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Case Report

Abnormalities in cardiac-induced brain tissue deformations are now detectable with MRI: A case-report of a patient who underwent craniotomy after trauma

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ABSTRACT

Background: Heartbeat and respiration induce cyclic brain tissue deformations, which receive increasing attention as potential driving force for brain clearance. These deformations can now be assessed using a novel 3D strain tensor imaging (STI) method at 7 T MRI.
Methods: An 18-year-old man had suffered a traumatic brain injury and was treated with a craniotomy with a maximal diameter of 12 cm. STI was employed to capture cardiac-induced brain tissue deformations and additional time-resolved 2D flow measurements were acquired to capture cerebrospinal fluid (CSF) flow towards the spinal canal.
Results: The craniotomy caused major changes in all aspects of the brain's mechanical dynamics as compared to healthy volunteer references. Tissue strains increased, particularly around the craniotomy, and directionality of deformations showed large abnormalities, also in the contralateral hemisphere. As the brain tissue could pulsate outward from the skull, physiological pulsatile CSF flow at the foramen magnum was abolished.
Conclusions: This work illustrates how STI can assess physiological patterns of brain tissue deformation and how craniotomy leads to widespread deformation abnormalities that can be detected at a single patient level. While this case is meant to provide proof of concept, application of STI in other conditions of abnormal brain mechanical dynamics warrants further study.

1. Introduction

Within the skull, the brain undergoes constant cyclic deformations driven by the pulsatile blood flow induced by heartbeat and respiration [1,2]. These pulsatile deformations can readily be observed during surgical interventions, but escape detection when the skull is intact. Furthermore, only the pulsations at the surface can be observed during surgery, while in fact the entire brain is deformed by changes in microvascular blood volume during the heartbeat and respiration cycles [1,2]. Currently, the pulsating brain receives increasing attention because of its potential role as driving force in the drainage of cerebral waste [3]. Furthermore, *in-vitro* studies have shown that tissue pulsations affect cellular function. The arterial waveform is crucial to regulate the formation and function of endothelial cells which constitute the blood-brain barrier [4]. Although the exact mechanism of drainage of cerebral waste is still controversial, it is likely that tissue deformations contribute to this process by mixing/stirring of the interstitial and paraarterial fluids [5,6]. Changes in brain tissue deformation may therefore have profound effects on tissue properties and be linked to diseases like Altzheimer's and cerebral small vessel disease [4,7]. However, medical interventions can influence the deformation of brain tissue as well, especially when the integrity of the skull is affected.

In this paper we present a first-ever case-study showing abnormal cardiac-induced brain tissue deformations after a craniotomy. We quantify the deformations by using a novel whole brain strain tensor imaging (STI) method at 7 T MRI [8] and show that the technique is sensitive enough to detect abnormal patterns of cardiac-induced tissue deformations throughout the brain on an individual subject level. Additionally, we assess the pulsatile cerebrospinal fluid (CSF) flow to and from the spinal canal, which in closed-skull situations

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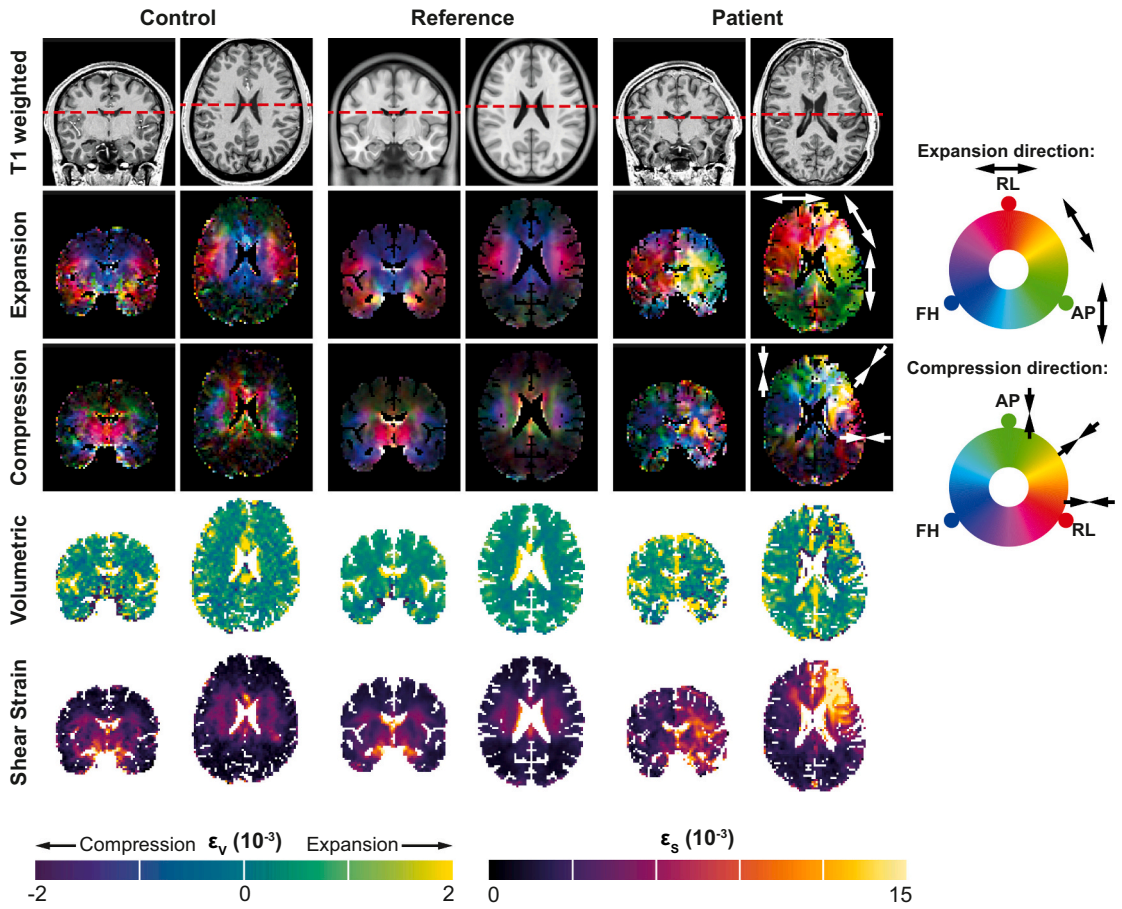

Fig. 1. Transverse and coronal slice in the center of the brain. Maps of a single control subject (left), a reference set in standard space composed of the average of nine subjects (middle) and the patient (right). T1-weighted images are shown as anatomical reference (top row), where dotted red lines indicate slice intersections. The second row represents the vector of primary tissue expansion: the color denotes the direction of this vector (Red: Right-to-Left, Green: Anterior-to-Posterior, Blue: Feet-to-Head) and the saturation indicates the magnitude of this expansion (increased saturation indicates larger expansion). The complementary tissue compression vector is represented in the middle row. This vector is (by definition) directed perpendicular to the stretch vector, reflecting the so-called Poisson effect. For the patient, the direction is also shown schematically with color circles that match the respective expansion and compression direction in the patient observed in the frontal and left-temporal part of the brain.
Volumetric strain and shear strain are indicated in the second bottom and bottom row, respectively. Volumetric strain reflects net expansion or compression of a voxel across the cardiac cycle. Shear strain signifies how much a voxel deforms, irrespective whether or not this deformation is accompanied by a change in volume. All maps represent peak-systole relative to end diastole.
The single control subject shows deformation maps that match the group mean reference. However, in the patient deformation patterns are very different. Much tissue expansion is observed around the surface of the craniotomy, directed parallel to the skull opening (indicated with white arrows). A main contrast to the group reference are the abnormal shear strains, which are most pronounced on the left frontal part of the brain, at the edge of the craniotomy. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

accommodates alterations in intracranial blood volume and/or brain tissue volume.

2. Material and methods

2.1. Patient

An 18-year-old man had suffered a traumatic brain injury. He was diagnosed with an acute left-sided subdural hematoma and was treated with a craniotomy. A cranial opening was created with a maximal diameter of 12 cm to reduce cranial pressure. At the time of MRI, one year after the accident, the patient had fully recovered and was about to get an operative skull reconstruction.

2.2. Data acquisition

Written informed consent was obtained from the patient, according to a protocol approved by our Institutional Review Board. Data was acquired at 7 T (Philips Healthcare, Best, The Netherlands) using a 32-channel receive head coil within an 8 channel transmit/receive head coil (Nova Medical), operating in quadrature mode.

Scan protocols were employed as previously described [8]. In brief, a displacement encoding with stimulated echo (DENSE) imaging sequence was used, which yielded time-resolved displacement measurements for the entire brain over the cardiac cycle, for motion in the right-left (RL), anterior-posterior (AP) and feet-head (FH) directions, respectively. The spatial and temporal resolutions of these maps were $3 \times 3 \times 3$ mm^3 and 50 ms, respectively. From these displacement maps the spatial derivatives were computed to obtain the strain tensor maps, which capture the cardiac-induced brain tissue deformations. The strain tensor describes the tissue deformation in terms of compression and expansion, and the associated directions along which the expansion and compression occur. Volumetric strain and shear strain can be computed from the strain tensor as well. Volumetric strain reflects net expansion or compression of a voxel, while shear strain signifies how much a voxel deforms, irrespective whether or not this deformation is accompanied by

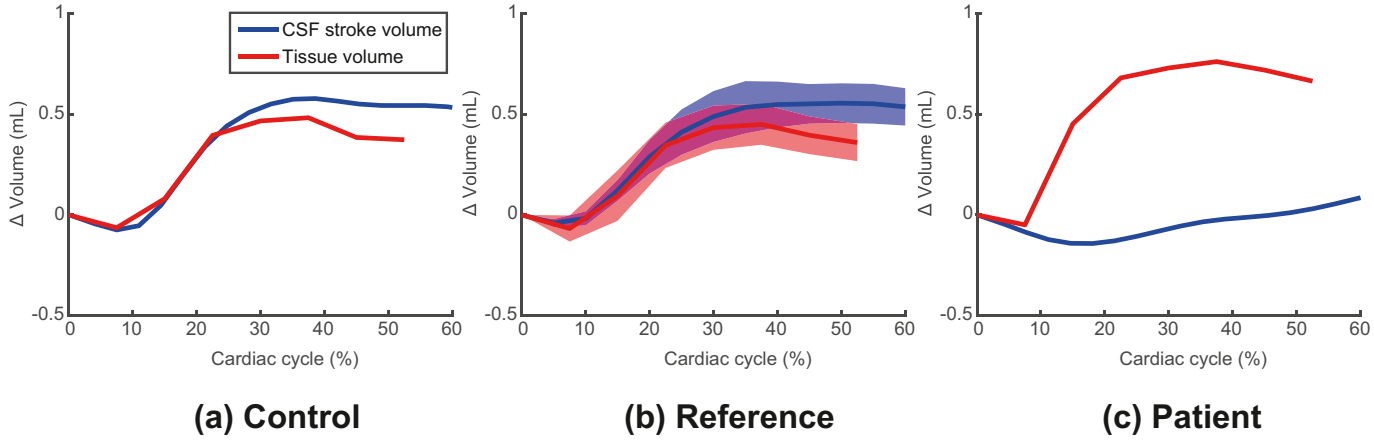

Fig. 2. CSF volume (blue) pushed out of the skull at peak systole (measured at the C2-C3 level) in comparison to whole brain tissue volume change (red) obtained from the volumetric strain measurements. As reference data was only available to 52.5% of the cardiac interval, the interval shown here reaches from 0 and 60% of the cardiac cycle. Data from an individual control subject (a) shows that tissue volume increase during systole is compensated by an outflow of CSF. The reference data (b) was obtained from nine subjects where the shaded area indicates 1 standard deviation over the subjects. (a) and (b) are in line with the Monro-Kellie doctrine, which implies a constant intracranial volume [1,8]. This doctrine is no longer valid for the patient (c), as the cranial opening changes the boundary conditions. Tissue volume increase is now compensated by tissue swelling through the cranial opening, for which intracranial CSF volume no longer has to compensate. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

a change in volume. Additional time-resolved 2D flow measurements were acquired at the C2-C3 level using retrospectively-gated phase-contrast MRI (PC-MRI) to compare cyclic compensatory CSF displacement with whole brain tissue volume change. Scan parameters included a spatial resolution of 0.45 × 0.45 × 3 mm^3 with 30 reconstructed cardiac phases over the cardiac interval. Velocity encoding sensitivities of 5 and 10 cm/s were used to obtain accurate measurements while avoiding phase wraps. See the previously described scan protocol for more details [8].

2.3. Data comparison

We included reference data from our previous study introducing STI for comparison [8]. The reference data originated from STI measurements in nine healthy subjects (6 males, 3 females, age 30 ± 4 years) that was averaged in standard MNI space (ICBM 2009c Nonlinear Symmetric [9]). Out of these nine subjects, the data of the youngest male participant (age 26 years) was selected as single subject comparator.

3. Results

The craniotomy causes major changes in all aspects of the brain's mechanical dynamics, including the healthy hemisphere. Fig. 1 shows that the deformation of brain tissue in the patient is disrupted by the intervention, with large regional differences. While the frontal part of the brain has a physiological AP oriented expansion in the reference, the patient shows an RL directed expansion in this part of the brain. On the left-temporal side at the craniotomy, the direction of expansion changes from RL in the reference to an AP direction in the patient. Furthermore, tissue shear strains are high at the frontal edge of the craniotomy, with pulsatile expansion of tissue in the frontal lobe directed towards the craniotomy. Moreover, the tissue that protrudes from the craniotomy expands parallel to the skin surface and shows compression ('thinning') in the direction perpendicular to the surface, similar to a bulging bicycle tire.

The hemisphere contralateral to the craniotomy shows large abnormalities as well, which illustrates the widespread disruption of the brain's mechanical dynamics. While total cyclic tissue volume variation in the patient remains comparable to the reference data, compensatory outflow of CSF according to the Monro-Kellie doctrine no longer occurs because brain tissue pulsates outward from the skull (see Fig. 2) [1,10].

4. Discussion

This case-report demonstrates for the first time how profound the effect of a craniotomy is on the cardiac-driven pulsatile deformation of brain tissue. As the rigid barrier of the skull was no longer present, tissue strains increased substantially, particular around the edge of the craniotomy. Moreover, alterations of the direction of brain tissue deformation were not limited to the area near the skull opening, but changed throughout the entire brain. Furthermore, CSF outflow was no longer required to compensate for the pulsatile volume changes of brain tissue, as tissue could swell outward from the skull.

Although the tissue strains increased, the total cardiac-cycle volumetric strain remained similar to that of healthy subjects. This indicates that the volumetric strain behavior is mainly determined by the properties of the vessel walls, rather than by the boundary conditions imposed by the tissue itself. At the same time, the reduction in CSF dynamics suggests changes in brain pulsations that might affect clearance.

5. Conclusions

The report demonstrates the strength of the STI technique, which is able to non-invasively and quantitatively measure these marked abnormalities of tissue deformation in a single patient. Direct application of the method includes understanding why some patients do not tolerate a craniotomy, but may also have much wider potential applications in the evaluation of conditions with aberrant brain deformation or tissue compliance, such as hydrocephalus or brain tumors. Application of the method in these settings, that will likely involve more subtle abnormalities in tissue deformation, warrants further study.

CRediT authorship contribution statement

Jacob-Jan Sloots: Conceptualization, Methodology, Software, Visualization, Data curation, Formal analysis, Writing – original draft. **Geert Jan Biessels:** Supervision, Funding acquisition, Writing – review & editing. **G. Johan Amelink:** Supervision, Writing – review & editing. **Jaco J.M. Zwanenburg:** Supervision, Conceptualization, Methodology, Funding acquisition, Writing – review & editing.

Declaration of Competing Interest

None.

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