A Digital Brain Atlas for Surgical Planning, Model-Driven Segmentation, and Teaching

Ron Kikinis, Martha E. Shenton, Dan V. Iosifescu, Robert W. McCarley, Pairash Saiviroonporn, Hiroto H. Hokama, Andre Robatino, David Metcalf, Cynthia G. Wible, Chiara M. Portas, Robert M. Donnino, and Ferenc A. Jolesz

Abstract—We developed a three-dimensional (3D) digitized atlas of the human brain to visualize spatially complex structures. It was designed for use with magnetic resonance (MR) imaging data sets. Thus far, we have used this atlas for surgical planning, model-driven segmentation, and teaching. We used a combination of automated and supervised segmentation methods to define regions of interest based on neuroanatomical knowledge. We also used 3D surface rendering techniques to create a brain atlas that would allow us to visualize complex 3D brain structures. We further linked this information to script files in order to preserve both spatial information and neuroanatomical knowledge. We present here the application of the atlas for visualization in surgical planning for model-driven segmentation and for the teaching of neuroanatomy. This digitized human brain has the potential to provide important reference information for the planning of surgical procedures. It can also serve as a powerful teaching tool, since spatial relationships among neuroanatomical structures can be more readily envisioned when the user can view and rotate the structures in 3D space. Moreover, each element of the brain atlas is associated with a name tag, displayed by a user-controlled pointer. The atlas holds a major promise as a template for model-driven segmentation. Using this technique, many regions of interest can be characterized simultaneously on new brain images.

Index Terms—Brain atlas, magnetic resonance imaging (MRI), 3D visualization, 3D surface rendering, biomedical visualization.

1 INTRODUCTION

With current imaging technology, it is possible to obtain isotropic, or nearly isotropic, data sets in a short period of time. Furthermore, improvements in the quality of images have made possible the use of three dimensional (3D) segmentation and 3D visualization techniques to develop a true 3D atlas of the human brain. Consequently, for the first time in medical imaging, anatomical details can be appreciated in 3D instead of being restricted to 2D images of 3D structures.

Accordingly, there is now a great deal of interest, by a number of independent investigators, in developing a 3D atlas of the human brain. Several groups have been working to generate digital 3D atlas data sets of the human brain for various applications. For example, Hoehne and coworkers [19], Hoehne et al. [20], Pommert et al. [32], Schiemann et al. [34], Tiede et al. [42] in Hamburg, Germany, have pioneered the development of a brain atlas for teaching neuroanatomy. However, since they used volume rendering on desktop workstations, their atlas is difficult to work with in interactive sessions. Furthermore, the data set that they have been using was derived from a patient with a localized pathology. Also, while this atlas is commercially available, the data set from which the atlas was built is not accessible for further development of new algorithms. Another atlas in use today comes from the Visible Human project of the National Library of Medicine. This project includes several research groups interested in various aspects of anatomical morphology (see URL1 for more information). Two other independent research groups have acquired brain morphology data at high resolution: Spitzer et al. in Colorado, collaborating with Toga and Evans at UCLA (Thompson et al. [41]) and the McGill University group. In both the latter two research efforts, the data sets were post-mortem frozen corpses cut with giant cryotomos. These efforts have generated huge data sets, some of which are available for downloading on the internet. However, the very time consuming and labor intensive labeling process has only just begun. Some MR and CT data were also acquired through these efforts. There are several other groups (Evans et al. [11], Greitz et al. [15], Mano et al. [30], Christensen et al. [41]) that have been working on digital atlas data sets, but to our knowledge none of these other efforts are as comprehensive as our atlas. Another effort to build a digital teaching tool for neuroanatomy is the digital anatomist project in Seattle (see Sundsten et al. [40] and URL2 for more information).

There is also a growing interest in automatically identifying regions of interest (ROIs) in multiple brains, starting with ROI identification in one brain (Bomans et al. [2],

1 http://www_hbp.scripps.edu/HBP_html/HBPfiles.html
2 http://www1.biostr.washington.edu/dar/references.html
Evans et al. [11], Christensen et al. [4], Collins et al. [9], Lehmann et al. [28]). This latter research interest frequently involves the construction of a brain atlas to be used as a template, which is the first step towards the automatic identification of 3D brain regions on new MR brain data sets. Currently, such identification is painstakingly slow and involves a cadre of workers who laboriously outline and edit each ROI. The development of a digitized anatomy atlas for registering new MR data sets would thus provide us with capabilities that have heretofore not been possible.

In our laboratory, we have created an MR-based 3D brain atlas using data from a single normal subject. The high definition images, with $1 \times 1 \times 1.5$ mm voxels, 3DFT SPGR (Fourier transform, spoiled gradient recalled acquisition) were classified by several operators (RD, HH, DVI, JMG, CMP, MES, CGW) into distinct anatomical regions (see below). The boundaries of the ROI, and the selection of neuroanatomical landmarks, were aided by using as references the textbook of Crosby et al. [10] and the structure-function correlation review of Radamacher et al. [33]. We created 3D representations of neuroanatomy by applying a series of image processing techniques to the MR data acquired from this single normal control subject. In this process we used automated segmentation methods, 3D editing techniques capable of reformatting MR slices in three different planes, and 3D surface rendering techniques. These procedures will be detailed below. To illustrate these methods, we have selected several neuroanatomical regions, including: cerebral cortical gray matter (subdivided by lobes and gyri), cerebellum, brainstem structures (including the pons and medulla), corpus callosum, basal ganglia structures, limbic system structures, eyes and optic chiasm, and the ventricular system. While this neuroanatomy list is not exhaustive, we have selected these regions because of their likely interest to neurologists and to psychiatric researchers.

2 METHODS

This section describes the manner in which the atlas was generated from an MR data set of a normal volunteer. It also details the type of rendering methods used, as well as providing an overview of the custom user-interface that was generated.

2.1 Generation of the Atlas

2.1.1 MR Acquisition

The MR images were acquired on a 1.5-tesla General Electric Signa System (GE Medical Systems, Milwaukee). We acquired a raster data set, consisting of $256 \times 256 \times 124$ elements (these are called voxels in the medical domain). Voxel dimensions were $0.92 \times 0.92 \times 1.5$ mm. The MR data set was transferred through the Ethernet connection to our Sun workstations (Sun Microsystems, Mountain View, California) where the images were processed using image processing techniques. A white, 25-year-old, right-handed male was the subject for this acquisition. The subject was part of the normal control group in a study. For more details about the acquisition see Shenton et al. [38].

2.1.2 Generation of Anatomical Labels

2.1.2.1 Improving Image Quality: Anisotropic Diffusion Filter.

The first step involved the use of a post-processing filter to reduce noise without blurring fine morphologic details (Giger et al. [13] and [14]). This filter is based on a simulation of anisotropic diffusion of heat, originally reported by Perona and Malik [31], but later applied to MR images by Giger and colleagues.

2.1.2.2 Semiautomated Segmentation. Following the filtering, we performed a supervised segmentation of the MR images to define distinct tissue classes. An operator picked sample points for each of the tissue classes that were distinguishable based on signal intensities. A classification was computed, using a nonparametric statistical classification algorithm. This allowed the translation of the gray-scale images into binary label maps, where each voxel was assigned a label such as gray matter, white matter, cerebrospinal fluid, etc. (for a more detailed description see Cline et al. [5], [6], [7], and [8]; see also Shenton et al. [37] and [38], and Kikinis et al. [25]).

2.1.2.3 Interactive ROI Definition. For further definition of anatomical ROIs it was necessary to use operator driven interactive editing, based on the results of the initial segmentation. For instance, there is no contrast mechanism available to separate the superior frontal gyrus from the middle frontal gyrus. Both would be classified as gray matter in the initial segmentation. To edit the labelmaps (i.e., ROI definitions), we used an interactive editing tool, allowing the user to review the original cross-sectional data, with a colored overlay of the label maps. The program displayed the data as cross-sectional slices parallel to each of the three main axes. In the medical domain, these directions are called sagittal, axial, and coronal.

We used both Crosby et al. [10] and Radamacher et al. [33] as references to assist in the definition of these ROIs. The ROIs were evaluated by several investigators knowledgeable in neuroanatomy (e.g., CGW, DVI, FAJ, HH, CMP, MES, RK, RWM from the list of authors).

A complete description of the landmarks will be made available to the reader upon request. Individual areas such as temporal lobe (Shenton et al. [38]), prefrontal cortex (Wible et al. [46]) and basal ganglia (Hokama et al. [23]) are defined in detail in previous publications. Briefly, the regions delineated include: cerebral cortical gray matter (subdivided by lobe), cerebellum, brainstem structures including the pons and medulla, corpus callosum, basal ganglia (subdivided), limbic system, eyes and optic chiasm, and the ventricular system. Several white matter tracts, including the corticospinal tract and the optic radiations were also delineated and reconstructed in 3D. Altogether, there are currently more than 150 labels in the atlas data set.

We found the reliability of the segmentation to be quite good, even for volume data from small structures (i.e., hippocampus, parahippocampal gyrus, amygdala, and superior temporal gyrus [STG]). To assess reliability, we acquired two scans consecutively, with the subject leaving the examination table and being repositioned between the two acquisitions. We expect all differences in the volume assessment in two such scans to be due to rasterization and processing artifacts.
We measured the volumes of the labeled structures by adding up the number of single voxels (pixel volumes) in each structure and multiplying it by the volume of each voxel, across all relevant slices. We observed less than 4% difference among the volumes of the aforementioned small brain structures, measured in the two consecutive scans, in a normal control subject. We performed the two acquisitions the same day, and we used for both images the same landmarks as in our previous study (Shenton et al. [38]). The results were: left STG = 7.63 ml (5,784 voxels) and 7.78 ml (5,907 voxels); right STG = 9.18 ml (6,964 voxels) and 9.36 ml (7,104 voxels); left amygdala = 1.76 ml (1,337 voxels) and 1.81 ml (1,372 voxels); right amygdala = 2.02 ml (1,533 voxels) and 1.98 ml (1,499 voxels); left hippocampus = 2.98 ml (2,265 voxels) and 2.88 ml (2,187 voxels); right hippocampus = 3.32 ml (2,519 voxels) and 3.41 ml (2,586 voxels); left parahippocampal gyrus = 2.39 ml (1,811 voxels) and 2.32 ml (1,757 voxels); and right parahippocampal gyrus = 2.59 ml (1,969 voxels) and 2.50 ml (1,899 voxels).

### 2.2 Hierarchical Browser

Anatomy is organized hierarchically. For instance, the superior frontal gyrus is part of the frontal lobe which is part of the neocortex, which is part of the brain, etc. Since the atlas contains the finest level of detail, the organizational information regarding the hierarchy was stored as a text file (see Table 1). Each line contained an identifier whether the item on the line was an end branch of the anatomical hierarchy or whether it contained substructures. Each structure was also assigned a color. The viewer can browse through the hierarchical representation and expand or collapse the level of detail displayed. The same voxel will have a different color, depending on the level of detail displayed. For instance, if we expand to the level of the brain, a belonging to the neocortex, and therefore part of the head, will be colored 020 205. The same voxel will be colored 64 203 208 if we display the level of cerebral hemispheres (see Table 1).

More specifically, the hierarchical browser is designed to provide a user friendly interface for visualizing the segmented images. The program automatically relates segmented images to the script files containing hierarchical names and pixel values. The user, however, has the option of displaying the image according to the pixel values or according to the hierarchical relations. We used the image display according to the pixel values to confirm the correlation between user-defined anatomical names and pixel values in the script file.

Display by hierarchical relations is, however, more friendly and flexible for the user than display by pixel values as there is an opportunity to group and ungroup different neuroanatomical regions and to use color to highlight different regions of interest. Once a hierarchy is established, different color groupings can also be used to appreciate the relation among neuroanatomical structures and the user is free to move up and down the hierarchy and to select smaller or larger groupings to appreciate the spatial relations among structures. This is an important adjunct to teaching medical students as students can learn at their own rate and they can teach themselves with an interactive tool.

### 2.3 Visualization of the Atlas Data

Once we have defined the labels, there are different ways to visualize and organize the data contained in the atlas. We currently have three principal modalities of visualization available to navigate the label data set. The first is a brute force rendering approach on a high performance computer for fast evaluation. The second uses surface models and
standard graphics hardware acceleration. The third approach uses a field of precalculated renderings to allow some form of interactivity when no hardware-accelerated rendering for surface models is available. These three approaches are characterized by decreasing levels of demand on computational resources, which are offset by decreasing the flexibility available to the user.

Speeds of a few renderings per second are a requirement for interactive work with data sets. Our data set contains more than 8 million voxels of binary labels. For a pleasant appearance, some form of interpolation or smoothing is necessary.

2.3.1 Fast Volume Rendering of Binary Labels on a Massively Parallel Computer

A fast volume rendering algorithm was implemented on a CM-200 with 16,000 Thinking Machines processors (Thinking Machines Corporation, Cambridge, Massachusetts). The algorithm is essentially based on the Z prebuffer algorithm. This is a brute force approach, optimized for speed and using a simple shading approach. The binary label data sets were rendered without any preprocessing in about 0.4 seconds (2.5 Hz) per frame.

We utilized the render engine in combination with the hierarchical browser to explore the data set and determine the appropriateness of color combinations and the correctness of the results of the rendering process. An additional tool allows us to produce annotated images. Fig. 1 gives an example of such an annotated rendering. It shows a view from the front with a small fraction of the frontal lobe removed and replaced with a textured cut plane. The annotation information has to be positioned manually, like a transparency in front of the rendering.

2.3.2 Surface Models for Hardware-Accelerated Rendering on Workstation

In order to generate surface models of sufficient quality from the individual binary labels, it was necessary to develop a processing pipeline. First, each label was converted into a binary data set. These data sets were converted into pseudo gray-scale data using a 3D Gaussian smoothing (Cline et al. [7]). Then we generated surface models, using either the dividing cubes or the marching cubes algorithm (Cline et al. [6] and Lorensen et al. [29]). We also adopted additional processing, since the models became prohibitively large compared to the render capabilities of desktop graphics acceleration. The surface models were reduced by more than 90% using a triangle reduction algorithm (Schroeder et al. [36]). To improve the appearance of the models, we used a triangle smoothing algorithm (Taubin et al. [43]). The models could then be imported into different rendering programs. We used two programs: Leotool, a demo program that is used by Sun Microsystems to demonstrate the use of XGL, and LYMB (Schroeder et al. [36]), a hybrid, object-oriented environment for visualization. The full atlas, consisting of approximately 600,000 triangles, can be rendered in approximately one sec-
ond on a Ultrasparc Creator 3D (Sun Microsystems, Palo Alto, California) using features like backface clipping, stereo display and Phong shading.

Fig. 2 demonstrates the quality of the renderings obtained with this approach. The ventricles of the brain (fluid filled structures in the center of the brain) are displayed on those images with different neighboring structures. Light sources have been positioned in different locations and highlights have been set to provide additional effect.

2.3.3 Prerendered Images for Use With Inexpensive Hardware

For situations when no graphics hardware is available, we developed a Java applet, using prerendered images. Using a Lymb-based render engine, we generated a series of renderings, providing views from different vantage points. We generated two images for each vantage point: A surface rendering providing the shaded surface and a second rendering providing the area occupied by each structure in the visible field. These images are linked to a hierarchical browser that uses the information in Table 1. The current implementation contains a field of $8 \times 8$ renderings, which is a compromise between the amount of angular resolution and the size of the dataset to be downloaded. The Java applet can be viewed in our website (URL3).

In our current implementation of this Java applet, we cannot determine which structures are visible and which are not (i.e., turn the skin on and off), but we can change the hierarchical representation. For instance, as in Fig. 3, the gyri can be highlighted such that each gyrus is colored differently, by changing settings on the hierarchical browser. Alternatively, the lobar organization of the neocortex can be displayed (frontal lobe, parietal lobe, etc.).
Fig. 4. An example of the use of the atlas for surgical planning. This case is of a 16-year-old woman with an oligodendroglioma. An axial high resolution MR image (a) can be seen with a 3D surface rendering of the tumor superimposed onto the image. A reformation of the images in the sagittal plane (b) also shows the tumor (gray) and the lateral ventricles (yellow). In the bottom panel (c), the tumor is registered to the atlas dataset along with the ventricles from the patient. Also in the bottom panel (d) we see the preoperative view of the patient in the expected surgical position. The ventricles and tumor of the patient are overlaid after registration using an experimental laser scanner device. The corticospinal tract is behind the tumor in this approach. This makes it critical for the surgeon to know the location of the corticospinal tract as precisely as possible. In addition, this view presents the position of the ventricles relative to the head, thus allowing a better understanding of Fig. 2.

3 RESULTS

This section presents several ways in which we have used the atlas over the past years. On one hand, a limited number of students have been using the atlas as a way to learn neuroanatomy. In addition, the atlas has been used to provide reference information on anatomical structures in a selected number of surgical cases. Furthermore, we have applied the atlas as a template, for the automated segmentation of new brain images into anatomical structures.

3.1 Teaching

Understanding the shape, configuration, and relations among different anatomical structures can be very difficult. A digital atlas can provide an intuitive way for students to learn neuroanatomy quickly and efficiently. We have used the atlas primarily to tutor students that were going to work on projects in the laboratory. In our context, the students were using the digital atlas in conjunction with conventional atlas books. The capability to change vantage points and to turn off structures at will with render speeds below one second for the whole atlas and with frequencies of 5-10 Hz for subsets of the atlas is a very important feature.

3.2 Surgical Planning

Fig. 4 is an example of the use of the atlas to provide reference information for the planning of a surgical procedure. This is the case of a 16-year-old woman with an oligodendroglioma. For a more detailed description of the concept of surgical planning in neurosurgery, see Kikinis et al. [26].

One of the challenges the surgeon faced in this case was to prevent damage to the corticospinal tract. We used the
Several approaches to align the structures are available. Current functional methods, on the other hand, which do not have the necessary spatial resolution. Accordingly, we need to rely on an atlas data set to provide anatomical information which is not obvious from contrast alone. Elastic matching is the main method used for the projection of atlas information into data sets of subjects and patients. There are several mathematical approaches to resolve the matching side of the problem, but one of the key issues is how the correspondence between structures is established. Several groups have been working on that topic for years (Bajcsy et al. [11], Gee et al. [12], Grenander et al. [16], Collins et al. [9]). Initial work to project the information contained in an atlas onto patient data sets have used structures that do not feature gross changes: Haller and coworkers [17] have used this approach to segment the hippocampus. Collins et al. [9] have used a similar method to build a probabilistic atlas. We have also worked on elastic registration for the segmentation of brain, deep gray matter and neocortical gray matter (Kikinis et al. [27], Iosifescu et al. [24]). Recently, we have started to perform elastic registration in patients with multiple sclerosis. In this illness, the topology of the white matter is not maintained. This problem required a combination of elastic warping and local optimization. The initial results are very promising (Warfield et al. [45]).

4 Discussion

We have presented our initial experience with a digitized MR-based brain atlas. This can serve multiple purposes: as an educational tool, as a tool for surgical planning and as a method for the automatic identification of regions of interest for new MR data sets.

Our approach differs from each of the other groups that have been doing work in the domain of digital atlases of the brain. The pioneering work done by the group in Hamburg (Hoehne et al. [19] and [20], Pommert et al. [32], Schiemann et al. [34], Tiede et al. [42]) is closest to our effort in its basic structure: an MR data set which is linked to a label data set. The Hamburg group uses a workstation based on a volume rendering engine for their visualization and has multiple features attached to each voxel. Their atlas is commercially available, but their data set is not generally available. The data set is derived from a patient with a tumor in the area of the frontal pole of the temporal lobe. There are significant differences between our effort and theirs: we have used a multitude of rendering techniques for the visualization of our data: volume rendering (Fig. 1), surface rendering (Fig. 2), and prerendering in a Java applet (Fig. 3). We have demonstrated the use of the atlas for planning of a neurosurgical procedure, and we have also used the atlas to develop model-based segmentation approaches (Warfield et al. [45]).

The digital anatomist program from Seattle has only been available as a teaching tool on video disk, CD-ROM and video tape. It has been used purely for visualization with surface models based on contours. To our knowledge it has not been used for surgical planning or model-based segmentation.

The group at the Montreal Neurologic Institute (Evans et al. [11] and Collins et al. [9]) has been building a probabilistic anatomical atlas based on more than 300 subjects. The atlas has been used for early work on model-based segmentation in the brain. However, their atlas is not as detailed as ours. In fact, they have requested and received our atlas data set as a complement to their work. To our knowledge, the Montreal probabilistic atlas is not being used for teaching of neuroanatomy.

The Denver (see URL4 for more information) and the UCLA groups (Sundsten et al. [40]) are building digital brain atlases based on giant microtome sections as part of the Visible Human project. They have acquired only partially the planned data sets. Some MR and CT data was also acquired. While there has been significant coverage of these efforts in the media, the labeling efforts (i.e., assigning
every voxel in the data set to a specific anatomical structure have barely begun and are extremely challenging. Accordingly, no teaching tool providing interactive 3D renderings of the brain is available at this time. When completed, these data sets (in particular the UCLA data), will represent extremely valuable data bases for teaching, surgical planning, and model-based segmentation. However, this is several years of work away. Our conceptual approach also differs significantly. By relying primarily on a noninvasive, nondestructive imaging method applied to a living human being, we can reimage our subject when needed. In fact, the subject used for the initial acquisition in 1990 has returned for additional imaging sessions, most recently a few weeks ago, when an MR angiogram was acquired. This data set will allow us to introduce in the future both morphology and function of the macroscopic vascular system into the atlas. When functional imaging methods will become available at our institution, we will probably be able to perform another data acquisition. This method contrasts the cryomicrotome-based acquisition, which is destructive and cannot be performed on live subjects. On the other hand, cryomicrotoms allow acquisitions at higher spatial resolutions.

There are several other groups working on the generation of atlas data sets based on 3D brain morphology (e.g., Greitz et al. [15] and Mano et al. [30]), but the basic approaches are similar to the ones discussed above in detail. Several more groups are working on developing algorithms for the use of atlases for model-based segmentation (Bajcsy et al. [11], Gee et al. [12], Collins et al. [19], Haller et al. [17]). However, we are currently not aware of other groups using a digital 3D atlas for surgical planning in neurosurgery.

In summary, our effort to develop a digital anatomical atlas of the brain differs from all the other similar efforts significantly.

By linking labels to a set of voxels, we were able to display many specific neuroanatomical structures. This labeling system also incorporated a hierarchical organization, so that neuroanatomical structures could be grouped according to specified relations among structures. Thus cortical gyri were subdivided into frontal, middle, and inferior frontal gyri, etc. and the ventricular system was subdivided into lateral, third, and fourth ventricles. The labels of component tissues were hierarchically arranged. Additionally, certain functionally related systems, such as the corticospinal tract, optic radiations, etc. were included. All of these features make the digitized human brain atlas particularly useful as a basis for teaching neuroanatomy, an implementation that has been discussed extensively by numerous investigators (Hoehne et al. [19] and [20], Pommert et al. [32], Schiemann et al. [34], Tiede et al. [42], Greitz et al. [15], Mano et al. [30], Evans et al. [11]).

The different visualization methods used for data exploration (from brute force volume rendering to web capable Java applet) allow flexibility, taking the users' available resources into account. This will allow medical students to use the atlas to evaluate the spatial relationships among structures. We believe anatomical structures can be better appreciated in 3D space, where structures can be readily grouped, viewed and rotated. The requirements for rendering in terms of computational hardware differ from a gigaflops level computer with brute force volume rendering at subsecond speeds, to the Java applet that can run on any PC or MAC with an 8 bit frame buffer. The flexibility available for the display is inversely related to the computational power of the render engines. Today, desktop workstations with graphics accelerators for triangle rendering represent a reasonable compromise between costs and capabilities.

Until now, identifying multiple ROIs for our brain atlas has been a tedious, painstaking task requiring about 12 months of work by several individuals. We plan to expand this atlas as well as to improve our ROI definitions by using an expert panel. We recognize, however, as noted by Rademacher et al. [33] the arbitrary nature of morphological classification. We plan to use the brain atlas described here, and to extend and modify it, as well as use an expert panel to review each region of the brain identified in order to have the best template possible.

Another purpose for developing the digitized brain atlas was to use it as a database for model-driven segmentation. Our initial results in that domain are very promising (Warfield et al. [45]).

5 Conclusion

We have presented a comprehensive effort to develop a digital anatomical atlas of the brain and to use the data set for multiple purposes: teaching, surgical planning and model-driven segmentation. Interactive visualization with multiple tools is at the core of this effort. It can be expected that digital atlases will become increasingly common in each of the three application areas.

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References

Ron Kikinis received his medical degree in 1982 from the University of Zurich, Switzerland. After a residency in radiology, with training in radiation oncology, general radiology, neuroradiology, and magnetic resonance imaging, he underwent additional training in biomedical engineering and image processing at the ETH in Zurich. In 1988, he moved to Boston and joined the medical staff at the Brigham and Women's Hospital. He is currently director of the surgical planning laboratory at the BWH, an assistant professor of radiology at the Harvard Medical School, and an adjunct assistant professor of biomedical engineering at Boston University. He has authored and coauthored more than 30 peer-reviewed papers. His URL is http://splweb.bwh.harvard.edu:8000.

Martha E. Shenton received her PhD in psychology in 1994 at Harvard University. She was a research fellow in biological psychiatry at the Harvard Medical School from 1984 to 1986 and, since 1983, has been an associate professor of psychology at the Harvard Medical School. In 1995, she became director of the Clinical Neuroscience Division, Neuroscience Laboratory, Department of Psychiatry, Harvard Medical School. She is the author of more than 40 peer-reviewed papers. Her current research interests include the computerized image analysis of MR scans to detect brain abnormalities, correlated with neuropsychological studies in schizophrenia patients. She is also involved in the MR study of schizotypal population.

Dan V. Ionescu received his MD in 1992 Bucharest, Romania, and did his internship there. He was a research fellow in the Psychiatry Department at the Harvard Medical School from 1994 to 1996. Since July 1996, he has been pursuing clinical training in psychiatry at Massachusetts General Hospital, Harvard Medical School. His current research interests include volumetric MR brain analyses in schizophrenia, particularly at the level of the basal ganglia and the parietal lobe. He is also involved in the development of new MR automated segmentation techniques, based on elastic matching.

Robert W. McCarley received his MD from the Harvard Medical School in 1984. He did his residency in psychiatry at the Massachusetts Mental Health Center in Boston. Since 1984, he has been a professor of psychiatry and director of the Laboratory of Neuroscience at the Harvard Medical School. He has published more than 180 papers in peer-reviewed journals, and is currently president of the Sleep Research Society and chairperson of the NIMH Clinical Neuroscience Study Committee. His current research interests include the neurophysiological study of schizophrenia, the biological basis of schizotypy, personality disorder, the neurophysiology of behavior, the synaptic basis of sleep-cycle control, and the glutametiregic neurotranscists in schizophrenia.

Paiphas Saliviraponporn received his BS in electrical engineering from the King Mongkuk's Institute of Technology, Ladkarkhang Campus, Thailand, in 1987. He worked for two years with the Signetics Thailand Company, a division of the North American Philips Corporation. In 1990, he received a scholarship from the Royal Thai government to pursure MS and PhD studies in the biomedical instrumentation field. He received his MS in biomedical engineering from Boston University in 1992, and is now a PhD candidate in the Biomedical Engineering Department there. His PhD research involves implementation and development of dynamically adaptive MRI methods using singular-value decomposition-encoded MRIs at Brigham and Women's Hospital. His interests also include development of medical image processing, and software development of SimD and MIMD architectural computers.

Hiroto H. Hokama graduated from the University of Ryukyus Medical School in Japan and received his MD in 1987. He was a research fellow in the Department of Psychiatry at the Harvard Medical School, from 1991 to 1994. Currently, he is an instructor in the Department of Neurology at the University of Ryukyus. His research interests include quantitative MRI analysis of the schizophrenic brain.

Cynthia G. Wible received her BS from the University of Pittsburgh in 1981, and her MA and PhD degrees from Johns Hopkins University in 1985 and 1989, respectively. Since 1993, she has been an instructor in the Department of Psychiatry at the Harvard Medical School. She has published more than 20 papers and book chapters. Her current research interests include hippocampal function in normal subjects and the role of hippocampal and temporal lobe dysfunction in schizophrenia.

Chiara M. Fortas graduated from the University of Cagliari, Italy, and received her MD there in 1988. She was an instructor in psychiatry at the Harvard Medical School from 1991 to 1995. Currently, she is a research fellow in the Wellcome Department of Cognitive Neurology at the Institute of Neurology of the University of London. Her current research interests include sleep/waking physiology as well as structural-functional MRI analysis of the human brain.

Robert M. Donnino received his BS in psychobiology from Harvard University in 1995. He began working for the Department of Psychiatry, Brockton Veteran Administration, Harvard Medical School, as an under-graduate in 1993 and continued as a research assistant until July 1996. In August 1996, he entered medical school at the State University of New York at Stony Brook. His current research interests include brain abnormalities in schizophrenia, particularly abnormalities in the inferior parietal region.

Ferenc A. Jolesz received his MD in Budapest, Hungary, and performed his residency in neurosurgery before moving to the United States in 1979. In Boston, he completed research fellowships in neurology at the Massachusetts General Hospital and in physiology at the Harvard Medical School, and a clinical residency and fellowship in radiology at the Brigham and Women's Hospital, where he joined the staff as a neuroradiologist. A professor or radiology at the Harvard Medical School, he has been director of the Division of Magnetic Resonance Imaging at Brigham and Women's Hospital and more recently director of the Image Guided Therapy Program there. His main research activities are in the areas of neuroradiology, neurophysiology, and developing new approaches to magnetic resonance imaging. Special interests include image-guided therapy, interventional MRI, and involvement in investigations of various diseases of the central nervous system demyelination, multiple sclerosis, schizophrenia, and Alzheimer's disease. Dr. Jolesz has been elected a member of the Institute of Medicine of the National Academy of Sciences and belongs to several professional societies and editorial boards of peer-reviewed journals.