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Incorporating DTI data as a Constraint in Deformation Tensor Morphometry Between T1 MR Images

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Abstract

Deformation tensor morphometry provides a sensitive approach to detecting and mapping subtle volume changes in the brain from conventional high resolution T1W MRI data. However, it is limited in its ability to localize volume changes within sub-regions of uniform white matter in T1W MRI. In contrast, lower resolution DTI data provides valuable complementary microstructural information within white matter. An approach to incorporating information from DTI data into deformation tensor morphometry of conventional high resolution T1W imaging is described. A novel mutual information (MI) derived criteria is proposed, termed diffusion paired MI, using an approximation to collective many-channel MI between all images. This approximation avoids the evaluation of high dimensional joint probability distributions, but allows a combination of conventional and diffusion data in a single registration criteria. The local gradient of this measure is used to drive a viscous fluid registration between repeated DTI-MRI imaging studies. Results on example data from clinical studies of Alzheimer's disease illustrate the improved localization of tissue loss patterns within regions of white matter.

1 Introduction

Tracking of change in brain anatomy over time has emerged as a powerful tool in detecting and studying changes relating to disease diagnosis and progression in neurodegeneration and development. In particular, non-rigid registration based methods have been developed to map subtle geometric changes in brain anatomy over time, and separate true volume changes from tissue displacements [8, 14, 5]. Such methods have been almost entirely focused toward the analysis of conventional T1 weighted (T1W), T2 weighted (T2W) or proton density weighted (PDW) structural MRI data. These images provide basic contrast between gray matter, white matter and cerebro-spinal fluid, but are limited in their ability to spatially localize geometric change within regions of uniform tissue. In particular, current serial morphometry of MRI cannot probe within the bulk of white matter that holds the underlying connections between functional brain regions. White matter is known to be lost during normal aging [10] and many forms of dementia. These regions are critically important in relating structural changes occurring over time in different anatomical regions, in a range of neurodegenerative conditions including Alzheimer's, Semantic and Fronto-Temporal Dementia, alcohol abuse and HIV.

DTI data [2] provides significant micro-structural information about tissues in the brain, which significantly compliments that provided by high resolution T1W imaging. There has been significant recent work on the alignment of DTI data to other DTI data, both within and between subjects. The alignment problem of DTI is more complex than the alignment of conventional scalar MRI values. This is because of the inherent local geometry of the diffusion measurements, which is modified by any spatial transformation of the data. DTI data itself, unlike T1W imaging, provides relatively calibrated measurements which are

consistent between studies and this motivates the direct application of tensor metrics to evaluate their alignment. Recent work has seen the incorporation of these ideas into deformable DTI registration algorithms such as the elegant work of [4, 3]. The work of [20] derives a novel method of incorporating this rotational information into an elastic registration scheme to align tensor orientations and locations simultaneously.

This paper examines a related but different problem: one of incorporating DTI alignment information within high resolution deformation morphometry of conventional T1W MRI data, in order to provide additional spatial constraints in deformation morphometry. T1W data is not directly compatible with the geometrically derived local diffusion measurements, but provides much greater spatial resolution in many areas of the brain (basic tissue boundaries and grey matter structure).

2 Method

Entropy based methods such as those using mutual information have been used to form a robust measure of image similarity between T1W images for accurate deformation morphometry, where, unlike the DTI tensor components, the intensity and contrast is essentially un-calibrated and can vary spatially within imaging studies. Given a pair of conventional T1 weighted images, with intensities $m^1(\mathbf{x})$ and $m^2(\mathbf{x})$ (superscripts denoting time point) in the same common space $\mathbf{x} \in X$, we can derive a measure of the mutual information between the sets of intensities M^1 and M^2 occurring together in the two images:

$$I(M^1;M^2)=H(M^1)+H(M^2) - H(H^1, M^2) \quad (1)$$

The local gradient of this criteria [9] can be used to drive a fluid registration allowing non-rigid alignment of images as in [7]. In this work we want to build on this by introducing information from DTI data.

If we assume that we additionally have sets of reconstructed diffusion tensor values over the same field of view of the T1 weighted MRI data at each time point $\mathbf{D}^1$ and $\mathbf{D}^2$, then we want to evaluate both MRI and DTI similarity simultaneously. In practice, here we will assume that the tensor contains six individual diffusion measures $\mathbf{D} = \{D_{xx}, D_{yy}, D_{xy}, D_{xz}, D_{yz}, D_{zz}\}$, but the methods can be extended to larger numbers of directions. For DTI data these calibrated tensor components can be related geometrically using methods such as [20, 4, 3] to derive a measure of similarity for DTI alignment. However, these measurements cannot be directly related conventional scalar image data. Ideally, a combined similarity measure is needed, which takes into account the changing relationship between the local orientation of the DTI data and the conventional structural data, as well as between the DTI information. A direct approach would be to evaluate the mutual information between all 7 image pairs (T1W intensity and the 6 diffusion tensor components) acquired for two imaging studies. This would make use of multi-channel mutual information methods previously proposed [15, 17, 11] to evaluate the collective mutual information between studies. For conventional matching where there is some shared information between image types, as illustrated in the upper part of figure 1, we can consider the shared information due to a combination of all the images. Given that the spatial relationships within studies is fixed [15], the registration similarity between studies can be evaluated from the mutual information between the two studies collectively:

$$I(M^1, \mathbf{D}^1;M^2, \mathbf{D}^2)=H(M^1, \mathbf{D}^1)+H(M^2, \mathbf{D}^2) - H(M^1, \mathbf{D}^1, M^2, \mathbf{D}^2) \quad (2)$$

where, $H(M^1, \mathbf{D}^1)$ is the collective information provided by the first study, $H(M^2, \mathbf{D}^2)$ is the collective information provided by the second study, and $H(M^1, \mathbf{D}^1, M^2, \mathbf{D}^2)$ is the

information of the combined studies. However, both of these criteria would require, for six DTI directions, the estimation of the (6 + 1) × 2 = 14 dimensional joint probability distribution for the joint entropy $H(M^1, \mathbf{D}^1, M^2, \mathbf{D}^2)$. i.e. we need to estimate the probability of co-occurrence of all possible combinations of 14 different values $(M^1, D^1_{xx}, \ldots\ M^2, D^2_{xx} \ldots\ D^2_{zz})$. This estimate would be extremely sparsely populated and require expensive computational methods to store and evaluate. One alternative approach is to simply ignore changes in shared information between different types of images and form a measure from a simple summation of MI between image pairs, each derived from the matching of one image type in one study to the same image type in the second study. This simplification however clearly ignores any influence that one image type may have in explaining the structure in the other image types.

An alternative formulation explored here is to use a simplification of the general case of equation (2). This simplification is based on the fact that the information provided by the different diffusion directions within a study is relatively un-correlated. For example: In conventional multi-channel MI based image registration, meaningful shared information between channels occurs when regions of a given intensity in one modality co-occur with intensities in a second modality (e.g. grey matter intensities in MRI co-occur with some fraction of a 'soft tissue' intensity range within CT). In DTI data complex curved tracts are exhibited as different combinations of diffusion strengths in each axis along its length. Thus, within a single DTI study, high values of diffusion components in the *X* axis D_{xx} would not be expected to co-occur more frequently with a particular diffusion strength in the *Y* axis D_{yy}. (i.e. given a diffusion strength in direction *X*, we cannot guess what the diffusion strength in direction *Y* is going to be.) However, considering the pairing conventional MRI with diffusion measurements: within regions of white matter as seen in T1W MRI, there will be a certain fraction of voxels exhibiting a specific level of *X* axis diffusion D_{xx}, and a certain fraction exhibiting *Y* axis diffusion D_{yy}, reflecting for example anterior-posterior or inferior-superior connections within white matter. In addition, low MRI T1W intensities delineate regions of unreliable diffusion measurements in CSF and bone. Thus, the statistical co-occurrence of DTI diffusion components and conventional structural MRI intensity can provide a meaningful partitioning of diffusion information to clarify the alignment measure. In order to account for this shared structure, a criteria formed by combining mutual information measures evaluated between T1/Diffusion image pairs, say M^1, D^1_{xx}, at each time point can be considered. For each diffusion image, its match to the same diffusion direction at the later time point is evaluated, together with the high resolution T1W image intensities at each time point. Denoting this by $I(M^1, D^1_\phi; M^2, D^2_\phi)$, where $\phi \in \{xx, xy, yy, xz, yz, zz\}$ are the set of directions considered, the measure can be expressed as:

$$I\rho(M^1, \mathbf{D}^1; M^2, \mathbf{D}^2) = \sum_{\forall \phi} I(M^1, D^1_\phi; M^2, D^2_\phi) \tag{3}$$

where

$$I(M^1, D^1_\phi; M^2, D^2_\phi) = H(M^1, D^1_\phi) + H(M^2, D^2_\phi) - H(M^1, D^1_\phi, M^2, D^2_\phi). \tag{4}$$

This combined measure, termed diffusion paired MI, requires only 4 dimensional joint intensity distributions to be estimated, but takes into account the co-occurrence of structural and diffusion measures as image alignment is evaluated. The local gradient of this global measure, $\nabla I\rho(M^1, \mathbf{D}^1; M^2, \mathbf{D}^2)$, with respect to the local deformation at a given spatial location, can be derived from the sum of the gradients of each of the paired MI terms

$I(M^1, D_\phi^1; M^2, D_\phi^2)$. These, in turn, can be derived using the approach of [9], to create a single force field driving the image sets into alignment.

2.1 Implementation

For these experiments in deformation tensor morphometry, a dense field image registration scheme is used, where the local voxel displacement mapping from one image to the other is given by a vector field such that:

$$\mathbf{x}_2 = \mathbf{x}_1 + \mathbf{u}(\mathbf{x}_1) \tag{5}$$

The registration force field $\mathbf{F}(\mathbf{x}) = \nabla I\rho(M^1, \mathbf{D}^1; M^2, \mathbf{D}^2)$ derived from the local gradient of the similarity measures with respect to the local displacement estimate is then used to drive a velocity based, viscous fluid deformation model to ensure topology preservation. The solution to the registration is formed by integrating steps along an instantaneous velocity field which is itself derived from a balance between the registration force field $\mathbf{F}(\mathbf{x})$ and the energy of a flowing viscous fluid. The instantaneous velocity vector $\mathbf{v}(\mathbf{x})$ of a point in the image is estimated such that:

$$\mu\nabla^2\mathbf{v}(\mathbf{x}) + (\mu+\lambda)\nabla(\nabla.\mathbf{v}(\mathbf{x})) = \mathbf{F}(\mathbf{x}), \tag{6}$$

where μ and λ are constants determining the relationships between stresses in the flow field. This is solved numerically in a similar way to [6] and [8], using Successive Over Relaxation [12]. From this velocity field estimate, a gradient ascent approach is used to refine the displacement estimate at each iteration. An iterative gradient ascent scheme is used to optimize the registration estimate. Although deformation will generally be small, larger changes can occur in serial studies. As a result we also include an updating of the local diffusion directions using the method of preserving the principal directions of diffusion [1], during the iterative registration.

At each step, the set of 6 4D joint probability distributions between the structural T1W MRI data paired each of the diffusion measurements at each time point is estimated. A discrete binned estimate, using 64 bins in each intensity range, is formed and smoothed using a recursive filter. From this probability distribution, a force field is estimated from the observed intensities and intensity gradients of the T1W and diffusion images. For the estimation of a given joint probability and its gradients with respect to intensity from this discrete binned histogram, a 4D Cubic B-Spline approximation [19] is used. As described by Thevenaz [18], the B-spline provides a positive function of data values essential for an interpolation model of probability estimates. Corresponding 2D histograms are formed for the marginal distributions and 2D Cubic B-Splines are used for approximation.

3 Results

3.1 Image Data

A subject with an initial clinical diagnosis of Alzheimer dementia was imaged on a 4T Siemens imaging system twice over a period of 9 months. Each imaging study included 3D T1 weighted MPRAGE acquisition with a resolution of 1 × 1 × 1*mm* (256 × 256 FOV with 256 × 256 matrix, 176 slices) acquired with a sagittal orientation with RF spoiling. The scan time is 5min 30sec. The phase encoding direction is anterior to posterior. The TR/TE/TI/flip angle=2300ms/3.37ms/950ms/7 degree. The acquisition was carried out using an 8 channel coil, using Grappa encoding and an acceleration factor of 2, with 50 reference lines of phase encoding. A diffusion tensor imaging protocol was then acquired consisting of a 2D double refocused spin-echo EPI sequence with a spatial resolution of 2×2×3mm with either 4

averages. The overall scan time was 3min with an axial acquisition of 40 slices without a gap between slices. The field of view 256 × 224*mm* and the slice thickness is 3mm. The acquisition uses an interleaved scan with TR/TE=6sec/77ms and a Matrix size of 128×128. An 8 channel coil is used with Grappa reconstruction using 2 acceleration factors and 35 reference lines. For directional encoding of diffusion, two b-values (0 and 800 sec/cm^2) and 6 diffusion directions were used.

3.2 Data Pre-Processing

The DTI data of each study was reconstructed into a rank 2 tensor and the b=0 image was rigidly and then non-rigidly aligned to the T1 MPRAGE data using a method derived from [13]. The non-rigid deformation estimate of the data was then applied to bring the diffusion tensors into the coordinate system and sampling resolution of the MPRAGE data (using cubic interpolation), taking into account the local change in geometry using the method of preservation of principal directions [1]. The initial rigid transformation mapping between the two MPRAGE images of the two studies was then estimated by maximization of normalized mutual information between scans [16].

3.3 Data and Registration Forces

Figure 2 shows a representation of the structural information being provided by the DTI dta and the MRI data together, in terms of the principal diffusion directions. This are displayed after initial rigid alignment, relative distortion correction and reorientation of the diffusion and MRI data (using the rview software tool http://rview.colin-studholme.net). In addition, a map of the components of the induced force field resulting from the conventional structural MRI and DTI data is shown, illustrating in particular, the alignment forces from DTI within bulk white matter.

3.4 Estimated Maps of Atrophy

The determinant of Jacobian matrix of the estimated deformation field was evaluated at each point in the first time point image and used to create a map of relative expansions and contractions required to force the anatomy at the first study to match the anatomy of the second. Results comparing the use of the proposed approach with conventional T1W deformation morphometry are shown in figure 3, for a subject diagnosed with Alzheimer's disease. The figure shows an improved localization of tissue contractions around the expanding ventricular space, when incorporating a measure of DTI alignment into the mapping process. Without DTI information, contractions of white matter around the expanding ventricle are significantly less constrained by the T1W imaging alone.

4 Discussion

This paper began be describing a new area of work in the general problem of deformation morphometry, that of using a combination of high resolution conventional scalar MRI data with diffusion tensor image data. The key motivation for this is the commonly observed loss of bulk white matter volume in conventional serial MRI of neurodegeneration. Without any structural features present within white matter in T1W MRI, this loss is simply distributed uniformly over large brain regions. By including information present within diffusion images, the aim is to provide improved localization of any volume losses in deformation morphometry studies, which may reveal characteristic losses related to cognitive decline.

An approach to solving this problem was described which makes use of an extension of mutual information based fluid registration techniques. The approach is aimed at making use of complimentary information provided by the modalities. Specifically, regions in brain diffusion images contain low or zero signal, particularly within fluid spaces, where they

provide unreliable directional information. However, regions of low or high diffusion signal correspond to different intensities within the structural MRI data (dark CSF and bright tissue). At its simplest level, the use of the paired MI of values between structural and diffusion images can be seen as partitioning the DTI data into more and less useful regions of directional information. The conventional structural MRI data provides the majority of shared content between the two studies, since it has highest resolution and contrast to noise. However, in regions of uniform white matter, the gradient of the criteria will contain stronger contributions from the DTI data.

An alternative approach would have been to derive scalar, orientation independent measures of image values from the DTI data, and combine these with conventional image data. However, sub-structures in white matter are characterized by both rotationally invariant microstructural tissue integrity (FA, diffusivity) and the microstructural orientation. Neighboring regions of white matter may have identical integrity but differing orientation of tracts. This information is provided by the orientation components of the diffusion tensor, not FA or diffusivity. By using the diffusion values directly, but including their re-orientation during the warping process, we can use their relationship between studies to more fully constrain the deformation solution within white matter.

An interesting extension of this work is to look at optimal smoothing of the DTI data to help to maximize the complimentary registration information it provides to the higher resolution, lower noise T1W images. Methods for dealing with regional variations in tissue contrast arising from disease in conventional MRI data, as in [14], also need to be developed for the case of fusing MRI and DTI data. However, these preliminary results showing the basic step of combining image data are promising, and work is under way to evaluate this approach further using phantom imaging, and to examine its value in studying patterns of white matter and grey matter tissue loss in different forms of neurodegenerative condition.

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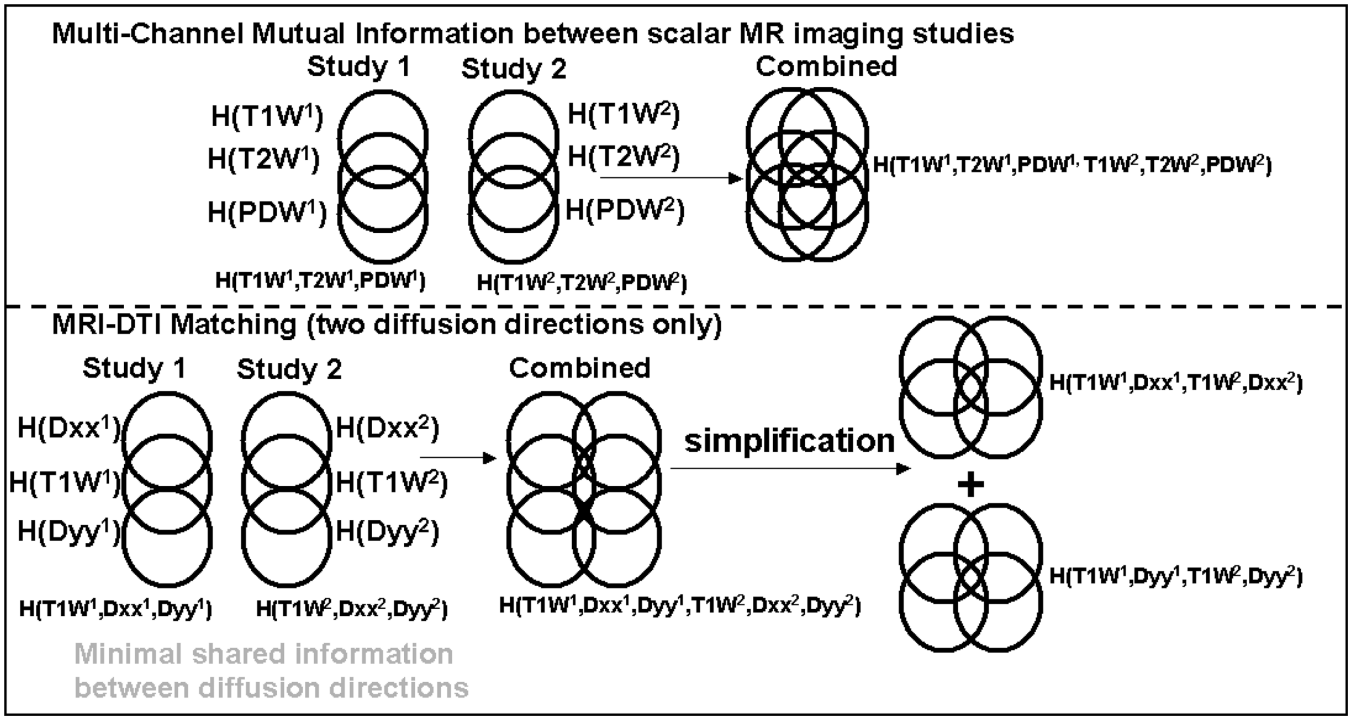

Fig. 1.

An illustration of the derivation of different MI measures of similarity between multiple sets of images for conventional scalar images (top) and combined scalar and DTI data types (bottom). In conventional MRI data sets (T1W,PDW,T2W) there is appreciable shared information. For DTI data there is little shared information between individual diffusion direction maps. We can therefore consider the simplified relationship between DTI directional measurements separately paired with conventional MRI.

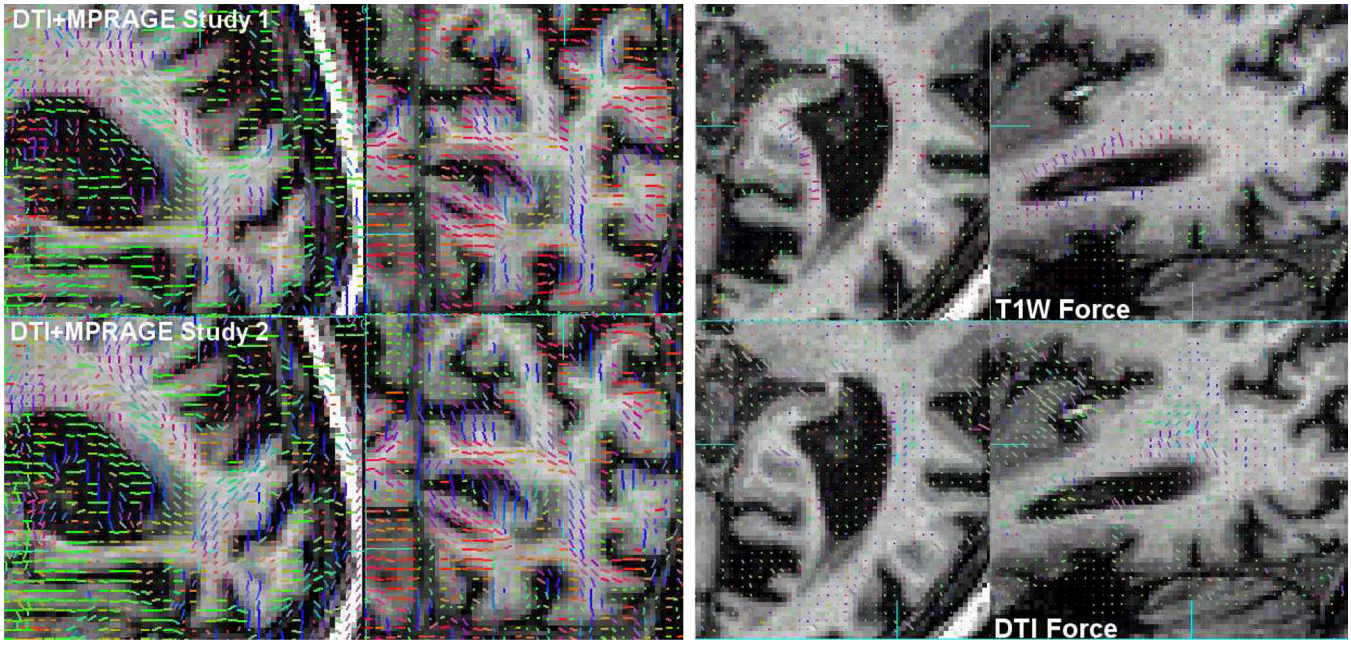

Fig. 2.

Left: Sagittal and coronal slices though DTI and MRI data for the two studies of the subject analyzed in figure 3, showing the principal direction vectors (colour coded by direction) of the two DTI datasets overlayed onto the corresponding T1W MPRAGE studies. Right: Components of the force fields driving the studies into alignment, derived from conventional T1W MRI and DTI data. Note expanding ventricular boundary force in conventional MRI and additional forces within uniform regions of white matter from DTI data.

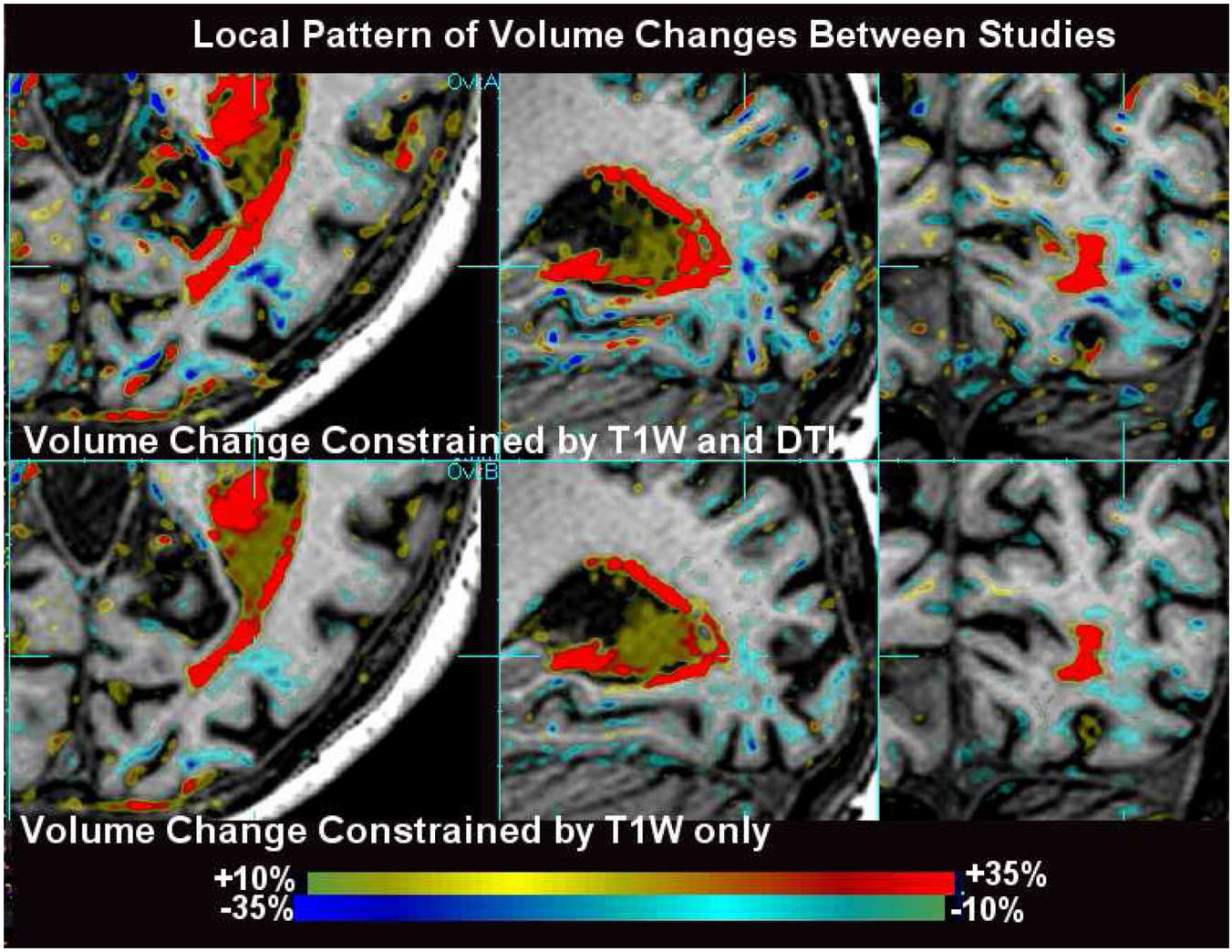

Fig. 3.

A subject diagnosed with Alzheimer's Dementia scanned twice with an interval of 9 months (MMSE 25, Age 61.7), exhibiting tissue loss and ventricular expansion. The scan pairs were fluidly aligned using T1 only (bottom right) and T1 with the full diffusion tensor (top right). The incorporation of the additional structural information on the internal white matter structure provided by DTI assists in constraining the local volume changes mapped by the fluid registration within a more focal region of white matter.)