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Clinical Study

Decompressive craniectomy causes a significant strain increase in axonal fiber tracts

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ABSTRACT

Decompressive craniectomy (DC) allows for the expansion of a swollen brain outside the skull and has the potential to reduce intracranial pressure. However, the stretching of axons may contribute to an unfavorable outcome in patients treated with DC. In this study, we present a method for quantifying and visualizing axonal fiber deformation during both the pre-craniectomy and post-craniectomy periods to provide more insight into the mechanical effects of this treatment on axonal fibers. The deformation of the brain tissue in the form of a Lagrangian finite strain tensor for the entire brain was obtained by a non-linear image registration method based on the CT scanning data sets of the patient. Axonal fiber tracts were extracted from diffusion-weighted images. Based on the calculated brain tissue strain tensor and the observed axonal fiber tracts, the deformation of axonal fiber tracts in the form of a first principal strain, axonal strain and axonal shear strain were quantified. The greatest axonal fiber displacement was predominantly located in the treated region of the craniectomy, accompanied by a large axonal deformation close to the skull edge of the craniectomy. The distortion (stretching or shearing) of axonal fibers in the treated area of the craniectomy may influence the axonal fibers in such a way that neurochemical events are disrupted. A quantitative model may clarify some of the potential problems with this treatment.

1. Introduction

The use of decompressive craniectomy (DC) has increased substantially in an effort to reduce intracranial pressure (ICP) following cerebral injury. However, a consensus on its effectiveness has not been achieved among clinicians[1–4] due to various complications.[5,6] There is debate on the interpretation of DC data reported by Cooper et al.[1] and its application in clinical practice.[7,8] DC allows expansion of the brain tissue outside the skull, thereby reducing the ICP.[5] However, the treatment also results in the stretching of axonal fibers, which has been suggested to contribute to unfavorable outcomes for patients treated with DC.[5] New methods, which may clarify the consequences of DC, are necessary to improve this treatment.

Axons transmit electrical-chemical impulses between neurons and intact axons, and they are critical for establishing normal neurological function. However, when axons are stretched, their capacity to transmit impulses is attenuated. Stretching even causes permanent loss of functional capability in severe cases.[9] Many *in vitro* injury models have been developed showing that axonal stretching causes neural injury in different forms, such as neurofilament structure alterations,[10] mechanical breaking of microtubules in axons[11] and axonal swelling.[12] Bain and Meaney[13] demonstrated, using an optic nerve stretch model, that a strain level of approximately 0.21 will elicit electrophysiological changes, while a strain of approximately 0.34 will cause morphological signs of damage to the white matter. These studies have yielded considerable insight into axonal alterations in response to mechanical stretching. In general, however, DC results in complex axonal deformation, and it is difficult to apply these cellular level thresholds to the tissue level because the axons within white matter do not necessarily lie along the same orientation as the direction of stretch. Therefore, incorporating the axonal fiber tracts into biomechanical models is necessary to quantify axonal stretching along the axons, thus allowing for comparisons with the thresholds obtained from previous experiments. Furthermore, information on axonal fiber deformation, such as axonal shear strain, could also be obtained.

The strain level representing the stretching of brain tissue has been quantified in a previous study.[14] It has been shown that following DC, the strain level and water content in the brain tissue were substantially increased. This may influence the axonal fibers in such a way that the neurochemical events are disrupted. Axonal fiber tracts extracted from diffusion-weighted images (DWI) have been included in a biomechanical model simulating an impact event in order to study the axonal elongation occurring during the primary injury stage.[15] However, axonal stretching during the

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post-craniectomy period, which may have prognostic value for the cognitive and neurological sequelae of patients treated with DC, has not been studied previously.

Thus, the aim of the present study was to quantify the strain level of axonal fibers following DC to gain better insight into the potential damage to axonal fibers caused by DC.

2. Patients and methods

2.1. Patient information

The patient was a 21-year-old male with a severe head injury due to a fall from a height of 4 m from a ladder at work. The patient was initially awake but then became unconscious, with a Glasgow Coma Scale (GCS) score of 7. A CT scan was performed on admission to the hospital. The scan showed extensive shallow subdural hemorrhage with underlying hemisphere swelling, including multiple contusions at the frontal, parietal and temporal lobes on the right side of the brain (Fig. 1a, b). Due to clinical deterioration with unconsciousness and increased ICP, the patient was treated with DC within 24 hours after the trauma. Following DC, there was evidence of edema in the frontal lobe. The CT scans after DC showed that the brain tissue expanded outside the skull at the treated area (Fig. 1c, d). After 23 days in the Department of Neurosurgery, the patient was discharged for further neurological rehabilitation due to a mild, left-sided hemiparesis from which he later recovered. Three months after the trauma, the GCS score was measured as 15, and 4 months after the trauma, the patient went back to his employment at 75% of his previous working hours.

2.2. Quantification of the brain displacement field in pre-craniectomy and post-craniectomy periods

Displacement fields representing the structural brain changes were obtained by a nonlinear image registration method based on the three-dimensional (3D) CT scanning data sets of the patient both before and after DC. The diffeomorphic demons (DD) algorithm[16] implemented in the open-source software Slicer 3D[17] was used to account for localized distortions and large deformations while simultaneously preserving the sample topology.[16] Quantification of the strain level in the pre-craniectomy period requires brain images of the patient obtained before the patient acquired the TBI. However, the healthy brain image was not available for our patient. Herein, we propose an approach of recovering a healthy brain image of the patient before TBI. This was performed by morphing the MRI from a similar-age healthy volunteer to the CT scan of the patient according to the cranial shape. The morphing result shows the image of the recovered healthy brain with one axial slice and the reconstructed surface (Supplementary Fig. 1, left column, upper row).

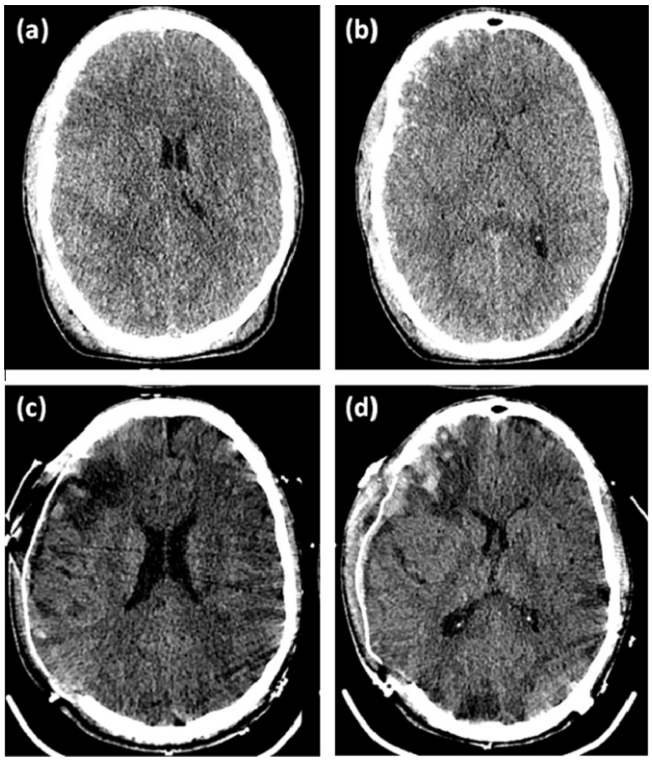

Fig. 1. Axial CT scans obtained (a,b) before craniectomy showing injuries and (c, d) following decompressive craniectomy showing brain tissue expansion.

The ventricles and the cranial geometry were segmented as binary images for the recovered healthy brain. This was also done for the pre-craniectomy and post-craniectomy CT scans. A rigid registration step was first used to center the images about the same point before applying the DD registration. Supplementary Fig. 1 (left column) shows the reconstructed surfaces of the segmented binary images. The images in Supplementary Fig. 1 (middle column, left) also show an overlay of the rigidly aligned images, which provided the basic initialization for subsequent DD deformable registration. In Supplementary Fig. 1 (middle column, right), we present the corresponding images after DD deformable registration. The images after DD registration show good alignment, which means that the displacement from normal to pre-craniectomy images (Supplementary Fig. 1, middle column, upper) and from pre-craniectomy to post-craniectomy images has been captured accurately (Supplementary Fig. 1, middle column, lower). A 3D matching field (Supplementary Fig. 1, right column, upper) representing the spatial transformation needed to displace the healthy brain images to that of the brain after injury (that is, pre-craniectomy) was then obtained from the DD registration. The resulting brain tissue deformation occurring at this stage, described by different strain measurements, is referred to as the "pre-craniectomy strain" throughout this manuscript. Similarly, the 3D matching field needed to displace the pre-craniectomy brain images to the post-craniectomy brain images is presented in Supplementary Fig. 1 (right column, lower).

2.3. Extraction of axonal fibers for the pre-craniectomy and post-craniectomy stages

Diffusion-weighted images (DWI) were acquired using a 3-Tesla scanner (Siemens Trio-Tim, Erlangen, Germany) on a healthy volunteer with the approval of the local Ethics Committee. T1-weighted images were taken simultaneously. The DWI were scanned with 30 gradient directions, and diffusion tensors were then estimated using a standard least-squares method implemented in the Slicer 3D software, which provides a comprehensive tool for DWI and diffusion tensor processing.[17] The extracted white matter tractography, using the streamline method,[18,19] contains polylines (Supplementary Fig. 2, left) with a corresponding diffusion tensor at each fiber point (Supplementary Fig. 2, middle). The maximum eigenvalue of the diffusion tensor, λ_1, with its corresponding eigenvector $\mathbf{N_1}$, is associated with the tangent to the fiber path. The two other eigenvalues, λ_2 and λ_3, together with their corresponding eigenvectors $\mathbf{N_2}$ and $\mathbf{N_3}$, are directly perpendicular to the fiber paths (Supplementary Fig. 2, right).

The extracted axonal fibers were matched to those in the brain of the patient by image registration using a similar procedure, as shown in Supplementary Fig. 1. First, the ventricles and cranial geometry from the corresponding T1-weighted MRI were segmented and converted to a binary image. Then, the resulting image