In vivo pons motion within the skull

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Abstract

Finite element (FE) models are used to identify head injury mechanisms and design new and improved injury prevention schemes. Although brain–skull boundary conditions strongly influence the model mechanical responses, limited experimental data are available to develop an informed representation. We hypothesize that the spinal cord tension and gravity contribute to the pons displacement in vivo. Static high-resolution T1-weighted sagittal MR images of the inferior portion of the head in neutral and flexion positions were acquired in 15 human volunteers in both supine and prone postures. Boundaries of the pons and clivus were extracted with a gradient-based algorithm, and the pontes were fitted into ellipses. Assuming rigid body motion of the skull, image pairs in different postures were co-registered with an autocorrelation technique. By comparing images before and after the motion, we found that while the rotation of the pons is negligible relative to the skull, the pons displaces significantly at the foramen magnum, on the order of $\approx 2$ mm. When the spinal cord tension and gravity act in concert, the pons moves caudally; when opposed, superiorly, such that the influence of gravity on the pons is six times that of the spinal cord tension. Based on these findings, we recommend that the brainstem–skull interface be treated as a sliding (with or without friction) boundary condition in FE models of the human head.

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1. Introduction

Traumatic brain injury (TBI) is the leading cause of injury deaths in the United States (32% in 2001, CDC). Computational finite element (FE) models of the human head play an increasingly important role in understanding the mechanisms of head injury and in designing new and improved injury prevention schemes. Together with injury thresholds from histopathological studies of animals, these models can be used to evaluate injury potential in accidental or inflicted head trauma.

Parametric studies have demonstrated that brain–skull boundary conditions over the cerebrum in FE models can strongly influence model predictions of local mechanical responses (Al-Bsharat et al., 1999; Bandak and Eppinger, 1994; Chu et al., 1994; DiMasi et al., 1991, 1995; Lighthall et al., 1989; Miller et al., 1998; Ruan et al., 1994; Takhounts et al., 2003; Ueno et al., 1989, 1995; Zhang et al., 2001), but limited experimental data are available for validation. With no consensus, the brain–skull interface has been represented as tied (no brain–skull relative slip) or sliding (with or without friction, with or without brain–skull separation). Most recently, Kleiven and Hardy (2002) concluded that a tied interface provides the best correlation with the measured cadaver intracranial marker displacements (Hardy et al., 2001).

Only a few FE simulations evaluated the brain–skull interface near the foramen magnum (Bandak and Eppinger, 1994; Chu et al., 1994; Horgan and Gilchrist, 2003, 2004; Kleiven and von Holst, 2002; Kuijpers et al., 1995; Lighthall et al., 1989; Trosselille et al., 1992; Ueno et al., 1989). However, the boundary condition near the foramen magnum has a strong influence on the
mechanical response of the brainstem tissue. Because the brainstem contains centers critical for regulating body temperature, respiration, heart rate and consciousness, it is important to accurately quantify the mechanical loading environment to understand the brainstem injury risk.

Accurate model predictions are strongly based on validation with experimental measurements of the local brain–skull displacements. Because of its accessibility, qualitative relative brain–skull motion in nonhuman primates during impact was observed using a transparent calvarium (Gosch et al., 1970; Pudenz and Shelden, 1946; Shelden et al., 1944). Later, X-ray systems were developed to quantitatively measure the relative brain–skull motion using radio-sensitive materials injected/implanted inside the vasculature, brain tissue or ventricles of live or dead animals as well as human cadavers (Hardy et al., 1997, 2001; Gurdjian et al., 1968; Hodgson et al., 1966; Nusholtz et al., 1984; Shatsky et al., 1974; Stalnaker et al., 1977).

However, few experiments measured the motion of the brainstem near the foramen magnum. Shatsky et al. (1974), Hodgson et al. (1966) and Gurdjian et al. (1968) used flash X-ray to visualize skull deformation and brain displacement in anesthetized dogs, rhesus monkeys, and intact human cadavers during impact. Using intravascular contrast media and implanted lead markers, Gurdjian et al. (1968) observed that the brainstem moved toward the foramen magnum during a midoccipital impact with the head upright. With neutral density targets implanted in inverted human cadaver heads, Hardy et al. (2001) found that the peak brain displacement just above the base of the skull was ~5 mm in frontal and occipital low-severity impacts.

More recently, we (Ji et al., 2004) reported the in vivo cerebellum rotation (2.7–4.3°) during voluntary flexion (over 50°) in live humans using a tissue tagging MR imaging technique. Similar to the occipital impact data in cadavers (Gurdjian et al., 1968), the brainstem moved toward the foramen magnum during flexion. However, only sagittal displacement of the brainstem along the neural axis was measured, due to the technical limitations of the tagging method.

We extend our studies to measure the in vivo pons displacements both parallel and normal to the clivus using high-resolution MR images. We investigate the role of gravity and spinal cord tension on the pons displacement. Specifically, we hypothesize that in supine flexion, both gravity and cord tension act in concert, but that in prone flexion, gravity and tension oppose each other. By comparing the pons displacement in these two postures at the same flexion angle, we determine the relative roles of gravity and cord tension. These in vivo pons displacement data guide the selection of the proper brainstem–skull boundary condition in future human head FE models.

2. Methods

Fifteen (N = 15) healthy human subjects (seven male, eight female, 23–46 years old) with no history of brain or spinal cord abnormalities were recruited, according to a protocol approved by the Institutional Review Board at the University of Pennsylvania. Mid-sagittal MR images of the inferior region of the head were obtained in neck flexion and neutral (with a natural lordosis, without neck flexion or extension) positions, in both supine and prone postures. Three subjects participated in more than one experiment (# of subjects in Figs. 4–6). All flexion images were at the subjects’ voluntary maximal head flexion position.

In supine (prone) postures, the height of the pad beneath the head (the torso) was adjusted to achieve either a neutral posture, or 43–68° (14–58°) flexion. In all postures, the torso remained horizontal, with the head’s sagittal midline aligned with the magnet bore. Proper head position was confirmed in coronal and transversal scout images (low pixel resolution images with coarse slice interspacing to position the imaging plane for the high-resolution images) and stabilized using sandbags during image acquisition (~3 min). In each position, a 10-mm-thick mid-sagittal T1-weighted image was acquired with 400 ms repetition time (TR), 14 ms echo time (TE), 120 mm field of view (FOV), base resolution of 256 × 256 in k space (Siemens Sonata 1.5 T), and was reconstructed as a 512 × 512 matrix (0.23 × 0.23 mm/pixel).

2.1. Data analysis

Pons motion was investigated in four motion sequences (“reference” to “displaced” posture): neutral supine to flexion supine (NS→FS), neutral prone to flexion prone (NP→FP), neutral supine to neutral prone (NS→NP) and flexion supine to flexion prone (FS→FP). Three steps were involved to determine the pons movement: (1) boundary extraction of the pons and clivus, (2) skull rigid body transformation and (3) comparison of image pairs to obtain pons relative motion.

2.1.1. Boundary extraction of the pons and clivus

A coordinate system (O₀) originated at the upper-left corner of the reference image was established (Fig. 1). Edge points of the pons and clivus in each image were identified (“edge” function in Matlab; The Mathworks, Natick, MA). The anterior edge of the pons was fitted into an ellipse using a direct least-squares optimization procedure (Fig. 1; Fitzgibbon et al., 1996, 1999; Josien et al., 2003; see Appendix A and B available at the Journal of Biomechanics website). Point P(x, y) in the reference image was written as

\[
P(x, y) = P(O_0; x, y).
\]
The pons orientation was defined as the angle between the long axis of the ellipse and the horizontal axis of $O_0$.

To verify that both the reference and displaced images had nearly identical imaging planes, we compared the shapes of the ellipses: if either of the axes differed in length by more than 5% between the reference and displaced images, images were discarded ($N = 5$). Potential reasons for this difference might be due to different imaging planes, motion artifacts or pons deformation.

2.1.2. Skull rigid body transformation

A rectangular region enclosing the clivus with margins of 5 pixels on all sides was identified in the reference and displaced images to establish local coordinate systems ($O_1$ and $O_2$ respectively; Fig. 2). A translational transformation between $O_0$ and $O_1$ ($T_1$) was obtained:

$$P(O_1; x', y') = T_1P(O_0; x, y).$$ (2)

Transformation from $O_1$ to $O_2$ was determined by image autocorrelation technique applied to these rectangular regions (see Appendix available at the Journal of Biomechanics website). A trial-and-error method was employed: for each rotational angle (step size: 0.1°) and translational displacement (step size: 1 pixel), the rectangular region in $O_1$ (Fig. 2a) was transformed to obtain its mutual information with the rectangular region in $O_2$. The optimal transformation with maximal mutual information was thus determined (Fig. 2c). To reduce the running time, an interactive procedure displacing and rotating the clivus boundary from the reference image to match that from the displaced image was first employed to estimate a start of the rotational angle. Typically, it took 30–120 min to register an image pair on a Pentium 4 PC (Intel 1.5 GHz, 1 G RAM, Windows 2000).

The rigid body transformation between $O_1$ and $O_2$ ($T_2$) was thus obtained:

$$P(O_2; x'', y'') = T_2P(O_1; x', y').$$ (3)

Combining Eqs. (1)–(3),

$$P(O_2; x'', y'') = T_2T_1P(O_0; x, y),$$ (4)

transforming the clivus and the ellipse from the reference image into the displaced image.

2.1.3. Comparison of images to obtain the pons relative motion

The rotational and translational displacements of the pons were obtained by comparing the transformed reference and displaced images (Fig. 3). For NS→FS and NP→FP where both gravity and cord tension may play a role, the translational displacement was decomposed as parallel and normal to the clivus ($d_{para}$ and $d_{perp}$). Positive values indicated sliding caudally or away from the clivus surface. For NS→NP and FS→FP where only gravity might cause the pons movement, we
analyzed the displacement along gravity (as defined positive).

Head rotational angle ($\theta$) was obtained from the image autocorrelation process. For NS→FS and NP→FP, $\theta$ was effectively the head flexion angle. For NS→NP and FS→FP, a head rotational angle of 180° was equivalent to identical alignment of the head and torso in prone and supine postures, thus allowing us to assume nearly identical cord tension in these two postures.

To verify the accuracy of the imaging analysis scheme, an idealized image with a “pons” (ellipse of $a = 125$ pixel and $b = 70$ pixel) and “clivus” was created and then blurred (Gaussian filter; $r = 2$) and added with Gaussian noise in Photoshop 7.0 (Adobe Systems Inc., San Jose, CA) to mimic the actual MR image. The fitted ellipse ($a = 125.8$ pixel, $b = 69.2$ pixel) matched well with the “pons” (fitting error ~1.1%). The “pons” was then translated along the “clivus” toward the “foramen magnum” 5 pixels and the image was further rotated 45° counterclockwise in Photoshop. The data analysis scheme determined a translation of 5 pixels and a rotation of 44.9°, demonstrating that the error associated with the pons displacement algorithm was negligible. The largest uncertainty in pons-displacement measurements was due to the pixel resolution, and was estimated to be 0.46 mm.

Regression analysis (assuming zero intercept) was performed to test the significance of the correlation between the pons displacement and head flexion angle for NS→FS and NP→FP. Significance was defined as $p<0.05$. For NS→NP and FS→FP, we examined the 95% confidence interval (CI) of the mean displacement to determine if gravity significantly influenced the pons movement. All the image analysis was performed in Matlab (Matlab 6.5; The Mathworks, Natick, MA), and statistical analysis was performed in JMP (SAS Institute Inc., Cary, NC).

3. Results

The pons rotation relative to the skull did not vary significantly with the head flexion angle ($p>0.16$, NS→FS, NP→FP), and the mean value did not significantly differ from zero. This finding agrees with our earlier results (Ji et al., 2004). However, the pons displaced significantly during flexion in both supine and prone postures. During supine flexion (NS→FS), both gravity and spinal cord tension acted in concert to pull the pons caudally, resulting in a significant caudal displacement toward the foramen magnum. In addition, the pons moved away from the clivus surface. The caudal and normal displacements increased significantly with the head flexion angle ($p<0.001$ and $p<0.05$, respectively, Fig. 4 and Table 1). Quantitatively, the regression coefficient between the pons caudal displacement along the clivus and head flexion angle (0.017, 95% CI: 0.012–0.021) was similar to that of the brainstem displacement along the neural axis near the foramen magnum (0.022, 95% CI: 0.015–0.029; Ji et al., 2004).

During prone flexion (NP→FP), gravity was directed superiorly, opposing the cord tension. The net result was a significant pons displacement away from the foramen magnum, with a magnitude 30% smaller than the pons displacement supine. Again, the pons superior displacement along clivus increased significantly with the head flexion angle ($p<0.05$, Fig. 5 and Table 1). However, the displacement normal to the clivus did not differ significantly from zero (Table 1), due to the balance between tension and gravity.

The causal effect of gravity is more evident when we examine the pons displacement along the gravitational axis, rather than normal or parallel to the clivus. Comparing the pons position in prone and supine postures for the same head position, the pons displacement along gravity was significantly greater than zero. Specifically, between prone and supine flexion positions,
the average displacement in the direction of gravity was 1.27 mm (95% CI: 0.86–1.68 mm), compared to 0.91 mm (95% CI: 0.69–1.14 mm) between prone and supine neutral positions (Fig. 6).

Combining the prone and supine data, we can extract the separate influences of spinal cord tension and gravity on pons displacement. We find that at a flexion angle of 60°, the pons displaced significantly under the influence...
of gravity (average 0.87 mm), but displacement due to cord tension was five times less than gravity (average 0.15 mm) and was within our measurement uncertainty.

4. Discussion

We report the pons displacement on the order of ~2 mm, consistent with the observation of the brainstem caudal movement during a mid-occipital head impact of upright anesthetized dogs and rhesus monkeys, and human cadavers (Gurdjian et al., 1968). In addition, this value is similar to the maximum displacement of the midline anterior cerebral artery (2.2 mm) at the level of the pterion (Shatsky et al., 1974) during a blunt temporoparietal head impact of upright anesthetized rhesus monkeys, but is less than the marker displacement (~5 mm) measured near the base of the skull during low-severity impacts of inverted human cadaver heads (Hardy et al., 2001; Kleiven and Hardy, 2002). However, unlike our in vivo static measurement of the pons displacement where gravity has the predominant influence on brain motion, these experiments examined the dynamic motion of the brain relative to the skull during impact where inertial forces are significantly more than gravitational forces. Displacement values from these impact studies are thus, not surprisingly, expected to be larger than those from our static studies. Nevertheless, our study extends our understanding of the human brain motion to voluntary static movements, and provides details regarding the pons motion near the foramen magnum.

Interestingly, the pons moves superiorly, away from the foramen magnum, during flexion in prone postures, but the magnitude was only 70% that of the caudal sliding in the supine posture, due to the opposing influences of gravity and cord tension. The reversed and smaller pons displacement in prone postures compared with that in supine indicates that gravity plays a larger role than the cord tension on the pons motion.

The pons displacement along gravity is consistent with the data of relative brain–skull motion with gravity (less than 1 mm for the cerebrum) reported by Hill et al. (1998). In addition, we find that the displacement along gravity in flexion is larger than that in the neutral position for more than half of our subjects (Fig. 6). On average, the pons displacement along the clivus is larger than displacement perpendicular to the clivus or in the direction of gravity (Fig. 4 and Table 1), suggesting that the pons moves most easily along the neural axis.

Several limitations of this study are noted. First, we assumed no out-of-plane displacement in a sagittal neck flexion and only captured sagittal motion, by ensuring a sagittal head position using scout images as well as by comparing the fitted ellipses of the pons. Second, it was important to have the same angle between the head and torso in prone and supine postures to ensure identical cord tension to study the effect of gravity. However, this was difficult to achieve, and subjects were positioned prone in a slight extension compared with supine (8–9° and 11–34° for neutral and flexion positions, respectively), resulting in an underestimation of the pons displacement along gravity. Because the majority of the subjects performed only flexion maneuver at maximum effort, we could not evaluate contributions of intra- and inter-subject variability to the large data scatter. Future studies may consider building a mechanical device to control the head motion and standardize the flexion angle.

One source of measurement error can be attributed to the misalignment of the reference and displaced MR images before and after head flexion. However, we have excluded extreme cases where the ellipse axes differed in length by more than 5%. Additionally, measurement error may be due to assuming a fixed size and shape of the pons, and neglecting any deformation between reference and deformed images. Finally, the uncertainty
in estimating pons displacement due to the 0.23 mm pixel resolution is 0.46 mm, and any displacements less than this value are not distinguishable from zero. Although the calculated pons displacement due to cord tension (0.15 mm) suffers from this technical limitation, most of the other calculated pons displacements are on the order of 1–2 mm, and are significantly larger than our measurement error.

Although all regressions yielded significant relationships (slopes all had \( p<0.05 \)), none of them yielded a significant \( R^2 \) value, indicating a large scatter of measurements. We have previously suggested that age and gender may influence the brainstem displacement (Ji et al., 2004). However, our current data set does not have sufficient power (\(<20\%\)) to ascertain the relationship of the three factors (flexion angle, age and gender).

Nevertheless, we confirm our hypothesis that the pons moves significantly near the base of the skull during static voluntary head motion, largely due to gravity. We speculate that these pons movements would be exacerbated during large inertial loads. Based on our results, we suggest that a sliding brainstem–skull boundary condition should be used in the human head FE models to capture the pons motion. These in vivo pons displacements help improve the boundary conditions in human head FE models, especially near the foramen magnum, thus allowing more life-like models to be developed.

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Appendix A. Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jbiomech.2005.11.009.

References


Further reading