

# Techniques for Measuring Brain Deformation

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## ***Introduction***

Image analysis provides tools to measure change in the size and shape of the brain. These changes can be caused by disease processes (eg: atrophy caused by Alzheimer's disease), therapies, normal aging or normal development (most dramatic in-utero and in neonates), neurosurgery, or changes in physiological parameters such as blood gas mixture or hydration.

The most widely used techniques for measuring brain deformation of all these types are based on longitudinal imaging with 3D gradient echo volume scans, normally T1 weighted. This tutorial reviews the methods that are widely used, and their applications. It also discusses the difficulties caused by image artefact.

## ***Methods for Quantification of the change in brain size or shape***

The oldest technique for measuring changes in brain size from MR scans is **volumetry**. Brain volumetry, at its most basic, involves using a mouse or similar device to draw around structures of interest in the brain, one slice at a time, at all the time points of interest, and count voxels within the boundaries to determine volume change between time-points. The limitations of this approach are firstly, the effort required from a skilled operator (can be several hours per brain), and secondly the subjectivity. The subjectivity can cause poor reproducibility, as inter-observer variability can be high.

The limitations of volumetry lead researchers to devise more computationally sophisticated approaches to reduce the interaction time and hence make the techniques more widely applicable, and/or to increase the precision to make the techniques more sensitive to change. Fully automatic brain extraction<sup>1</sup> can be used for volumetry, but these techniques have not yet been shown to have sufficient precision to quantify the subtle changes over time that are of interest. Alternative approaches can use intensity information to increase the precision.

The Boundary shift integral<sup>2</sup> makes use of accurate segmentations obtained interactively, but rather than just calculating volumes, registers the repeat scans back to the baseline using rigid registration, and uses this transformation to transform the repeat segmentation into base-line coordinates. The algorithm then creates a "between borders" region using an XOR operation on the two segmentations in baseline coordinates. Differences in the scans that lie in a defined intensity range are then integrated over this "between borders" region, approximating the volume traversed by the brain/ CSF boundary over time. The technique is less sensitive to segmentation errors than volumetry as it ignores differences where the paired intensities are

similar (e.g., CSF on both scans) and at the upper or lower ends of the voxel range (i.e., not representing a change from brain to non-brain tissue). The BSI has been shown to have a reproducibility about 5 times greater than interactive delineation.

The SIENA<sup>3</sup> algorithm uses intensity gradients in registered and transformed images to estimate atrophy, but is entirely automatic.

An alternative approach is to use non-rigid registration rather than rigid registration and intensity information. Non-rigid registration of MRI images of the brain can be performed with several different algorithms, including methods based on fluid<sup>4</sup> or B-splines control points<sup>5</sup> or HAMMER<sup>6</sup>. All these techniques carry out an initial rigid or affine transformation to approximately align the different time points, then use local transformations to determine the local deformation. These local deformations can be parameterised in many ways, but in most cases, are driven by some image similarity measure derived from the voxel intensities. These algorithms generate a 3D displacement or deformation field, from which the volume change at each voxel can be calculated with a Jacobian operator. The Jacobian values can be integrated over regions of interest to generate volume changes in structures of interest, or the deformation field can be used to transform reference features by “segmentation propagation”<sup>7</sup>. These techniques have undergone rapid development in the last few years, and their reliability and precision is increasing. The advantage of these approaches compared to the intensity integration approaches is that they can determine volume change over arbitrary size regions of interest.

It is also possible to measure change in time in brain size and shape using methods based on the cortex. These include direct application of differential geometry to the brain surface<sup>8</sup>, or measurement of cortical thickness at different time points<sup>9</sup>.

### ***Application of volume change measurement techniques.***

The methods described above are becoming used for an increasingly large number of applications. The more sophisticated approaches are often referred to as computational neuroanatomy. Some example applications of these techniques are atrophy biomarkers used in the evaluation of novel treatments of Alzheimer’s disease<sup>10</sup>, the study of brain deformation during neurosurgery in order to quantify the accuracy of image guided surgery systems<sup>11</sup>, and studying the developing brain<sup>12</sup>. There is rapid development of new methods, but validation of these techniques remains a research areas of its own right. For most real data, there is no gold standard. Validation methods that can be used include measures of consistency, group separation of normal and diseased groups (where this is known from pathology), and the use of sophisticated simulations of the disease. It is likely that effective validation of these techniques will require aspects of all these approaches.

### ***Causes of error***

Image artefact can be a major cause of errors in the quantification of brain deformation<sup>13</sup>. Since artefacts are endemic in MR images, it is important that any method for measuring brain

deformation is characterised in terms of its sensitivity to artefact. Three main categories of artefact are described below:

## **1. intensity distortion**

MRI images often suffer from substantial intensity inhomogeneity. This inhomogeneity has been well studied for 1.5T scanners with birdcage coils, and techniques to correct it have been proposed eg: <sup>14</sup>. However with increasing use of higher field strength scanners and array coils for neuro-imaging, the types of artefact that arise is becoming more complex, and new methods for correcting for intensity distortion are becoming necessary. With array coils, the signal to noise ratio can be substantially improved, but the B1 receive field is much less uniform than with a birdcage coils. Image-acquisition based corrections (using a calibration scan to measure the coil sensitivities) are becoming available from all scanner vendors, but while these techniques reduce the intensity inhomogeneity, they lead to spatially varying noise that can also cause difficulties for image analysis algorithms. Furthermore, at field strengths above 1.5T, field focusing leads to B1 transmit inhomogeneity which not-only causes position dependent intensity, but also position dependent contrast changes. Acquisition based methods can be used to reduce the impact of these effects (eg: by changes in the flip angles used in IR prep'd gradient echo sequences), but post-processing methods are also likely to be required.

## **2. Geometric distortion**

Distortion can arise in MRI images due to inhomogeneities in the main field (B0) which can be caused by imperfections in the magnet, or from object-induced inhomogeneities. The latter are most severe where the patient has metallic implants, but are always present. Various methods to correct these distortions have been proposed, but they are not widely used.

A further cause of geometric distortion is the gradients. Design restrictions lead to imperfect gradients. The main consequence of this is that if an object is imaged at the isocentre, then at the edge of the field of view, the object will be notably distorted between scans. Some scanners have post-processing methods built-in to correct for these distortion, but these correction schemes are usually 2D, not fully 3D. In practice, careful patient positioning and scan planning is advisable to ensure that patients are always imaged within a few millimetries of the same position with respect to the isocentre for quantitative studies. Furthermore, even after correcting for distortion, there may be residual scaling terms, which can be corrected using phantom measurements or, in some cases, can be removed by affine registration during the analysis.

## **3. Motion artefact**

Motion artefact can be a major problem in MRI investigations, and causes particular problems for image analysis techniques. Bulk motion can cause ghosting and blurring, and pulsatile motion in blood vessels or eye-ball motion can cause streaks across the brain.

## Conclusions

There are many image analysis techniques that can be used for measuring brain deformation. This tutorial has focused on those methods based on longitudinal structural MRI images. Where deformation takes place over a shorter timeframe (eg: brain pulsation with the cardiac cycle), then alternative methods are required to quantify it, and methods such as displacement encoding, tagging or velocity encoding can be used.

The methods described here have been shown to have great potential in a number of applications, but validation and robustness to artefact remain important challenges that need further research.

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