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Registration, segmentation, and visualization of multimodal brain images

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Abstract

This paper gives an overview of the studies performed at our institute over the last decade on the processing and visualization of brain images, in the context of international developments in the field. The focus is on multimodal image registration and multimodal visualization, while segmentation is touched upon as a preprocessing step for visualization. The state-of-the-art in these areas is discussed and suggestions for future research are given. © 2001 Elsevier Science Ltd. All rights reserved.

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1. Introduction

In a growing number of clinical studies, images are acquired from multiple imaging modalities. For an optimal interpretation of the multimodal information, integration of the images is called for.

Image integration (or image fusion) consists of two steps:

(1) (co)registration (or matching, or alignment), where the images are brought into spatial agreement; and
(2) integrated or multimodality display (or presentation, or visualization), where the registered multimodality (or intermodality) information is rendered.

The second step implies some form of image segmentation or classification.

The scope of the present paper is the registration and integrated presentation of intermodality, intrasubject volumetric clinical brain images. The work of the last decade in Utrecht, in registering, segmenting and visualizing multimodal brain images is briefly described, and the state-of-the-art developments in the field are briefly reviewed so as to put our work into perspective; a full coverage of the field is not aimed at. In Section 5, a number of open questions will be discussed and directions for further research will be suggested.

2. Registration

Techniques to bring multimodal images into register can be classified according to various criteria as, e.g. elasticity of the transformation (rigid, affine, projective, curved), or extrinsic vs. intrinsic matching (i.e. using external fiducial markers vs. using the image information per se). A recent, comprehensive review of medical image registration with a classification scheme comprising the above criteria as well as many others is given in Refs. [1,2].

Registration in intermodality brain imaging is usually restricted to rigid transformations. Curved (elastic) transformations are relevant for intramodality matching, which occurs in atlas based registration, in comparative population studies, and in longitudinal studies of a single patient; however, this is beyond the scope of the present paper. Scaling may be important, but scaling parameters can generally be derived from the header information and thus be disregarded in the computational registration process, leaving only rotation and translation to be considered.

Extrinsic and intrinsic matching have both been applied extensively in brain image registration. The artificial fiducial markers that underlie extrinsic matching may be skull screws, stereotactic frames, head or dental adapters, or skin markers. Skin markers are the most patient-friendly fiducials, applicable in all imaging modalities, and are — slightly surprisingly — at least as accurate as the invasive frames [3]. However, extrinsic matching cannot be applied retrospectively; the marker placement has to be included in the clinical protocol, which is a serious disadvantage. Furthermore, since intrinsic matching has improved significantly over the last few years,

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extrinsic registration is loosing ground, and is applied only when image information is sparse (as in EEG or MEG) or when markers have to be applied anyway, notably in stereotactic frame based neurosurgery.

The oldest form of intrinsic matching is based on manual placement of corresponding landmarks in two images. This procedure is subjective, inaccurate and time-consuming, and is thus no longer used in rigid registration; for elastic registration, landmarks are still quite useful. Surface-based matching requires the segmentation of the skin or the cerebral cortex from the images to be registered. This is a high-level image processing operation which may be performed accurately, but is inherently imprecise (non-robust). Surface-based registration is still used in many centres, but is ripe for replacement.

The method of choice for multimodality brain image registration has become voxel based matching. There are two approaches: (i) based on the image intensities directly; and (ii) based on feature images derived from the original images by, e.g., edge or ridge detectors. The latter approach has been studied extensively by us [1,3–5] and has been quite successful. Nonetheless, approach (i) seems preferable because it provides results that are at least as good [6], at less computational costs. The paradigm is simple: the histograms of two images to be registered define a 2D feature space (a scatter plot, see Fig. 1), which has the property of becoming more fuzzy with increasing misregistration. The registration of two images can thus be performed by maximizing the 'crispness' in some sense. The optimum criterion has been derived to be maximization of the mutual information of the two images, an information theory measure that is a generalization of joint entropy minimization. An extensive description and a comparison with similar, earlier attempts can be found in Refs. [7–13].

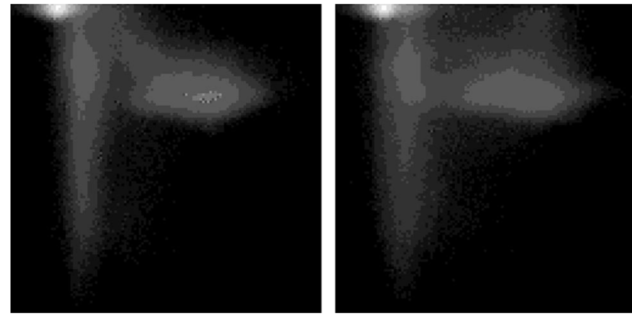

Fig. 1. Scatter-plot of the histograms of a pair of PET (horizontal axis) and MR (vertical axis) images. Left frame: images in register. Right frame: images misregistered by a translation of 10 mm along the two in-plane axes.

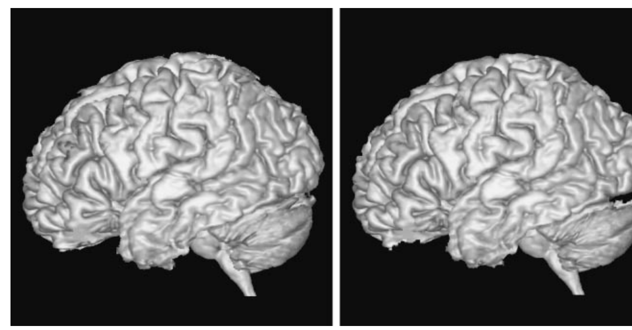

Fig. 2. Comparison of volume renderings of the brain, based on automatic (left) and manual (right) segmentation of T_1-weighted MR data.

3. Segmentation

Segmentation has been, is, and probably will long remain the key problem of image analysis. It is well beyond the scope of this paper to give a survey of image segmentation, or even of medical image segmentation. We will confine ourselves to the segmentation of brain images in so far as it is relevant to multimodality image integration. The main segmentation task in brain image matching is the extraction of the total brain (i.e., distinction between brain tissue and CSF). This task can be automated for a given MR protocol, even with a simple threshold-based technique [14,15]. Automated segmentation has proven sufficiently accurate for volumetric display (Fig. 2) and may also be adequate for estimates of total brain volume [16,17]. However, more detailed studies of brain anatomy and physiology will require more powerful segmentation methods.

Multiscale image analysis [18–20] has appeared pre-eminently suited for intricate segmentation tasks in a variety of applications. The inclusion of partial volume effects in the segmentation paradigm has especially proven valuable [19,21]. The 'hyperstack' segmentation approach has yielded reproducible results for tasks like grey matter/white matter separation or segmentation of the ventricles. The approach deliberately provides an oversegmentation of the object to be defined, typically by a factor of five, whereupon a merging process completes the segmentation. The merging process is usually performed manually, but can be automated for well-defined tasks [22].

4. Visualization

Registered volumetric images can be displayed in 2D (single slices) without a pre-segmentation, e.g., by juxtaposition with a linked cursor or by non-selective integration as subtraction, alternate pixel ('chessboard') display or colour washing [14]. However, the information transfer of this type of display is limited.

Contoured 2D or 3D display (Fig. 3) paradigms all require some form of segmentation or classification. In contoured 2D display the delineation of the cerebral cortex is generally required, while other structures like the ventricles or the lesion at issue may also be outlined. However simple these techniques may seem, the gain in accuracy in localizing lesions may be considerable [14,17].

Volumetric visualization is more powerful still. There are basically two approaches to 3D display [23]. One is by defining the surfaces to be visualized by a binary segmentation

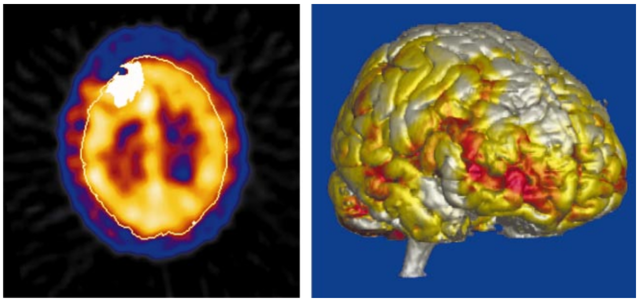

Fig. 3. SPECT/MRI multimodality display of a patient with a right frontal lobe tumour. Left frame: 2D contoured display. The grey values represent a slice of the SPECT image; the brain contour and the tumour area were delineated in a corresponding registered MR slice. Right frame: 3D normal fusion display. The brain surface was (automatically) segmented from an MR-T_1 image; the SPECT perfusion values were integrated along the surface normal and colour coded onto the surface. The dark area in the right frontal lobe signals increased perfusion and was found to surround the tumour.

(i.e. a voxel is either on one side of the surface, or on the other). This approach, surface rendering, has the advantage of allowing visualization by standard graphics tools, but has the drawback that the binary segmentation leads to errors in the surface definition. The second approach, volume rendering, has the significant advantage that a 'hard' segmentation is not needed. The method just requires a rough classification of the tissues traversed by the rays cast into the volume. The partial volume hyperstack segmentation [19] has turned out to be a good preprocessor for volume rendering, although in many cases simpler methods, e.g. based on histograms, may suffice.

Volume rendering is — much more than surface rendering — suitable for multimodality display [23,24]. The 'fuzzy' surface definition allows a more natural integration of the functional image modality (SPECT, PET). We have developed an approach (normal fusion) where the functional information is integrated along the inward normal to the cortical surface; the result is colour coded onto the cortex. An example of SPECT/MRI fusion is given in Fig. 3b. By varying the depth of integration of the functional modality, an insight can be gained into the functional anatomy of the cortical processes; see Fig. 4.

For neurosurgical procedures, the combined visualization of cortical structures and functional information is beneficial both in the planning phase and for intraoperative guidance. Fig. 5 gives an integrated presentation of cortical anatomy and functional MRI information, which shows critical cortical areas (the motor strip) in relation to a nearby tumour which is to be surgically removed.

For more examples of multimodality visualization, we refer the interested reader to our website: http://www.isi.uu.nl.

5. Conclusions and discussion

Maximization of mutual information has appeared to be a powerful method for registering volumetric (CT/MRI, PET/MRI, SPECT/MRI) brain image pairs [6–13]. It has also appeared successful for rigid monomodality (MRI/MRI, etc.) registration [10]. Despite its success in the comprehensive Vanderbilt multicentre trial [6], the approach still needs to be evaluated extensively, in particular as concerns its dependency on the choice of entropy in the information measure, on the optimization paradigm,

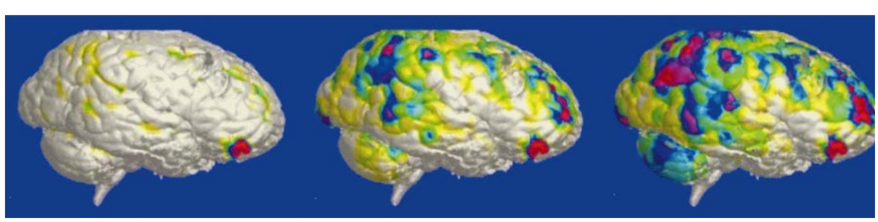

Fig. 4. Integrated SPECT/MRI visualization of a patient with Gilles de la Tourette syndrome. The normal fusion paradigm was used. The three frames show integration of functional SPECT information over 1 mm (left), 5 mm (middle), 15 mm (right).

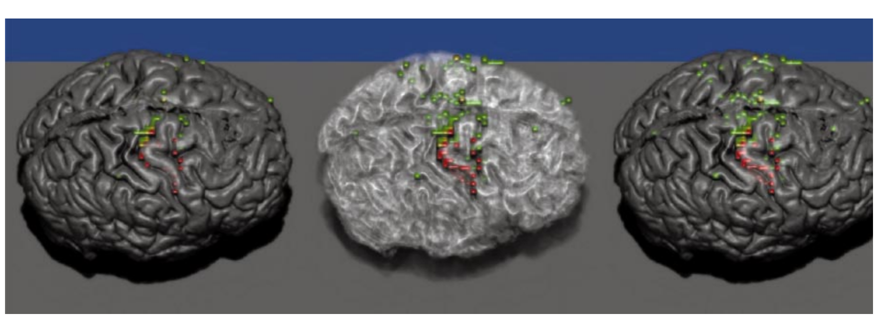

Fig. 5. Integrated visualization of functional MRI information and cortical anatomy. In the left frame, the standard visualization approach is shown. The deeper fMRI voxels are not visible owing to occlusion by brain tissue. In the middle frame, transparency has been used to bring out the deeper fMRI voxels, at the expense of a degraded view of the gyral–sulcal pattern. The right frame presents a multispectral display (see Ref. [25] for details of the technique). The brain is transparent for light scattered by the fMRI voxels. The subcortical fMRI areas are visible without disturbing the view on the cortex.

and on the resampling technique [26] applied in the transformations. An as yet underrated issue is that mutual information does not include spatial connectivity. Paradigms which would combine the advantageous statistical characteristics of mutual information maximization with spatial correlation as exhibited, e.g. by feature-based methods, are worthy of further investigation. Another interesting point of research is the influence of the imaging physics on the registration. MRI distortion correction [6] and SPECT or PET scatter modelling may aid significantly in reducing the registration error. The main directions of future research in image registration will, however, be real-time matching for intraoperative image guidance and curved (elastic) matching for both intermodality and intramodality image alignment.

Segmentation of brain images can be done automatically for well-defined tasks as total brain segmentation or white matter/grey matter differentiation. More complex tasks require an interactive procedure. Interactive segmentation will require substantial guidance by model knowledge, which may include both imaging physics and characteristics of the object to be segmented. Interactive segmentation of volumetric data furthermore calls for fast visualization techniques and suitable user interfaces. Finally, registered multimodal images facilitate multimodality (multispectral, multiparameter) segmentation methods. This is a largely unexplored research area, which will probably be developed in the coming years.

Multimodality visualization has proven to have great clinical potential [14,17]. A major research issue is the design and evaluation of display approaches for specific applications, since visualization is highly task-driven. Clinical validation of such procedures requires both a thorough methodological set-up and significant efforts of multiple experts. The latter aspect especially makes the evaluation of visualization techniques a rarity in scientific literature.

For interventional multimodality visualization, where preoperative images are combined with intraoperative images, other problems have to be solved first, notably as regards computational speed. While the preoperatively acquired images can be pre-segmented, which removes the need for on-line segmentation, real-time multimodality visualization does require real-time registration. Fiducial markers can provide on-line alignment, except for changes in geometry during the intervention as, notably, the brain shift occurring upon trepanation. Accordingly, correction for such changes will be the primary research objective in interventional image guidance.

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