, \ldots x_{id \times n} \end{bmatrix}^T, \quad i = 1 \ldots m
\]

The average shape \( \mathbf{\bar{x}} \) of the \( m \) training set objects is calculated as in Figure 1-7. Figure 1-8 illustrates this procedure using a simple 2-D example involving training the outline of a set of electrical resistors, as it was presented in the seminal shape modeling paper by Cootes et al. Each resistor is defined using 32 corresponding landmarks (i.e., \( n = 32 \)), where each landmark is defined by an x- and y-coordinate (i.e., \( d = 2 \)). Thus, each resistor represents one point in the domain of a 64-dimensionsal shape space (i.e., \( d \times n = 64 \)).
Figure 1-7 – Shape instances $x_i$ within an allowable shape space, along with the average shape $\bar{x}$. The shape space in this figure is represented by a 3-D ellipsoidal volume for illustrative purposes, however, in reality, shape domains are commonly of many more dimensions.

$$\bar{x} = \frac{1}{m} \sum_{i=1}^{m} x_i$$

Figure 1-8 – a) A training set of electrical resistors, taken from Cootes et al. 1995, with a set of 32 landmarks used to define each resistor in the training set. b) The average shape of the resistors showing the spread of selected individual landmarks.
Principal component analysis (PCA) is then used to describe the variation between the training set objects within the shape space. First, the deviation of each object from \( \bar{x} \) is calculated:

\[
dx_i = x_i - \bar{x}
\]

(3)

from which a covariance matrix is calculated:

\[
S = \frac{1}{m} \sum_{i=1}^{m} dx_i dx_i^T
\]

(4)

The eigenvectors \( \phi_k \), and corresponding eigenvalues \( \lambda_k \), of \( S \) are:

\[
S \phi_k = \lambda_k \phi_k
\]

(5)

where each eigenvector \( \phi_k \) \( (k = 1...m - 1) \) describes one mode of variation (i.e., a way in which landmarks change with respect to one another). An eigenvector’s influence on object shape is related to the magnitude of its corresponding eigenvalue, such that large eigenvalues indicate dominant eigenvectors. Thus, the \( n \times d \)-dimensional shape space can be simplified to \( t \)-dimensions, \( t < n \times d \), where \( \phi_1, \phi_2, ..., \phi_t \) encapsulate the majority of the shape variation (Figure 1-9).
14

Figure 1-9 – The modes of variation of points within the shape space are defined by three principal components in this simplified 3-dimensional example. Since the thickness of the space in the direction of PC3 is small (the 3-D volume is squished into a thin disk) compared to PCs 1 and 2, most of the variation of the data occurs with respect to PCs 1 and 2, and the 3-D shape space can be approximated as a 2-D circle without sacrificing much information of the total variability in the shape space.

Combining the average shape plus a linear combination of eigenvectors creates a unique shape within the shape space:

\[ x = \bar{x} + \Phi b \]  \hspace{1cm} (6)

where \( \Phi = (\varphi_1, \varphi_2, ..., \varphi_t) \) is the collection of eigenvectors, and \( b = (b_1, b_2, ..., b_t)^T \) is a vector of weightings. The range of values \( b_1, b_2, ..., b_t \) must be large enough to encapsulate sufficient population variance, while still creating instances of valid geometry. As it can be shown that the variance of \( b_k \) is \( \lambda_k \), Cootes et al. suggest the range of \( b_k \) as three standard variations, \(-3\sqrt{\lambda_k} \leq b_k \leq 3\sqrt{\lambda_k}\). Continuing with the example of the electrical resistors, Figure 1-10 shows the influence of weighting \( b_1 \) on the first mode of variation \( \varphi_1 \):
1.2.4.2 SSM in Biomechanics

Due to computing constraints at the time of its development, early implementations of SSM in biomechanics used only 2-dimensional landmarks \((d = 2)\)\(^{43,44}\). Since computing capabilities have progressed, 3-D, 4-D, and higher dimensional landmarks (dimensions higher than three involve assigning scalar values, such as temperature, concentration, or density to nodes in addition to coordinates) have been incorporated as well.

Using a training set of 21 femurs, Bryan et al. \(^{10}\) used SSM to drive a Monte Carlo analysis of hip fracture (Figure 1-11), the epidemiology of which matched closely with clinical reports. When the training set was expanded to 41 femurs, variability in anatomic measurements of the specimens generated by the SSM displayed good agreement with a public database\(^{12}\).

**Figure 1-10** – The impact of varying the weighting of the largest and most influential eigenmode on resistor shape from the example in Cootes 1995\(^{42}\). Note how each resistor is still of the same class (\(i.e.\) is still resistor-shaped), but has a unique geometry.
Figure 1-11 – The influence on shape and material distribution due to varying the weighting of the first and most influential eigenmode between $-\sqrt{\lambda_1} \leq b_1 \leq \sqrt{\lambda_1}$ in a statistical shape model of the femur. It is apparent that this eigenmode mostly scales the femur axially, with some effect on cortical thickness.

Statistical shape modeling has also been applied to systems of multiple structures. Yang et al. applied SSM to the primate shoulder, modeling humerus and scapula alignment, while Baldwin et al. applied SSM to soft tissue structures, predicting variations in cartilage thickness and alignment in the knee joint.

There is currently only one study which applies SSM to the skull. The training set for this model contained infants of 0–3 months of age, a developmental period that displays extreme changes shape. The goal of this study was to understand how certain craniometric measurements of the skull related to one another over time during early human development.

This study did not enjoy the same automation potential afforded other shape models. Particularly important to the development of the adolescent skull is the tracking of skull suture boundaries, and thus, each specimen in the training set needed to be manually digitized at landmarks of interest such as at suture boundaries. A total of 92 landmarks were used, however some were automatically generated through parametric definitions.
with other landmarks. Skull thickness was also of interest, and thus thickness values were manually measured at each landmark, requiring further manual intervention. These requirements resulted in a much increased time requirement to develop the training set as compared to previously described automated studies investigating the femur\textsuperscript{10}.

1.3 Outline of Research Performed

The goal of this thesis is to develop computational tools necessary to create and validate a SSM of the CFS of the adult human, to use these tools to automatically generate unique FE meshes of the CFS, and to use these meshes in a MC analysis investigating the relationship between CFS geometry, bone density distribution, and the structural characteristics of specific craniofacial features. In achieving these objectives, not only will the full potential of computational automation in biomechanical studies incorporating geometric variability be demonstrated, but these tools will be fully transferable to investigations involving other anatomical parts of interest. These objectives will be accomplished in a series of four studies.

1.3.1 Validation of a FE Model of Facial Impact

The first study will involve the creation of FE meshes capable of representing the elastic response of the human CFS. This will not only serve to create baseline models upon which to build a SSM, but also serve as a compliment to the recently completed development of a customized craniofacial impact device (of which the author has played a major role).

The geometry of the five skull specimens used in these \textit{in-vitro} experiments will be extracted from CT images and be used to create a custom FE mesh for each specimen. The
natural frequencies of these models will be extracted in a modal analysis and the results compared to previously collected experimental values.

The hypothesis of this study is that finite element modelling can accurately predict the natural frequencies of existing human CFS specimens, thus establishing a set of baseline FE meshes validated with respect to their ability to model the geometry and material properties of physical skulls, upon which a SSM will be built.

1.3.2 Creation of a Mesh Morphing Algorithm for the Human CFS

In order to create a SSM of the human CFS, a means of describing the training set of CFS geometries using FE meshes with corresponding nodes and elements will need to be established.

One specimen from the first study will be randomly selected to be the baseline mesh. A morphing algorithm will be developed to map the mesh of the baseline specimen onto the geometry of the remaining four specimens. In order to minimize the amount of manual intervention, it will be a requirement of the morphing procedure that it will be able to operate without having to manually identify anatomic landmarks. The quality of mesh elements will be analyzed using several element quality measures to ensure that the mesh quality degradation is kept to a minimum during the morphing process. Finally, the meshes produced by morphing the baseline to the remaining target geometries will be subjected to FE analyses using the same conditions as in the first study, and the FE results compared to those of the manually made meshes for the same specimen, in order to establish that meshes made through a morphing procedure perform comparably to those made manually,
establishing a means of morphing one mesh to other geometries without compromising on FE performance.

**The hypothesis of this study is that there will be no appreciable difference in the results of an FE analysis whether using a mesh produced from morphing a baseline mesh to an arbitrary target geometry of the same class (i.e. another CFS geometry), or using a mesh created manually from contemporary methods.**

**1.3.3 SSM of the human CFS**

Once a means of morphing a baseline mesh to target geometries has been shown to create meshes suitable for use in a FE analysis, a mechanism with which to build a training set for a SSM will have been established.

The morphed meshes produced in the second study will thus comprise this training set in the establishment of a SSM of the human CFS. (Note that the second study will only involve five specimens, so in order to increase the available number of eigenmodes in the SSM, new specimens will need to be sourced, their geometries extracted, and the baseline mesh mapped onto them as was done with the original set of specimens in the second study.) Elastic modulus values will also be incorporated into the SSM by interpolating a value for each mesh node from mesh elements.

After building the training set and applying the principal component analysis, a sample of 1000 specimens will be produced. In order to ensure that the shape variation displayed by these samples represents that of the general human population, the distribution and correlations between specific craniometric measurements between the SSM sample and a database of human measurements will be compared.

---

*Note that the number of specimens in the second study is reduced to five in order to increase the available number of eigenmodes in the SSM. New specimens will need to be sourced, their geometries extracted, and the baseline mesh mapped onto them as was done with the original set of specimens in the second study.*
The hypothesis of this study is that the sample of SSM produced CFS meshes will accurately reflect the diversity of geometries observed in the human population, both with respect to the magnitudes of individual measurements, as well as in terms of how these measurements vary with respect to one another.

1.3.4 Monte Carlo Analysis of Zygoma Fracture

Once it has been established that meshes produced by the SSM a) produce geometry representative of the variability observed in the human population and b) perform just as well in a FE analysis as meshes made from current manual techniques, the SSM will be used to demonstrate how it can be applied as an alternative to in-vitro experimentation in biomechanical investigations establishing safety standards.

A previous investigation used in-vitro testing to predict the fracture probability of the zygoma in terms of applied load used a sample of eighteen cadaveric specimens, and a qualitative fracture criteria based on a subjective 1-5 scale to indicate fracture severity. In the fourth study, the 1000 SSM produced CFS meshes develop in the previous studies will be used in an FE analyses modeling the experimental setup of these past experiments. Using a fracture criteria based on maximum principal strain, the predicted threshold 50% probability fracture force will be applied in the FE analysis, and the percentage of models experiencing fracture will be compared to the predicted 50% criterion. Further to this, an investigation into the relationship between fracture of select craniofacial structures and craniometric measurements and/or bone density distribution will be performed.46

The hypothesis of this study is that the FE-based Monte Carlo analysis of facial impact implemented using SSM will match experimentally reported data, and provide
constructive feedback on the state of modern surrogates used in craniofacial impact studies.

1.4 Significance

The ability to study the impact of parameter variation on biomechanical outcomes using an automated computer program has been one of the most useful applications of FE analysis since it has been applied to biomechanical investigations. However, the ability to implement geometric variation, a source of variation that can have a significant impact on biomechanical outcomes, has been a persistent barrier to fully understand how questions regarding implant design, surgical procedures, or other interventions, vary among the human population. It is the aim of this thesis to contribute to the body of knowledge addressing this barrier.
1.5 References


36. Lapeer RJ, Prager RW. Fetal head moulding: Finite element analysis of a fetal skull
subjected to uterine pressures during the first stage of labour. *J Biomech.* 2001;34(9):1125-1133.


Validation of a Finite Element Model of the Human Craniofacial Skeleton Through Modal Analysis

2.1 Introduction

Finite element analysis (FEA) is a popular simulation tool used in biomechanics to perform investigations that cannot be evaluated analytically due to complex geometry, material properties, and other nonlinearities inherent in biomechanical systems. These numerical simulations provide a means of exploring the impact of several interacting variables simultaneously in a way that is often more time- and cost-effective than \textit{in-vitro} alternatives. Furthermore, FEA allows for the visualization of field variables which can provide a unique perspective not possible with many physical sensing systems. Advances in computer hardware and analysis software have made this tool ever more available to researchers, resulting in more robust orthopaedic implant designs, a better understanding of the function of anatomical structures, and an ability to investigate injury mechanisms.

The utility of a model depends on its ability to replicate physical phenomena; that is, before a FE model can be used to predict outcomes in the physical world, it must at minimum reproduce existing physical data to some standard of accuracy. Furthermore, a model is most useful if it displays robustness by maintaining accuracy in the face of changing input conditions. In recent years, there has been an increased emphasis on the validation of biomechanical studies incorporating FE analysis, particularly reporting of mesh element quality and mesh density independence\textsuperscript{1}.

Model validation is often achieved by correlating \textit{in-vitro} strain gauge output with corresponding locations on a FE model. While this ensures model accuracy at discrete points of interest, it is also important that the bulk behavior of the FE model reflect that of
the entire physical object throughout the analysis domain. Modal FE analyses are one way to do this. A modal analysis seeks to find a structure’s natural frequencies of vibration and corresponding mode shapes, which are respectively the frequencies at which a structure vibrates when subject to a sharp impulse, and the physical oscillation pattern of those vibrations. These characteristics are functions of an object’s mass and stiffness distributions, as well as its geometry, all of which are acquired from CT images. Thus, a modal analysis provides a means of evaluating a FE model’s performance, taking into account how well its geometry, density distribution, and stiffness represent those of the physical object it is simulating.

Early investigations using modal analyses to validate FE models of human bone focused on the lower extremities and used homogeneous material properties. Later studies incorporated inhomogeneous and orthotropic material models which were able to replicate mode shapes and resonant frequency values derived from accelerometer data. Neugebauer performed an experimental modal analysis of the hemi-pelvis using optical vibrometry, which was followed up by Scholz who evaluated various density-modulus material relationships in their ability to reproduce experimental results.

Due to its applications in audiology and craniofacial injury, the vibrational response of the craniofacial skeleton (CFS) has a long history of experimental investigation; however, calculation of resonant frequencies and visualization of mode shapes have often used idealized geometries, or limited analysis to the cranium. Recent experimental data using strain gauges to determine the vibrational response of the craniofacial skeleton to blunt impact has provided an opportunity for FE model validation. This study is presented as a follow-up to this work, where experimentally derived resonant frequency values will
be used to validate FE models of the same experimental CFS specimens. It is hypothesized that the FE models of the CFS will be validated using the experimental resonant frequency values.

2.2 Methods

2.2.1 Experimental Resonant Frequency Acquisition

The results of previous craniofacial impact tests were used to validate the FE models created in the present study\(^\text{16}\). For context, the testing procedure will be briefly reviewed (note that while 6 skulls were originally tested, only 5 had data of sufficient quality to validate FE models.)

Five fresh frozen cadaveric head specimens (mean 78.2 yrs, std. dev. 12.6 yrs; 2 female, 4 male) were stripped of soft tissue via surgical dissection and denuded using a colony of Dermestidae beetles. The mandibles were discarded, and strain gauges applied bilaterally to the cranium on the parietal and frontal bones, on the supra-orbital rim, lateral orbital rim, infra-orbital rim, nasal bone, zygomatic arches, and maxilla. One additional gauge was placed just superior to the glabella for 17 total strain gauges.

Two holes were drilled into the occiput lateral of the foramen magnum to allow the placement of two carriage bolts. The bolts protruded inferiorly from the cranium and were fixed to the occiput with an assembly of lock nuts, washers, and rubber grommets, allowing a flexion-extension degree of freedom simulating that between the occiput and C1 vertebrae.

The protruding portions of the carriage bolts were embedded in a section of PVC pipe using dental cement, ensuring sufficient clearance between the top of the pipe and the skull so
there would be no interference between the two. The whole potting assembly was then secured to the impact apparatus using a custom jig and subjected to a series of sub-fractural impacts across five different impact locations on the cranium and face.

The strain gauge voltage signals were sampled at 50 kHz filtered to 5 kHz with a low-pass filter in order to capture the short impact duration. The time signal was transformed into the frequency domain using the Fast Fourier Transform (FFT) algorithm, and resonant frequency values were identified from peaks in the single-sided amplitude spectrum.

2.2.2 Model Creation

CT scans of each specimen were taken prior to experimental testing (GE Discovery CT750 HD, 80 kV, 450 mAs). Scans were imported into Mimics® v. 16.0 (Materialise®, Leuven, Belgium), where a mask of the CFS geometry was created using both automatic and manual segmentation procedures. Bone and sinus cavities were included in the mask, while the inner cranial cavity was left hollow. Triangular surface meshes were then created in 3-Matic® v. 8.0 (Materialise®, Leuven, Belgium).

2.2.3 Mesh Evaluation

2.2.3.1 Convergence

To investigate mesh independence, three surface meshes with varying degrees of coarseness were made for each specimen. This was done by limiting the maximum allowable edge length of surface mesh seed elements to 1 mm, 2 mm, and no limit. The surface meshes were then imported to Abaqus® 6.13 (Simulia, Providence, RI, USA) where solid meshing using 10-node quadratic solid tetrahedral elements was completed. Percent change in resonant frequency values were used to examine mesh dependence.
2.2.3.2 Quality

Mesh quality was quantified by calculating radius ratio ($\rho$), mean ratio ($\eta$), and element condition number ($\kappa$) for all mesh elements:

$$\rho = \frac{3r}{R}, \quad \eta = \frac{\sigma^{2/3}}{|S|^2}, \quad \kappa = \frac{3\sigma}{|S||\Sigma|}$$

Where, $r$ and $R$ are respectively the radii of the element insphere and circumsphere $^{17}$, $S$ is the nodally invariant Jacobian matrix $^{18–20}$, and $|S|$, $\Sigma$, and $\sigma$ are respectively the Frobenius norm, adjoint, and determinant of $S$. Each of these measures are invariant under translation, rotation, reflection, and uniform scaling, and attain a maximum value of 1 for equilateral and 0 for degenerate (0-volume) tetrahedrons, making them suitable measures of mesh quality independent of the scale or geometry of the feature being modeled $^{17,19–21}$. Each measure has a different geometrical interpretation: $\rho$ can be considered a measure of aspect ratio $^{21}$, $\eta$ a measure of element distortion $^{17}$, and $\kappa$ the distance of an element from the set of inverted elements $^{18,19}$.

2.2.4 Materials Assignment

The equation $E = 2017.3\rho^{2.46}$, where $E$ and $\rho$ are respectively elastic modulus (MPa) and apparent density (g/cm$^3$), was developed from experimental tests involving the pelvis $^{22}$ and has shown better performance among density-modulus relations in FE investigations involving flat bone $^{23}$. Strain rate effects were ignored because vibrationally induced strains would be negligibly small $^{24}$.

Note that since the entire sinus volume was modeled as a volumetric mesh the contribution to stiffness and strength of the thin bone structures within this volume were not specifically
segmented and modeled; rather, the model relied on the density-modulus relationship to indicate strength stiffness. Thus, elements corresponding to air added no contribution to the stiffness of the structure, while those that contained some bone volume provided some stiffness. Due to the incredibly thin structure of sinus bones, these approximations were assumed to not impact the results of any FE analysis not directly testing the response of these bones.

The CT scans used were taken with a clinical scanner known to be calibrated regularly to the Hounsfield scale. Thus, density values were related to HU under the assumption of a linear relationship where -1024 and 0 HU corresponded to 0.0 g/cm$^3$ and 1.0 g/cm$^3$, respectively.

2.2.5 Boundary Conditions

Prior to potting, the drill holes used to insert the carriage bolts and the cranial surface on each specimen were digitized using an Optotrak Certus® (NDI, Waterloo, ON, Canada). This allowed for the drill holes to be registered in the coordinate system of the FE mesh so that the nodes corresponding to the boundary of the drill holes could be selected and set to a pinned boundary condition.

2.2.6 Data Analysis

Resonant frequencies up to 3.5 kHz were calculated in the FE simulation, corresponding to frequencies with the highest power content in the experimental tests. RMS error was calculated to gauge the magnitude of error between simulated and experimental frequency values. Intra-class correlations were calculated and Bland-Altman plots constructed to
compare the ability of experimental and computational methods of calculating resonant frequency values.25

2.3 Results

2.3.1 Rigid Body Motion

For each specimen, the FE simulation calculated four resonant frequencies that were between ~50 and 700 Hz, well below the lowest resonant frequency collected experimentally. Observing the mode shapes calculated by the FE analysis revealed that these four modes corresponded to rigid body motion of the CFS about its occiput boundary condition in flexion-extension, lateral, internal-external rotations, as well as inferior-superior translation. Since these modes would not cause bone deflection at the strain gauge sites, they were not detected via strain gauge instrumentation, and were not considered in comparisons between experimental resonant frequency values.

2.3.2 Mesh Evaluation

Figure 2-1 and Table 2-1 display the results of the mesh convergence analysis. Percentage differences in resonant frequency values calculated at the three different element densities were very low (between 0.1% and 3.8%), and thus these values were considered mesh independent. When run entirely on computer memory (24 GB available) using 12 processing cores, simulations ran on average 20 and 27 minutes for Mesh Cases 1 and 2, respectively. Due to the increased degrees of freedom of Mesh Case 3, simulations could not run entirely on memory, contributing to their considerably longer runtimes at 16-25 hours. Thus, Mesh Case 2 was used for all further analysis as it was considered the best balance between mesh fineness and computational cost. Figure 2-2 charts the average and
standard deviation cumulative distribution corridors of element quality metrics $\rho$, $\eta$, and $\kappa$ for all meshes. The 10th percentile values (i.e. values which 90% of mesh elements exceeded) for $\rho$, $\eta$, and $\kappa$ are 0.66, 0.72, and 0.70, respectively.

![Graph](image)

**Figure 2-1** - Resonant frequency values for specimen 1641 using mesh densities with 1) no restriction on maximum edge length 2) maximum edge length restricted to 2 mm 3) maximum edge length restricted to 1 mm.

**Table 2-1** - Percent change in numerically derived resonant frequency values across different mesh densities for each specimen.

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Number of Elements in Mesh Cases</th>
<th>Average (±stddev) % change in frequency across mesh densities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1622</td>
<td>306,381 -747,216</td>
<td>2.3% (0.9%)</td>
</tr>
<tr>
<td>1652</td>
<td>227,512 -717,085</td>
<td>1.7% (0.7%)</td>
</tr>
<tr>
<td>1643</td>
<td>268,434 -665,362</td>
<td>1.5% (1.2%)</td>
</tr>
<tr>
<td>1641</td>
<td>245,844 -640,183</td>
<td>2.7% (0.9%)</td>
</tr>
<tr>
<td>1653</td>
<td>306,381 -747,216</td>
<td>1.4% (0.7%)</td>
</tr>
</tbody>
</table>
Figure 2-2 - Mesh element distributions for a) radius ratio ($\rho$), b) mean ratio ($\eta$), and c) element condition ($\kappa$) number.
2.3.3 Resonant Frequencies

Table 2-2 lists the absolute percent error (2.3% – 18.2%) and RMSE (88.4 – 599.5 Hz) between computed and experimental resonant frequencies for each specimen. Intraclass correlation coefficients ranged between 0.66 and 0.99 individually, with a value of 0.83 for all skulls pooled together (Table 2-3). Graphical comparisons of experimental and FE frequency values are presented in Figure 2-3.

Table 2-2 – Difference between experimental and calculated resonant frequency values for each specimen in terms of root mean square error, average percent error, and absolute % error.

<table>
<thead>
<tr>
<th>Specimen ID</th>
<th>RMSE</th>
<th>Ave % error</th>
<th>Ave</th>
<th>% error</th>
</tr>
</thead>
<tbody>
<tr>
<td>1652</td>
<td>88.4</td>
<td>0.6%</td>
<td>2.3%</td>
<td></td>
</tr>
<tr>
<td>1643</td>
<td>599.5</td>
<td>-16.2%</td>
<td>18.2%</td>
<td></td>
</tr>
<tr>
<td>1641</td>
<td>136.1</td>
<td>2.0%</td>
<td>7.4%</td>
<td></td>
</tr>
<tr>
<td>1653</td>
<td>401.1</td>
<td>-12.8%</td>
<td>12.8%</td>
<td></td>
</tr>
<tr>
<td>1622</td>
<td>296.0</td>
<td>-11.8%</td>
<td>13.3%</td>
<td></td>
</tr>
</tbody>
</table>

Table 2-3 – Intra-class correlations between experimental and calculated resonant frequencies.

<table>
<thead>
<tr>
<th>Specimen ID</th>
<th>ICC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1652</td>
<td>0.99</td>
</tr>
<tr>
<td>1643</td>
<td>0.66</td>
</tr>
<tr>
<td>1641</td>
<td>0.98</td>
</tr>
<tr>
<td>1653</td>
<td>0.86</td>
</tr>
<tr>
<td>1622</td>
<td>0.81</td>
</tr>
<tr>
<td>Pooled</td>
<td>0.83</td>
</tr>
</tbody>
</table>
Figure 2-3 – Comparison of numerically and experimentally derived resonant frequency values for each CFS specimen.
A Bland-Altman plot (Figure 2-4) yielded an average error for all specimens of -206 Hz (standard deviation 296 Hz), indicating simulated resonant frequency values tended to underestimate experimental values overall. Looking at Bland-Altman plots for individual specimens (Figure 2-5), a consistent negative bias was observed for the simulation versus experimental results. Table 2-4 lists the average and standard deviations of the frequency pair deviations corresponding to the Bland-Altman plots.

Figure 2-4 - Bland-Altman plot comparing experimental (gold standard) and calculated values for all resonant frequencies of all specimens. The average error is -206 Hz with a standard deviation of 296 Hz. The blue line is the average deviation and the red lines represent a 95% confidence interval (±1.96σ).
Figure 2-5 – Bland-Altman plots comparing experimental (gold standard) and calculated values for all resonant frequencies for individual specimens. The blue line is the average deviation and the red lines represent a 95% confidence interval ($\pm 1.96\sigma$).
Table 2-4 – Average deviation and standard deviation values of frequency pairs corresponding to Bland-Altman plots.

<table>
<thead>
<tr>
<th>Specimen ID</th>
<th>Average Deviation (Hz)</th>
<th>Standard Deviation (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1652</td>
<td>23.4</td>
<td>95.4</td>
</tr>
<tr>
<td>1643</td>
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<tr>
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</tr>
<tr>
<td>1622</td>
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<td>206.1</td>
</tr>
<tr>
<td>Pooled</td>
<td>-206.0</td>
<td>296.5</td>
</tr>
</tbody>
</table>

2.3.4 Mode Shapes

In addition to resonant frequencies, the FE method also calculates the system’s eigenvectors, allowing for the visualization of each CFS specimen’s vibrational mode shapes. While resonant frequency values at each mode number differed, consistent mode shape patterns were observed across all specimens. Three-view illustrations of these mode shapes are displayed for one specimen in Figure 2-6. Mode shape five shows the facial bones and maxilla stretching into and out of the anterior-posterior (a-p) axis. Mode shape six showed the maxilla and alveolar process translating in the medial-lateral direction relative to the cranium, flexing the zygomatic processes. Mode shape seven showed the maxillae, zygomatic arches, temporal bones, and occiput folding together towards and away from the cranium. Mode shape eight showed the face twisting in the transverse plane about a superior-inferior directed axis passing through the hard palate of the maxilla. Mode shape nine had the same character as mode shape six, and was likely a harmonic thereof. Mode shape ten showed the same character as mode shape seven, with the slight difference of the maxilla pulsing inward/outward in the a-p direction.
5. Maxilla and face stretching and compressing away/towards cranium.

6. Maxilla and face twisting side to side wrt the cranium.

7. Maxilla and face stretching and compressing away and towards cranium, individual maxilla twisting out wrt one another, bulging of temporal bones.

8. Face and cranium rotating on superior-inferior axes with respect to skull, the connection of face to cranium seems to be a node.

9. Lower maxilla translating side to side with top of face and rest of cranium seemingly motionless. Large zygoma strains.

10. Maxillae rotating on a-p axis.

Figure 2-6 – Mode shape visualizations and descriptions for Specimen 1652
2.4 Discussion

Resonant frequency analysis has been used to validate FE models in both long\textsuperscript{2–4,6} and flat bones\textsuperscript{8}. While there have been several experimental investigations into the resonant frequencies of the human CFS\textsuperscript{9–11}, as well as investigations using in-vitro strain gauge data to validate FE models of the CFS\textsuperscript{26,27}, these approaches have not yet been combined. This study used experimentally determined resonant frequency values to validate FE models of the human CFS, and has presented a visualization of the calculated mode shapes using accurate human geometry.

While there is much room for improvement in terms of matching experimental and FE resonant frequency values, the results obtained from this analysis

Overall, there were mixed results with respect to the agreement between calculated and experimental resonant frequency values. ICC values ranged from poor (0.66) to excellent (0.99). The Bland-Altman plot show that the calculated data generally tended to underestimate experimental values.

Average percent error between simulated and experimental resonant frequency values was found to range between -16.2\% - 2\%, with an average of -10.8\% over all specimens and resonant frequencies. This represents an improvement in accuracy when compared to the results of Scholz \textit{et al}., who in a comparable study using experimental resonant frequency values of the pelvis reported overall percent differences in modal frequency values between -15.5\% and -45.0\%\textsuperscript{8}. Notable in this comparison is the fact that Scholz \textit{et al}. tested three material models of bone that were derived from long bone data\textsuperscript{28–30}, concluding that their large error values indicated that FE models involving flat bone structures cannot rely on material
models produced for long bone. While the present study did not look at the pelvis specifically, the CFS is still considered flat bone, and the reduced error values observed as compared to Scholz et al. add further support to the hypothesis that density-modulus relationships used in material models of bone for FE analysis are highly dependent on anatomical location and the type of bone they are intended to represent\textsuperscript{30}. For these reasons, it was concluded that the results of this FE analysis are representative of the state of the art within the field for similar analysis types at time of writing, and are suitable to use as a basis for further mesh morphing and statistical shape modeling procedures.

Resonant frequency values varied widely between specimens, which was expected considering the general anatomic variability present in the human population. However, there was a distinct similarity in the motion of mode shapes for corresponding mode numbers across specimens, suggesting an underlying consistency in the geometric structure and density distribution of human CFS anatomy. This motion was dominated by the facial skeleton translating and/or rotating with respect to the cranial skeleton, highlighting the relative flexibility of the facial bones compared to the cranium. This suggests that any kinetic energy dissipated through vibrations of CFS would largely be through the structures of the face rather than the cranium, particularly with the added mass of soft tissue. This would support current hypotheses of the face as an energy absorption device that might dissipate energy from impacts, protecting the brain from injury much like the crumple zone of a vehicle protects its occupants\textsuperscript{31}.

Despite the insights provided by the present study, the considerable gap between experimental and simulated resonant frequency values for some specimens indicate that there are several ways in which it could be improved. Strain gauges were used to measure resonant frequency values because they are relatively inexpensive, easy to apply, and offer robust performance in
impact environments. Furthermore, their low weight and stiffness compared to the CFS would not appreciably alter its vibrational characteristics. However, strain gauges measure deflection only, not displacement, and as such could not be used to calculate the modal assurance criterion (MAC) values to quantitatively compare experimental and calculated mode shapes. This would require a means of measuring the displacement of the skull at multiple locations on the CFS. Ideally, this would be achieved using non-contact measurement methods such as a scanning laser vibrometer, which collects data at many points across the target surface, the coordinates of which can be imported to FE models\textsuperscript{32}. Another alternative would be the use of triaxial accelerometers, which while much less expensive than vibrometry systems, could potentially alter the vibrational characteristics of the system being measured through their added mass.

Also, the experimental data on which the analysis in this study was based was acquired from dry skulls. While this might make the results of this specific FE analysis less complex, as no damping or influence from soft tissue was incorporated, it limits the direct clinical applicability of the data.

These deficiencies notwithstanding, the results produced in this study still serve as a validation of FE models of the human CFS, lending to a deeper understanding of its biomechanics that are applicable to several branches of applied research. In the field of acoustics and audiology, the structural vibrational modes of the craniofacial skeleton play an important role in bone-conducted sound\textsuperscript{10,33,34}. It has also been hypothesized that the vibrational characteristics of the human CFS could lead to better understanding of the mechanisms and risk of mild traumatic brain injury\textsuperscript{11}. While many safety standards for sporting and industrial helmets use reduction in linear accelerations as a safety accreditation target, reductions in linear acceleration alone have not been shown to reduce the incidence of concussive injury, suggesting injury
mechanisms other than linear acceleration are at play\textsuperscript{35–37}. Incorporation of vibration reduction strategies observed in the structure of the woodpecker’s skull have been successfully used to reduce failure of micro electro-mechanical systems (MEMS) due to impact\textsuperscript{38,39}, and the current research might guide a similar approach in the design of human protective equipment.

2.5 Conclusion

The preceding study used modal analysis to validate FE models of the human CFS by comparing experimentally measured and numerically calculated resonant frequency values for five specimens. Errors between calculated and experimental modal frequencies performed favourably compared to similar analyses involving other thin bones, and skull mode shapes were also visualized. These mode shapes were similar in character across specimens, suggesting that despite differences in frequency values, the vibrational mode shapes of the CFS is consistent among individuals.
2.6 References


3 Development of a Mesh Morphing Algorithm Applied to the Craniofacial Skeleton

3.1 Introduction

The development of computer hardware and software has made finite element (FE) modeling an important tool in understanding human biomechanical systems and prosthetic implants. The ability to perform experiments virtually significantly reduces the time and cost investments that come with procuring human specimens, obtaining ethics approvals, and building experimental apparatuses. This flexibility facilitates parametric analyses which can determine how variables such as a system’s material properties or loading environment might impact bone remodeling patterns, implant performance, or biomechanical behavior following surgery\textsuperscript{1}.

Despite these developments, there are still difficulties in accounting for variation in anatomical geometry present in human populations\textsuperscript{2-5}. This is because the most common method of creating specimen-specific FE meshes from CT scans is highly laborious and time consuming. The first step in this process is the segmentation of target anatomy. While automated segmentation techniques do exist, manual intervention is still required in many cases to ensure the segmented volume accurately represents the target geometry. Once complete, the CT voxels contained within the segmented volume are used to form a FE mesh. The simplest way to do this is to turn each voxel into a hexahedral mesh element, however, this produces rough boundaries which could lead to erroneous results where surface and/or contact variables are important. Many contemporary segmenting programs are able to extract a smoothed surface from the segmented region to produce a triangulated surface mesh that better represents the
bone surface, which can be turned into a volume and meshed using any number of available CAD and/or meshing programs.

The development of mesh morphing algorithms has made specimen-specific mesh generation more flexible and somewhat less labor intensive. A high quality template mesh developed as described above can be morphed to target segmented surfaces. While the target surfaces still require segmentation, a robust mesh morphing procedure can automatically map a high quality mesh to many target subjects. Beyond automation, morphing has the added advantage of maintaining correspondence of elements and nodes \( (i.e. \) consistent topology) between the FE meshes under investigation. This facilitates the automation of FE analysis pre- and post-processing using node and element groups, and can be used to create a training set of meshes for use in statistical shape models (SSM) and other probabilistic applications\(^6\text{–}^8\).

Several morphing algorithms have been described in the literature\(^9\text{–}^{13}\). Many work by first morphing a source surface mesh to a target surface mesh, from which interior volumetric nodal displacements are interpolated. Bah \textit{et al.} developed a morphing scheme to examine the effects of bone implant placement where the equations of linear elasticity were solved for interior nodes after rigidly moving the bone-implant boundary while keeping the external bone boundary fixed\(^{11}\). O’Reilly \textit{et al.} used a tracking tool to project surface nodes of a template mesh onto a target surface, while a smoothing algorithm moved interior nodes and improved mesh quality\(^{12}\). Sigal and Whyne compared two methods of mesh morphing with respect to their abilities to reproduce target geometry and FE performance of morphed and manually created meshes: one calculated surface transformations by first wrapping a simple auxiliary surface onto the more complex source and target anatomical surfaces using an energy minimization function, while the other used manual landmarking with radial basis function
(RBF) interpolation using a thin plate spline RBF function. It was found that both methods adequately morphed the geometry of the source surface to the target and performed well in FE analyses, but manual landmarking was better able to match specific landmarks between meshes\textsuperscript{13}, which is useful in cases where the landmarks confer some anatomical meaning. Manual landmarking with interpolation of surface nodes followed by volume nodes, often using some form of RBF interpolation, has become one of the more popular approaches among subsequent mesh morphing studies\textsuperscript{14–19}. 

A common drawback of the above mentioned strategies is that they all require some manual intervention beyond manual segmentation. Choosing an intermediate auxiliary surface is not always trivial, especially when dealing with intricate geometry, or if both inner and outer surfaces require morphing. Manual landmarking is also time consuming, especially if there are many target specimens to be processed. Furthermore, in cases where target landmarks have significant anatomical meaning, landmarks should be identified by trained individuals, and there is always inter-operator error to consider. While it has been demonstrated that as few as 10 landmarks are needed to adequately morph a source to target mesh in the femur\textsuperscript{14}, more complex geometry requires more landmarking. For example, in morphing in the craniofacial skeleton (CFS), 92 landmarks were required to adequately define only half the CFS geometry\textsuperscript{16}. In a study of the spine-pelvis-femur system, 40 landmarks were reported to be required (after the creation of a landmark atlas), which also required visual inspection of automated landmark placement around thin bone structures. (It should be noted that this morphing algorithm did not require segmentation of a target surface, as CT voxel thresholds were used to guide surface node movement.)\textsuperscript{18}
It is useful to minimize the amount of manual intervention involved in specimen specific mesh creation. A 3-D generalization\textsuperscript{20} of a 2-D surface matching algorithm\textsuperscript{21} that requires no manual landmarking has been shown to successfully morph FE meshes of the femur\textsuperscript{6,7}. The purpose of the present study is to apply this morphing algorithm to the more geometrically intricate CFS models developed manually in Chapter 2. A 3-D interpolation algorithm based on solving the diffusion equation will be used to interpolate volumetric node displacements, and a combined element untangling and optimization algorithm will maintain mesh quality\textsuperscript{22}. In order to determine the viability of the mesh morphing algorithm as a substitute for manual mesh production in FE CFS investigations, the same modal FE simulations performed in Chapter 2 will be applied to the morphed meshes, whose results will be compared to the those obtained from the manually created meshes. It is hypothesized that there will be no practical difference between FE results produced using manually created and morphed CFS meshes.

### 3.2 Methods

#### 3.2.1 Mesh Morphing Algorithm

Of the volumetric meshes created in Chapter 2, one was chosen randomly to be used as a baseline mesh to be morphed to all others. Triangular surface meshes of each specimen were created to be used in the surface-based mesh morphing procedure. In order to maintain correspondence between volume and surface meshes for later morphing steps, the node numbers and nodal coordinates of the surface mesh nodes and surface nodes of the volume meshes were consistent.

The morphing of the baseline volume mesh to that of the other skulls was driven by a three step iterative procedure. First, surface nodes of the baseline mesh were displaced towards the
surface of the target mesh. Second, the surface node displacements were used to generate displacement values for interior nodes. Third, automated volumetric element untangling and optimization was performed.

A copy of the Matlab code used to develop the morphing algorithm has been submitted with this thesis. Appendix D outlines the pseudocode framework used in its implementation.

### 3.2.1.1 Surface Mesh Morphing

The source surface mesh \( S_S \) and volumetric mesh \( V_S \) were first simultaneously aligned with the target specimen’s surface mesh \( S_T \) in 3-Matic using a combination of manual translations, rotations, and scaling. This initial manual alignment was followed by a fine adjustment using 3-Matic’s Iterative Global Registration function. This process took approximately 2 minutes per specimen, and was the only manual intervention required in the entire morphing process.

Next, an iterative surface-based morphing algorithm modified from Moshfeghi et al.\(^{20}\) was used to morph \( S_S \) to \( S_T \) (Figure 3-1). For each node \( n_i \) on \( S_S \), its nearest triangle \( t_T \) on \( S_T \) was identified by finding the target triangle centroid nearest \( n_i \) using Matlab’s (Mathworks® Inc., Natick, MA) `knnsearch` function. A new point \( G \) was then constructed by perpendicularly projecting \( n_i \) onto the plane formed by \( t_T \). A distance vector \( \mathbf{D}_{SI} \) was then calculated, defined as the position vector directed from \( n_i \) to \( G \) if \( G \) was inside the area of \( t_T \), or from \( n_i \) to the closest vertex of \( t_T \) otherwise. This process was then repeated for all nodes of \( S_T \), with a new set of distance vectors \( \mathbf{D}_{TI} \) directed from \( S_T \) to \( S_S \). This resulted in \( N \) source-to-target distance vectors \( \mathbf{D}_{SI} \) and \( M \) target-to-source distance vectors \( \mathbf{D}_{TI} \), where \( N \) and \( M \) are the number of nodes on the source and target surface meshes respectively.
Figure 3-1 - Visualization of the determination of two distance vectors $D_{S_i}$ and $D_{S_{i+1}}$ corresponding to nodes $n_i$ and $n_{i+1}$ in the mesh morphing algorithm. Note that once all the $D_{S_i}$ are determined going from $S_S$ to $S_T$, $D_{S_j}$ will be determined for $S_T$ to $S_S$.

The calculated distance vectors $\bar{D}_{S_i}$ and $\bar{D}_{T_j}$ were then used to determine the surface node displacement field $\bar{d}_S(x, y, z)$ using the following equation:

$$\bar{d}_S(x, y, z) = \frac{1}{\gamma} \left[ \sum_{i=1}^{N} G_{1i} \bar{D}_{S_i} - \frac{\sum_{j=1}^{M} G_{2j} \bar{D}_{T_j}}{\sum_{i=1}^{N} G_{1i}} \right]$$
Here $\gamma$ is a scalar which moderates displacement magnitude, and $G_1$ and $G_2$ are Gaussian radial basis functions which incorporate the effect of all distance vectors $\overline{D}_i$ and $\overline{D}_{T_j}$:

$$G_1_i = e^{\frac{-[(x-x_i)^2+(y-y_i)^2+(z-z_i)^2]}{\sigma_k^2}}$$

$$G_2_j = e^{\frac{-[(x-x_j-D_{T_x})^2+(y-y_j-D_{T_y})^2+(z-z_j-D_{T_z})^2]}{\sigma_k^2}}$$

The basis functions $G_1$ and $G_2$ depend on $\sigma_k$, which controls the influence of distance vectors based on their proximity to $p(x,y,z)$:

$$\sigma_k = \sigma_0 c^{-k}$$

In this equation, $\sigma_0$ and $c$ are constants and $k$ corresponds to iteration number. As $k$ increases, the influence of deformation vectors distant from the point of interest have diminishing influence. This results in bulk nodal movement initially, with finer nodal adjustments coming at higher iteration numbers. Values for $\sigma_0$, $c$, and $\gamma$ used in this study were respectively 10, 1.07, and 2.

The displacement $\overline{D}_{si}(x,y,z)$ of each surface node $n_i$ on $S_S$ was then calculated by evaluating the displacement field at $n_i(x,y,z)$. Modified Laplacian Smoothing was applied after each iteration to avoid surface triangle entanglement (i.e. surface triangles with negative volumes). Iterations continued until the average distance of all surface nodes to the target surface was equal to or less than 0.05 mm (with no distance greater than 0.5 mm), or stopped decreasing.
3.2.1.2 Volume Morphing

The use of the diffusion equation to calculate volumetric mesh nodal displacements from surface nodal displacements has been shown to be a flexible and efficient process, and is used in many dynamic meshing applications\textsuperscript{24,25}. In this approach, homogeneous 3-D diffusion equations are solved independently for each component of the displacement field $\vec{d}_V = (d_{Vx}\hat{i} + d_{Vy}\hat{j} + d_{Vz}\hat{k})$:

$$
\nabla^2 d_{Vx} = 0, \nabla^2 d_{Vy} = 0, \nabla^2 d_{Vz} = 0
$$

The above equation uses the surface nodal displacement values calculated from the surface morphing step as Dirichlet boundary conditions. This approach is especially attractive considering that the FE method can be used to solve for the displacement components at each internal node, and the skull geometry is already discretized into a volumetric mesh.

3.2.1.3 Mesh Untangling and Optimization

Volumetric node displacement sometimes resulted in tangled elements (i.e. elements with negative volumes.) Mesh untangling was achieved by minimizing a function derived from modified versions of the tetrahedral element quality metrics $\eta$ and $\kappa$\textsuperscript{22}.

First, all nodes that were connected to elements with negative volumes (i.e. tangled elements) and not part of the surface mesh were assigned to a sub-set. The algorithm then worked its way serially through the sub-set, where at each node, a local sub-mesh comprised of all elements connected to the current node $\vec{x}_{C}(x, y, z)$ was created. A sub-mesh objective function was then defined as:
Here, $p$ was taken as 2 and $f_i$ is a modified version of either the tetrahedron mean ratio $\eta$ or element condition number $\kappa^{22,26}$ evaluated for element $i$ of the submesh. In these modified functions, the term $\sigma$ is replaced with the function $h(\sigma)$, which eliminates the discontinuity in $F(\bar{x}_c)$ which occurs when a node crosses its element boundary in transitioning from tangled to untangled$^{22}$, allowing for the utilization of Matlab’s `fmincon` function to operate on $F(\bar{x}_c)$:

$$
\eta_m = \frac{h(\sigma)^{2/3}}{|S|^2}, \kappa_m = \frac{3h(\sigma)}{|S||\Sigma|}
$$

For each node in the sub-set, the algorithm first used $\eta_m$ for $f_i$. If that failed, $\kappa_m$ was used. If neither function succeeded in untangling the sub-mesh, that node was skipped. If tangled elements remained after the initial node sub-set was processed, the untangling algorithm was repeated using the newly reduced set of tangled elements. A 2-dimensional visualization of the untangling algorithm is presented in Figure 3-2. Minimizing $F$ serves to improve element quality in untangled elements. Thus, once the entire mesh was untangled, the algorithm was applied to all interior volume nodes using the unmodified $\eta$ for $f_i$ in one final mesh quality improvement step.
Figure 3-2 – 2-D illustration of mesh untangling process. a) Tangled elements (red) are identified, and their connected nodes (light blue) grouped into a sub-set. b) Proceeding serially through the node sub-set, a sub-mesh is created (green and red) by selecting all elements connected to the current node (dark blue). c) The untangling algorithm operates on the sub-mesh by minimizing the sum of the inverse element scores of the submesh, simultaneously untangling elements and improving element quality. d) The algorithm moves to the next node in the sub-set (dark blue). If the submesh produced by this node is already untangled, the algorithm proceeds to the next node.
3.2.2 Morphed Mesh Quality and Performance

The element quality metrics mean ratio ($\eta$), element condition number ($\kappa$), and radius ratio ($\rho$), were calculated for the morphed meshes and compared with those of the manually created meshes from Chapter 2. For reference, these metrics are defined as:

$$\eta = \frac{\sigma^{2/3}}{|S|^2} \quad \kappa = \frac{3\sigma}{|S||\Sigma|} \quad \rho = \frac{3r}{R}$$

where, $r$ and $R$ are respectively the radii of the element insphere and circumsphere, $S$ is the nodally invariant Jacobian matrix$^{22,27}$, and $|S|$, $\Sigma$, and $\sigma$ are respectively the Frobenius norm, adjoint, and determinant of $S$. Each of these measures are invariant under translation, rotation, reflection, and uniform scaling, and attain a maximum value of 1 for equilateral and 0 for degenerate (0-volume) tetrahedrons, making them suitable measures of mesh quality independent of the scale or geometry of the feature being modeled. Each measure has a different geometric interpretation: $\eta$ can be considered a measure of element distortion, $\kappa$ the distance of an element from the set of inverted elements, and $\rho$ a measure of aspect ratio.

The modal analyses used to validate the manually created meshes from Chapter 2 was reproduced using the morphed meshes. The direct comparison between the resonant frequencies produced from both methods allowed for the determination of whether morphed meshes were a suitable substitute for manually created meshes in FE investigations. Furthermore, since a structure’s natural frequencies depend in large part on its geometry and material properties, a modal analysis is especially suited to judge how well morphed meshes were able to match the geometry of their manually created counterparts, as well as their
position in 3-D space, which would influence the assignment of material properties when imported into CT scans.

The morphed meshes were imported into Mimics and registered with their corresponding CT scans. Inhomogeneous linear-elastic material properties were assigned based on a power-law relationship between the radiodensity of the voxels contained within each element and elastic modulus:

\[ E = 2017.3 \rho_{app}^{2.46} \]

Here, \( E \) is elastic modulus (MPa) and \( \rho_{app} \) is apparent density (g/cm\(^3\)), which was calculated knowing that CT grayvalues were calibrated to the HU scale, where 0 and -1024 HU correspond to the density of water (1.0 g/cm\(^3\)) and air (~0 g/cm\(^3\)), respectively. Poisson’s ratio \( \nu \) was set to 0.3, and strain rate effects were not included in the model. The meshes were then imported into Abaqus, where the same rigid boundary conditions at the occiput as in Chapter 2 were applied and a frequency linear perturbation step was executed calculating all free natural frequencies under 3.5 kHz.

The natural frequencies calculated from the FE simulations using the morphed meshes were compared to those determined from Chapter 2 using the manually created meshes. The amount of agreement between the results was evaluated by calculating the same measures as in Chapter 2: average error and Bland-Altman plots to determine any biases, root mean square error (RMSE) values calculated to describe deviation in absolute frequency values (Hz), and intra-class correlation coefficients as an additional measure of agreement between.
3.3 Results

3.3.1 Mesh Morphing

After morphing was completed on all specimens, the average mean distance between baseline surface nodes and target surfaces was 0.05 mm. The cutoff distance of 0.05 mm was reached by 3 of the 4 morphed specimens, with the remaining specimen managing 0.06 mm. The size of the voxels for all CT scans was 0.49 X 0.49 X 0.63 mm, thus in all cases the average surface distance was within the resolution of the CT scan. The morphing process ranged between 5 and 8 hours, depending on the quality of initial alignment of meshes, and the similarity of skull shapes.

3.3.1.1 Mesh Quality

Figure 3-3 shows the cumulative distribution corridors (average ±1.5 standard deviations) of the manually created and morphed meshes for element quality metrics $\eta$, $\kappa$, and $\rho$, along with the 10th percentile value of the averaged cumulative distribution curves (the value above which, on average, 90% of the mesh elements scored). For all measures, the corridor width at the widest point was 0.03 for manual meshes and 0.06 for morphed meshes. In all cases the 10th percentile values of the averaged morphed mesh quality metrics were lower than their manually created counterparts: 0.68 vs. 0.72 for $\eta$, 0.67 vs. 0.70 for $\kappa$, and 0.61 vs 0.66 for $\rho$. 
Figure 3-3 – Averaged cumulative distribution curves of $\rho$, $\kappa$, and $\eta$ for morphed (red) and manually created (black) meshes. For all measures, maximum corridor width was 0.02 for manual meshes and 0.05 for morphed meshes.
3.3.2 Model Validation

3.3.2.1 Finite Element Modeling Performance

Excellent agreement between frequencies calculated using morphed versus manually created meshes was observed (Figure 3-4). Average absolute percent difference in frequencies ranged from 0.0 – 1.2 Hz and RMSEs from 6.4 – 19.5 Hz (Table 3-1). ICC values were also quite high, with values of 0.99 and 1.00 for individual skulls and a value of 1.00 when data from all skull specimens was pooled together (Table 3-2).

Figure 3-4 – Comparison of resonant frequency values as calculated using manually created and morphed meshes.
Table 3-1 – Difference between resonant frequency values calculated using manually created and morphed meshes in terms of root mean square error, average percent error, and absolute % error.

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<th>Specimen ID</th>
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<th>Ave % error</th>
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<th>% error</th>
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Table 3-2 – Intra-class correlations calculated for resonant frequency values as calculated using manually created and morphed meshes

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<th>Specimen ID</th>
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<tr>
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Figure 3-5 and Figure 3-6 show the Bland-Altman plots comparing the FE calculated resonant frequencies using the manually created (“gold standard”) and morphed meshes by specimen as well as with all simulation data pooled together. The morphed meshes tended to slightly overestimate resonant frequencies calculated by the original meshes. Table 3-3 lists the average and standard deviations of the frequency pair deviations corresponding to the Bland-Altman plots.
Figure 3-5 – Pooled Bland-Altman plot comparing the resonant frequencies using manually created (gold standard) and morphed meshes. The blue line represents the average deviation with red lines representing a 95% confidence interval.

Figure 3-6 – Bland-Altman plots of FE calculated resonant frequencies using manually created (gold standard) and morphed meshes. The blue line represents the average deviation with red lines representing a 95% confidence interval.
Table 3-3 – Average deviation and standard deviation values of frequency pairs corresponding to Bland-Altman plots.

<table>
<thead>
<tr>
<th>Specimen ID</th>
<th>Average Deviation (Hz)</th>
<th>Standard Deviation (Hz)</th>
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</table>

3.4 Discussion

Collectively, the results presented in this study demonstrate that the morphed meshes produced by the 3-D elastic morphing algorithm are suitable substitutes to those produced using conventional manual methods. The average distance error between morphed mesh nodes and their target surfaces (0.05-0.06 mm) was an order of magnitude below the resolution of a clinical CT scan. Not only does this ensure a faithful reproduction of the target specimen’s geometry, but also that the material properties assigned to elements of the morphed mesh are calculated from the appropriate CT voxels. Overall mesh quality and consistency suffered somewhat, as the element quality metrics scores ($\rho$, $\eta$, and $\kappa$) and corridor widths respectively decreased and increased in morphed meshes versus their manually created counterparts. However, FE performance was essentially unchanged, with average error calculations, Bland-Altman plots, and ICC values all indicating a high degree of consistency between natural frequency values calculated using morphed versus manually created meshes.

Despite these successes, the 5-8 hours it took to morph a source mesh to its target was significant, especially considering sub-hour morphing times have been reported in studies using other morphing schemes$^{6,14}$. (Although it should be noted that in these studies, morphing
was performed on meshes of the femur, whose geometry is significantly less intricate than that of the CFS.)

While the morphing process was automated, freeing user time for other tasks, there are several ways in which the morphing speed could be increased. The main bottleneck in the morphing procedure was the untangling step. Mesh untangling was applied serially, that is, a tangled node’s optimal position was calculated and immediately moved before any subsequent elements were processed. An alternative would be to wait to calculate the optimized positions of tangled element nodes before effecting the calculated displacement, allowing nodal displacements to be calculated in parallel. Parallel processing has been suggested for the untangling algorithm used in the present study, however no investigation into the impact serial and parallel untangling has on element quality has been reported\textsuperscript{22}, which could be the basis of future investigations.

Other untangling algorithms were also investigated. Freitag and Plassman developed a mesh untangling algorithm that also worked on creating sub-meshes composed of tangled elements, however, instead of optimizing mesh element quality, the volume of the sub-mesh was maximized (inverted elements create negative volume values)\textsuperscript{28}. While this works to untangle meshes, the resulting elements were often of poor quality, and thus a second mesh optimizing step was required. Furthermore, element untangling was executed using linear programming, which would not be as fast as the second-order methods used in the present study. Still, mesh untangling is an active area of research and new methods of parallel untangling could increase the morphing speeds observed in the present study\textsuperscript{29,30}. 
Another factor influencing morphing speed is the magnitude of displacement applied to surface mesh nodes during each morphing iteration. In principal, it would be possible to move source surface nodes to the target surface all at once, completing the surface morphing in one iteration, however, initial trials with this method lead to large numbers of tangled elements. Furthermore, it has been reported that small iterative steps improve the quality of the morphed mesh, albeit at the expense of more computation time\textsuperscript{31}. The average 0.05 mm cutoff value was achieved in 15 to 18 iterations (Figure 3-7). While the nodal displacements per iteration used (controlled largely by the parameters $\gamma$, $\sigma_k$, and $\sigma_0$ from) performed adequately for purposes of the present study, no attempt was made to optimize these parameters. Furthermore, the cutoff value of 0.05 mm average error was arbitrary, and was selected because initial tests revealed it to be towards the upper limit of what the morphing algorithm could achieve for the CFS meshes used. As shown in Figure 3-7, the average error between source nodes and target surface became less than 0.5 mm at around iteration 5 for all specimens, which is still below CT resolution. Further investigations may reveal that larger iteration steps and/or more relaxed surface matching criteria result in FE meshes that still adequately reproduce the results obtained from manually created FE meshes, significantly cutting down on morphing time.
The alignment of source mesh to its target was the only manual intervention required in the morphing process. While this procedure was fairly trivial and took no more than a few minutes per specimen, it represents a break in an otherwise fully automated mesh morphing scheme, and an opportunity for future improvement. Automatic coarse alignment has been achieved using only three landmarks, but these need to be manually selected\textsuperscript{14,18}. Alternatively, it has been shown that the bilateral symmetry plane in the CFS can be automatically calculated using principal component analysis (PCA)\textsuperscript{32,33}. Automated alignment between source and target meshes could be achieved by first translating the geometric centers of source and target meshes, aligning symmetry planes, and implementing a final automated fine adjustment algorithm such as iterative closest point (ICP).

Figure 3-7 – Mesh morphing iteration number versus mean distance of all nodes on CFS specimen source meshes to their targets (mm). All specimens were morphed for 20 even if the cutoff of 0.05 mm before all iterations were completed.
3.5 Conclusion

This study successfully morphed a template FE mesh of an arbitrary human CFS to several target CFS geometries with an error less than that of a standard clinical CT scan. While mesh quality suffered somewhat during the morphing process, FE analysis results using the morphed meshes were not significantly different than those obtained with manually created meshes, thus validating the main hypothesis of this study. The ability to morph meshes between specimens goes a long way towards the ultimate goal of simplifying CFS mesh creation in order to perform FE analyses that can account for variation in anatomical shape of the CFS. However, manual segmentation of specimens is still a necessary and time-consuming step. The next chapter aims to use the morphing procedure employed in this study to develop a statistical shape model of the human CFS, which will be able to automatically generate new human CFS meshes without the need of CT segmentation.
3.6 References


4 Validation of a Statistical Shape Model of the Human Craniofacial Skeleton

4.1 Introduction

Finite element (FE) analysis is a tool used in biomechanical engineering to investigate research questions that are otherwise too expensive, time-intensive, or technically difficult to examine experimentally. Physical systems modeled virtually and executed numerically allow for parameterization of loading conditions, material properties, and many other variables that might affect their understanding.

One aspect of biomechanics that is difficult to parameterize, however, is shape. This becomes an issue when trying to generalize FE results to the broader human population. Unlike in industrial applications involving rigid, tightly tolerated, and functionally specific objects, there is a high degree of variation in the geometry and material properties of human bones which must be accounted for before any research conclusions can be applied to the broader human population\textsuperscript{1,2}. At the same time, the construction of FE meshes used to represent human anatomy requires segmenting bone geometry from clinical or CT scans. While the development of automated segmentation techniques is an active field of research\textsuperscript{3–7}, there is still a great deal of tedious manual segmentation required to convert a CT scan into an FE mesh, making FE studies with few specimens common\textsuperscript{8–11}.

The concept of varying an FE mesh’s shape by first fitting geometric primitives to key landmarks (\textit{e.g.} a sphere to a femoral head) and varying parameters defining those primitives (\textit{e.g.} spherical radius) is at first appealing considering the fact that geometric primitives are already used to define the geometry and mechanics of human joints\textsuperscript{12}. However, this becomes problematic when dealing with highly complex geometry, such as the craniofacial skeleton...
(CFS). Furthermore, there is strong evidence of co-variation between anatomical features due to genetic and environmental factors\textsuperscript{13–15}, and without this information, any imposed shape variation may not be reflective of the population it is intended to represent.

Statistical shape modeling (SSM) is one way to address these challenges. A SSM uses principal component analysis (PCA) on a training set of a particular class of objects to extract information about the variation in shape and/or material properties of that object\textsuperscript{16,17}. The PCA eigenvectors correspond to independent directions of variation within the shape space (also known as “shape modes”), and the eigenvalues to the variance represented by its corresponding eigenvector. Once established, the SSM can be used to produce new instances of the object of interest by forming linear combinations of the eigenvectors. The result is a population of unique objects of the same shape class whose geometric and material variation is consistent with that expressed in the training set, and hopefully, the population it is intended to model.

An essential part of SSM is defining shape geometry and other values of interest of the training set in terms of a collection of corresponding points. In constructing a SSM of the CFS of the developing human, Li \textit{et al.} identified anatomical landmarks on a sagittally symmetric model, and defined additional points in relation to these landmarks in order to adequately describe CFS geometry\textsuperscript{11‡}. Manual landmark identification is a time-consuming process and must be

\[\text{‡In between thesis submission and defense, the author has learned of two recent studies by this group that performed statistical shape modeling of the developing CFS using automated landmarking:}\]


performed by experienced personnel. A more straightforward approach is to use a mesh morphing algorithm to fit a template mesh to each instance in the training set, achieving correspondence between mesh nodes which themselves act as landmarks.$^{18}$

In this chapter, the mesh morphing algorithm from Chapter 3 will be used to create sample of 22 human CFS meshes with corresponding nodes, which will comprise a training set in the production of a statistical shape model of the human CFS. The SSM will be used to build a population of 1000 CFS geometries. The SSM produced population will be evaluated by its ability to create CFS geometries that are both anatomically valid and model the geometric variation of the human population through measures of symmetry, as well as the value and covariation of a selection of craniometric measurements.

4.2 Methods

4.2.1 Statistical Shape Model

4.2.1.1 CFS Training Set Creation

CT scans (GE Discovery CT750 HD, 80 kV, 450 mAs) of 17 human cadaveric heads were performed and imported to Mimics® (Materialise®, Leuven, Belgium), where a geometric mask of the CFS was created using a combination of automated and manual segmenting procedures. Bone and sinus cavities were included in the mask, but the inner cranial cavity was left hollow. Triangular surface meshes were created from the masks using 3-Matic v. 8.0 (Materialise®, Leuven, Belgium) by specifying a maximum edge length of 2 mm. Including the specimens from Chapter 3, this provided a total of 22 specimens to use for a SSM training set (11 M, 11 F, average age 70.9, std. dev. 20.3)
The morphing algorithm developed in Chapter 3 was used to morph the same randomly selected volumetric mesh from Chapter 3 to each of the new 17 CFS specimens. The performance of the morphing algorithm on these remaining specimens was comparable to that of Chapter 3. Appendix C goes into detail about the morphing performance in terms of mesh quality, morphing accuracy, and processing time.

The morphed meshes were imported to their respective CT scans where material properties were assigned to mesh elements as in Chapter 2 and 3. This produced a training set of 22 CFS meshes with corresponding nodes and elements that included elastic modulus values at mesh elements.

4.2.1.2 CFS Coordinate System

A SSM determines the modes of shape variation present in the training set used in its composition. Thus, it was important to first eliminate any artificial or irrelevant forms of variability between training set instances. To this end, each skull was transformed into a common coordinate system to minimize variation in skull models occurring due to its 3-D spatial positioning. Skulls were not normalized with respect to scale, as skull size was a variable that was of interest.

The coordinates of the orbitales and porions were identified on each skull’s CT scan. These were used to form the Frankfurt Plane, which served as the X-Z plane for the common coordinate system (Figure 4-1). The origin was set equidistant between the porions, which also formed the X-axis with the positive direction pointing towards the specimen’s left. The Y axis was defined perpendicularly downwards from the Frankfurt plan, with the Z axis perpendicular to both the X and Y axes.
Figure 4-1 – Common coordinate system defined for CFS specimens in the SSM Training Set. The Frankfurt Plane is illustrated, and the porions and orbitales used in its definition highlighted.

4.2.1.3 Material Properties

The meshes produced from the morphing procedure in Chapter 3 assigned material properties to mesh elements, however in order to include variation in skull stiffness in the SSM, it was necessary to carry this information at mesh nodes. This was accomplished by calculating the volume-weighted average modulus from all elements connected to each node. The rationale for this procedure stemmed from the fact that mesh element density values were originally calculated for each training set mesh using the material assignment module in Mimics® (Materialise®, Leuven, Belgium), which bases the calculation of bone density within an element on the information from all voxels contained within its volume, so elements with greater volume carried more raw CT information with them.
4.2.1.4 SSM Construction

Each node was then defined by 4 degrees of freedom: an \( x \), \( y \), and \( z \) coordinate (mm), and an elastic modulus, \( E \) (MPa). At 58,334 nodes per mesh, each CFS specimen constituted one data point in 233,336 (4 \( \times \) 58,334) dimensional space. Each specimen was expressed in the vector form

\[
\mathbf{x}_i = [x_{i1}, x_{i2}, x_{i3}, \ldots, x_{ij}, \ldots, x_{i4n}]^T, \quad i = 1 \ldots m
\]

where \( m \) represents the number of specimens in the training set (22 in this study), \( n \) the number of nodes, and \( x_{ij} \) the \( j \)th degree of freedom of the \( i \)th specimen. Degrees of freedom were grouped by node, so that for specimen \( i \), variables \( x_{i1} \ldots x_{i4} \) corresponded to \( x, y, z, \) and \( E \) for node 1, variables \( x_{i5} \ldots x_{i8} \) to \( x, y, z, \) and \( E \) for node 2, \( \text{etc.} \)

A principal component analysis (PCA) was performed on the training set to determine the main modes of variation in geometry and stiffness within the allowable shape space. First, the average value was subtracted from each degree of freedom:

\[
x'_{ij} = x_{ij} - \bar{x}_i = x_{ij} - \frac{\sum_{i=1}^{m} x_{ij}}{m}
\]

The mixing of units for coordinates (mm) and modulus (MPa) resulted in values with widely different magnitudes. Thus, each \( x'_{ij} \) was normalized with respect to its standard deviation:\(^{20}\)

\[
x^*_{ij} = \frac{x'_{ij}}{\sigma^j_{1/2}}
\]
Where $\sigma_j$ is the variance of the $j$th degree of freedom. Specimen vectors were then expressed in terms of $x_{ij}^*$:

$$x_i^* = [x_{i1}^*, x_{i2}^*, x_{i3}^*, ..., x_{i4n}^*]^T$$

The modified vectors were then collected into a matrix

$$X^* = [x_1^*, x_2^*, ..., x_m^*]$$

Multiplying $X^*$ by itself and dividing by $m - 1$ gives the correlation matrix $S$ for the training set:

$$S = \frac{1}{m - 1} X^* X^{*T}$$

The eigenvectors $\varphi_i^* (i = 1 ... m - 1)$ of $S$ represent the modes of variation of the training set in the shape space, ranked according to its corresponding eigenvalue $\lambda_i$. Thus, $\varphi_1^*$ is the mode of maximum variance in the training set with a variance of $\lambda_1$, while $\varphi_{m-1}^*$ is the direction of smallest variation with a variance of $\lambda_{m-1}$. Eigenvalue decomposition of $S$, a 233,336 $\times$ 233,336 matrix, was easily handled using the pca function in Matlab® (Mathworks® Inc., Natick, MA), which utilizes the singular value decomposition (SVD) algorithm.

The components within $\varphi_i^*$ were multiplied by each degree of freedom’s standard deviation to transform them back into the original variable space:

$$\varphi_{ij} = \varphi_{ij}^* \sigma_j^{1/2}, i = 1 .. m, j = 1 .. 4n.$$
The resulting \( \boldsymbol{\varphi}_l \) formed an orthogonal basis within the shape space that was used to produce new instances of CFS geometry using linear combinations of the eigenvectors:

\[
x_{new} = \bar{x} + \sum_{i=1}^{m-1} b_i \varphi_i
\]

where \( b_i \) are user-defined weightings. With \( \bar{x} \) and \( \varphi_i \) calculated, new CFS instances could be readily generated by simply assigning values for \( b_i \). This was done using a Sobolov Sequence\(^{21} \), which was transformed into a normal distribution through a domain of \( \pm 3 \) standard deviations (i.e. \( -3\sqrt{\lambda_i} < b_i < +3\sqrt{\lambda_i} \)), creating 1000 unique CFS meshes. The mesh untangling and optimization algorithm described in Chapter 3 was used to refine all new mesh elements to ensure they were geometrically valid and of high quality. The process of calculating, untangling, optimizing, and writing to file all 1000 meshes took approximately 8 hours and was fully automated.

### 4.2.2 Validation of SSM Generated Geometry

While the CFS geometries produced by the SSM may qualitatively appear human-like, this is not ensured nor is it feasible through a simple visual inspection. A rigorous, quantitative comparison of geometric characteristics, including craniometric measurement values, their relationships with one another, and facial symmetry, are required to confirm that the CFS geometry produced by the SSM is comparable to humans in general.

#### 4.2.2.1 Facial Symmetry

Symmetry plays a large role in the perception of human attractiveness\(^{22} \). This has motivated extensive research into developing techniques to identify a CFS symmetry plane, and quantifying symmetry\(^{23–25} \).
Recently, an automated method of calculating CFS symmetry planes that combines iterative closest point (ICP) alignment and PCA was shown to be more accurate and less time consuming to than past techniques involving manual identification of anatomical landmarks\textsuperscript{26}. This technique uses surface meshes derived CT-scans to determine the symmetry plane, and thus serves as a convenient method to quantify the symmetry of SSM created CFS meshes.

For a given mesh, the automated symmetry plane algorithm calculates a model based symmetry score $SS_{\text{model}}$ by first mirroring half of the model about the calculated symmetry plane, and averaging the area-weighted distances between the centroids of mirrored- and original-mesh triangle pairs. This procedure has previously been applied to 32 human CFS scans\textsuperscript{27}, whose $SS_{\text{model}}$ scores were compared to those of the SSM generated meshes in the current study.

4.2.2.2 Craniometric Measurements

4.2.2.2.1 Morphological Integration

The hypothesis of morphological integration posits that morphological traits of anatomical structures will co-vary due to their functional, genetic, or developmental relationships\textsuperscript{14}. As manifested in the CFS, it has been hypothesized that CFS morphology exists on a spectrum with two extremes: a dolicocephalic type, in which the face is extended supero-inferiorly and the skull is longer in the sagittal plane and narrow in the coronal plane, and a brachycephalic type, in which the extremes are reversed\textsuperscript{28}. This would be detected through a positive correlation between neurocranial breadth and facial breadth, and negative correlations between neurocranial breadth and length, as well as neurocranial breadth and facial height.

To test that the CFS meshes produced from the SSM support morphological integration, mesh nodes corresponding to craniometric landmarks were located on the averaged CFS geometry
Taking advantage of correspondence of nodes between individual SSM meshes, neurocranial breadth and length, as well as facial breadth and height, could automatically be measured for all SSM geometries.

![Figure 4-2 – Representation of the average skull shape from the training set.](image)

4.2.2.2.2 The Howells Dataset

In addition to the covariation of measurements, comparisons of raw measurement values between SSM and human CFS geometries would lend support to the geometric validity of SSM produced CFS meshes. Such a database exists in the Howells craniometric dataset.

This dataset was compiled by W.W. Howells across several decades, and is made up of 2524 individual human crania from 28 different tribal/ethnic human populations distributed across 6 continents, and is freely available on the internet. Measures for neurocranial breadth, neurocranial length, facial breadth, and facial height (labeled as XCB, GOL, ZYB, and NPH, respectively).
respectively, by Howells) from the SSM meshes were compared to those in the Howells set using 2 sample t-tests. Cohen’s $d$ effect sizes were also calculated.

### 4.2.2.2.3 Validation of Automated Measurement Methods

As with previous studies$^8,^9$, craniometric measurements relied on the consistent relative positions of mesh nodes to automate the taking of anatomical measurements of SSM produced meshes. This assumption was tested by having a volunteer manually locate the craniometric landmarks listed in Table 4-1 on a sub-sample of 150 SSM produced CFS geometries in 3-Matic® (Materialise®, Leuven, Belgium), from which manual measurements were calculated for XCB, GOL, ZYB, and NPH. Symmetry planes calculated from Section 4.2.2.1 were used to aid in locating the landmarks located in the sagittal plane (i.e. the prosthion, glabella, nasion, and opisthocranion.)

The same volunteer then identified the same landmarks on the mean CFS specimen $\bar{x}$. Craniometric measurements were taken on the same 150 CFS geometries by assuming nodes identified on the mean CFS specimen represented the same landmarks on all geometries in the 150 specimen sub-sample. The manually and automatically determined craniometric measurements were then compared through the construction of Bland-Altman plots and calculation of intraclass correlation coefficients (ICCs).
Table 4-1 – List of craniometric measures used in the geometric validation of SSM produced skull sample.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Landmarks used in measurement</th>
<th>Landmark description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial breadth</td>
<td>L/R Zygion</td>
<td>Most extremely lateral points on zygomas</td>
</tr>
<tr>
<td>(ZYB)</td>
<td>(zyl/zyr)</td>
<td></td>
</tr>
<tr>
<td>Facial height</td>
<td>Nasion</td>
<td>Point in the midline of the face where the nasal and frontal bones intersect</td>
</tr>
<tr>
<td>(NPH)</td>
<td>(n)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prosthion</td>
<td>The most anterior point on the maxillary alveolar process in the sagittal plane</td>
</tr>
<tr>
<td></td>
<td>(p)</td>
<td></td>
</tr>
<tr>
<td>Cranial breadth</td>
<td>L/R Euryon</td>
<td>Most extremely lateral points on the cranial braincase</td>
</tr>
<tr>
<td>(XCB)</td>
<td>(eul/eur)</td>
<td></td>
</tr>
<tr>
<td>Cranial length</td>
<td>Glabella</td>
<td>A smooth, raised region on the frontal bone just above the nasion and between the eyebrows</td>
</tr>
<tr>
<td>(GOL)</td>
<td>(g)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Opisthocranion</td>
<td>Most extremely posterior point on the cranium in the sagittal plane</td>
</tr>
</tbody>
</table>
4.3 Results

4.3.1 Facial Symmetry

Figure 4-3 shows the eigenvalue decay of the SSM. The first eigenvector contained 33% of the total variation, with 80% variation achieved in the first 9 eigenvectors.

![Eigenvalue decay](image)

**Figure 4-3 – Eigenvalue decay representing the accumulated percentage of shape and stiffness variation inherent in the SSM training set.**

The first eigenvector was largely an increase or decrease in overall CFS size, indicating that CFS scale was the main mode of variation between the specimens in the training set. Some variation in cranial stiffness was also observed in this mode. The second eigenvector corresponded to an elongation of the CFS in the sagittal plane, with little change in stiffness distribution. The third mode showed some moderate variation in the alveolar process, but was largely dominated by large changes in cranial stiffness. The manifestations of the first 9 eigenvectors are illustrated in Figure 4-4 and Figure 4-5.
<table>
<thead>
<tr>
<th>E1 Sagittal</th>
<th>E1 Coronal</th>
<th>E6 Sagittal</th>
<th>E6 Coronal</th>
</tr>
</thead>
<tbody>
<tr>
<td>E2 Sagittal</td>
<td>E2 Coronal</td>
<td>E7 Sagittal</td>
<td>E7 Coronal</td>
</tr>
<tr>
<td>E3 Sagittal</td>
<td>E3 Coronal</td>
<td>E8 Sagittal</td>
<td>E8 Coronal</td>
</tr>
<tr>
<td>E4 Sagittal</td>
<td>E4 Coronal</td>
<td>E9 Sagittal</td>
<td>E9 Coronal</td>
</tr>
<tr>
<td>E5 Sagittal</td>
<td>E5 Coronal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 4-4 – Visualizations of +/-2σ (green/red) of the first 9 (E1-E9) eigenvectors for CFS geometry
Figure 4-5 – Visualizations of +/-2σ of the first 9 (E1-E9) eigenvectors for CFS stiffness distribution
4.3.2 Validation of SSM Generated Geometry

4.3.2.1 Facial Symmetry

Figure 4-6 compares the symmetry scores $SS_{\text{model}}$ between a sample human population examined by Roumeliotis et al. ($n = 32$) and the models produced by the SSM, which were significantly more symmetric than the human sample\textsuperscript{27}.

![Comparison of symmetry scores between SSM produced CFS models and a population of 32 specimens from Willing et al using a whisker plot. The red line represents the median, the lower and upper blue boundaries represent the 25\textsuperscript{th} and 75\textsuperscript{th} percentiles respectively, and the whiskers extend to the most extreme values.](image)

4.3.2.2 Craniometric Measurements

4.3.2.2.1 Morphological Integration

Table 4-2 shows the correlation matrices for GOL, XCB, NPH, and ZYB for both the SSM and Howells geometries, revealing positive correlations for all combinations of measurements. Specific to the integration hypothesis, neurocranial breadth (XCB) was positively correlated with facial breadth (ZYB), facial height (NPH), and neurocranial length (GOL). Figure 4-7 contains scatterplots of these relationships.
Figure 4-7 – Scatterplots of the relationship between cranial breadth (XCB) and a) facial breadth (ZYB), facial height (NPH), and cranial length (GOL).
Table 4-2– Howells (sub-populations) and SSM correlation matrices. All off-diagonal correlations were significant at p < 0.01.

<table>
<thead>
<tr>
<th></th>
<th>xcb</th>
<th>zyb</th>
<th>nph</th>
<th>gol</th>
</tr>
</thead>
<tbody>
<tr>
<td>xcb</td>
<td>1</td>
<td>0.66</td>
<td>0.28</td>
<td>0.23</td>
</tr>
<tr>
<td>zyb</td>
<td>-</td>
<td>1</td>
<td>0.50</td>
<td>0.47</td>
</tr>
<tr>
<td>nph</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>0.50</td>
</tr>
<tr>
<td>gol</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>xcb</th>
<th>zyb</th>
<th>nph</th>
<th>gol</th>
</tr>
</thead>
<tbody>
<tr>
<td>xcb</td>
<td>1</td>
<td>0.69</td>
<td>0.26</td>
<td>0.32</td>
</tr>
<tr>
<td>zyb</td>
<td>-</td>
<td>1</td>
<td>0.59</td>
<td>0.66</td>
</tr>
<tr>
<td>nph</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>0.67</td>
</tr>
<tr>
<td>gol</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

4.3.2.2.2 The Howells Dataset

The SSM model sample was compared to all 28 populations in the Howells dataset. This yielded significant differences between the two groups for all four craniometric measurements examined in the integration analysis, with Cohen’s $d$ effect sizes of 0.65, 0.34, 0.82, and 0.12 for GOL, NPH, XCB, and ZYB, respectively (Table 4-3). Normalized distributions of SSM and Howells measurement values are displayed in Figure 4-8.

CFS morphology is known to be a heritable trait$^{33,34}$, and as such, comparing craniometric measurements from individuals of ethnic populations different than those used to build the SSM may not be consistent. Considering that the SSM produced in the present study was entirely made up of Caucasian specimens, the t-tests were performed once again after limiting the Howells data set to populations of European origin (Norse, Zalavar, and Berg) only. This yielded no significant difference between groups for the ZYB measurement, with significant differences persisting for GOL, NPH, and XCB measurements. Effect sizes, however, had decreased to 0.49, 0.31, and 0.31, respectively (Table 4-3)
Figure 4-8 – Comparison of normalized craniometric measurement distributions using a) all Howells data and b) Howells specimens of European descent. Measurement values (mm) are on the x-axis, with proportion of total population on the y-axis.

Table 4-3 – 95% confidence intervals with Cohen’s d and p-values calculated from t-tests conducted between Howells and SSM generated skull populations.

<table>
<thead>
<tr>
<th>Population</th>
<th>GOL</th>
<th>NPH</th>
<th>XCB</th>
<th>ZYB</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>[4.99 – 6.29]</td>
<td>[1.39 – 2.18]</td>
<td>[5.28 – 6.35]</td>
<td>[-1.45 – -0.35]</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.01, d=0.65</td>
<td>p&lt;0.01, d=0.34</td>
<td>p&lt;0.01, d=0.82</td>
<td>p&lt;0.01, d=-0.12</td>
</tr>
<tr>
<td>European</td>
<td>[3.25 – 5.50]</td>
<td>[0.82 – 1.95]</td>
<td>[1.11 – 2.63]</td>
<td>[-1.08 – 0.40]</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.01, d=0.49</td>
<td>p&lt;0.01, d=0.31</td>
<td>p&lt;0.01, d=0.31</td>
<td>p=0.40, d=-0.06</td>
</tr>
</tbody>
</table>

Power (@ d = 0.2) = 0.87
4.3.2.2.3 Validation of Automated Measurement Methods

Excellent agreement was observed between manual and automated measurement methods as shown in the Bland-Altman plots (Figure 4-9 and Table 4-4). ICC values for GOL, XCB, NPH, and ZYB were 0.99, 0.97, 0.80, and 0.99, respectively (Table 4-5).

Table 4-4 – Comparison of craniometric measurements between Howells populations and SSM generated models using average error (±σ) in mm.

<table>
<thead>
<tr>
<th>GOL</th>
<th>NPH</th>
<th>XCB</th>
<th>ZYB</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.02 ±2.49</td>
<td>-0.33 ±0.53</td>
<td>-0.71 ±1.13</td>
<td>0.23 ±1.55</td>
</tr>
</tbody>
</table>

Table 4-5 – ICC values comparing automated and manual CFS metric measurements.

<table>
<thead>
<tr>
<th>GOL</th>
<th>NPH</th>
<th>XCB</th>
<th>ZYB</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.99</td>
<td>0.80</td>
<td>0.97</td>
<td>0.99</td>
</tr>
</tbody>
</table>
Figure 4-9 – Bland-Altman plots comparing CFS dimensions measured using manual and automated methods (mm).
4.4 Discussion

This study used corresponding meshes of 22 human CFS geometries to create a SSM, defining independent modes of variation in geometry and stiffness distribution in the human CFS. This enabled the production of unique, FE analysis-ready meshes of CFS geometries complete with stiffness distribution information. The mesh creation process, along with element untangling and optimization, was fully automated, taking approximately 8 hours to produce a population of 1000 unique meshes. Correspondence of mesh nodes and elements between meshes allowed for key craniometric measurements of the meshes, and will facilitate the preparation and data extraction of future FE analyses performed using these meshes.

Comparison with the Howells dataset of human CFS measurements revealed that the extent and nature of geometric variability present in the SSM meshes are a good representation of that observed in humans of European origin. SSM produced meshes exhibited a high degree of symmetry, with average $SS_{\text{model}} = 0.76$ mm. While $SS_{\text{model}}$ refers to a measure of surface-based symmetry, it has been shown to correlate with symmetry of cephalometric landmarks\textsuperscript{26}, and thus indicates a high degree of symmetry between CFS features as well. This low symmetry score (higher degree of symmetry) is supportive of the human-likeness of the SSM produced population, as the human face is highly symmetric. Although SSM produced meshes were significantly more symmetric than those of Roumeliotis et al. (average $SS_{\text{model}} = 1.02$ mm)\textsuperscript{27}, this could be attributed to the fact that the meshes produced by the SSM were idealized and featureless to facilitate FE analyses, which would eliminate sources of asymmetry found in a CFS scan of higher fidelity. Further studies could investigate the symmetry of each mode of variation individually to determine if symmetry
in bilateral CFS symmetry corresponds with one shape mode in particular, or if perhaps symmetry emerges from the combination of all shape variation modes working together.

For both the SSM generated meshes and Howells measurements, maximum cranial breadth (XCB) was found to be positively correlated with facial breadth (ZYB), but also with facial height (NPH) and cranial length (GOL), which is counter to the dolico-brachycephalic spectrum posited by Enlow and Hans’ traditional theory of integration\textsuperscript{28}. Despite the fact that this paradigm is still used to characterize CFS geometry\textsuperscript{35,36}, the data from the present study are consistent with a growing body of research critical of this model of integration. Several studies have shown that while there is still strong evidence of co-variation in various anatomical structures, the strongest phenotypic expression in the CFS in particular is that of positive correlations between cranial and facial breadth, which has been demonstrated previously in mice\textsuperscript{37}. More recently this finding has been extended to humans in a study looking at a population of 351 human skulls with recorded familial relationships from Hallstadt, Austria, which found the strongest correlations were between cranial and facial breadth, with weaker positive correlations with facial height and cranial length\textsuperscript{33}, all consistent with the present results.

Significant differences (p < 0.05) between Howells and SSM mesh measurements were detected for all measurements GOL, NPH, XCB, and ZYB, with effects sizes of 0.65, 0.34, 0.82, and 0.12, respectively. Better correspondence between measurements was achieved by limiting comparisons to only those Howells sub-populations that were of European origin \textit{(i.e.} Norse, Berg, and Zalavar populations), a hypothesis based on the fact that the training set was completely made up of Caucasian specimens. This had the effect of increasing the p-value from < 0.05 to 0.40 for the ZYB measurement. While p-values
remained below 0.05 for comparisons of GOL, NPH, and XCB measurements, effects sizes decreased for comparisons of GOL, NPH, and XCB decreased, ranging from 0.31 to 0.49, (small to moderate\textsuperscript{38}).

One explanation for low p-values despite small effect sizes between groups is the large sample sizes used\textsuperscript{39} (1000 and 317 for SSM models and Howells sub-populations respectively), leading to the possibility of an overpowered comparison. The power of a statistical test refers to its ability to detect small differences in sample means at a given p-value, and an overpowered test occurs when a statistically significant difference between sample means is so small as to be inconsequential to the question at hand. For the present study, the differences between population means as a percentage of mean Howells values for XCB, NPH, and GOL are quite small at 1.3\%, 2.1\%, and 2.4\%. Furthermore, a power calculation reveals that even if these differences were assumed to actually be 0.86\%, 1.4\%, and 1.0\% (all corresponding to an effect size of 0.2, considered small\textsuperscript{38}), the power value is 0.89, corresponding to the probability of detecting a difference between samples at the p=0.05 level. For these reasons, it was concluded that the geometry of the CFS meshes produced by the SSM reasonably represented that of humans of European descent.

While these preliminary results are encouraging, it is fairly trivial to improve upon the robustness of a SSM by adding additional instances to the training set. The training set in the present study used 22 specimens. While training sets of this size have been used to create SSMs capable of producing viable human geometries\textsuperscript{9}, increasing the size of the training set would allow for the determination of a greater number of variability modes, and allow for a more geometrically diverse population of meshes.
At some point, increasing the size of the training set encounters diminishing benefits as any additional modes of variation realized by an increased training set account for less and less of the overall variability in the set. The ability of the training set to describe a particular geometry can still be improved, however, through creating separate SSMs based on characteristics of sub-populations, as demonstrated in the present study by limiting comparisons with the Howells sub-populations that were of European origin. Extending this idea, training sets made out of only male or female specimens could be used to create sex-specific geometries. The fact that distribution of craniometric measurements from the Howells’ dataset in Figure 4-8 appear somewhat bi-modal supports the idea that sex-specific SSMs could better represent male and female CFS geometries, an idea that could prove fruitful for future research.

The advent of digital image analysis has made automated measurement techniques common in the field of biomechanics, which often leads to faster and/or more accurate measurements than manual identification on images. While this is advantageous, it is crucial that these automated techniques are validated against manual counterparts to justify their use. Past work utilizing SSM generated geometries have assumed that correspondence between mesh nodes equates with correspondence between anatomical landmarks. The present study was the first attempt at testing this theory, showing excellent agreement between craniometric measurements made manually and those made by assuming nodal correspondence implies correspondence of cephalometric landmarks.
4.5 Conclusion

The work presented in this study demonstrated the first SSM of the human CFS that requires no manual landmarking and produces FE analysis ready CFS meshes that accurately describe the variation in geometry observed in the adult human population. This work will aid in future computational analyses of the human CFS in several ways. First, it eliminates the need to acquire CT images from human candidates to perform FE analyses of the human CFS, eliminating the time and money needed to acquire cadaveric specimens or patient records. Second, CFS meshes are produced automatically with corresponding nodes and elements, eliminating the time-consuming process of manual geometry segmentation and mesh generation, and facilitates the pre- and post-processing of FE analyses. Third, it enables researchers to use a large population of CFS specimens with different geometries to acquire FE data that is more representative of the human population at large.
4.6 References


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5 Implementation of a Statistical Shape Model of the Craniofacial Skeleton in a Monte Carlo Analysis of Zygomatic Fracture

5.1 Introduction

Anthropomorphic testing devices (ATDs) have long been established as a valuable tool in biomechanical investigations of the physical response of the human body. They are less sensitive to testing conditions, offer more instrumentation options, and present fewer ethical considerations compared to cadavers. As a result, ATDs have been used to quantify the damage incurred from traumatic physical events, as well as to evaluate the efficacy of injury prevention devices\textsuperscript{1–3}.

A crucial property of an ATD is its biofidelity, which describes how well it is able to mimic the kinetic and kinematic response of a corresponding human subject. This objective is confounded by the high degree of variability present in the human population. Addressing this variability usually involves designing classes of ATDs to represent different body types or conditions of interest, such as a certain percentile of a child or adult\textsuperscript{4,5}.

In order to properly characterize a human response, data on the variables of interest are needed. Collecting these data from a population of human subjects can be a relatively simple task for commonly or easily measured variables such as height and weight. However, attributes such as bone fracture thresholds require \textit{in-vitro} testing of human cadaveric specimens. The financial and technical challenges that come with these kinds of tests can inhibit the ability of researchers to use larger sample sizes, resulting in high variability or inconsistencies between studies.
With respect to the craniofacial skeleton (CFS), frangible or crushable inserts have been developed for use with modern ATDs to indicate whether or not an event is likely to result in fracture. The technical literature used to inform the development of these inserts have reported much variation in fracture force thresholds. In a study involving forty-five cadaveric experiments and an array of impactor sizes, Swearingen measured the minimum fracture point of the zygoma to be 489.3 N. Hodgson reported zygomatic fractures occurring anywhere from 150 to 1000 lbs (667 – 4448 N) depending on the contact area and impactor size, as well as the duration of the impact itself. Gadd, however, concluded that fracture tolerance values were most dependent on peak force, measuring this to be 225 lbs (1001 N). The conclusion of peak force being the main contributor to fracture risk (as opposed impact area, duration, velocity, etc.) has since been well corroborated by several subsequent studies. This is likely explained by the fact that the zygoma is a flat bone with relatively little marrow content, reducing the potential for viscoelastic effects compared to long bones. Further studies of zygoma fracture force thresholds estimated fracture tolerances to be between 200 and 540 lbs (890 – 2402 N).

While these studies reported comparable ranges of zygomatic fracture tolerances, the size of these ranges indicate a high degree of variability. This is unsurprising considering the high number of potentially confounding variables determining fracture tolerance, such as zygoma size, geometry, and bone density, not to mention inconsistencies in experimental trials. A more appropriate way of describing fracture risk would be to use a probabilistic distribution as opposed to a singular force threshold. Yoganandan was the first to develop a fracture risk distribution for the zygomatic complex using experimental data from drop tests performed on 18 whole unembalmed human cadaver heads. Each specimen was
oriented such that its zygoma impacted the spoke-rim junction of a steering wheel at the zygomatic eminence. Impact velocities were varied to generate a spectrum of impact forces with corresponding fracture scores, which were used to generate a cumulative fracture risk probability curve using a Weibull distribution. It was found that a force of 1525 N corresponded to a 50% probability of facial fracture.

In recent years, advances in computer software and hardware have made it possible to combine finite element (FE) and Monte Carlo (MC) techniques to explore the interaction between variation in anatomical parameters and the physical response of biomechanical systems. In this approach, a large number of FE simulations are executed with values for input variables randomly assigned from predetermined probabilistic distributions. The aggregate of the resulting deterministic FE solutions is then used to describe the distribution of an outcome measure, as well as evaluate the relative importance of input variables. This approach has been used to evaluate how geometric variation of the femur relates to fracture patterns collected from clinical data, but has not yet to be applied to study the CFS.

One objective of this chapter is to provide a demonstration of how a validated statistical shape model (SSM) and the FE method can be used to inform ATD fracture thresholds using a combined FE and MC analysis. The set of 1000 FE meshes created by the SSM developed in Chapter 4 represent a population of CFS geometries whose geometric principal component weightings were randomly selected from normal distributions. These meshes were loaded with the 1525 N fracture threshold at the zygomatic eminence, and the proportion of those simulations experiencing fracture compared to the predicted value of 50%.
In addition, the zygomatic fracture classification system first described by Zingg\textsuperscript{20} has been noted for its ability to characterize clinical fracture cases with little ambiguity, and has been implemented in several clinical reviews of zygomatic fracture in Switzerland\textsuperscript{20}, Australia/New Zealand\textsuperscript{21} and Tunisia\textsuperscript{22}. There is some discrepancy in the relative frequency of the occurrence of various fracture types, and it remains unclear whether or not this is chiefly due to the conditions of the fracture event itself, or if certain geometric or anatomical factors play a significant role in fracture outcome. The ability to automatically take craniometric measurements demonstrated in Chapter 4 will be used to determine if particular CFS characteristics such as geometry or density distribution are associated with a particular fracture pattern. The consistency in the magnitude and location of the applied forces afforded by corresponding meshes and FE software will ensure that the only variability present in the model is CFS geometry and bone density distributions.

5.2 Methods

5.2.1 FE Model creation

5.2.1.1 Mesh Generation and Model Setup

The sample of 1000 CFS meshes created in Chapter 4 were modified to create analysis-ready FE meshes. Elastic modulus values were calculated for each element by averaging the modulus values at the associated nodes, and linear tetrahedral mesh elements were converted to second order elements through the addition of mid-side nodes. A density value was also calculated for each element using a power law relation between density and elastic modulus developed for flat bone structures\textsuperscript{23}. 
To model contact with the rim of a steering wheel used by Yoganandan to develop the facial fracture probability distribution\cite{yoganandan2015}, a strip of nodes approximately 8 mm wide covering the external surface of the zygomatic eminence composed a loading node set (Figure 5-1). A plane with a medially directed normal vector was fit to the loading node set using principal component analysis. The 50\% fracture threshold force of 1525 N was evenly distributed over the loading node set, and was directed along the fitted plane’s medially directed normal vector to ensure the force acted normal to the loading surface (Figure 5-1).

![Figure 5-1 –a) Loading node set and b) load direction axis used for the FE simulations.](image)

A region consisting of the contralateral zygomatic and temporal processes, lateral aspect of the maxilla, and lateral orbital rim were held fixed in order to ensure that the applied load was not shared by both zygomatic structures (Figure 5-2).
The above FE model preparation process was applied to all 1000 FE meshes automatically through the use of a Python script.

5.2.2 Fracture Categorization

Element groups were defined corresponding to three regions of interest (ROIs) used in the zygoma fracture categorizations defined by Zingg et al. The elements of the zygomatic arch were designated as ROI1; the elements of the lateral orbital wall and rim were designated as ROI2; and the elements of the infraorbital rim were designated as ROI3 (Figure 5-3).
Figure 5-3 - Regions of interest used in FE model fracture classification system
Mesh elements with a maximum principal strain exceeding 0.42% were considered yielded. An FE simulation was considered to have resulted in fracture if the volume fraction of failed elements for one or more ROIs exceeded 10%. The ratio of simulations resulting in fracture was calculated and compared to the rate of 50% as predicted by Yoganandan et al.

Simulation fractures were classified depending on the number and location of failed ROIs. If only one of ROI 1, 2, or 3 failed, the fracture was classified as type A1, A2, or A3, respectively. If at least two ROIs failed, the fracture was classified as type B, as it was assumed that the remaining point of support would not be able to support the loading by itself. There were no specific criteria included for fractures of type C as these fractures are simply a subset of type B, and the simplified model used was not able to differentiate between dislocation or dislocation plus comminution. Thus, fracture types B and C were combined into a single category. The proportion of fractures occurring in each category were compared to the proportions reported by clinical studies.

5.2.3 Correlation Between Model Features and Incidence of Fracture

Chapter 4 established that craniometric measurements on meshes created by the SSM can be automatically taken by assuming corresponding nodes from different meshes remain in the same relative position with respect to cranial landmarks. This provides an efficient means by which to investigate what relationships, if any, exist between CFS characteristics and the vulnerability of ROIs to fracture.

To this end, several craniofacial dimensions relating to the zygoma were quantified to determine their relationship with volume of failed elements in any ROI. These included
Zygomatic Length (ZYL), defined by the distance between the base of the zygomatic arch and its insertion into the zygomatic buttress; Zygomatic Thickness (ZYT), defined as the thickness of the zygomatic arch at mid span; and Zygomatic Prominence (ZYP), defined by the difference between facial breadth (ZYB) and intertemporal distance (ITD), which is the distance between the most medial aspect of each temporalis groove$^{25,26}$ (Figure 5-4).

Furthermore, since the SSM produced a unique bone mineral density distribution in each mesh, it was possible to analyze the relationship between bone density distribution and volume of zygomatic fracture. Thus, element-volume-weighted-density (VWD) values VWD1, VWD2, and VWD3 were calculated for each of ROI1, ROI2, and ROI3 respectively.
These six measurement- and material-based variables were entered as independent variables in a multivariate multiple linear regression analysis. The volume of failed elements in ROI1, ROI2, and ROI3, indicated as FVOL1, FVOL2, and FVOL3 respectively, were used as dependent variables. Significance was set at $p < 0.05$.

5.3 Results

5.3.1 Fracture Categorization and Historical Comparison

The results of the probabilistic FE analysis are summarized in Figure 5-5. Of the 1000 FE simulations, fracture in at least one ROI occurred in only 61 (6.1%).

![Figure 5-5 - Proportion of finite element simulation resulting in at least one ROI experiencing fracture.](image)

Figure 5-6 breaks down the simulations resulting in fracture by fracture classification. The occurrence of A1 (8% of fractures) and A2 (3% of fractures) fracture types observed in the MC analysis are similar to those reported clinically. Similarly, type B and C fractures made up the largest proportion of overall fractures (48%). However, there was a much higher proportion of type A3 fractures observed in the MC analysis (41%) than in any of the other clinical studies. Figure 5-7 gives representations of the manifestation of each fracture type.
Figure 5-6 – Breakdown of fracture types as predicted by finite element simulations.

Figure 5-7 - Representative examples of FE simulations resulting in fractures of types A1, A2, A3, and B/C.
5.3.2 Correlation Between Model Features and Incidence of Fracture

The results of the multivariate multiple linear regression are summarized in Table 5-1. The linear model was found to generally fit the data well, with $r^2$ values of 0.73, 0.64, and 0.87 for FVOL1, FVOL2, and FVOL3, respectively ($p<0.001$). All independent variables except for ZYP were found to be significant.

Geometric factors that influenced the volume of failed elements in each region were Zygomatic Length (ZYL) and Zygomatic Thickness (ZYT). ZYL was positively correlated with FVOL3 ($p<0.001$), while ZYT was negatively correlated with FVOL2 ($p<0.05$).

The volume-weighted average density of each region was most strongly correlated with failure in its corresponding ROI, and inversely correlated with the amount of failed volume in that same region ($p < 0.001$). Additionally, VWD3 was also negatively correlated with the FVOL1 and FVOL2 ($p < 0.05$), indicating that, for the present model bone density distribution in this region is particularly predictive of fracture of the zygomatic complex.

Multiple regression analyses were also performed on each dependent variable using both backwards and forwards elimination methods. In all cases, independent variables found to be significant in the multivariate regression were also found to be significant in the multiple regressions.
Table 5-1 – Summary of results from multivariate multiple linear regression analysis. Significant effects are bolded. The Model Significance row lists each independent variable’s p-value for the entire linear model. The Between-Subjects Effects row lists each independent variable’s p-value for a corresponding dependent variable, with beta values underneath in brackets.

<table>
<thead>
<tr>
<th>Model Significance</th>
<th>p-value</th>
<th>ZYP</th>
<th>ZYT</th>
<th>ZYL</th>
<th>VWD1</th>
<th>VWD2</th>
<th>VWD3</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVOL1 (R²=0.73)</td>
<td>0.282</td>
<td>0.852</td>
<td>0.813</td>
<td>&lt;0.001</td>
<td>0.850</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(-17.8)</td>
<td>14.7</td>
<td>-5.5</td>
<td>(-1750e3)</td>
<td>(44e3)</td>
<td>(-487e3)</td>
<td></td>
</tr>
<tr>
<td>FVOL2 (R²=0.64)</td>
<td>0.933</td>
<td>0.014</td>
<td>0.669</td>
<td>0.400</td>
<td>&lt;0.001</td>
<td>0.019</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.1</td>
<td>(-154.0)</td>
<td>-7.6</td>
<td>(-256e3)</td>
<td>(-713e3)</td>
<td>(-409e3)</td>
<td></td>
</tr>
<tr>
<td>FVOL3 (R²=0.87)</td>
<td>0.441</td>
<td>0.142</td>
<td>&lt;0.001</td>
<td>0.275</td>
<td>0.496</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(-11.0)</td>
<td>(-100.0)</td>
<td>(77.0)</td>
<td>(-371e3)</td>
<td>(-136e3)</td>
<td>(-2148e3)</td>
<td></td>
</tr>
</tbody>
</table>


5.4 Discussion

The purpose of this investigation was to demonstrate the utility of a SSM in evaluating experimentally derived failure thresholds by using the outcome of a Monte Carlo analysis implemented using FE analysis. Furthermore, the role of craniofacial geometry and bone density in zygomatic loading distributions was analyzed and compared with clinically observed zygomatic fracture patterns.

Only 6.1% of simulations predicted fracture of some kind based on the 10% by volume failure criteria, which is considerably lower than the 50% fracture risk predicted by Yoganandan et al. This indicates that the experimentally derived fracture tolerances of the zygoma at 1525 N severely underestimate the resistance of the zygoma to fracture. While designing to a standard set by a 1525 N threshold would err on the side of safety, it could also lead to overly stringent regulations which might manifest in product costs.

Table 5-2 compares the proportion of fracture categories between the results of the Monte Carlo analysis and past clinical investigations. While isolated fractures of the zygomatic arch (type A1) and lateral orbital rim (type A2) are comparable across studies, the Monte Carlo analysis predicted far more isolated fractures of the infraorbital rim. This outcome may indicate a particular susceptibility of ROI3 to the laterally directed loading employed by the FE models used in this study, as the fractures reported in the clinical studies were caused by a variety of incidents (e.g. assaults, vehicular accidents, etc.) where the applied loading would be inconsistent.

As a result of the increased proportion of FE models resulting in fractures of type A3, there was significant drop in the proportion of fractures exhibiting full zygomatic dislocation.
(types B and C) as compared to the clinical studies; however, these fracture types still represented the largest proportion of fractures in both the Monte Carlo analysis and clinical studies.

The results of the multivariate analysis indicate that there is some association with craniofacial measurements and fracture risk. In particular, zygomatic length was positively correlated with failed element volume in ROI3, which is reasonable from a structural perspective; a longer zygomatic arch would create a larger moment arm at the insertion of the zygomatic and temporal processes, resulting in increased stresses and strains. There was also a negative correlation between zygomatic arch thickness and failed element volume in ROI2, perhaps indicating that a thicker zygomatic arch has a somewhat protective effect on ROI2 by reducing the strain in this region.

A ROI’s volume weighted density was the strongest indicator of the volume of elements exceeding the failure strain within that same region. This mirrors results of similar FE and experimental investigations\textsuperscript{19,27}, and is unsurprising as the relationship between bone density and strength has been well established in biomechanics.

The volume weighted density of ROI3 was also associated with the volume of elements exceeding yield strain in all three ROIs. This indicates that the inferior portion of the zygomatic bone extending to the infraorbital rim (ROI 3) plays a significant role in resistance of the entire zygomatic complex to fracture subject to a medial force applied on the zygomatic eminence, as might be experienced in contact with a steering wheel. In particular, these results seem to suggest that ROI 3 acts as kind of lynch-pin, where weakness in this region would translate to weakness in ROIs 1 and 2.
The results of this study offer unique insight into the relationship between the anatomical characteristics of the zygoma and the loading experienced in steering wheel contact; however, these results must be interpreted within the context of the assumptions imposed on the FE simulations.

The FE simulation was performed as a static analysis, which assumes certain loading considerations are negligible; namely, impact duration and viscoelastic properties of bone. These assumptions were considered reasonable because the role of peak force as the main indicator of fracture risk is well established from previous investigations that have reported little rate-dependence on zygomatic fracture\textsuperscript{3,9–12}.

Furthermore, the initial craniofacial FE models upon which the mesh morphing and subsequent SSM produced models were built were validated using a modal analysis. While a modal analysis does overall elastic response of the structure, it is no guarantee that discrete strain values are reflective of the actual physical response. This is especially important at the surface mesh boundary, where partial volume effects can cause element stiffness to be underestimated. With respect to the present study, this may artificially inflate strain values on surface elements, and potentially increase the incidence of fracture according to the 0.42% failure strain value.

Suture lines of the zygomatic complex were not incorporated into the fracture model. The geometric discontinuities and changes in material properties across these boundaries are likely to have an impact on the threshold force required to produce fracture, as well as the degree and pattern of the fracture itself. Future investigations should incorporate these factors, as there is much clinical evidence that fracture does occur along the sutures\textsuperscript{20}. 
The age of the individuals used in the training set to develop the SSM in Chapter 4 was not incorporated into the SSM itself; that is, it was implicitly assumed that factors such as CFS geometry and bone density distribution did not change with age. While it has been established that bone density distribution depends on age (especially in females) in the femur and vertebrae, it has been well established that this same correlation has not been observed in the CFS due to its relatively high content of cortical bone.\textsuperscript{15,17,27}

There are several ways in which fracture thresholds can be defined for a FE simulation. A fracture threshold of 153 MPa has been suggested in the past to indicate fracture of the CFS.\textsuperscript{28} However, when applied to the current investigation, it was found to be overly conservative as no fractures occurred. The threshold of 0.42% principal strain was chosen for several reasons. It was based off of a comprehensive validation study in which a FE model of a human head including all bony structures and soft tissues was validated against 35 experimental cases, and was the most comprehensive CFS FE model validation found. Furthermore, previous studies have reported strain-based strength criteria to hold several advantages over stress-based strength criteria, such as being statistically more powerful, independent of bone density, and isotropic.\textsuperscript{29–33}

The fracture threshold of 10% is also unverified, however it has previously been described as conservative in that the actual threshold is likely higher, which still reinforces the idea that a 50% probability fracture threshold of 1525 N is an underestimation.\textsuperscript{19}

While the threshold value of failed volume may be imprecise, the advantage of using a FE analysis is demonstrated by the ability to objectively compare the consequences of loading on each ROI using a quantitative assessment, namely, the volume of elements exceeding...
some threshold yield strain value. The method used by Yoganandan to develop a fracture risk curve employed a subjective fracture scale with values of one to five, and is subject to inter-rater error. Using a fracture criteria based on an FE outcome leaves no ambiguity to the potential damage caused by a loading scenario and has higher fidelity with respect to damage quantification, allowing for a more accurate damage assessment.

5.5 Conclusion

The goal of combining FE and MC analysis to evaluate experimentally derived fracture criteria for the CFS and comparing outcomes with clinical reports was achieved. This is the first study to the author’s knowledge to investigate the interaction between anatomical characteristics and loading distribution in the zygoma while controlling for force magnitude, that uses a statistical shape model to study the loading capacity of the human CFS, and that uses probabilistic methods to evaluate ATD design specifications.

While there were some limitations to this analysis, there is much potential for future improvement and expansion on the ideas presented in this study. A training set of 22 specimens was used to develop the SSM in Chapter 4 used to produce the FE meshes for this study. While this was shown to adequately capture human anatomical variation, it would be relatively simple to continually add specimens to this training set over time. Not only would this add more information to the current model, but statistical shape models of sub-groups of interest could also be developed. For example, it has been shown that the CFS of females generally has lower bone density values. With the development of an adequate fracture criteria and more complex FE model, the methods used in this study could be used to create fracture criteria tailored to these specific groups, allowing safety engineers even more flexibility in the development of specialized ATD devices.
Table 5-2 - Comparison of fracture classification proportions between the Monte Carlo analysis and previous clinical investigations.

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<th>Adj <em>et al.</em></th>
<th>Bougulia <em>et al.</em></th>
<th>Monte Carlo</th>
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<td>1%</td>
<td>41%</td>
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<td>61%</td>
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<tr>
<td>C</td>
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Number of Fractures

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<td>363</td>
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<tr>
<td>1000</td>
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5.6 References


26. Waitzman AA, Posnick JC, Armstrong DC, Pron GE. Craniofacial skeletal


6 Conclusion

6.1 Research Goal

The main motivation of this thesis was to develop a means of addressing a pervasive deficiency of existing biomechanical investigations of the human craniofacial skeleton (CFS) that utilize finite element (FE) analysis; namely, that these studies are severely underpowered with respect to sample size. Statistical shape modeling is a technique adapted from computer vision and facial recognition research that can be employed to automate the usually tedious process of generating FE meshes representing human anatomy. This thesis was conceived as a means of using statistical shape models (SSM) to enable FE investigations of the human CFS that utilize large samples, and this goal was achieved through the conception and execution of four studies, each building off the results of its predecessor.

6.2 Summary of Research Performed

Since all subsequent CFS meshes produced by the SSM would be based on manually created models, it was important to first verify that manually created models could reliably represent the elastic response of the CFS (Hypothesis 1). Thus, the first step was the validation of manually created FE meshes using experimental results. In Chapter 1, a modal FE analysis was performed on 5 CFS specimens that were part of another experimental investigation into the resonant frequencies of the CFS. Meshes were created from CT scans of experimental specimens using the more common method of semi-automatic geometry masking, geometry extraction, node seeding and finally meshing. The resonant frequencies calculated by the FE analysis matched the experimental values to a higher standard than past reports of modeling the modal response of flat bone (e.g. the pelvis), owing largely to
the use of a material model developed specifically for flat bone. This study established that contemporary FE techniques could adequately model the geometry and linear response of the human CFS (Hypothesis 1 accepted).

In Chapter 3, a mesh morphing algorithm was developed to adapt a single mesh to the set of experimental meshes used in Chapter 2, a step that was necessary to create the SSM itself. It was also important to ensure this morphing process did not degrade the quality of the manually created baseline mesh, and to verify that morphed meshes performed as well as manually created meshes in FE analyses (Hypothesis 2). This was accomplished using a two-step iterative surface- and volume-morphing algorithm that mapped baseline meshes onto target geometry. The initial surface morphing algorithm was implemented using radial basis function interpolation and a Laplacian smoothing algorithm to maintain surface element quality. Surface displacements were used as boundary conditions for calculating volumetric node displacements by solving three independent boundary value problems using the diffusion equation: one each for the x-, y-, and z-directions. Material properties were assigned to nodes by registering the morphed mesh with the CT scan of its target combined with established CT greyscale-bone density relationships. An optimization procedure was developed to maintain volumetric mesh quality, where objective functions constructed using element quality metrics were minimized. The morphed meshes were then subjected to the same simulations as the manually created ones in Chapter 2, and it was found that the results of the FE analyses using the morphed meshes were in excellent agreement with those of the manually created meshes, with only slight reductions in overall mesh quality (Hypothesis 2 accepted).
In Chapter 4, the morphing procedure developed in Chapter 3 was used to create a training set of 22 CFS meshes for a SSM that included shape and density information. It was important to confirm that the shape variation produced by SSM-created meshes reflected that of the general human population (Hypothesis 3). A sample of 1000 CFS meshes were produced, and were subsequently compared with human specimens in terms of symmetry, as well as the distribution and relationship between several craniometric measurements including cranial breadth, cranial length, facial breadth, and facial height. It was found that the CFS meshes produced by the SSM generally represented the geometry of the broader human population well (Hypothesis 3 accepted). The ability of SSM produced meshes to represent human geometry improved when comparisons were limited to individuals of European descent. It was hypothesized that this is because the SSM model was made up of only Caucasian specimens, which would bias SSM produced geometries towards this population. This result highlighted the importance of ensuring that the specimens used to make up the training set of an SSM are sourced from a broad cross-section of the population intended to be modeled. It also highlighted further opportunities for population-specific SSMs useful in situations where specific human demographics or perhaps medical conditions affecting bone geometry or bone density, are of interest.

As an additional sub-study, Chapter 4 also confirmed an assumption implicit in several past investigations employing SSMs; namely, that correspondence of nodes between SSM produced meshes can be relied upon to automatically take measurements of the shape under investigation.

Chapter 5 represented the culmination of the foundational work performed in Chapters 2-4. After establishing that the 1000 CFS meshes created by the SSM capably represented
the elastic response of the CFS (Chapters 2 and 3), and that the geometric variation present in these meshes adequately represented that of the human population (Chapter 4), the use of the SSM produced meshes to represent the human population in a Monte Carlo analysis was justified. The Monte Carlo analysis performed in Chapter 5 assessed the conclusion of a previous experimental investigation that used only 18 human cadaver heads and reported a 50% fracture probability threshold for the human zygoma of 1525 N (Hypothesis 4). Of the 1000 FE simulations run, only 6% resulted in fracture based on previously established fracture criteria, indicating that the resistance of the zygoma is potentially much higher than reported (Hypothesis 4 not fully accepted – conflicting Monte Carlo and experimental results, but useful information gained). Furthermore, the amount of damage incurred by the bony structures of the CFS were more quantifiable using the objective measures determined from the FE results (i.e. principal strains, von mises stresses, etc.). This offers advantages over the qualitative scale that has been used previously for the zygoma and other fracture types, which is subject to inter-rater error, subjective biases, and ambiguity of the degree of damage caused. This is significant because studies like the ones the Monte Carlo analysis was compared against are used to determine properties of anthropomorphic testing devices (ATDs), where biofidelity is relied upon to develop effective safety systems for use in vehicles or personal protective equipment.

Beyond fracture characterization, the ability to automatically measure anatomical features and density distributions in regions of interest afforded by correspondence of nodes and elements in the SSM produced meshes facilitated an investigation into the relationship between these measurements and fracture characteristics by highlighting the importance of the sub-orbital region of the zygoma to the integrity of the zygomatic complex. This
information is valuable to plastic surgeons who depend on an understanding of the structural significance of craniofacial structures to restore function and comfort to patients suffering craniofacial fractures.

6.3 Significance

The work presented in this thesis provides novel insights into the biomechanics of the CFS with respect to its elastic response and structural integrity; into mesh generation and optimization in the field of biomechanical FEA; and the incorporation of probabilistic methods to account for variability in anatomical geometry and material properties in biomechanical studies employing FE techniques.

Chapter 2 is, to the author’s knowledge, the only study to use FE analysis to determine the resonant frequencies of the human CFS, and to have these models validated using experimental results. Furthermore, mode shapes of the skull have only been estimated using idealized analytical models, whereas the FE analysis was able to visually illustrate the physical manifestations of these mode shapes on anatomically accurate models.

The surface and mesh morphing algorithms, as well as the mesh untangling algorithms, presented in Chapter 3 were all independently developed in separate fields; however, they had never been assembled into an automated mesh processing pipeline for the purpose of creating a SSM training set. The tools developed in this chapter can be used independently to morph or optimize any anatomical geometry of interest.

Chapter 4 was the first study to use a SSM to model the geometric variation of the adult human CFS without requiring the use of manually placed landmarks. The placement of landmarks can itself be a tedious process, and is best done by individuals with specialized
training. Even then, inter-rater reliability is a confounding source of error. The automated morphing procedure described in this thesis offers a more accurate and less time-consuming alternative. Chapter 4 is also, to the authors knowledge, the first study in which the assumption of nodal correspondence between morphed meshes to automatically take anatomical measurements has been explicitly validated. Furthermore, Chapter 4 is the first time a SSM of the human CFS has been validated against a database of craniometric measurements from an actual human population, while simultaneously investigating the hypothesis of morphological integration.

Finally, Chapter 5 introduced a novel approach to evaluating anthropomorphic test device (ATD) design by employing the Monte Carlo method to assess a zygomatic fracture probability curve. Beyond simply investigating fracture thresholds, Chapter 5 demonstrated the advantage of using validated FE results in Monte Carlo analysis, as relationships between anatomical measurements and density distributions of craniofacial structures were related biomechanical function and fracture risk.

6.4 Future Directions

The tools developed in the present body of work have many applications beyond that which has been demonstrated.

While the results of Chapter 4 demonstrated that the SSM of the human CFS represented the geometric variation present in the human population to a reasonable degree, better agreement was found on the sub-sample of humans of European descent. This finding opens up options in further development and refinement of the SSM. One option would be to add more specimens of various different ethnic groups to the training set, better
encapsulating the entirety of the human population. An example of where this approach would hold value is in the design of orthopaedic implants.

One of the goals of orthopaedic implants is to stabilize a joint to allow healing post-surgery, or to restore motion and function to an afflicted joint. The degree to which the implant fits, or conforms, to a patient’s bone or joint has a significant effect on how well the implant achieves its goal. An implant’s shape is often assessed by fitting a prototype to a limited selection of cadaveric samples, and altered to optimally fit this sample. Past studies have used previously developed level set segmentation tools to demonstrated how a SSM can be employed to better improve the design of an implant with respect to specific shape criteria, demonstrating the technique in the context of tibial plate design used in internal fracture fixation\(^1\). In the field of cosmetic and reconstructive surgery, the degree to which craniofacial shape and function are restored is highly important to improving a patient’s quality of life. The SSM developed in this study could thus be used to develop new CFS implant designs that are optimized with respect to specific geometric criteria that offer a better fit to a larger proportion of the human population (or that of a specific segment of the population) than do existing implants.

Another option would be to create specialized training sets of sub-populations to develop SSMs representing groups of interest, such as specifically male/female models, or models representing groups displaying a particular pathology. Recent research into the pathoanatomy of osteoarthritis of the shoulder has revealed that the geometry of the humeral head influences the progression of osteoarthritis (OA) in the glenoid\(^2\). However, it remains to be determined what (or even if) anatomical factors play a role in the pattern of this erosion. This thesis has demonstrated the ability of a SSM to relate anatomical
measurements to clinical outcomes, and a SSM developed for individuals exhibiting shoulder OA could shed some light on the issue. The University of Western Ontario would be a particularly suitable place for this research to occur, as the Hand and Upper Limb Clinic contains one of the largest databases of upper limb OA cases in the world, allowing for very large training sets.

Furthermore, the code developed for this thesis is capable of morphing meshes of any anatomical body part as it stands, and successful pilot tests of morphing with the humerus have already been conducted. However, long bones like the humerus are more amenable to meshing with hexahedral elements as opposed to tetrahedral elements. Hexahedral elements generally are more accurate and robust than tetrahedral elements with the disadvantage of being less flexible when it comes to meshing complicated geometries. If a hexahedral mesh could be developed for a long bone such as the humerus, the morphing procedure developed in Chapter 3 could be adapted to work for hexahedral elements. Specifically, the neither surface or the volumetric morphing procedures would have to be changed at all; only the mesh quality metrics used in the untangling procedure would need to be updated for hexahedral elements.

These suggestions represent a narrow sample of the potential impact of the tools developed in this thesis. As the ability to further automate FE analyses and mesh generation continue, the true potential of the combination of probabilistic methods and biomechanics will be realized.
6.5 References


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Appendix C – Mesh Morphing and Natural Frequency Results for Non-Experimental Craniofacial Specimens

The 17 CFS specimens used in addition to the 5 specimens used in experimental modal analyses (Chapter 2) that were used in Chapter 4 to supplement the SSM were each represented by both manually created and morphed meshes. As further validation of the use of morphed meshes in place of manually created ones, each of these additional specimens were subject to an FE modal analysis using both morphed and manually created meshes. The morphing process ranged between 7 and 8 hours, depending on the quality of initial alignment of meshes, and the similarity of skull shapes.

As in Chapters 2 and 3, mesh quality was measured using the measures radius ratio ($\rho$), mean ratio ($\eta$), and element condition number ($\kappa$). In place of fixing the skulls at the occiput, the skulls were allowed to freely vibrate, and natural frequencies up to 3.5 kHz were recorded.

Figure C-1 shows the cumulative distribution corridors (average ±1.5 standard deviations) of the manually created and morphed meshes for element quality metrics $\rho$, $\eta$, and $\kappa$, along with the 10th percentile value of the averaged cumulative distribution curves (the value above which, on average, 90% of the mesh elements scored). For all measures, the corridor width at the widest point was 0.02 for manual meshes and 0.05 for morphed meshes.
Figure C-1 - Averaged cumulative distribution element quality curves of $\rho$, $\kappa$, and $\eta$ for morphed (red) and manually created (black) meshes. For all measures, maximum corridor width was 0.02 for manual and 0.05 for morphed meshes.
In all cases the 10\textsuperscript{th} percentile values of the averaged morphed mesh quality metrics were lower than their manually created counterparts: 0.65 vs. 0.70 for $\kappa$, 0.59 vs 0.66 for $\rho$, and 0.72 vs 0.67 for $\eta$. The morphed meshes also had larger maximum standard deviations than the manually created meshes: 0.05 vs 0.02 for all metrics.

Figure C-2 shows a Bland-Altman plot of resonant frequencies as calculated by the FE analysis using manually created and morphed meshes. The Intraclass Correlation Coefficient between the two sets of data was 0.99.

![Figure C-2 – Bland-Altman plot comparing the FE calculated free vibration natural frequency values using manually created (the gold standard reference) and morphed meshes.](image-url)
Appendix D – Pseudocode for the Morphing Algorithm

The code used to write implement the Mesh Morphing algorithm was entirely written in Matlab®, and comprises many hundreds of lines of code. The pseudocode used to develop the code itself is presented here. An electronic copy of the morphing has been submitted to The University of Western Ontario School of Graduate and Postdoctoral Studies along with this thesis.

The main program is called Morph (Figure D-1). Two key functions that calculate the surface morphing parameters are calc_def_field_subset (Figure D-2) and calc_disp_field (Figure D-3). The key function that directs the volumetric node morphing is diffusion_main (Figure D-4), which also calls untangle_main (Figure D-5) in the case of tangled elements.
Figure D-1 – Pseudocode for Morph
Figure D-2 – Pseudocode for `calc_def_field_subset`

For all i baseline surface nodes

No

Find subset of target surface elements with same normal orientation as baseline elements surrounding node i (prevents morphing inner surfaces to out surfaces & vice versa)

All i nodes finished?

Yes

Find nearest target triangle element centroid to node i (uses Matlab’s knnsearch)

Determine distance vector from node i to target surface triangle as in Cootes et al. 1995 using `find_def_field_vector`

Return distance field back to Morph
Figure D-3 – Pseudocode for \texttt{calc\_disp\_field}
Figure D-4 – Pseudocode for **diffusion_main**
Figure D-5 – Pseudocode for untangle_main

1. Initialize Jacobian Matrix of mapping element \( W \)
2. Find all tangled elements in mesh
3. For all tangled elements:
   - Identify nodes connected to tangled element
   - For all \( j \) nodes in tangled element:
     - Is node \( j \) a surface node?
       - Yes: Create sub-mesh of all elements connected with node \( j \) using \texttt{gen_submesh}
       - No: Continue
   - Move on to the next element
4. Did \( \geq 1 \) element get untangled?
   - Yes: Untangle failed
   - No: Have you gone through all tangled elements?
     - Yes: Have all element nodes been tested?
       - Yes: Is element \( i \) still tangled?
         - No: No
         - Yes: Calculate new node coordinates by minimizing with respect to \( \eta \)
       - No: Is element \( i \) still tangled?
         - Yes: Calculate new node coordinates by minimizing with respect to \( \kappa \)
         - No: No
     - No: Untangle failed

untangle_main
Curriculum Vitae

Mark A.C. Neuert

Education
University of Western Ontario: Mechanical & Materials Eng., PhD 2011-2016
Current Thesis: The Development And Application Of A Statistical Shape Model Of The Human Craniofacial Skeleton with Dr. Tom Jenkyn

University of Western Ontario: Mechanical & Materials Eng., MESc 2009-2011
Thesis: Development of a Strain-Adaptive Material Model of Bone Tissue in the Distal Ulna Implemented through a Finite Element Analysis with Dr. Cynthia Dunning

University of Alberta: Mechanical Engineering, BSc (Co-op) 2003-2008

Selected Academic Honours and Awards
Queen Elizabeth II Graduate Scholarship ($15,000/a) 2014-2015
NSERC Canadian Graduate Scholarship P ($21,000/a) 2011-2014
NSERC Canadian Graduate Scholarship M ($17,500/a) 2010-2011
Louis McKinney Scholarship (GPA in top 1.5-2% – $2500/a) 2004 – 2007

Related Work Experience
C-FER Technologies, Research Engineer Feb 2016-Present

Peer Reviewed Journal Articles
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Conference Talks

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Teaching Experience

Teaching Assistantships
1. MME 3379A – Materials Selection 2010 – 2015
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3. MME 2260A – Industrial Materials: 2015

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