Hybrid simulation of brain–skull growth

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Abstract
This paper describes a hybrid model that includes both a standard finite element model and also volume-preserving structural modeling for a clinical application involving skull development in infants, with particular application to craniosynostosis modeling. To accommodate the growing brain, the skull needs to grow quickly in the first few months of life, and most of the growth of the skull at that time occurs at the sutures. Craniosynostosis, which is a developmental abnormality, occurs when one or more sutures are fused early in life (even in utero) while the skull is growing, resulting in an abnormal skull shape. To study normal brain–skull growth and to develop a model of craniosynostosis, we have developed a hybrid computational model to simulate the relationship between the growing deformable brain and the rigid skull. Our model is composed of the nine segmented skull plates as rigid surfaces, deformable sutures, and a volumetrically controllable deformable brain. The Cranial Index (ratio of biparietal width to fronto-occipital length) is measured during the simulation, showing a characteristic peak during development. Measures of linear growth along each dimension show characteristic increases over time. The hybrid simulation framework shows promise to support further investigations into abnormal skull development. By varying the properties of the sutures in our model, we can now simulate different craniosynostosis models, such as scaphocephaly and trigonocephaly. In this paper, we show results on the evolution of the Cranial Index as calculated using standard landmarks and compare to the normal index, and thereby evaluate our model by comparing it with patient data.

Keywords
Hybrid deformation model, surgical simulation, brain–skull growth, craniosynostosis

1. Introduction
In this paper, we start by considering the physical development of the brain and skull. The growth of the human brain starts prenatally, and has a steep growth curve until the age of 8–10 months.¹–⁴ During this time, the skull accommodates this growth by stretching the dura at the sutures as they expand.³–⁵ The dura in the suture area is a membranous soft tissue separating the skull plates from each other, and compensates for the rapidly increasing volume of the brain.⁶,⁷ However, the mechanism of this process remains largely unknown.⁸ Our study makes use of a hybrid simulation in order to investigate the interactions between rigid skull places, the increasing volume of the brain, and the growth of the sutures between these plates in order to accommodate the developmental growth.

In craniosynostosis, the premature fusion of one of the sutures leads to a pattern of growth in which the increasing volume must be accommodated by other sutures, thereby changing the normal shape of the skull.⁹ The causes of suture fusion are not well known, but seem to be linked to abnormal signaling from the dura (for example in mutations of the fibroblast growth factor receptors).⁹ There are a few types of craniosynostosis, among which scaphocephaly and trigonocephaly are the most common types.¹⁰ In scaphocephaly, the sagittal suture is fused, causing a long, ‘boat-shaped’ head.¹¹ Trigonocephaly occurs when the metopic suture is fused, leading to a triangular forehead.

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Those pathologies are usually treated by surgery, and different surgical techniques have been described.

The proposed use of our modeling framework is to predict the result of various surgical interventions on the pattern of skull growth. Our model is implemented on the ArtiSynth software package, which is a biomechanical simulation platform for complex anatomical structures modeling. Within this package, a number of types of components can be chosen, such as rigid body, finite element materials, and point-to-point force-based articulations. We utilize rigid-body meshes for the skull plates, derived from computed tomography (CT) imagery, and make use of different finite element components for the sutures and brain.

2. Materials and methods

The brain is a soft tissue incompressible deformable body, and is therefore modeled as a deformable volumetric mesh. Incompressible deformable object modeling has always caused problems for finite element modeling software. In this hybrid model, we have chosen to model the brain as a volumetrically controlled soft body. It behaves as an independent parametric object, where the volume is controlled, and the remaining components must react. The skull is composed of several rigid bone plates, which are separated by sutures. Accordingly, we assign plates to rigid bodies in our model, while connecting to each other by finite element components functioning as sutures. These three component types form the basis of our hybrid model.

Figure 1 demonstrates the workflow of our simulation. First of all, imaging data from a clinical case study is acquired, and then segmented to separate the brain and skull. Rigid-body meshes are then generated for each skull plate and a volumetric mesh delineated for the brain. The suture was also generated manually by setting a field of hexahedral meshes. These assets are then imported into the ArtiSynth package and are assigned material properties, such as Young’s modulus, Poisson’s ratio, and the density for these rigid-body objects. These local linear parameters are simply the initial conditions for the model, which may vary away from local initialization to encompass the global deformations. Accordingly, six markers were set on the skull to monitor the maximum length, breadth, and height of the skull during the simulation. After all these steps were set up, we established a schedule of volumetric changes for the entire brain volume.

2.1 Simulation software

ArtiSynth is a powerful and extensible platform for three-dimensional (3D) object modeling and finite element model (FEM) simulations, which is flexible enough to allow us to implement our hybrid model. Our approach of 3D modeling is mesh generation, also known as grid generation, which is a technique to describe a geometric structure with polygonal or volumetric meshes. Polygonal meshes delineate the surface of 3D objects with a set of vertices, edges, and (triangular, quadrilateral, or simple polygonal) faces, while volumetric meshes represent the whole volume of 3D objects with finite elements such as pyramids, tetrahedral, and hexahedral elements. Volumetric meshes are often used to characterize deformable models for finite element analysis (FEA), which analyze the response of stressed volumetric elements, taking into account a number of factors: mass, volume, temperature, force, displacement, and so on.

ArtiSynth can be used to create or import numerous items, such as rigid bodies, finite elements components, and particles, enabling us to build our hybrid model. In addition to supporting various solvers, it is capable of dealing with interactions between any two components, showing the pressures and forces involved, so that we can interact, display, and ultimately animate a playback of the contact of growing brain and growing skull, as well as calculate the intracranial pressure. The view point can be changed to let the user focus on any part of the model, in accord with volumetric visualization methods. Any points on the model can be marked and traced during the simulation so that we can produce reports of the evolution of our model across various metrics.
2.2 Virtual brain–skull growth

2.2.1 Development of the virtual head. We acquired a head CT scan from a normal three-week-old baby. The parameters of this CT series are described as follows:

- patient position: head first – supine (HFS);
- image type: DICOM;
- gantry tilt: 0.0;
- image size: 512*512*82;
- gray level: –1024–1758;
- coordinate: uniform;
- voxel size: 0.253906*0.253906*1.25 (mm).

We auto-segmented this baby’s skull with the threshold algorithm in Amira software, which is a platform for two-dimensional (2D) or 3D image data visualization and manipulation. We utilized Amira as an interactive viewing platform to manually segment the skull into nine plates.\(^{16}\)

Figure 2 shows 3D skull plates with different colors, including sphenoid bone in gray, frontal left in bright yellow, frontal right in red, parietal left in green, parietal right in blue, temporal right in sky blue, temporal left in yellow, occipital bone in purple, and a bone at the bottom in gray to fill the spinal cord hole. The jaw was excluded in our skull model since it is not relevant with brain–skull growth. Each of the skull plates was represented by a surface mesh, treating the skull as a rigid body with no need for finite element modeling. This is a feature of our hybrid modeling approach.

We manually segmented the brain within this volume to be used as the initial volumetric shape. It was then increased systematically to develop a simulated stress on the skull plates and sutures. Figure 3 shows the model of brain, represented as a simplified tetrahedral mesh. This is one aspect of the ‘hybrid’ approach that needs to be emphasized: the brain is modeled by a volumetric mesh (rather than a 2D polygonal surface enclosure). This allows for our simulation to provide controlled volumes and changes of volume, which then interact with the rigid-body skull plates. The sutures then respond as FEM elements.

Since the suture play a critical role in our modeling, as the only zones where there is skull growth to accommodate the rapid increasing brain volume, these were setup as FEM elements between the rigid skull plates. It is important to note that these ‘joins’ between the skull plates are the points at which new skull mass is developed. As it develops, it hardens and becomes part of the rigid body. As a consequence, its material spring properties are not to be used quantitatively, but rather for qualitative comparison to derive the regions of growth of the skull plates. Consequently, after importing the nine separated skull plates as simulation assets, we generated hexahedral mesh elements and adjusted their position to fit into the space between the plates, until all the space was filled. The sutures linking the skull plates are shown in blue in Figure 4.
2.3 Simulation preparation

Using ArtiSynth, the physical properties of each object in our hybrid model below needed to be initialized in accord with nominal values accepted in the literature.

**Skull plates:** density: 2070 kg/m$^3$; visible: true; alpha: 0.2; bottom plate: fixed. (Where alpha is the graphical transparency. We fixed the bottom plate to provide a stable reference for the graphical playback.)

**Brain:** density: 1040 kg/m$^3$; Young’s modulus: 1.0* $10^6$ Pa; Poisson’s ratio: 0.48; visible: true; alpha: 0.2.

**Sutures:** density: 1130 kg/m$^3$; Young’s modulus: 200 MPa; Poisson’s ratio: 0.28; visible: true; alpha: 0.2.

As the reference data indicated, the proportion of brain Young’s modulus to suture Young’s modulus is 1:200, which means the suture is hard to deform with regard to the brain. However, in this paper, we would anticipate seeing a relatively great deformation of suture to compensate the extension of the skull edge, since in our hybrid simulation, the skull is rigid and does not grow. As a result, we tuned the proportion from 1:200 to 1:2 in order to make the suture soft enough to be stretched. This stretching phase was then used to initialize the proposed growth phase of the rigid skull plates. It is again important to note that the material properties within the sutures are inconsequent, and are non-existent in the brain volume since the volume is the independent parameter, and is increased systematically in order to examine the effect on the suture profiles. This is the key point in the hybrid simulation model. Furthermore, we are not modeling cerebro-spinal fluid and therefore there is no viscosity model needed. The choice of parameters for the skull makes them ‘rigid’, and the choice of material properties for the sutures allows them to deform readily. The use of a locally linear model in these cases allows us to use the FEM solver to resolve the forces that develop in response to the pressure from the expanding volume of the brain. To be sure, we could have simply set a pressure and applied it to the skull plates, but his would have been a uniform pressure. By allowing the pressure to be applied from an expanding brain shape volumetric model, we were able to model the non-uniform expanding forces as they develop within the non-uniform concavities of the skull plates. By setting the position of the centroid of our brain model, we expanded the volume of the brain from that centroid (uniformly across the three spatial directions).

The reference landmarks were placed on the skull to measure the length, breadth, and width of the head during the simulation. Therefore, six markers were chosen on the left, right, top, bottom, front, and back of the skull, shown in Figure 5 as red points.

3. Results and discussion

By measuring the length, breadth, and height of the skull as established by these reference landmarks, we were able to measure the standard Cranial Index (CI), which is a clinical measure of the pattern of growth of the skull. We were also able to calculate the skull volume development over time. A qualitative representation of the resulting suture stresses was prepared for illustration. The cross-sectional stress developed through the sutures in tension, colorized by color from blue as no tension to red as maximum, was also observed during the simulation for our analysis. We ran the normal brain–skull growth simulation several times by changing the ratio of the growing speed, the duration of the time, the time step, and time interval as we monitored the parameters. The results from a wide set of these simulation runs are similar. The properties were setup as follows in this simulation run: ratio = 0.02; time step = 0.001; time duration = 6.3 s; calculating time interval = 0.1 s. The result is shown in Figures 6 and 7.

In Figure 6, the x-axis is the time line with units of seconds. The blue diamonds are the maximum length of the head, while the blue ‘+’ shapes are the maximum breadth of the head and the blue asterisks are the height. The unit of these three is millimeters (mm) referred to in the left blue y-axis. The red circles show the volume of the head in units of cm$^3$, indicated by the right red y-axis. Figure 7 illustrates the CI, which is simply the relation between the skull width and the skull length over time. The simulation was run as a set of 1 second epochs, except where multiple surface-to-surface collisions required finer temporal step analysis. The head length grew from 106.46 to 123.07 mm with 15.6% increment, whereas the head width increased 24.6% at the end of the simulation. In other words, the head circumference increased by approximately 20%. Clinically, the 20% increment of head circumference takes 9 months for a nearly newborn baby to achieve. Therefore, this simulation from 2.4 to 6.3 s is a description of 9 months of skull development.
From time 0 to 2.3 s, the length, breadth, and height were all maintained at the same level, since we initialize the brain at 5% lower volume to ensure the hybrid model was totally stable while initializing the run sequences within the ArtiSynth software. As the brain was allowed to increase in volume, the surface contacts were then transformed into stresses along the sutures. After 2.4 s, the height began to grow first, the breadth grew more rapidly

**Figure 6.** The length, width, height, and volume measurement [mm] during brain–skull growth, plotted with regard to simulation time [s]. (Color online only.)

**Figure 7.** The Cranial Index, which is the relation between skull width and skull length, plotted with regard to simulation time [s].
in the following two time intervals, and the length stayed relatively constant until 3 s. As in normal developmental cases, the breadth of the head grew faster than height. At 6 s, the breadth and the height seem to be at apogee, and the values plateaued, whereas the length was still growing. Figure 8 was captured at the end of the animation, showing two yellow areas for the potential further growth of length, and also stretched to accommodate through breadth and height.

The volume of the skull was set to increase quickly along the initial timeline, and the ratio of growth decreased monotonically after reaching a peak. The CI increased slowly from 81.64 at 2.6 s to 88.62 at 6.2 s, which is the peak of this line, then started to decrease; the breadth began to saturate while the length was still growing. Figure 9 was captured at the end of the animation, showing two yellow areas for the potential further growth of length, and also stretched to accommodate through breadth and height.

We were able to compare our modeled observations with clinical data measuring cranial parameters, for different ages of volunteers. Table 1 shows that the width, length, and height of the skull increase at different rates, with the height having the most salient changes. The CI decreases slightly as a function of that growth. In our model, we observe that right after birth, the brain growth rate far exceeds the growth of skull, with large stretching of the sutures, which in turn can signal the skull to grow more rapidly. Meanwhile, the stresses developing within the sutures and the skull restrict the growth of the brain. The length of the skull grows steadily, and then the breadth, still leaving some space to grow, which all contributes to the evolution of the CI. Our measures are similar to these clinical results, except for the CI, where we have an increase. The difference is not significant, and might be due to their sample size or to our model being based on one particular subject. As a future direction, we will be using an available database of pediatric images to estimate these measures on an independent sample.

4. Conclusions

It is difficult to develop empirical measures of the stresses that develop in developmental brain/skull growth. However, simulation with computational models provides a tool to investigate modeling skull development of infants to characterize craniosynostosis and different abnormalities due to the skull growth. In this paper, we have simulated

<table>
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<th>Age</th>
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<th>Head breadth Mean</th>
<th>Head breadth SD</th>
<th>Head length Mean</th>
<th>Head length SD</th>
<th>Head height Mean</th>
<th>Head height SD</th>
<th>Mean Cranial Index</th>
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<tr>
<td>7 days</td>
<td>19</td>
<td>9.6</td>
<td>0.32</td>
<td>11.9</td>
<td>0.57</td>
<td>8.5</td>
<td>0.52</td>
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<td>10.1</td>
<td>0.45</td>
<td>12.7</td>
<td>0.70</td>
<td>9.2</td>
<td>0.57</td>
<td>79.5</td>
</tr>
<tr>
<td>2 mo</td>
<td>22</td>
<td>10.3</td>
<td>0.54</td>
<td>13.7</td>
<td>0.61</td>
<td>9.8</td>
<td>0.62</td>
<td>78.5</td>
</tr>
<tr>
<td>4 mo</td>
<td>20</td>
<td>11.3</td>
<td>0.50</td>
<td>14.4</td>
<td>0.81</td>
<td>10.5</td>
<td>0.60</td>
<td>78.2</td>
</tr>
<tr>
<td>6 mo</td>
<td>21</td>
<td>11.8</td>
<td>0.59</td>
<td>15.2</td>
<td>0.91</td>
<td>11.0</td>
<td>0.46</td>
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</tr>
<tr>
<td>9 mo</td>
<td>19</td>
<td>12.0</td>
<td>0.71</td>
<td>15.4</td>
<td>0.93</td>
<td>11.1</td>
<td>0.59</td>
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the surface-based interaction between a growing brain interacting with skull, leading to growth at the skull sutures. A number of standard craniometric indices were measured to quantify the skull growth pattern. The results from our simulation match the evolution of these parameters in normal skull growth: the breadth has rapid initial growth compared to the length, while the length continues to grow over the long term, but at a slower rate. The volume of the skull follows the same profile as for normal infants.

Our future work will explore measures of the infant’s cranial diameters in three dimensions between birth and 10 months, as compared to a US database of normal skull development in collaboration with the Montreal Neurological Institute [Collins]. We will also attempt to simulate abnormal growth – scaphocephaly and trigonocephaly – by fusing specific sutures, and comparing the CI with our normal growth data.

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References

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Appendix: Idealized hybrid model

To demonstrate the interactions for a non-clinical geometrical simulation, or for more general clinical data, we demonstrate our method as an idealized hybrid model. A rigid cubic enclosing frame was composed of six square plates, which were connected together by a finite elements frame as the deformable binding. A tetrahedron ellipsoid functioning as the expanding volume was enclosed in the cubic frame. Figure 10 shows the idealized model.

These were coded within ArtiSynth, and the ‘ellipsoid’ was provided by ArtiSynth as a primitive element. We set the density of all the objects to 5000 kg/mm$^3$, and set the Young’s modulus to 80,000 Pa and the Poisson’s ratio to 0.45 for the volume and the bindings. During the simulation, as the ellipsoid grows under programmed control within ArtiSynth, it reaches the left and right plates first, pushing these outwards. Part of the frame, which was attached to left and right plates, gets stretched out while the other part remains. In order to show stress changes on the frame, colorization is used, which varies from blue as no tension to red implying maximum. This purely geometrical model provides a demonstration and a starting point for other more generic human hybrid modeling. Figure 11 shows the interaction between the expanding volume, rigid plates, and deformable expansion bindings.

Figure 10. Idealized model with cubic frame and ellipsoid. (Color online only.)

Figure 11. The volume increases until surface-based collisions for an idealized geometry. In this case the stresses are uniform.