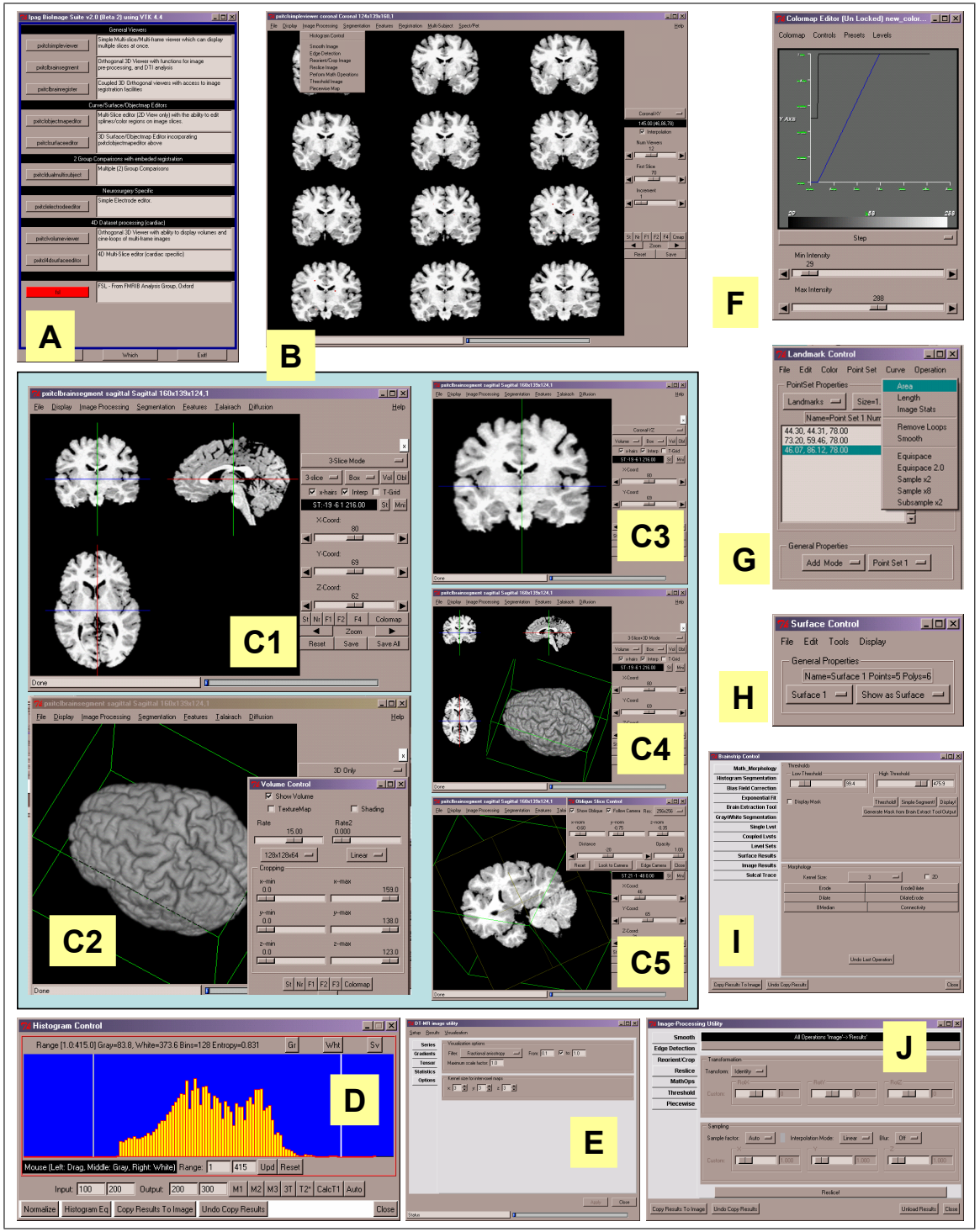

Figure 1: **Example Views of the BioImage Suite Graphical User Interface. A.** The initial menu. **B** The mosaic viewer capable of displaying multiple parallel slices in the three orthogonal orientation. **C1-C5** The multifunctional orthogonal viewer tool displaying orthogonal sections with linked cursors (C1), volume rendering (c2), single slice (C3) combination of 3D and slice views (c4), oblique slice (C5). **D** Histogram Tool. **E** Image Processing Tool. **F** Colormap editor. **G** Landmark Tool. **H** Surface Processing Tool. **I** Segmentation/Bias Field Correction Tool. **J** Basic Diffusion Tensor Tool.

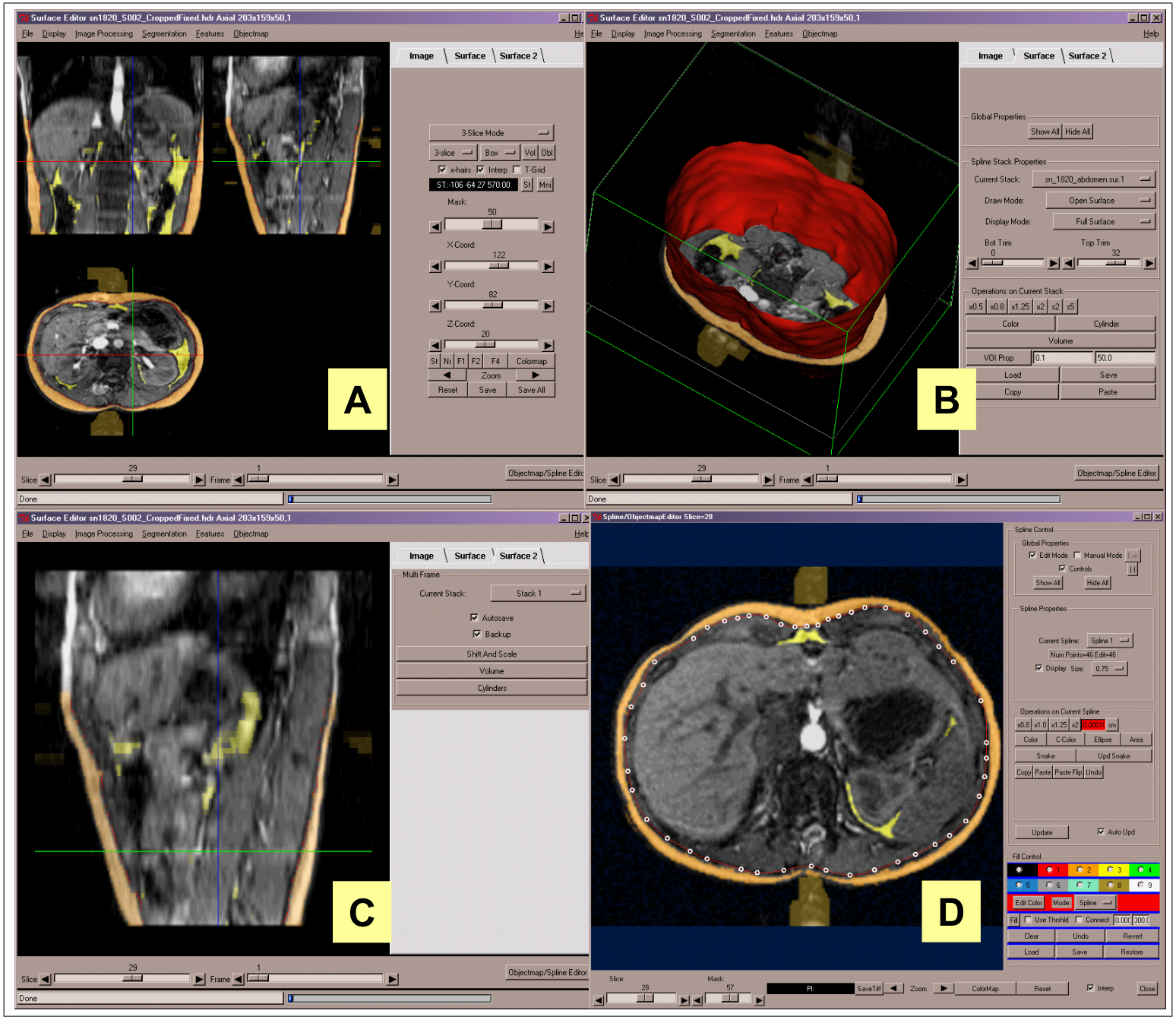

Figure 2: **The interactive surface/objectmap editor tool,** as used to quantify abdominal fat. **A** Main viewer showing three orthogonal slices of the objectmap image (yellow=abdominal fat,red=subcutaneous fat) and the abdominal surface overlaid on the original MR image. **B** The main viewer in 3D display mode showing the surface. **C** Main viewer in single slice mode. **D** The slice editor which enables manipulation of the slice-by-slice surface by editing the spline and intelligent voxel coloring by using thresholding and connectivity under the mouse cursor.

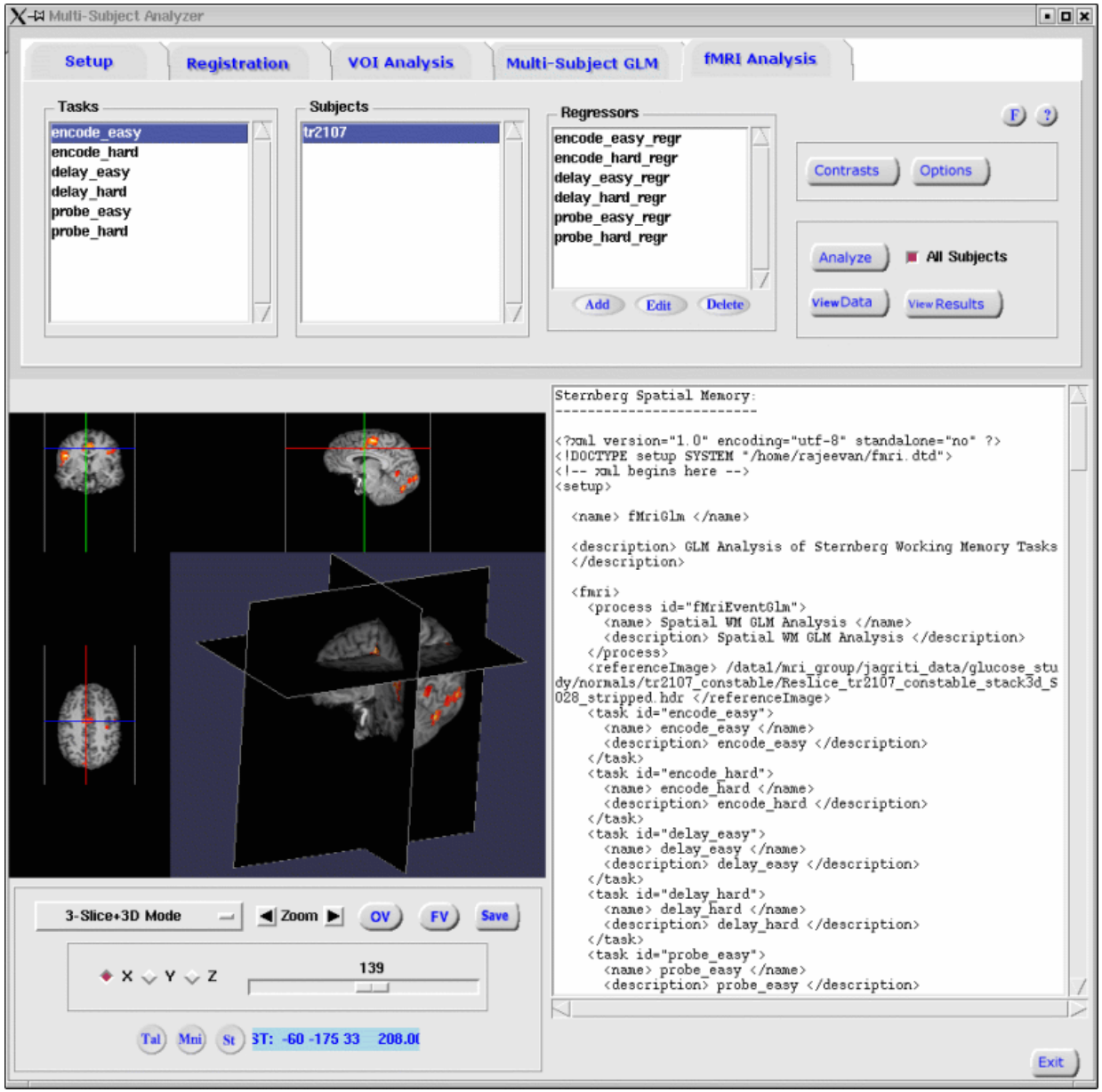

Figure 3: **The fMRI processing tool**, which includes functionality for registration, volume of interest analysis (VOI), single subject GLM and multi-subject group analysis using analysis of variance and covariance (ANOVA and ANCOVA). The definition for the entire fMRI experiment and processing is defined through an XML (extensible markup language) setup file following a standard DTD (document type definition) or schema. The single subject GLM has options for incorporating spatial and temporal correlations and user define hemodynamic response functions. This tool has the ability to visualize the activation results overlaid on the underlying anatomy using the embedded orthogonal viewer control (shown in the bottom left hand corner).

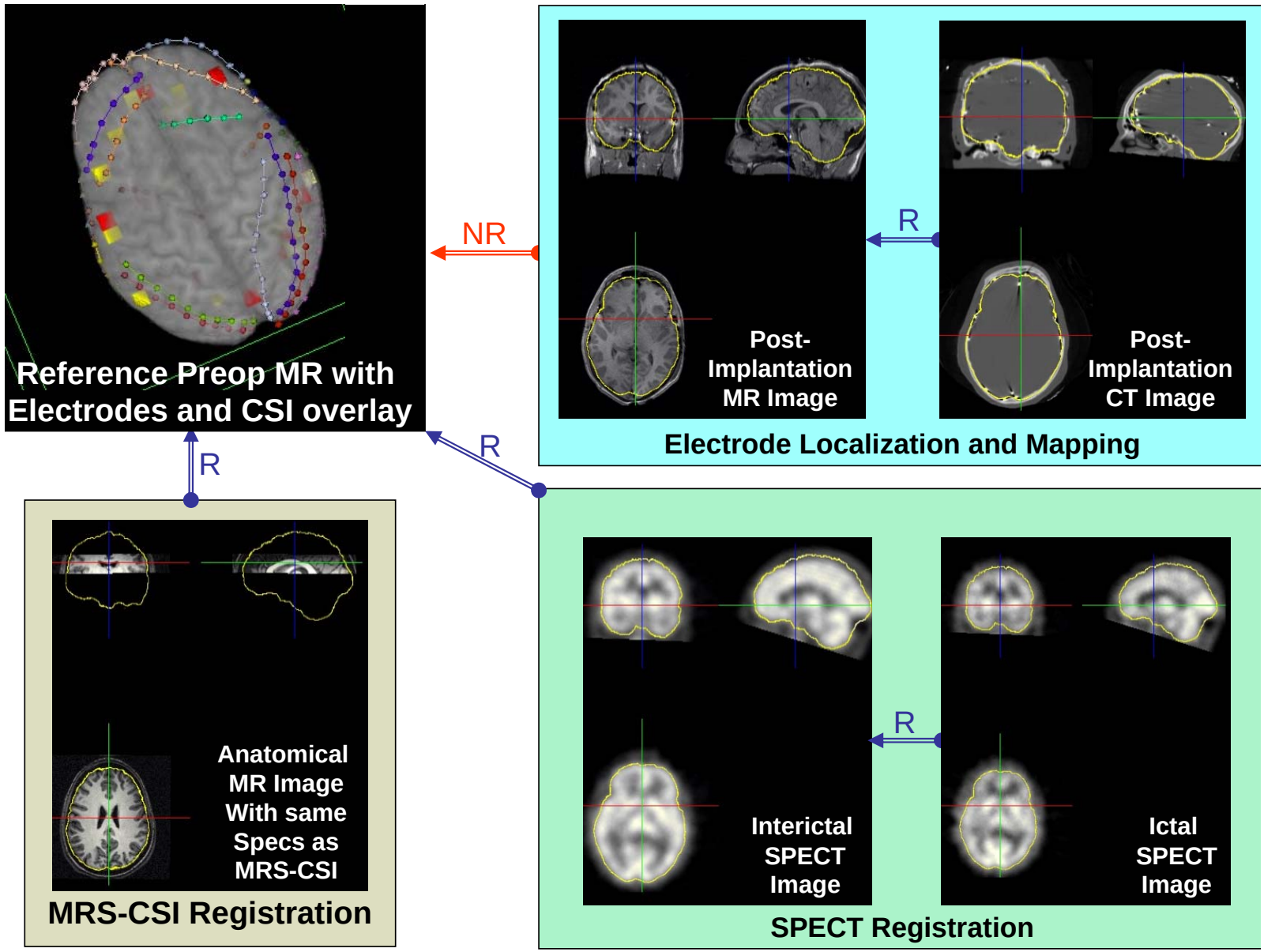

Figure 4: **Applications of rigid and non-rigid registration in neurosurgical planning.** Rigid and non-rigid registrations as applied for epilepsy neurosurgical planning. Here we demonstrate mapping nuclear images (SPECT), pre and post electrode implantation MR images, post electrode implantation CT images, and small-coverage MR images acquired together with MRS measurements to the same coordinate space.

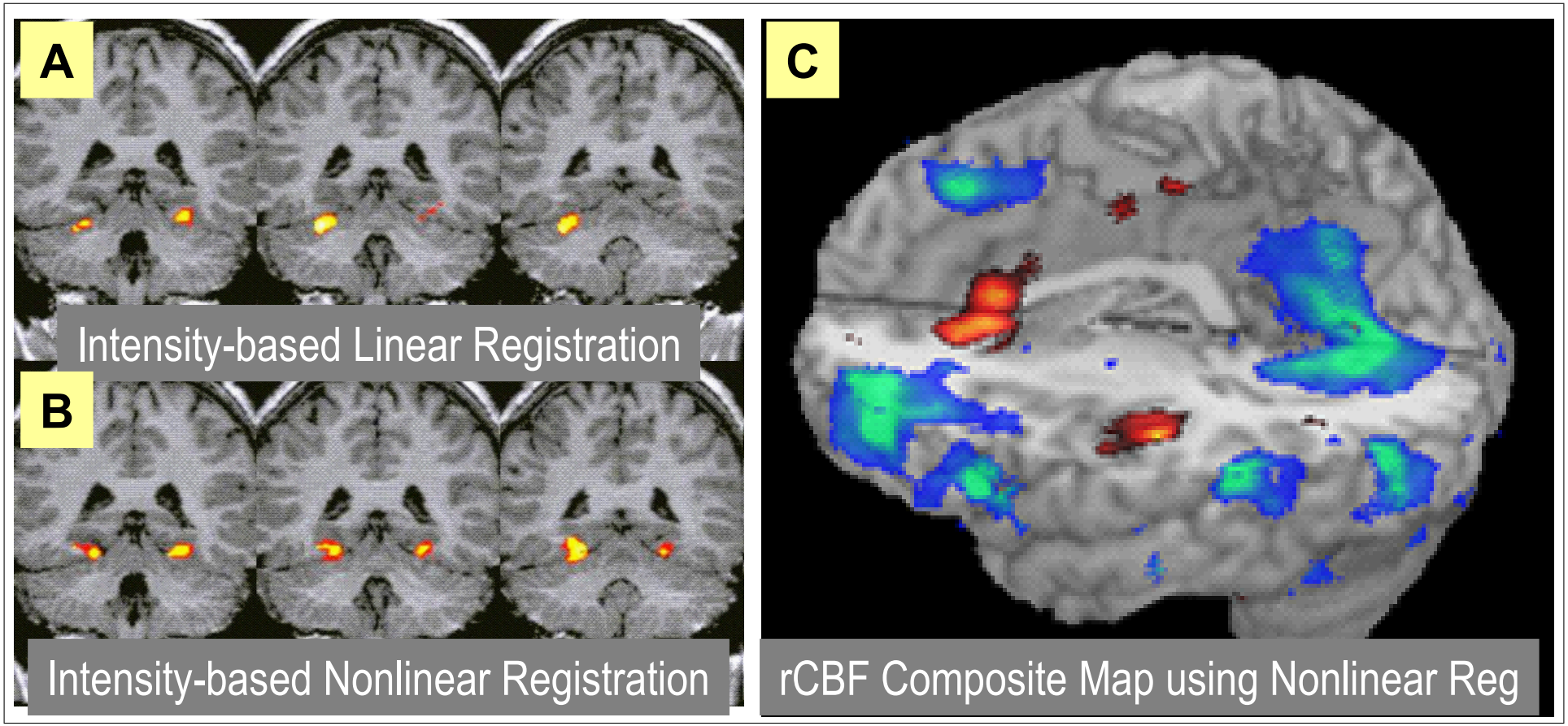

Figure 5: **Composite functional maps.** (A) and (B) Conventional BOLD fMRI composite activation maps obtained using intensity-based linear and nonlinear registrations in an object vs faces task. Coronal slices through the fusiform gyrus are shown each spaced 6mm apart. The linear registration misplaces the activation focus to the cerebellum (in A) as opposed to properly locating it in the fusiform gyrus (in B). (C) Composite map of regions of significant changes in cerebral blood flow (rCBF) between baseline and post 0.25 MAC dose of Sevoflurane anesthetic.

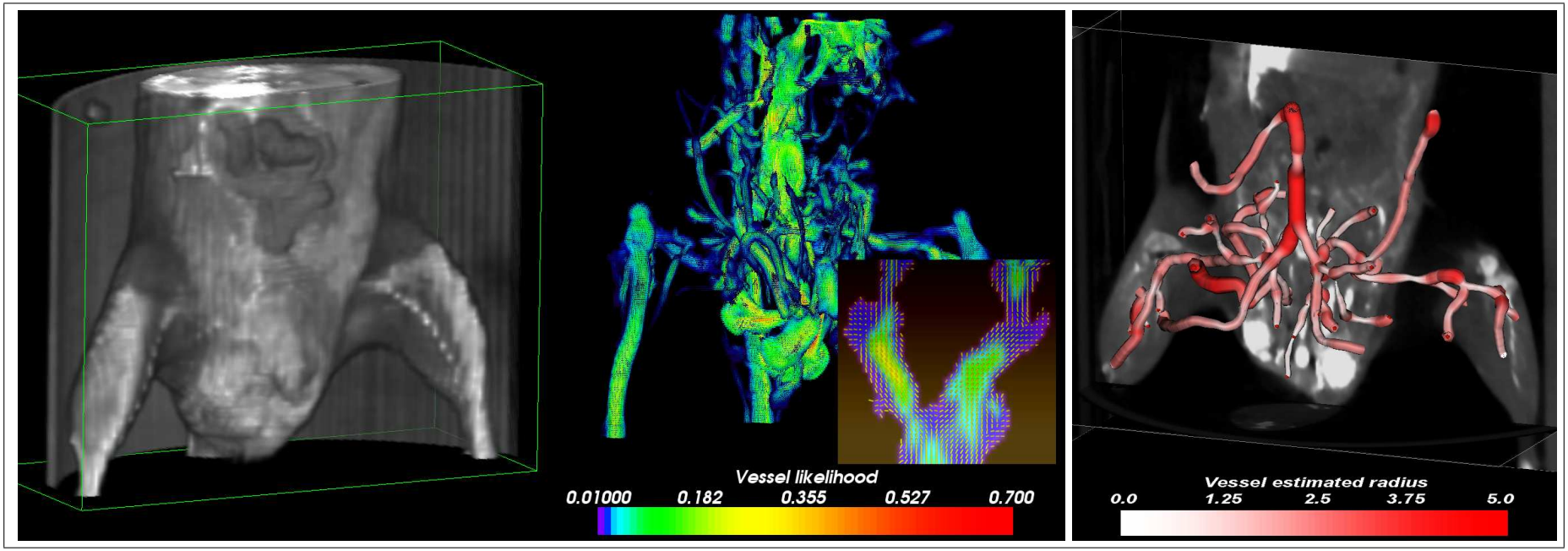

Figure 6: **Angiography** (Top) Volume rendering of original CT angiographic data. (Middle) 3D view of the extracted vector field indicating the presence and orientation of possible vessels. (Right) Reconstruction of the major vessels connecting to the aorta, colored according to their estimated size.

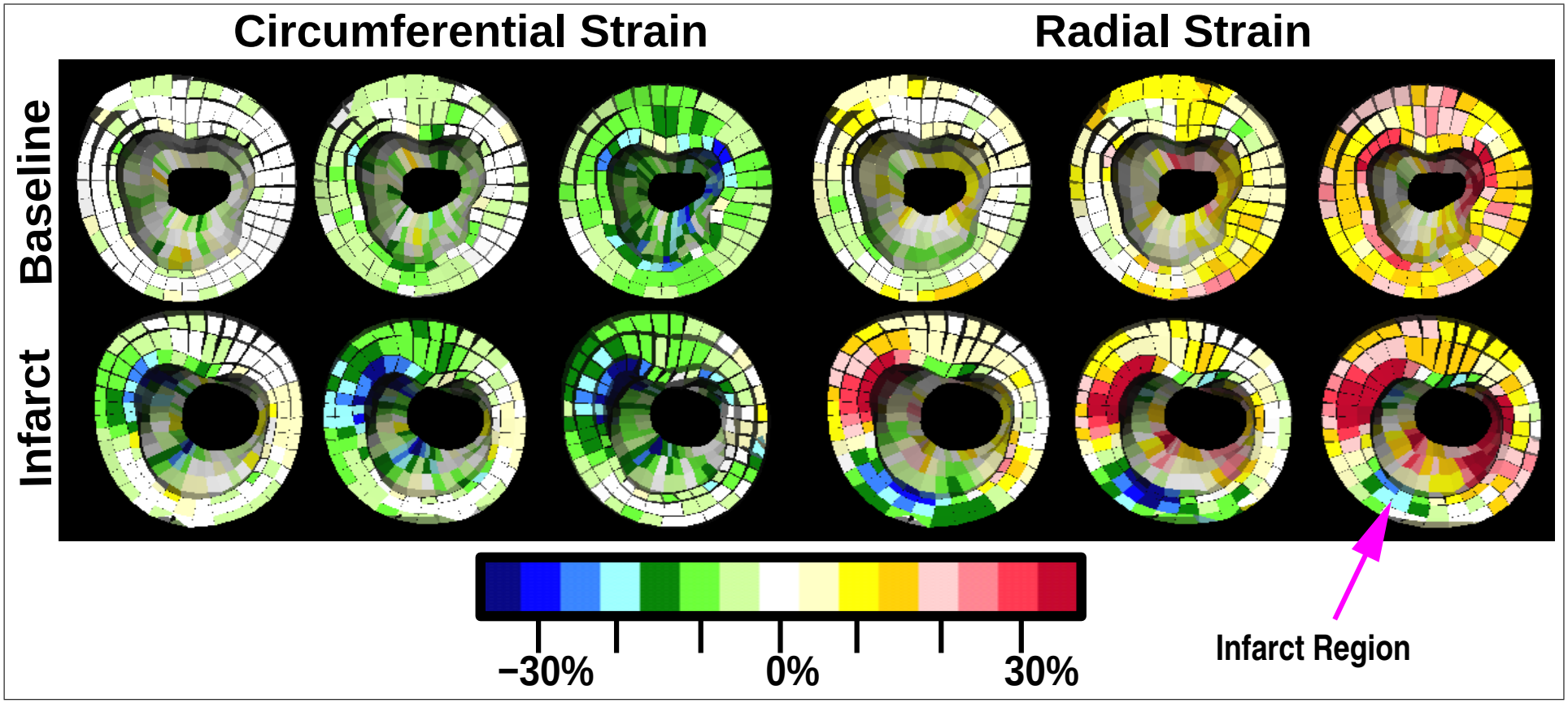

Figure 7: **Cardiac Deformation.** Strain Development Post-Infarction (bottom) vs. Baseline (top) in canine left ventricle quantified from cine-MRI by our methods. Mid-ventricle cutaway views through the 3D reconstructed volume show the strain patterns that develop at 3 points in the cardiac cycle.Left: circumferential strains (normal shortening is in the blue-green region). Right: radial strains (normal thickening in yellow-red region).

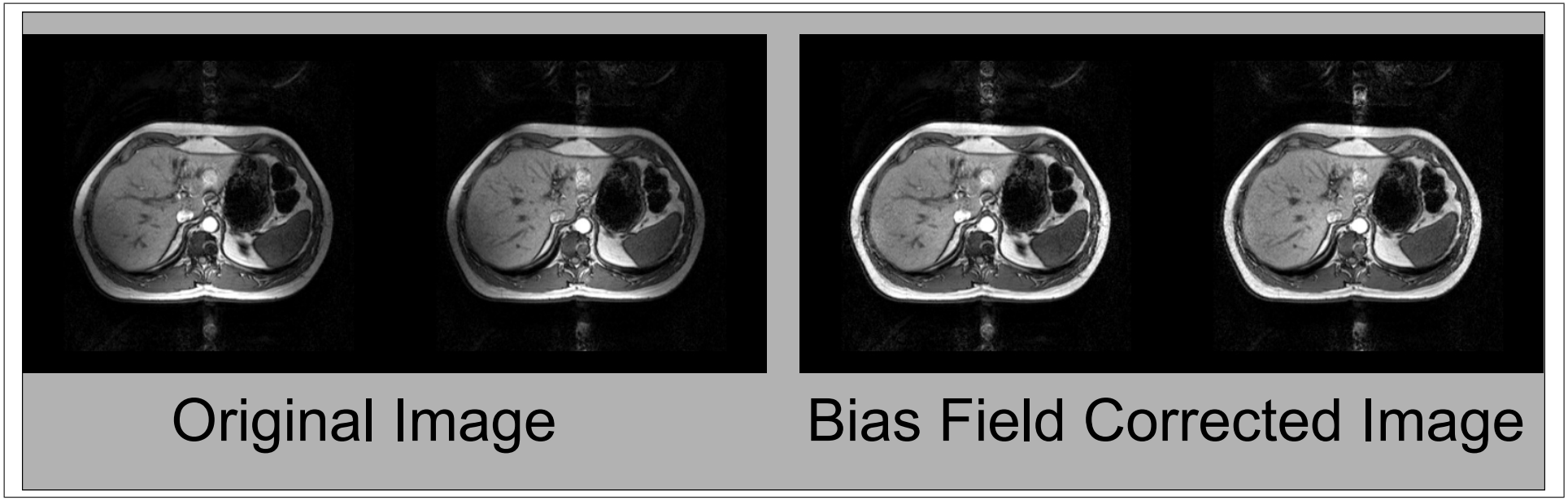

Figure 8: **Abdominal Image Bias Field Correction.** *Left:* Consecutive slices from an abdominal MRI image acquired with a parallel image sequence. Note the strong shading artifacts especially in the outer fat layer and the liver on the lower left. *Right:* Bias field corrected abdominal image exhibiting much improved contrast and fat layer homogeneity.

BioImage Suite: An integrated medical image analysis suite

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Abstract. BioImage Suite is an integrated image analysis software suite developed at Yale. It uses a combination of C++ and Tcl in the same fashion as that pioneered by the Visualization Toolkit (VTK) and it leverages both VTK and the Insight Toolkit. It has extensive capabilities for both neuro/cardiac and abdominal image analysis and state of the art visualization. It is currently in use at Yale; a first public release is expected before the end of 2005.

1 Introduction

Biomedical imaging and image analysis technology have made substantial progress over the last 20 years. However, a major bottleneck that blocks the full use of these techniques is still the relative lack of easy-to-use, readily-available software. The key reason for this problem is that while sophisticated image analysis methods are constantly being developed, these methods are not being translated into user-friendly well documented software packages. Part of the reason, in our experience, is that software development obeys the 80/20 rule which suggests that 80% of the work is done in 20% of the time. While 80% of the package makes the methods usable in the hands of its developers and perhaps closely supported collaborators, it is insufficient for making the software truly available to a wider audience.

Over the last ten years, we have developed a body of software collectively known as BioImage Suite as a result of the needs of different projects in structural [4] and functional neuroimaging, cardiac image analysis[12], image guided epilepsy neurosurgery [17], abdominal fat quantification [22], targeted imaging of angiogenesis and diffusion tensor imaging [4]. BioImage Suite is in wide use in the Yale Image Analysis and Processing Group, the Yale Magnetic Resonance Research Center and the laboratories of local close collaborators. While the software development has focused on the analysis of human images, it has also been applied to mouse CT and MRI and to a lesser extent optical microscopy data.

There are a number of software packages available for medical image analysis that provide some overlapping capabilities; some are commercial but most are research-based. The neuroimaging packages such as Slicer [18], Brainsuite [16] and SPM [19] are the best developed. AIR [1] is limited to image registration. The general purpose commercial software package Analyze [2] has strengths in visualization, segmentation, registration and measurement.

2 Current State of the Software

BioImage Suite is developed using a combination of C++ and Tcl in the same fashion as that pioneered by VTK [15]. In practice, most of the underlying computationally expensive algorithms are implemented in C++ (as classes deriving from related VTK or ITK [7] classes) and the user interface is for the most part developed in the Tcl/Tk scripting environment. Further, a custom written C++ wrapper around the Tk graphical user interface library enables the creation of complex graphical components from C++. BioImage Suite is a collection of programs utilizing the same underlying code infrastructure and look and feel but tuned to specific applications. This modular design encourages the creation of reusable components (e.g. viewers). The current version of BioImage Suite consists of (a) a number of a graphical applications (GUI) and (b) a set of command-line utilities thus providing support for and batch-mode processing. All software has been tested on Linux, Windows (via cygwin) and IRIX 6.5.

Algorithms currently in BioImage Suite: In addition to the extensive set of methods available within the above libraries, we have implemented and customized the following algorithms: *Pre-processing:* A custom reimplementation of the bias field correction method of Styner *et al.* [21] has been performed which incorporates automated histogram fitting for determining the appropriate numbers of classes, and additional spatial constraints. *Voxel Classification:* Methods for voxel classification are available using simple histogram, single channel MRF and exponential-fit methods [11]. *Deformable Surface Segmentation:* BioImage Suite has a strong and unique interactive deformable surface editor tool [12] which allows for easy semi-interactive segmentation of different anatomical structures and embeds common snake-like deformable models [9]. *Registration:* BioImage suite includes a clean reimplementation of the work of Studholme *et al.* [20] for rigid/affine registration using a highly efficient conjugate gradient optimization scheme is included in BioImage Suite. These methods have been successfully used to align serial MRI data as well as multimodal data (e.g. CT/PET/SPECT to MRI). It also includes a full complement of non-rigid point-based registration methods [4], intensity-only and integrated feature intensity methods [10]. *Diffusion Weighted MR Imaging:* BioImage suite has methods for computation and visualization of basic voxel-wise measures from diffusion tensor images (e.g. fractional anisotropy) as well as fiber tracking methods using traditional (streamlining) and novel (anisotropic front propagation) methods [4]. *Cardiac Image Analysis:* The shape-based cardiac deformation method of Papademetris *et al.* [12] is included in BioImage Suite (but requires in addition the presence of the Abaqus finite element package [8]). *fMRI Activation Detection:* BioImage Suite has a clean and fast reimplementation of the standard General Linear Model (GLM) [5] method for fMRI activation detection, in addition to tools for performing region of interest analysis (ROI), multisubject composite maps, etc. The registration tools (described above) can be used for motion correction, distortion correction and intra-subject registration.

Key Components: An illustration of several key components of BioImage Suite are shown in Figure 1. These include the two core viewers (the mosaic multi-

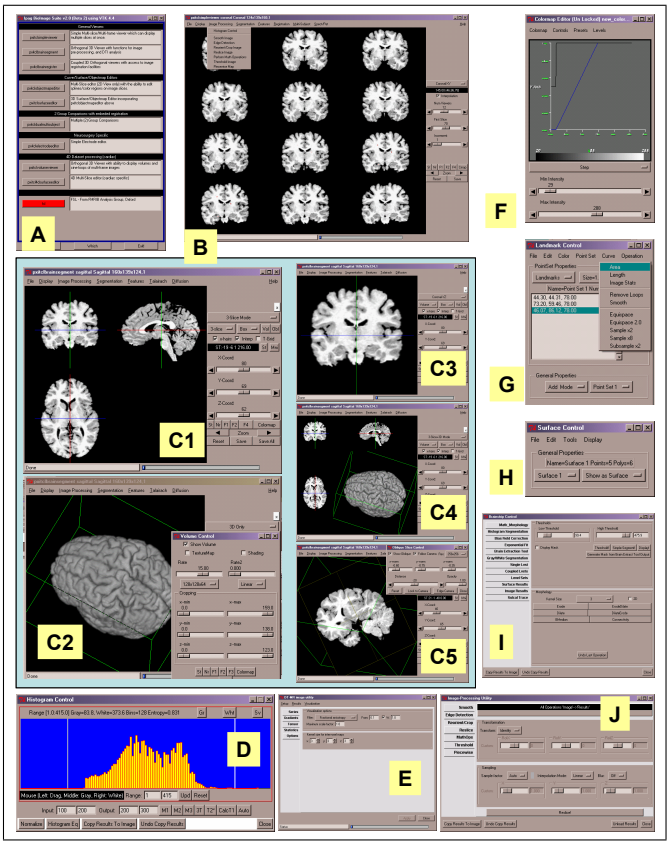

Fig. 1. Example Views of BioImage Suite. A. Initial menu. **B** The mosaic viewer capable of displaying multiple parallel slices in any orthogonal orientation. **C1-C5** The multifunctional viewer tool displaying orthogonal sections with linked cursors (C1), volume rendering (C2), single slice (C3) combination of 3D and slice views (C4), oblique slice (C5). **D** Histogram Tool. **E** Image Processing Tool. **F** Colormap editor. **G** Landmark Tool. **H** Surface Processing Tool. **I** Segmentation/Bias Field Correction Tool. **J** Basic DTI Tool.

ple slice viewer and the orthogonal viewer); the landmark tool which includes common functionality for drawing and processing curves on any given slice (or on volume renderings and surfaces) as well as simple ROI analysis; the surface processing tool which includes functions for surface decimation and smoothing, marching cubes ISO-contour extraction etc. and the colormap editor for manipulating how images are displayed. In addition there are common controls grouping related algorithms such as the histogram control, the image processing control and the segmentation/bias field correction control also shown in Figure 1. These components are building blocks for creating application specific programs.

Graphical Applications: The components are linked together to yield several individual applications including the `Brainsegment` and `Brainregister` tools for brain segmentation and registration. The later also includes the multisubject compositing tool for creating composite functional maps, and the distortion correction algorithms for fMRI. The `Surfaceeditor` tool is for manual/interactive segmentation of both brain, cardiac and abdominal image data. In `surfaceeditor`, each surface consists of a stack of curves (one per slice) and each curve is parameterized using a non-uniform b-spline. The user is able to edit the b-spline in a curve editor window and have the surface updated inter-

actively. These techniques enable the generation of surfaces which are smooth in all three orthogonal directions, unlike the more common slice-by-slice editing packages which typically display the result in only one orientation. The `ElectrodeEditor` tool is used for intra-cranial electrode localization in epilepsy neurosurgery planning. (v) The `fMRITool` includes both individual and group fMRI activation analysis methods. (vi) `DTITool` is a diffusion weighted MR image analysis package and (vii) `Vessel` is a tool for vessel extraction from angiography images. All of these programs have the same look and feel as they use much of the same underlying components.

Command Line Tools All of the registration tools in BioImage Suite, plus some support utilities, e.g. for reslicing of images, can be accessed through command line programs, in addition to being available in the `Brainregister` graphical tool. We provide these because: (a) they enable access to the registration algorithms from custom software packages already in use in other laboratories and (b) given that nonlinear registration is a computationally intensive task, the command line tools are more easily used for batch mode processing. A custom batch mode registration generation script was also developed and takes as input a well defined setup file consisting of reference and target images/surfaces. The batch file generates as output a standard Unix `makefile` consisting of all the commands that need to be executed for registration with appropriately defined dependencies. Using the make utility enables us to leverage its flexibility for partitioning jobs into multiple processors (using the -j flag) and recovery after system crashes (the dependency mechanism of the makefile enables the process to restart exactly where it was stopped as a result of a system crash, etc.).

3 Ongoing work and future plans

BioImage Suite is constantly being enhanced by the addition of newly developed algorithms. In the near future we hope to add recently published methods such as the constrained multi-object segmentation work of Jing et al. [4]). In addition we plan to integrate into BioImage Suite three related software packages developed at Yale, namely (a) the Magnetic Resonance Spectroscopy processing tool written by Dr. Robin de Graaf [3], the SPECT processing tool written by Dr. Rajeevan [14] and the PET processing package developed by Dr. Richard Carson of the Yale PET Center (previously at the NIH). Further we have recently successfully implemented a module to seamlessly integrate BioImage Suite with the Brainlab VectorVision image guided surgery platform.

Licensing Issues and Release Plans: The major obstacle prior to a public release of BioImage Suite is that it uses code originally derived from the Numerical Recipes book[13] for some numerical operations. Given the stringent restrictions in the use of Numerical Recipes code in open source applications, this code must be replaced prior to public release. We anticipate a first public release by the end of 2005 using a dual licensing scheme. All underlying algorithms will be release using the GNU General Public License (GPL) (The original implementation of *some* of our registration algorithms also used portions of code from the vtkCISG registration toolkit by T. Harktens [6] which was also released using the GPL.),

whereas the graphical user interface will be probably released using a less restrictive dual licensing scheme such the one used in the mySQL project. While the exact licensing scheme is still uncertain, we will ensure that all software will be available as open source to non-commercial research users.

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