

# Suggested papers for BME650

## VBM analysis

Ashburner, J., Friston, K.J.

### **Voxel-based morphometry - The methods**

(2000) *NeuroImage*, 11 (6 I), pp. 805-821. Cited 1624 times.

Bookstein, F.L.

### **"voxel-based morphometry" should not be used with imperfectly registered images**

(2001) *NeuroImage*, 14 (6), pp. 1454-1462. Cited 242 times.

Ashburner, J., Friston, K.J.

### **Why Voxel-based morphometry should be used**

(2001) *NeuroImage*, 14 (6), pp. 1238-1243. Cited 247 times.

Good, C.D.<sup>a</sup>, Johnsruide, I.S.<sup>b</sup>, Ashburner, J.<sup>a</sup>, Henson, R.N.A.<sup>a c</sup>, Friston, K.J.<sup>a</sup>, Frackowiak, R.S.J.<sup>a</sup>

### **A voxel-based morphometric study of ageing in 465 normal adult human brains**

(2001) *NeuroImage*, 14 (1 I), pp. 21-36. Cited 1174 times.

## REGISTRATION

Maes, F., Collignon, A., Vandermeulen, D., Marchal, G., Suetens, P.

### **Multimodality image registration by maximization of mutual information**

(1997) *IEEE Transactions on Medical Imaging*, 16 (2), pp. 187-198. Cited 1512 times.

Wells III, W.M.<sup>a b</sup>, Viola, P.<sup>b c</sup>, Atsumi, H.<sup>d</sup>, Nakajima, S.<sup>e</sup>, Kikinis, R.<sup>e</sup>

### **Multi-modal volume registration by maximization of mutual information**

(1996) *Medical Image Analysis*, 1 (1), pp. 35-51. Cited 675 times.

Maintz, J.B.A., Viergever, M.A.

### **A survey of medical image registration**

(1998) *Medical Image Analysis*, 2 (1), pp. 1-36. Cited 1075 times.

Zitová, B., Flusser, J.

### **Image registration methods: A survey**

(2003) *Image and Vision Computing*, 21 (11), pp. 977-1000. Cited 982 times.

Woods, R.P.<sup>a b f</sup>, Grafton, S.T.<sup>e</sup>, Holmes, C.J.<sup>a b</sup>, Cherry, S.R.<sup>c</sup>, Mazziotta, J.C.<sup>a b c d</sup>

### **Automated image registration: I. General methods and intrasubject, intramodality validation**

(1998) *Journal of Computer Assisted Tomography*, 22 (1), pp. 139-152. Cited 942 times.

Woods, R.P.<sup>a b f</sup>, Grafton, S.T.<sup>e</sup>, Holmes, C.J.<sup>a b</sup>, Cherry, S.R.<sup>c</sup>, Mazziotta, J.C.<sup>a b c d</sup>

### **Automated image registration: I. General methods and intrasubject, intramodality validation**

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Rueckert, D.

### **Nonrigid registration using free-form deformations: Application to breast mr images**

(1999) *IEEE Transactions on Medical Imaging*, 18 (8), pp. 712-721. Cited 929 times.

Ashburner, J.<sup>a b</sup>, Friston, K.J.<sup>a</sup>

### **Nonlinear spatial normalization using basis functions**

(1999) *Human Brain Mapping*, 7 (4), pp. 254-266. Cited 698 times.

Jenkinson, M., Smith, S.

### **A global optimisation method for robust affine registration of brain images**

(2001) *Medical Image Analysis*, 5 (2), pp. 143-156. Cited 596 times.

Thirion, J.-P.

### **Image matching as a diffusion process: An analogy with Maxwell's demons**

(1998) *Medical Image Analysis*, 2 (3), pp. 243-260. Cited 463 times.

Hill, D.L.G., Batchelor, P.G., Holden, M., Hawkes, D.J.

### **Medical image registration**

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### **Comparison and evaluation of retrospective intermodality brain image registration techniques**

(1997) *Journal of Computer Assisted Tomography*, 21 (4), pp. 554-566. Cited 399 times.

## **CORTICAL SURFACE EXTRACTION/ANALYSIS**

Dale, A.M.<sup>a</sup>, Fischl, B.<sup>a</sup>, Sereno, M.I.<sup>b</sup>

### **Cortical surface-based analysis: I. Segmentation and surface reconstruction**

(1999) *NeuroImage*, 9 (2), pp. 179-194. Cited 668 times.

Fischl, B.<sup>a</sup>, Sereno, M.I.<sup>b</sup>, Dale, A.M.<sup>a</sup>

### **Cortical surface-based analysis: II. Inflation, flattening, and a surface-based coordinate system**

(1999) *NeuroImage*, 9 (2), pp. 195-207. Cited 557 times.

MacDonald, D.<sup>a</sup>, Kabani, N.<sup>a</sup>, Avis, D.<sup>b</sup>, Evans, A.C.<sup>a</sup>

### **Automated 3-D extraction of inner and outer surfaces of cerebral cortex from MRI**

(2000) *NeuroImage*, 12 (3), pp. 340-356. Cited 221 times.

## **PREPROCESSING**

Sied, J.G.<sup>a b</sup>, Zijdenbos, A.P.<sup>a b</sup>, Evans, A.C.<sup>a b</sup>

### **A nonparametric method for automatic correction of intensity nonuniformity in mri data**

(1998) *IEEE Transactions on Medical Imaging*, 17 (1), pp. 87-97. Cited 658 times.

Van Leemput, K., Maes, F., Vandermeulen, D., Suetens, P.

**Automated model-based bias field correction of MR images of the brain**  
(1999) *IEEE Transactions on Medical Imaging*, 18 (10), pp. 885-896. Cited 188 times.

## VALIDATION

Collins, D.L., Zijdenbos, A.P., Kollokian, V., Sied, J.G., Kabani, N.J., Holmes, C.J., Evans, A.C.  
**Design and construction of a realistic digital brain phantom**  
(1998) *IEEE Transactions on Medical Imaging*, 17 (3), pp. 463-468. Cited 517 times.

## Tissue classification and segmentation

Wells III, W.M.<sup>a b</sup>, Crimson, W.E.L.<sup>a b</sup>, Kikinis, R.<sup>a b</sup>, Jolesz, F.A.<sup>a b</sup>  
**Adaptive segmentation of MRI data**  
(1996) *IEEE Transactions on Medical Imaging*, 15 (4), pp. 429-442. Cited 464 times.

Van Leemput, K., Maes, F., Vandermeulen, D., Suetens, P.  
**A unifying framework for partial volume segmentation of brain MR images**  
(2003) *IEEE Transactions on Medical Imaging*, 22 (1), pp. 105-119. Cited 81 times.

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**Unified segmentation**  
(2005) *NeuroImage*, 26 (3), pp. 839-851. Cited 346 times.

Fischl, B.<sup>a</sup>, Salat, D.H.<sup>a</sup>, Busa, E.<sup>a</sup>, Albert, M.<sup>b c</sup>, Dieterich, M.<sup>e</sup>, Haselgrove, C.<sup>e</sup>, Van Der Kouwe, A.<sup>a</sup>, Killiany, R.<sup>d</sup>, Kennedy, D.<sup>e</sup>, Klaveness, S.<sup>e</sup>, Montillo, A.<sup>f</sup>, Makris, N.<sup>e</sup>, Rosen, B.<sup>a</sup>, Dale, A.M.<sup>a</sup>  
**Whole brain segmentation: Automated labeling of neuroanatomical structures in the human brain**  
(2002) *Neuron*, 33 (3), pp. 341-355. Cited 336 times.

Smith, S.M.<sup>a</sup>, Zhang, Y.<sup>a</sup>, Jenkinson, M.<sup>a</sup>, Chen, J.<sup>a c</sup>, Matthews, P.M.<sup>a</sup>, Federico, A.<sup>b</sup>, De Stefano, N.<sup>b</sup>  
**Accurate, robust, and automated longitudinal and cross-sectional brain change analysis**  
(2002) *NeuroImage*, 17 (1), pp. 479-489. Cited 280 times.

Pham, D.L.<sup>a b</sup>, Xu, C.<sup>a</sup>, Prince, J.L.<sup>a</sup>  
**Current methods in medical image segmentation**  
(2000) *Annual Review of Biomedical Engineering*, 2 (2000), pp. 315-337. Cited 274 times.

Shattuck, D.W.<sup>a</sup>, Sandor-Leahy, S.R.<sup>b</sup>, Schaper, K.A.<sup>c</sup>, Rottenberg, D.A.<sup>c d</sup>, Leahy, R.M.<sup>a</sup>  
**Magnetic resonance image tissue classification using a partial volume model**  
(2001) *NeuroImage*, 13 (5), pp. 856-876. Cited 239 times.

## OTHER IMAGING/PROCESSING

Basser, P.J.<sup>a</sup>, Jones, D.K.<sup>b</sup>  
**Diffusion-tensor MRI: Theory, experimental design and data analysis - A technical review**  
(2002) *NMR in Biomedicine*, 15 (7-8), pp. 456-467. Cited 243 times.

Fenster, A., Downey, D.B., Cardinal, H.N.

**Three-dimensional ultrasound imaging**

(2001) *Physics in Medicine and Biology*, 46 (5), pp. R67-R99. Cited 216 times.

Vedantham, S.<sup>a</sup>, Karellas, A.<sup>a</sup>, Suryanarayanan, S.<sup>a</sup>, Albagli, D.<sup>b</sup>, Han, S.<sup>b</sup>, Tkaczyk, E.J.<sup>b</sup>, Landberg, C.E.<sup>b</sup>, Opsahl-Ong, B.<sup>b</sup>, Granfors, P.R.<sup>c</sup>, Levis, I.<sup>a</sup>, D'Orsi, C.J.<sup>a</sup>, Hendrick, R.E.<sup>d e</sup>

**Full breast digital mammography with an amorphous silicon-based flat panel detector: Physical characteristics of a clinical prototype**

(2000) *Medical Physics*, 27 (3), pp. 558-567. Cited 213 times.

Ntziachristos, V., Bremer, C., Weissleder, R.

**Fluorescence imaging with near-infrared light: New technological advances that enable in vivo molecular imaging**

(2003) *European Radiology*, 13 (1), pp. 195-208. Cited 195 times.

Johansen-Berg, H.<sup>a</sup>, Dawes, H.<sup>b</sup>, Guy, C.<sup>b</sup>, Smith, S.M.<sup>a</sup>, Wade, D.T.<sup>b</sup>, Matthews, P.M.<sup>a</sup>

**Correlation between motor improvements and altered fMRI activity after rehabilitative therapy**

(2002) *Brain*, 125 (12), pp. 2731-2742. Cited 195 times.

Smith, S.M.<sup>a b</sup>

**Fast robust automated brain extraction**

(2002) *Human Brain Mapping*, 17 (3), pp. 143-155. Cited 765 times.

Xu, C.<sup>a b</sup>, Prince, J.L.<sup>a b</sup>

**Snakes, shapes, and gradient vector flow**

(1998) *IEEE Transactions on Image Processing*, 7 (3), pp. 359-369. Cited 1235 times.

**fMRI and Neurophysiology**

Boas DA, Jones SR, Devor A, Huppert TJ, Dale AM (A vascular anatomical network model of the spatio-temporal response to brain activation. *Neuroimage* 40:1116-1129.2008).

Devor A, Hillman EM, Tian P, Waeber C, Teng IC, Ruvinskaya L, Shalinsky MH, Zhu H, Haslinger RH, Narayanan SN, Ulbert I, Dunn AK, Lo EH, Rosen BR, Dale AM, Kleinfeld D, Boas DA (Stimulus-induced changes in blood flow and 2-deoxyglucose uptake dissociate in ipsilateral somatosensory cortex. *J Neurosci* 28:14347-14357.2008).

Devor A, Tian P, Nishimura N, Teng IC, Hillman EM, Narayanan SN, Ulbert I, Boas DA, Kleinfeld D, Dale AM (Suppressed neuronal activity and concurrent arteriolar vasoconstriction may explain negative blood oxygenation level-dependent signal. *J Neurosci* 27:4452-4459.2007).

Dunn AK, Devor A, Dale AM, Boas DA (Spatial extent of oxygen metabolism and hemodynamic changes during functional activation of the rat somatosensory cortex. *Neuroimage* 27:279-290.2005).

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Kriegeskorte N, Cusack R, Bandettini P (How does an fMRI voxel sample the neuronal activity pattern: Compact-kernel or complex spatiotemporal filter? *Neuroimage* 49:1965-1976.2010).

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Allen EA, Pasley BN, Duong T, Freeman RD (Transcranial magnetic stimulation elicits coupled neural and hemodynamic consequences. *Science* 317:1918-1921.2007).

Pasley BN, Allen EA, Freeman RD (State-dependent variability of neuronal responses to transcranial magnetic stimulation of the visual cortex. *Neuron* 62:291-303.2009).

## Detailed list with abstracts

### VBM papers

Ashburner, J., Friston, K.J.

#### **Voxel-based morphometry - The methods**

(2000) *NeuroImage*, 11 (6 1), pp. 805-821. Cited 1624 times.

Wellcome Dept. of Cogn. Neurology, Institute of Neurology, Queen Square, London WC1N 3BG, United Kingdom

#### **Abstract**

At its simplest, voxel-based morphometry (VBM) involves a voxel-wise comparison of the local concentration of gray matter between two groups of subjects. The procedure is relatively straightforward and involves spatially normalizing high-resolution images from all the subjects in the study into the same stereotactic space. This is followed by segmenting the gray matter from the spatially normalized images and smoothing the gray-matter segments. Voxel-wise parametric statistical tests which compare the smoothed gray-matter images from the two groups are performed. Corrections for multiple comparisons are made using the theory of Gaussian random fields. This paper describes the steps involved in VBM, with particular emphasis on segmenting gray matter from MR images with nonuniformity artifact. We provide evaluations of the assumptions that underpin the method, including the accuracy of the segmentation and the assumptions made about the statistical distribution of the data. (C) 2000 Academic Press.

**Document Type:** Article

**Source:** Scopus

Bookstein, F.L.

#### **"voxel-based morphometry" should not be used with imperfectly registered images**

(2001) *NeuroImage*, 14 (6), pp. 1454-1462. Cited 242 times.

University of Michigan

#### **Abstract**

John Ashburner and Karl Friston (2000) introduced a standardized method of "voxel-based morphometry" (VBM) for comparisons of local concentrations of gray matter between two groups of subjects. Segmented images of gray matter from grossly normalized high-resolution images are smoothed and their group differences analyzed by the now-conventional voxelwise Worsley approach to Gaussian random fields of differences. This comment concerns an unfortunate interaction between the algorithm's spatial normalization and voxelwise comparison steps, whereby several obvious quantitative confounds are injected at the core of the inference engine the authors put forward. Specifically, the statistics of the resulting voxelwise comparisons are uninformative about group differences wherever the spatial normalization algorithm has failed to register on any robustly appearing image gradient. The method of Ashburner and Friston is defensible only far from all image gradients. © 2001 Academic Press.

**Document Type:** Article

**Source:** Scopus

Ashburner, J., Friston, K.J.

**Why Voxel-based morphometry should be used**

(2001) *NeuroImage*, 14 (6), pp. 1238-1243. Cited 247 times.

The Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London, WC1N 3BG, United Kingdom

**Abstract**

This article has been written in response to Dr. Fred L. Bookstein's article entitled "Voxel-Based Morphometry" Should Not Be Used with Imperfectly Registered Images' in this issue of *NeuroImage*. We will address three main issues: (i) Dr. Bookstein appears to have misunderstood the objective of voxel-based morphometry (VBM) and the nature of the continuum we referred to. (ii) We agree with him when he states that findings from VBM can pertain to systematic registration errors during spatial normalization. (iii) His argument about voxelwise tests on smooth data holds in the absence of error variance, but is of no consequence when using actual data. We first review the tenets of VBM, paying particular attention to the relationship between VBM and tensor-based morphometry. The last two sections of this response deal with the specific concerns raised by Dr. Bookstein. © 2001 Academic Press.

**Document Type:** Review

**Source:** Scopus

Good, C.D.<sup>a</sup>, Johnsrude, I.S.<sup>b</sup>, Ashburner, J.<sup>a</sup>, Henson, R.N.A.<sup>a c</sup>, Friston, K.J.<sup>a</sup>, Frackowiak, R.S.J.<sup>a</sup>

**A voxel-based morphometric study of ageing in 465 normal adult human brains**

(2001) *NeuroImage*, 14 (1 I), pp. 21-36. Cited 1174 times.

<sup>a</sup> Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London

<sup>b</sup> MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge

<sup>c</sup> Institute of Cognitive Neuroscience, University College London, 17, Queen Square, London, WC1N 3BG, United Kingdom

**Abstract**

Voxel-based-morphometry (VBM) is a whole-brain, unbiased technique for characterizing regional cerebral volume and tissue concentration differences in structural magnetic resonance images. We describe an optimized method of VBM to examine the effects of age on grey and white matter and CSF in 465 normal adults. Global grey matter volume decreased linearly with age, with a significantly steeper decline in males. Local areas of accelerated loss were observed bilaterally in the insula, superior parietal

gyri, central sulci, and cingulate sulci. Areas exhibiting little or no age effect (relative preservation) were noted in the amygdala, hippocampi, and entorhinal cortex. Global white matter did not decline with age, but local areas of relative accelerated loss and preservation were seen. There was no interaction of age with sex for regionally specific effects. These results corroborate previous reports and indicate that VBM is a useful technique for studying structural brain correlates of ageing through life in humans. © 2001 Academic Press.

#### **Author Keywords**

Ageing; MRI; Normal; Voxel based morphometry

## **REGISTRATION**

Maes, F., Collignon, A., Vandermeulen, D., Marchal, G., Suetens, P.

#### **Multimodality image registration by maximization of mutual information**

(1997) *IEEE Transactions on Medical Imaging*, 16 (2), pp. 187-198. Cited 1512 times.

Laboratory for Medical Imaging Research, Katholieke Universiteit Leuven, Universitair Ziekenhuis Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium

#### **Abstract**

A new approach to the problem of multimodality medical image registration is proposed using a basic concept from information theory mutual information (MI) or relative entropy as a new matching criterion. The method presented in this paper applies MI to measure the statistical dependence or information redundancy between the image intensities of corresponding voxels in both images which is assumed to be maximal if the images are geometrically aligned. Maximization of MI is a very general and powerful criterion because no assumptions are made regarding the nature of this dependence and no limiting constraints are imposed on the image content of the modalities involved. The accuracy of the MI criterion is validated for rigid body registration of computed tomography (CT) magnetic resonance (MR) and photon emission tomography (PET) images by comparison with the stereotactic registration solution while robustness is evaluated with respect to implementation issues such as interpolation and optimization and image content including partial overlap and image degradation. Our results demonstrate that subvoxel accuracy with respect to the stereotactic reference solution can be achieved completely automatically and without any prior segmentation feature extraction or other preprocessing steps which makes this method very well suited for clinical applications. © 1997 IEEE.

#### **Author Keywords**

Matching criterion; Multimodality images; Mutual information; Registration

**Document Type:** Article

**Source:** Scopus

Wells III, W.M.<sup>a b</sup>, Viola, P.<sup>b c</sup>, Atsumi, H.<sup>d</sup>, Nakajima, S.<sup>e</sup>, Kikinis, R.<sup>e</sup>

#### **Multi-modal volume registration by maximization of mutual information**

(1996) *Medical Image Analysis*, 1 (1), pp. 35-51. Cited 675 times.

<sup>a</sup> Harvard Medical School, Brigham Women's Hospital, Department of Radiology, Boston, MA, United States

<sup>b</sup> Massachusetts Inst. of Technology, Artificial Intelligence Laboratory

<sup>c</sup> Salk Institute, Compl. Neurobiology Laboratory

<sup>d</sup> Harvard Medical School, Brigham Women's Hospital, Department of Neurosurgery

<sup>e</sup> Harvard Medical School, Brigham Women's Hospital, Department of Radiology

### **Abstract**

A new information-theoretic approach is presented for finding the registration of volumetric medical images of differing modalities. Registration is achieved by adjustment of the relative position and orientation until the mutual information between the images is maximized. In our derivation of the registration procedure, few assumptions are made about the nature of the imaging process. As a result the algorithms are quite general and can foreseeably be used with a wide variety of imaging devices. This approach works directly with image data; no pre-processing or segmentation is required. This technique is, however, more flexible and robust than other intensity-based techniques like correlation. Additionally, it has an efficient implementation that is based on stochastic approximation. Experiments are presented that demonstrate the approach registering magnetic resonance (MR) images with computed tomography (CT) images, and with positron-emission tomography (PET) images. Surgical applications of the registration method are described.

### **Author Keywords**

Information theory; Multi-modality volume registration; Mutual information

**Document Type:** Article

**Source:** Scopus

Maintz, J.B.A., Viergever, M.A.

### **A survey of medical image registration**

(1998) *Medical Image Analysis*, 2 (1), pp. 1-36. Cited 1075 times.

Image Sciences Institute, Utrecht University Hospital, Utrecht, Netherlands

### **Abstract**

The purpose of this paper is to present a survey of recent (published in 1993 or later) publications concerning medical image registration techniques. These publications will be classified according to a model based on nine salient criteria, the main dichotomy of which is extrinsic versus intrinsic methods. The statistics of the classification show definite trends in the evolving registration techniques, which will be discussed. At this moment, the bulk of interesting intrinsic methods is based on either segmented points or surfaces, or on techniques endeavouring to use the full information content of the images involved.

### **Author Keywords**

Matching; Registration

**Document Type:** Article

**Source:** Scopus

Zitová, B., Flusser, J.

### **Image registration methods: A survey**

(2003) *Image and Vision Computing*, 21 (11), pp. 977-1000. Cited 982 times.

Department of Image Processing, Inst. of Info. Theory and Automation, Acad. of Sci. of the Czech Republic, Pod vodarenskou vezi 4, 182 08 Prague 8, Czech Republic

### **Abstract**

This paper aims to present a review of recent as well as classic image registration methods. Image registration is the process of overlaying images (two or more) of the same scene taken at different times, from different viewpoints, and/or by different sensors. The registration geometrically align two images (the reference and sensed images). The reviewed approaches are classified according to their nature (area-based and feature-based) and according to four basic steps of image registration procedure: feature detection, feature matching, mapping function design, and image transformation and resampling. Main contributions, advantages, and drawbacks of the methods are mentioned in the paper. Problematic issues of image registration and outlook for the future research are discussed too. The major goal of the paper is to provide a comprehensive reference source for the researchers involved in image registration, regardless of particular application areas. © 2003 Elsevier B.V. All rights reserved.

### **Author Keywords**

Feature detection; Feature matching; Image registration; Mapping function; Resampling

**Document Type:** Review

**Source:** Scopus

Woods, R.P.<sup>a b f</sup>, Grafton, S.T.<sup>e</sup>, Holmes, C.J.<sup>a b</sup>, Cherry, S.R.<sup>c</sup>, Mazziotta, J.C.<sup>a b c d</sup>

**Automated image registration: I. General methods and intrasubject, intramodality validation**

(1998) *Journal of Computer Assisted Tomography*, 22 (1), pp. 139-152. Cited 942 times.

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<sup>b</sup> Department of Neurology, UCLA, School of Medicine, Los Angeles, CA, United States

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### **Abstract**

**Purpose:** We sought to describe and validate an automated image registration method (AIR 3.0) based on matching of voxel intensities. **Method:** Different cost functions, different minimization methods, and various sampling, smoothing, and editing strategies were compared. Internal consistency measures were used to place limits on registration accuracy for MRI data, and absolute accuracy was measured using a brain phantom for PET data. **Results:** All strategies were consistent with subvoxel accuracy for intrasubject, intramodality registration. Estimated accuracy of registration of structural MRI images was in the 75 to 150  $\mu\text{m}$  range. Sparse data sampling strategies reduced registration times to minutes with only modest loss of accuracy. **Conclusion:** The registration algorithm described is a robust and flexible tool that can be used to address a variety of image registration problems. Registration strategies can be tailored to meet different needs by optimizing tradeoffs between speed and accuracy.

### **Author Keywords**

Brain mapping; Emission computed tomography; Image registration; Magnetic resonance imaging

**Document Type:** Article

**Source:** Scopus

Rueckert, D.

**Nonrigid registration using free-form deformations: Application to breast mr images**

(1999) *IEEE Transactions on Medical Imaging*, 18 (8), pp. 712-721. Cited 929 times.

Division of Radiological Sciences and Medical Engineering, Guy'S, king'S, and St. Thomas' School of Medicine, King's College London, London SE1 9RT, United Kingdom

**Abstract**

In this paper we present a new approach for the nonrigid registration of contrast-enhanced breast MRI. A hierarchical transformation model of the motion of the breast has been developed. The global motion of the breast is modeled by an affine transformation while the local breast motion is described by a free-form deformation (FFD) based on B-splines. Normalized mutual information is used as a voxel-based similarity measure which is insensitive to intensity changes as a result of the contrast enhancement. Registration is achieved by minimizing a cost function, which represents a combination of the cost associated with the smoothness of the transformation and the cost associated with the image similarity. The algorithm has been applied to the fully automated registration of three-dimensional (3-D) breast MRI in volunteers and patients. In particular, we have compared the results of the proposed nonrigid registration algorithm to those obtained using rigid and affine registration techniques. The results clearly indicate that the nonrigid registration algorithm is much better able to recover the motion and deformation of the breast than rigid or affine registration algorithms. © 1999 IEEE.

**Document Type:** Article

**Source:** Scopus

Ashburner, J.<sup>a b</sup>, Friston, K.J.<sup>a</sup>

**Nonlinear spatial normalization using basis functions**

(1999) *Human Brain Mapping*, 7 (4), pp. 254-266. Cited 698 times.

<sup>a</sup> Functional Imaging Laboratory, Wellcome Dept. of Cogn. Neurology, Institute of Neurology, London, United Kingdom

<sup>b</sup> Functional Imaging Laboratory, Wellcome Dept. of Cogn. Neurology, Institute of Neurology, 12 Queen Square, London WC1N 3BG, United Kingdom

**Abstract**

We describe a comprehensive framework for performing rapid and automatic nonlabel-based nonlinear spatial normalizations. The approach adopted minimizes the residual squared difference between an image and a template of the same modality. In order to reduce the number of parameters to be fitted, the nonlinear warps are described by a linear combination of low spatial frequency basis functions. The objective is to determine the optimum coefficients for each of the bases by minimizing the sum of squared differences between the image and template, while simultaneously maximizing the smoothness of the

transformation using a maximum a posteriori (MAP) approach. Most MAP approaches assume that the variance associated with each voxel is already known and that there is no covariance between neighboring voxels. The approach described here attempts to estimate this variance from the data, and also corrects for the correlations between neighboring voxels. This makes the same approach suitable for the spatial normalization of both high-quality magnetic resonance images, and low-resolution noisy positron emission tomography images. A fast algorithm has been developed that utilizes Taylor's theorem and the separable nature of the basis functions, meaning that most of the nonlinear spatial variability between images can be automatically corrected within a few minutes.

#### **Author Keywords**

Anatomy; Basis functions; Functional mapping; Imaging; MRI; PET; Registration; Spatial normalization; Stereotaxy

**Document Type:** Article

**Source:** Scopus

Jenkinson, M., Smith, S.

#### **A global optimisation method for robust affine registration of brain images**

(2001) *Medical Image Analysis*, 5 (2), pp. 143-156. Cited 596 times.

University of Oxford, John Radcliffe Hospital, FMRIB Centre, Oxford OX3 9DU, United Kingdom

#### **Abstract**

Registration is an important component of medical image analysis and for analysing large amounts of data it is desirable to have fully automatic registration methods. Many different automatic registration methods have been proposed to date, and almost all share a common mathematical framework - one of optimising a cost function. To date little attention has been focused on the optimisation method itself, even though the success of most registration methods hinges on the quality of this optimisation. This paper examines the assumptions underlying the problem of registration for brain images using inter-modal voxel similarity measures. It is demonstrated that the use of local optimisation methods together with the standard multi-resolution approach is not sufficient to reliably find the global minimum. To address this problem, a global optimisation method is proposed that is specifically tailored to this form of registration. A full discussion of all the necessary implementation details is included as this is an important part of any practical method. Furthermore, results are presented for inter-modal, inter-subject registration experiments that show that the proposed method is more reliable at finding the global minimum than several of the currently available registration packages in common usage. © 2001 Elsevier Science B.V. All rights reserved.

#### **Author Keywords**

Affine transformation; Global optimisation; Multi-resolution search; Multimodal registration; Robustness

**Document Type:** Article

**Source:** Scopus

Thirion, J.-P.

**Image matching as a diffusion process: An analogy with Maxwell's demons**

(1998) *Medical Image Analysis*, 2 (3), pp. 243-260. Cited 463 times.

INRIA, Equipe Epidaure, 2004 Route des Lucioles, 06902 Sophia-Antipolis, France

**Abstract**

In this paper, we present the concept of diffusing models to perform image-to-image matching. Having two images to match, the main idea is to consider the objects boundaries in one image as semi-permeable membranes and to let the other image, considered as a deformable grid model, diffuse through these interfaces, by the action of effectors situated within the membranes. We illustrate this concept by an analogy with Maxwell's demons. We show that this concept relates to more traditional ones, based on attraction, with an intermediate step being optical flow techniques. We use the concept of diffusing models to derive three different non-rigid matching algorithms, one using all the intensity levels in the static image, one using only contour points, and a last one operating on already segmented images. Finally, we present results with synthesized deformations and real medical images, with applications to heart motion tracking and three-dimensional inter-patients matching.

**Author Keywords**

Deformable model; Elastic matching; Image sequence analysis; Inter-patient registration; Non-rigid matching

**Document Type:** Article

**Source:** Scopus

Hill, D.L.G., Batchelor, P.G., Holden, M., Hawkes, D.J.

**Medical image registration**

(2001) *Physics in Medicine and Biology*, 46 (3), pp. R1-R45. Cited 401 times.

Radiological Sciences, King's College London, Guy's Hospital, St Thomas' Street, London SE1 9RT, United Kingdom

**Abstract**

Radiological images are increasingly being used in healthcare and medical research. There is, consequently, widespread interest in accurately relating information in the different images for diagnosis, treatment and basic science. This article reviews registration techniques used to solve this problem, and describes the wide variety of applications to which these techniques are applied. Applications of image registration include combining images of the same subject from different modalities, aligning temporal sequences of images to compensate for motion of the subject between scans, image guidance during interventions and aligning images from multiple subjects in cohort studies. Current registration algorithms can, in many cases, automatically register images that are related by a rigid body transformation (i.e. where tissue deformation can be ignored). There has also been substantial progress in non-rigid registration algorithms that can compensate for tissue deformation, or align images from different

subjects. Nevertheless many registration problems remain unsolved, and this is likely to continue to be an active field of research in the future.

**Document Type:** Review

**Source:** Scopus

West, J., Fitzpatrick, J.M., Wang, M.Y., Dawant, B.M., Maurer Jr., C.R., Kessler, R.M., Maciunas, R.J., Barillot, C., Lemoine, D., Collignon, A., Maes, F., Suetens, P., Vandermeulen, D., Van Den Elsen, P.A., Napel, S., Sumanaweera, T.S., Harkness, B., Hemler, P.F., Hill, D.L.G., Hawkes, D.J., Studholme, C., Maintz, J.B.A., Viergever, M.A., Malandain, G., Pennec, X., Noz, M.E., Maguire Jr., G.Q., Pollack, M., Pelizzari, C.A., Robb, R.A., Hanson, D., Woods, R.P.

**Comparison and evaluation of retrospective intermodality brain image registration techniques**

(1997) *Journal of Computer Assisted Tomography*, 21 (4), pp. 554-566. Cited 399 times.

#### **Abstract**

**Purpose:** The primary objective of this study is to perform a blinded evaluation of a group of retrospective image registration techniques using as a gold standard a prospective, marker-based registration method. To ensure blindedness, all retrospective registrations were performed by participants who had no knowledge of the gold standard results until after their results had been submitted. A secondary goal of the project is to evaluate the importance of correcting geometrical distortion in MR images by comparing the retrospective registration error in the rectified images, i.e., those that have had the distortion correction applied, with that of the same images before rectification. **Method:** Image volumes of three modalities (CT, MR, and PET) were obtained from patients undergoing neurosurgery at Vanderbilt University Medical Center on whom bone-implanted fiducial markers were mounted. These volumes had all traces of the markers removed and were provided via the Internet to project collaborators outside Vanderbilt, who then performed retrospective registrations on the volumes, calculating transformations from CT to MR and/or from PET to MR. These investigators communicated their transformations again via the Internet to Vanderbilt, where the accuracy of each registration was evaluated. In this evaluation, the accuracy is measured at multiple volumes of interest (VOIs), i.e., areas in the brain that would commonly be areas of neurological interest. A VOI is defined in the MR image and its centroid  $c$  is determined. Then, the prospective registration is used to obtain the corresponding point  $c'$  in CT or PET. To this point, the retrospective registration is then applied, producing  $c''$  in MR. Statistics are gathered on the target registration error (TRE), which is the distance between the original point  $e$  and its corresponding point  $c''$ . **Results:** This article presents statistics on the TRE calculated for each registration technique in this study and provides a brief description of each technique and an estimate of both preparation and execution time needed to perform the registration. **Conclusion:** Our results indicate that retrospective techniques have the potential to produce satisfactory results much of the time, but that visual inspection is necessary to guard against large errors.

#### **Author Keywords**

Computed tomography; Emission computed tomography; Image quality; Image registration; Magnetic resonance imaging; Magnetic resonance imaging, physics and instrumentation

**Document Type:** Article

**Source:** Scopus

## CORTICAL SURFACE EXTRACTION/ANALYSIS

Dale, A.M.<sup>a</sup>, Fischl, B.<sup>a</sup>, Sereno, M.I.<sup>b</sup>

### **Cortical surface-based analysis: I. Segmentation and surface reconstruction**

(1999) *NeuroImage*, 9 (2), pp. 179-194. Cited 668 times.

<sup>a</sup> Nuclear Magnetic Resonance Center, Massachusetts General Hosp, Harvard Medical School, 13th Street, Charlestown, MA 02129, United States

<sup>b</sup> Department of Cognitive Science, Univ. of California at San Diego, Mail Code 0515, 9500 Gilman Drive, San Diego, CA 92093-0515, United States

### **Abstract**

Several properties of the cerebral cortex, including its columnar and laminar organization, as well as the topographic organization of cortical areas, can only be properly understood in the context of the intrinsic two-dimensional structure of the cortical surface. In order to study such cortical properties in humans, it is necessary to obtain an accurate and explicit representation of the cortical surface in individual subjects. Here we describe a set of automated procedures for obtaining accurate reconstructions of the cortical surface, which have been applied to data from more than 100 subjects, requiring little or no manual intervention. Automated routines for unfolding and flattening the cortical surface are described in a companion paper. These procedures allow for the routine use of cortical surface-based analysis and visualization methods in functional brain imaging.

### **Author Keywords**

Cortical surface reconstruction; Segmentation

**Document Type:** Article

**Source:** Scopus

Fischl, B.<sup>a</sup>, Sereno, M.I.<sup>b</sup>, Dale, A.M.<sup>a</sup>

### **Cortical surface-based analysis: II. Inflation, flattening, and a surface-based coordinate system**

(1999) *NeuroImage*, 9 (2), pp. 195-207. Cited 557 times.

<sup>a</sup> Nuclear Magnetic Resonance Center, Massachusetts General Hosp, Harvard Medical School, 13th Street, Charlestown, MA 02129, United States

<sup>b</sup> Department of Cognitive Science, Univ. of California at San Diego, Mailcode 0515, 9500 Gilman Drive, San Diego, CA 92093-0515, United States

### **Abstract**

The surface of the human cerebral cortex is a highly folded sheet with the majority of its surface area buried within folds. As such, it is a difficult domain for computational as well as visualization purposes. We have therefore designed a set of procedures for modifying the representation of the cortical surface to (i) inflate it so that activity buried inside sulci may be visualized, (ii) cut and flatten an entire hemisphere, and (iii) transform a hemisphere into a simple parameterizable surface such as a sphere for the purpose of establishing a surface-based coordinate system.

**Author Keywords**

Atlas; Coordinate systems; Cortical surface reconstruction; Flattening

**Document Type:** Review

**Source:** Scopus

MacDonald, D.<sup>a</sup>, Kabani, N.<sup>a</sup>, Avis, D.<sup>b</sup>, Evans, A.C.<sup>a</sup>

**Automated 3-D extraction of inner and outer surfaces of cerebral cortex from MRI**

(2000) *NeuroImage*, 12 (3), pp. 340-356. Cited 221 times.

<sup>a</sup> McConnell Brain Imaging Centre, Montréal Neurological Institute, 3801 University, Montréal, Que. H3A 2B4, Canada

<sup>b</sup> School of Computer Science, McGill University, Montréal, Que., Canada

**Abstract**

Automatic computer processing of large multidimensional images such as those produced by magnetic resonance imaging (MRI) is greatly aided by deformable models, which are used to extract, identify, and quantify specific neuroanatomic structures. A general method of deforming polyhedra is presented here, with two novel features. First, explicit prevention of self-intersecting surface geometries is provided, unlike conventional deformable models, which use regularization constraints to discourage but not necessarily prevent such behavior. Second, deformation of multiple surfaces with intersurface proximity constraints allows each surface to help guide other surfaces into place using model-based constraints such as expected thickness of an anatomic surface. These two features are used advantageously to identify automatically the total surface of the outer and inner boundaries of cerebral cortical gray matter from normal human MR images, accurately locating the depths of the sulci, even where noise and partial volume artifacts in the image obscure the visibility of sulci. The extracted surfaces are enforced to be simple two-dimensional manifolds (having the topology of a sphere), even though the data may have topological holes. This automatic 3-D cortex segmentation technique has been applied to 150 normal subjects, simultaneously extracting both the gray/white and gray/cerebrospinal fluid interface from each individual. The collection of surfaces has been used to create a spatial map of the mean and standard deviation for the location and the thickness of cortical gray matter. Three alternative criteria for defining cortical thickness at each cortical location were developed and compared. These results are shown to corroborate published postmortem and in vivo measurements of cortical thickness. (C) 2000 Academic Press.

**Document Type:** Article

**Source:** Scopus

**PREPROCESSING**

Sied, J.G.<sup>a b</sup>, Zijdenbos, A.P.<sup>a b</sup>, Evans, A.C.<sup>a b</sup>

**A nonparametric method for automatic correction of intensity nonuniformity in mri data**  
(1998) *IEEE Transactions on Medical Imaging*, 17 (1), pp. 87-97. Cited 658 times.

<sup>a</sup> McConnell Brain Imaging Centre, Montréal Neurological Institute, McGill University, 3801 University Street, Montréal, PQ, H3A 2B4, Canada

<sup>b</sup> McConnell Brain Imaging Centre, Montréal Neurological Institute, Montreal, PQ, H3A 2B4, Canada

### **Abstract**

A novel approach to correcting for intensity nonuniformity in magnetic resonance (MR) data is described that achieves high performance without requiring a model of the tissue classes present. The method has the advantage that it can be applied at an early stage in an automated data analysis, before a tissue model is available. Described as nonparametric nonuniform intensity normalization (N3), the method is independent of pulse sequence and insensitive to pathological data that might otherwise violate model assumptions. To eliminate the dependence of the field estimate on anatomy, an iterative approach is employed to estimate both the multiplicative bias field and the distribution of the true tissue intensities. The performance of this method is evaluated using both real and simulated MR data. © 1998 IEEE.

### **Author Keywords**

Intensity nonuniformity; Magnetic resonance imaging; Rf field inhomogeneity; Shading artifact

**Document Type:** Article

**Source:** Scopus

Van Leemput, K., Maes, F., Vandermeulen, D., Suetens, P.

**Automated model-based bias field correction of MR images of the brain**  
(1999) *IEEE Transactions on Medical Imaging*, 18 (10), pp. 885-896. Cited 188 times.

Group of Medical Image Computing, Faculties of Med. and Engineering, University Hospital Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium

### **Abstract**

We propose a model-based method for fully automated bias field correction of MR brain images. The MR signal is modeled as a realization of a random process with a parametric probability distribution that is corrupted by a smooth polynomial inhomogeneity or bias field. The method we propose applies an iterative expectation-maximization (EM) strategy that interleaves pixel classification with estimation of class distribution and bias field parameters, improving the likelihood of the model parameters at each iteration. The algorithm, which can handle multichannel data and slice-by-slice constant intensity offsets, is initialized with information from a digital brain atlas about the a priori expected location of tissue classes. This allows full automation of the method without need for user interaction, yielding more objective and reproducible results. We have validated the bias correction algorithm on simulated data and we illustrate its performance on various MR images with important field inhomogeneities. We also relate the proposed algorithm to other bias correction algorithms. © 1999 IEEE.

### **Author Keywords**

Bias field; Digital brain atlas; MRI; Tissue classification

**Document Type:** Article

**Source:** Scopus

## VALIDATION

Collins, D.L., Zijdenbos, A.P., Kollokian, V., Sied, J.G., Kabani, N.J., Holmes, C.J., Evans, A.C.

### **Design and construction of a realistic digital brain phantom**

(1998) *IEEE Transactions on Medical Imaging*, 17 (3), pp. 463-468. Cited 517 times.

Montréal Neurological Institute, McGill University, McConnell Brain Imaging Centre, 3801 University, Montréal, Que. H3A 2B4, Canada

### **Abstract**

After conception and implementation of any new medical image processing algorithm, validation is an important step to ensure that the procedure fulfills all requirements set forth at the initial design stage. Although the algorithm must be evaluated on real data, a comprehensive validation requires the additional use of simulated data since it is impossible to establish ground truth with in vivo data. Experiments with simulated data permit controlled evaluation over a wide range of conditions (e.g., different levels of noise, contrast, intensity artefacts, or geometric distortion). Such considerations have become increasingly important with the rapid growth of neuroimaging, i.e., computational analysis of brain structure and function using brain scanning methods such as positron emission tomography and magnetic resonance imaging. Since simple objects such as ellipsoids or parallélépipèdes do not reflect the complexity of natural brain anatomy, we present the design and creation of a realistic, high-resolution, digital, volumetric phantom of the human brain. This three-dimensional digital brain phantom is made up of ten volumetric data sets that define the spatial distribution for different tissues (e.g., grey matter, white matter, muscle, skin, etc.), where voxel intensity is proportional to the fraction of tissue within the voxel. The digital brain phantom can be used to simulate tomographic images of the head. Since the contribution of each tissue type to each voxel in the brain phantom is known, it can be used as the gold standard to test analysis algorithms such as classification procedures which seek to identify the tissue "type" of each image voxel. Furthermore, since the same anatomical phantom may be used to drive simulators for different modalities, it is the ideal tool to test intermodality registration algorithms. The brain phantom and simulated MR images have been made publicly available on the Internet (<http://www.bic.mni.mcgill.ca/brainweb>). © 1998 IEEE.

### **Author Keywords**

Brain phantom; Magnetic resonance imaging; Positron emission tomography; Simulation, testing; Validation

**Document Type:** Article

**Source:** Scopus

## Tissue classification and segmentation

Wells III, W.M.<sup>a b</sup>, Crimson, W.E.L.<sup>a b</sup>, Kikinis, R.<sup>a b</sup>, Jolesz, F.A.<sup>a b</sup>

### **Adaptive segmentation of MRI data**

(1996) *IEEE Transactions on Medical Imaging*, 15 (4), pp. 429-442. Cited 464 times.

<sup>a</sup> Department of Radiology, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, United States

<sup>b</sup> Department of Radiology, Harvard Medical School, Brigham and Women's Hospital, Boston, MA 02115, United States

### **Abstract**

Intensity-based classification of MR images has proven problematic, even when advanced techniques are used. Intrascan and InterScan intensity inhomogeneities are a common source of difficulty. While reported methods have had some success in correcting intrascan inhomogeneities, such methods require supervision for the individual scan. This paper describes a new method called adaptive segmentation that uses knowledge of tissue intensity properties and intensity inhomogeneities to correct and segment MR images. Use of the expectation-maximization (F.M) algorithm leads to a method that allows for more accurate segmentation of tissue types as well as better visualization of magnetic resonance imaging (MRI) data, that has proven to be effective in a study that includes more than 1000 brain scans. Implementation and results are described for segmenting the brain in the following types of images: axial (dual-echo spin-echo), coronal [three dimensional Fourier transform (3-DFT) gradient-echo T1-weighted] all using a conventional head coil, and a sagittal section acquired using a surface coil. The accuracy of adaptive segmentation was found to be comparable with manual segmentation, and closer to manual segmentation than supervised multivariant classification while segmenting gray and white matter, © 1996 IEEE.

**Document Type:** Article

**Source:** Scopus

Van Leemput, K., Maes, F., Vandermeulen, D., Suetens, P.

**A unifying framework for partial volume segmentation of brain MR images**

(2003) *IEEE Transactions on Medical Imaging*, 22 (1), pp. 105-119. Cited 81 times.

Med. Image Comp. (Rad.-ESAT/PSI), Faculties of Medicine and Eng., University Hospital Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium

### **Abstract**

Accurate brain tissue segmentation by intensity-based voxel classification of magnetic resonance (MR) images is complicated by partial volume (PV) voxels that contain a mixture of two or more tissue types. In this paper, we present a statistical framework for PV segmentation that encompasses and extends existing techniques. We start from a commonly used parametric statistical image model in which each voxel belongs to one single tissue type, and introduce an additional downsampling step that causes partial voluming along the borders between tissues. An expectation-maximization approach is used to simultaneously estimate the parameters of the resulting model and perform a PV classification. We present results on well-chosen simulated images and on real MR images of the brain, and demonstrate that the use of appropriate spatial prior knowledge not only improves the classifications, but is often

indispensable for robust parameter estimation as well. We conclude that general robust PV segmentation of MR brain images requires statistical models that describe the spatial distribution of brain tissues more accurately than currently available models.

**Author Keywords**

Expectation-maximization; Markov random field; Monte Carlo sampling; MRI; Partial volume; Segmentation

**Document Type:** Article

**Source:** Scopus

Van Leemput, K., Maes, F., Vandermeulen, D., Suetens, P.

**Automated model-based tissue classification of MR images of the brain**

(1999) *IEEE Transactions on Medical Imaging*, 18 (10), pp. 897-908. Cited 313 times.

Group of Medical Image Computing, Faculties of Med. and Engineering, University Hospital Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium

**Abstract**

We describe a fully automated method for modelbased tissue classification of magnetic resonance (MR) images of the brain. The method interleaves classification with estimation of the model parameters, improving the classification at each iteration. The algorithm is able to segment single- and multispectral MR images, corrects for MR signal inhomogeneities, and incorporates contextual information by means of Markov random Fields (MRF's). A digital brain atlas containing prior expectations about the spatial location of tissue classes is used to initialize the algorithm. This makes the method fully automated and therefore it provides objective and reproducible segmentations. We have validated the technique on simulated as well as on real MR images of the brain. © 1999 IEEE.

**Author Keywords**

Digital brain atlas; Markov random fields; MRI; Segmentation; Tissue classification

**Document Type:** Article

**Source:** Scopus

Ashburner, J., Friston, K.J.

**Unified segmentation**

(2005) *NeuroImage*, 26 (3), pp. 839-851. Cited 346 times.

Wellcome Department of Imaging Neuroscience, Functional Imaging Laboratory, 12 Queen Square, London, WC1N 3BG, United Kingdom

## Abstract

A probabilistic framework is presented that enables image registration, tissue classification, and bias correction to be combined within the same generative model. A derivation of a log-likelihood objective function for the unified model is provided. The model is based on a mixture of Gaussians and is extended to incorporate a smooth intensity variation and nonlinear registration with tissue probability maps. A strategy for optimising the model parameters is described, along with the requisite partial derivatives of the objective function. © 2005 Elsevier Inc. All rights reserved.

## Author Keywords

Bias correction; Image registration; Mixture of Gaussians; Tissue classification; Tissue probability maps

**Document Type:** Article

**Source:** Scopus

Fischl, B.<sup>a</sup>, Salat, D.H.<sup>a</sup>, Busa, E.<sup>a</sup>, Albert, M.<sup>b,c</sup>, Dieterich, M.<sup>e</sup>, Haselgrove, C.<sup>e</sup>, Van Der Kouwe, A.<sup>a</sup>, Killiany, R.<sup>d</sup>, Kennedy, D.<sup>e</sup>, Klaveness, S.<sup>e</sup>, Montillo, A.<sup>f</sup>, Makris, N.<sup>e</sup>, Rosen, B.<sup>a</sup>, Dale, A.M.<sup>a</sup>

**Whole brain segmentation: Automated labeling of neuroanatomical structures in the human brain** (2002) *Neuron*, 33 (3), pp. 341-355. Cited 336 times.

<sup>a</sup> Massachusetts General Hospital, Nuclear Magnetic Resonance Center, Building 149, 13th Street, Charlestown, MA 02129, United States

<sup>b</sup> Department of Neurology, Massachusetts General Hospital, Harvard Medical School, 55 Fruit Street, VBK 901, Boston, MA 02114, United States

<sup>c</sup> Department of Psychiatry, CNY-9, Massachusetts General Hospital, Boston, MA 02114, United States

<sup>d</sup> Department of Anatomy and Neurobiology, Boston University School of Medicine, 715 Albany Street, Boston, MA 02118, United States

<sup>e</sup> Center for Morphometric Analysis, Neuroscience Center, MGH-East, 13th Street, Charlestown, MA 02129, United States

<sup>f</sup> Computer Science Department, University of Pennsylvania, 111 Towne Building, 220 South 33rd Street, Philadelphia, PA 19104, United States

## Abstract

We present a technique for automatically assigning a neuroanatomical label to each voxel in an MRI volume based on probabilistic information automatically estimated from a manually labeled training set. In contrast to existing segmentation procedures that only label a small number of tissue classes, the current method assigns one of 37 labels to each voxel, including left and right caudate, putamen, pallidum, thalamus, lateral ventricles, hippocampus, and amygdala. The classification technique employs a registration procedure that is robust to anatomical variability, including the ventricular enlargement typically associated with neurological diseases and aging. The technique is shown to be comparable in accuracy to manual labeling, and of sufficient sensitivity to robustly detect changes in the volume of noncortical structures that presage the onset of probable Alzheimer's disease.

**Document Type:** Article

**Source:** Scopus

Smith, S.M.<sup>a</sup>, Zhang, Y.<sup>a</sup>, Jenkinson, M.<sup>a</sup>, Chen, J.<sup>a,c</sup>, Matthews, P.M.<sup>a</sup>, Federico, A.<sup>b</sup>, De Stefano, N.<sup>b</sup>  
**Accurate, robust, and automated longitudinal and cross-sectional brain change analysis**

(2002) *NeuroImage*, 17 (1), pp. 479-489. Cited 280 times.

<sup>a</sup> Oxford Centre for Functional Magnetic Resonance Imaging of the Brain, Department of Clinical Neurology, University of Oxford, Headley Way, Headington, Oxford, United Kingdom

<sup>b</sup> Neurometabolic Unit, NMR Centre, University of Siena, Italy

<sup>c</sup> MRS Lab, McConnell Brain Imaging Centre, MNI, Canada

### **Abstract**

Quantitative measurement of brain size, shape, and temporal change (for example, in order to estimate atrophy) is increasingly important in biomedical image analysis applications. New methods of structural analysis attempt to improve robustness, accuracy, and extent of automation. A fully automated method of longitudinal (temporal change) analysis, SIENA, was presented previously. In this paper, improvements to this method are described, and also an extension of SIENA to a new method for cross-sectional (single time point) analysis. The methods are fully automated, robust, and accurate: 0.15% brain volume change error (longitudinal); 0.5-1% brain volume accuracy for single-time point (cross-sectional). A particular advantage is the relative insensitivity to differences in scanning parameters. The methods provide easy manual review of their output by the automatic production of summary images which show the results of the brain extraction, registration, tissue segmentation, and final atrophy estimation. © 2002 Elsevier Science (USA).

### **Author Keywords**

Atrophy measurement; Normalized registration; Structural brain analysis

**Document Type:** Article

**Source:** Scopus

Pham, D.L.<sup>a b</sup>, Xu, C.<sup>a</sup>, Prince, J.L.<sup>a</sup>

### **Current methods in medical image segmentation**

(2000) *Annual Review of Biomedical Engineering*, 2 (2000), pp. 315-337. Cited 274 times.

<sup>a</sup> Dept. of Elec. and Comp. Engineering, Johns Hopkins University, Baltimore, MD 21218, United States

<sup>b</sup> Lab. of Personality and Cognition, National Institute on Aging, Baltimore, MD 21224, United States

### **Abstract**

Image segmentation plays a crucial role in many medical-imaging applications, by automating or facilitating the delineation of anatomical structures and other regions of interest. We present a critical appraisal of the current status of semi-automated and automated methods for the segmentation of anatomical medical images. Terminology and important issues in image segmentation are first presented. Current segmentation approaches are then reviewed with an emphasis on the advantages and disadvantages of these methods for medical imaging applications. We conclude with a discussion on the future of image segmentation methods in biomedical research.

### **Author Keywords**

Classification; Deformable models; Image processing; Magnetic resonance imaging; Medical imaging

**Document Type:** Article

**Source:** Scopus

Basser, P.J.<sup>a</sup>, Jones, D.K.<sup>b</sup>

**Diffusion-tensor MRI: Theory, experimental design and data analysis - A technical review**  
(2002) *NMR in Biomedicine*, 15 (7-8), pp. 456-467. Cited 243 times.

<sup>a</sup> Sec. on Tissue Biophys./Biomimetics, NICHD, National Institutes of Health, Bethesda, MD 20892, United States

<sup>b</sup> Section of Old Psychiatry, Institute of Psychiatry, London, United Kingdom

### **Abstract**

This article treats the theoretical underpinnings of diffusion-tensor magnetic resonance imaging (DT-MRI), as well as experimental design and data analysis issues. We review the mathematical model underlying DT-MRI, discuss the quantitative parameters that are derived from the measured effective diffusion tensor, and describe artifacts that arise in typical DT-MRI acquisitions. We also discuss difficulties in identifying appropriate models to describe water diffusion in heterogeneous tissues, as well as in interpreting experimental data obtained in such issues. Finally, we describe new statistical methods that have been developed to analyse DT-MRI data, and their potential uses in clinical and multi-site studies. Copyright © 2002 John Wiley & Sons, Ltd.

### **Author Keywords**

Diffusion; Methods; MRI; Tensor

**Document Type:** Review

**Source:** Scopus

Shattuck, D.W.<sup>a</sup>, Sandor-Leahy, S.R.<sup>b</sup>, Schaper, K.A.<sup>c</sup>, Rottenberg, D.A.<sup>c d</sup>, Leahy, R.M.<sup>a</sup>

**Magnetic resonance image tissue classification using a partial volume model**  
(2001) *NeuroImage*, 13 (5), pp. 856-876. Cited 239 times.

<sup>a</sup> Signal and Image Processing Institute, University of Southern California, Los Angeles, CA 90089, United States

<sup>b</sup> TRW, Inc., Redondo Beach, CA 90278, United States

<sup>c</sup> PET Imaging Center, VA Medical Center, Minneapolis, MN 55417, United States

<sup>d</sup> Department of Neurology, University of Minnesota, Minneapolis, MN 55455, United States

### **Abstract**

We describe a sequence of low-level operations to isolate and classify brain tissue within T1-weighted magnetic resonance images (MRI). Our method first removes nonbrain tissue using a combination of anisotropic diffusion filtering, edge detection, and mathematical morphology. We compensate for image non-uniformities due to magnetic field inhomogeneities by fitting a tricubic B-spline gain field to local

estimates of the image nonuniformity spaced throughout the MRI volume. The local estimates are computed by fitting a partial volume tissue measurement model to histograms of neighborhoods about each estimate point. The measurement model uses mean tissue intensity and noise variance values computed from the global image and a multiplicative bias parameter that is estimated for each region during the histogram fit. Voxels in the intensity-normalized image are then classified into six tissue types using a maximum a posteriori classifier. This classifier combines the partial volume tissue measurement model with a Gibbs prior that models the spatial properties of the brain. We validate each stage of our algorithm on real and phantom data. Using data from the 20 normal MRI brain data sets of the Internet Brain Segmentation Repository, our method achieved average  $\kappa$  indices of  $\kappa = 0.746 \pm 0.114$  for gray matter (GM) and  $\kappa = 0.798 \pm 0.089$  for white matter (WM) compared to expert labeled data. Our method achieved average  $\kappa$  indices  $\kappa = 0.893 \pm 0.041$  for GM and  $\kappa = 0.928 \pm 0.039$  for WM compared to the ground truth labeling on 12 volumes from the Montreal Neurological Institute's BrainWeb phantom. © 2001 Academic Press.

**Document Type:** Article

**Source:** Scopus

Fenster, A., Downey, D.B., Cardinal, H.N.

**Three-dimensional ultrasound imaging**

(2001) *Physics in Medicine and Biology*, 46 (5), pp. R67-R99. Cited 216 times.

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**Abstract**

Ultrasound is an inexpensive and widely used imaging modality for the diagnosis and staging of a number of diseases. In the past two decades, it has benefited from major advances in technology and has become an indispensable imaging modality, due to its flexibility and non-invasive character. In the last decade, research investigators and commercial companies have further advanced ultrasound imaging with the development of 3D ultrasound. This new imaging approach is rapidly achieving widespread use with numerous applications. The major reason for the increase in the use of 3D ultrasound is related to the limitations of 2D viewing of 3D anatomy, using conventional ultrasound. This occurs because: (a) Conventional ultrasound images are 2D, yet the anatomy is 3D, hence the diagnostician must integrate multiple images in his mind. This practice is inefficient, and may lead to variability and incorrect diagnoses. (b) The 2D ultrasound image represents a thin plane at some arbitrary angle in the body. It is difficult to localize the image plane and reproduce it at a later time for follow-up studies. In this review article we describe how 3D ultrasound imaging overcomes these limitations. Specifically, we describe the developments of a number of 3D ultrasound imaging systems using mechanical, free-hand and 2D array scanning techniques. Reconstruction and viewing methods of the 3D images are described with specific examples. Since 3D ultrasound is used to quantify the volume of organs and pathology, the sources of errors in the reconstruction techniques as well as formulae relating design specification to geometric errors are provided. Finally, methods to measure organ volume from the 3D ultrasound images and sources of errors are described.

**Document Type:** Review

**Source:** Scopus

Vedantham, S.<sup>a</sup>, Karellas, A.<sup>a</sup>, Suryanarayanan, S.<sup>a</sup>, Albagli, D.<sup>b</sup>, Han, S.<sup>b</sup>, Tkaczyk, E.J.<sup>b</sup>, Landberg, C.E.<sup>b</sup>, Opsahl-Ong, B.<sup>b</sup>, Granfors, P.R.<sup>c</sup>, Levis, I.<sup>a</sup>, D'Orsi, C.J.<sup>a</sup>, Hendrick, R.E.<sup>d,e</sup>

**Full breast digital mammography with an amorphous silicon-based flat panel detector: Physical characteristics of a clinical prototype**

(2000) *Medical Physics*, 27 (3), pp. 558-567. Cited 213 times.

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**Abstract**

The physical characteristics of a clinical prototype amorphous silicon-based flat panel imager for full-breast digital mammography have been investigated. The imager employs a thin thallium doped CsI scintillator on an amorphous silicon matrix of detector elements with a pixel pitch of 100  $\mu$ . Objective criteria such as modulation transfer function (MTF), noise power spectrum, detective quantum efficiency (DQE), and noise equivalent quanta were employed for this evaluation. The presampling MTF was found to be 0.73, 0.42, and 0.28 at 2, 4, and 5 cycles/mm, respectively. The measured DQE of the current prototype utilizing a 28 kVp, Mo-Mo spectrum beam hardened with 4.5 cm Lucite is -55% at close to zero spatial frequency at an exposure of 32.8 mR, and decreases to -40% at a low exposure of 1.3 mR. Detector element nonuniformity and electronic gain variations were not significant after appropriate calibration and software corrections. The response of the imager was linear and did not exhibit signal saturation under tested exposure conditions. (C) 2000 American Association of Physicists in Medicine.

**Author Keywords**

Breast imaging; Detective quantum efficiency (DQE); Digital mammography; Image quality; Physics

**Document Type:** Article

**Source:** Scopus

Ntziachristos, V., Bremer, C., Weissleder, R.

**Fluorescence imaging with near-infrared light: New technological advances that enable in vivo molecular imaging**

(2003) *European Radiology*, 13 (1), pp. 195-208. Cited 195 times.

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**Abstract**

A recent development in biomedical imaging is the non-invasive mapping of molecular events in intact tissues using fluorescence. Underpinning to this development is the discovery of bio-compatible, specific fluorescent probes and proteins and the development of highly sensitive imaging technologies for in vivo fluorescent detection. Of particular interest are fluorochromes that emit in the near infrared (NIR), a spectral window, whereas hemoglobin and water absorb minimally so as to allow photons to penetrate for

several centimetres in tissue. In this review article we concentrate on optical imaging technologies used for non-invasive imaging of the distribution of such probes. We illuminate the advantages and limitations of simple photographic methods and turn our attention to fluorescence-mediated molecular tomography (FMT), a technique that can three-dimensionally image gene expression by resolving fluorescence activation in deep tissues. We describe theoretical specifics, and we provide insight into its in vivo capacity and the sensitivity achieved. Finally, we discuss its clinical feasibility.

#### **Author Keywords**

Fluorescence; In vivo; Molecular imaging; Near infrared

**Document Type:** Review

**Source:** Scopus

Johansen-Berg, H.<sup>a</sup>, Dawes, H.<sup>b</sup>, Guy, C.<sup>b</sup>, Smith, S.M.<sup>a</sup>, Wade, D.T.<sup>b</sup>, Matthews, P.M.<sup>a</sup>

**Correlation between motor improvements and altered fMRI activity after rehabilitative therapy** (2002) *Brain*, 125 (12), pp. 2731-2742. Cited 195 times.

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<sup>b</sup> Rivermead Rehabilitation Centre, Oxford, United Kingdom

#### **Abstract**

Motor rehabilitation therapy is commonly employed after strokes, but outcomes are variable and there is little specific information about the changes in brain activity that are associated with improved function. We performed serial functional MRI (fMRI) on a group of seven patients receiving a form of rehabilitation therapy after stroke in order to characterize functional changes in the brain that correlate with behavioural improvements. Patients were scanned while performing a hand flexion-extension movement twice before and twice after a two-week home-based therapy programme combining restraint of the unaffected limb with progressive exercises for the affected limb. As expected, the extent of improvement in hand function after therapy varied between patients. Therapy-related improvements in hand function correlated with increases in fMRI activity in the premotor cortex and secondary somatosensory cortex contralateral to the affected hand, and in superior posterior regions of the cerebellar hemispheres bilaterally (Crus I and lobule VI). fMRI offers a promising, objective approach for specifically identifying changes in brain activity potentially responsible for rehabilitation-mediated recovery of function after stroke. Our results suggest that activity changes in sensorimotor regions are associated with successful motor rehabilitation.

#### **Author Keywords**

Cerebellum; FMRI; Premotor cortex; Rehabilitation; Stroke

**Document Type:** Article

**Source:** Scopus

Smith, S.M.<sup>a b</sup>

### **Fast robust automated brain extraction**

(2002) *Human Brain Mapping*, 17 (3), pp. 143-155. Cited 765 times.

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#### **Abstract**

An automated method for segmenting magnetic resonance head images into brain and non-brain has been developed. It is very robust and accurate and has been tested on thousands of data sets from a wide variety of scanners and taken with a wide variety of MR sequences. The method, Brain Extraction Tool (BET), uses a deformable model that evolves to fit the brain's surface by the application of a set of locally adaptive model forces. The method is very fast and requires no preregistration or other pre-processing before being applied. We describe the new method and give examples of results and the results of extensive quantitative testing against "gold-standard" hand segmentations, and two other popular automated methods. © 2002 Wiley-Liss, Inc.

#### **Author Keywords**

Brain segmentation; Cortical surface modeling

Xu, C.<sup>a b</sup>, Prince, J.L.<sup>a b</sup>

### **Snakes, shapes, and gradient vector flow**

(1998) *IEEE Transactions on Image Processing*, 7 (3), pp. 359-369. Cited 1235 times.

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<sup>b</sup> IEEE

#### **Abstract**

Snakes, or active contours, are used extensively in computer vision and image processing applications, particularly to locate object boundaries. Problems associated with initialization and poor convergence to boundary concavities, however, have limited their utility. This paper presents a new external force for active contours, largely solving both problems. This external force, which we call gradient vector flow (GVF), is computed as a diffusion of the gradient vectors of a gray-level or binary edge map derived from the image. It differs fundamentally from traditional snake external forces in that it cannot be written as the negative gradient of a potential function, and the corresponding snake is formulated directly from a force balance condition rather than a variational formulation. Using several two-dimensional (2-D) examples and one three-dimensional (3-D) example, we show that GVF has a large capture range and is able to move snakes into boundary concavities. © 1998 IEEE.

#### **Author Keywords**

Active contour models; Deformable surface models; Edge detection; Gradient vector flow; Image segmentation; Shape representation and recovery; Snakes

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