A Sensitivity Analysis of Brain Morphometry Based on MRI-Derived Surface Models

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ABSTRACT

Quantification of brain structure is important for evaluating changes in brain size with growth and aging and for characterizing neurodegeneration disorders. Previous quantification efforts using *ex vivo* techniques suffered considerable error due to shrinkage of the cerebrum after extraction from the skull, deformation of slices during sectioning, and numerous other factors. *In vivo* imaging studies of brain anatomy avoid these problems and allow repetitive studies following progression of brain structure changes due to disease or natural processes. We have developed a methodology for obtaining triangular mesh models of the cortical surface from MRI brain datasets. The cortex is segmented from nonbrain tissue using a 2D region-growing technique combined with occasional manual edits. Once segmented, thresholding and image morphological operations (erosions and openings) are used to expose the regions between adjacent surfaces in deep cortical folds. A 2D region-following procedure is then used to find a set of contours outlining the cortical boundary on each slice. The contours on all slices are tiled together to form a closed triangular mesh model approximating the cortical surface. This model can be used for calculation of cortical surface area and volume, as well as other parameters of interest. Except for the initial segmentation of the cortex from the skull, the technique is automatic and requires only modest computation time on modern workstations.

Though the use of image data avoids many of the pitfalls of *ex vivo* and sectioning techniques, our MRI-based technique is still vulnerable to errors that may impact the accuracy of estimated brain structure parameters. Potential inaccuracies include segmentation errors due to incorrect thresholding, missed deep sulcal surfaces, falsely segmented holes due to image noise and surface tiling artifacts. The focus of this paper is the characterization of these errors and how they affect measurements of cortical surface area and volume.

Keywords: brain morphometry, surface models, segmentation

1. INTRODUCTION

Quantitative measurements of the brain geometry are desirable in studies of neurodegeneration and correlation studies of function and anatomy. The complexities of anatomy of the human brain present a challenge to automated measurements. Because the relation between cortical volume and surface area may indicate some level of organizational efficiency as well as numerous other theoretical implications, these two measures have attracted considerable attention from past researchers. Both *in vivo* and *ex vivo* attempts have been made to quantify brain surface area and volume. In 1910, the human brain surface area of the cerebral cortex was estimated to be about 2000-2500 cm^2 by applying gold foil to the surface and peeling it off onto scaled paper [1]. Estimates of surface area of 1400-1700 cm^2 were made in 1968 by summing the product of the perimeter length and the slice thickness on each slice and correcting the sum by 35-50% for cutting artifacts and shrinkage [2]. A stereological method used in 1969 gave 1715 to 3031 cm^2 as the range of brain surface area [3].

With the advent of magnetic resonance imaging, volumetric datasets of gray matter, white matter and cerebral spinal fluid (CSF) spaces can be routinely acquired for studies of the normal and abnormal human brain. Many geometric models have been proposed to describe and quantify the subcortical area (gray-white interfaces) or outer cortical area (gray-CSF interfaces) and their complexity from these MRI datasets. For subcortical area, a model-based voxel counting method for estimation of surface area and its fractal dimension were recently presented by Sisodiya [4],[5] and Free [6]. A surface-based approach to determining surface area of the outer cortex has been described by Griffin [7] and Loftus et. al. [8]. In a related surface-based

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method, Jouandet [9] has proposed a method for projecting the cortical surface onto unfolded 2D maps. Most surface-based techniques to date rely on manually traced contours to derive the cortical surface models. Though accurate determination of the cortex boundary can be achieved by outlining the cortex edge manually on MR image slices, this method is very time consuming and not a practical approach for processing and comparing many different brain datasets.

Parametric representations of the outer cortical surface have recently been obtained using a deformable surface algorithm [10]. These techniques attempt to wrap a flexible sheet around the cortex to obtain an accurate parametric representation of the cortical surface. Because of the difficulty of forcing these deformable models to follow areas of high curvature, like the curves of the cortical sucli, these techniques are primarily used for surface rendering and for the elastic matching of gross anatomical features between different brain datasets. They do not follow the cortical surface adequately enough for accurate cortex surface area and volume quantification.

In this work, a method is descibed which uses a reconstruction of a whole brain outer cortical surface from a single protocol MRI dataset to determine surface area and brain volume of both gray and white matter. The method is validated by studies on a 3D mathematical phantom and a MRI dataset of sphere phantom. The implementation of the technique is nearly automatic once the proper brain segmentation is completed.

2. BRAIN SURFACE EXTRACTION

To obtain the brain cortex surface area and brain volume using 3D MRI data, segmentation of the brain is accomplished first. After thresholding and processing with morphological operators, the boundary between the brain cortex and the cerebral spinal fluid (CSF) is defined by using a 2D contour following program. The contours are tiled to form a 3D surface from which a surface area and volume are computed. Details of these procedures are given below.

2.1 Data acquisition

The MRI brain image data were obtained using a 1.5 Tesla GE Signa magnet. A 3D gradient-echo technique (fast spoiled GRASS, or SPGR) was used with a TR of 32 msec, TE of 8 msec, field of view of 24 cm and flip angle of 45^0. The data sampling dimensions are 256 x 256 x 124, and the voxel size is 0.94 x 0.94 x 1.5 mm^3. The data acquisition procedure requires 9 min. TR values of 32-50ms and TE's > 5ms with flip angles of 35^0-45^0 will also give good quality separations between cerebrum and the cerebral spinal fluid, but acquisition time will be larger (e.g. 13 min).

2.2 Brain segmentation

Segmentation of the brain soft tissue from the head is accomplished using the segmentation toolkit provided by the VIDA image display and processing software package [11]. A gray level threshold which separates brain parenchyma (gray and white matter) from CSF is selected from the gray level distribution (histogram) obtained from the 3D dataset. On each data slice, an arbitrary brain region is seeded and adjacent pixels above the threshold are flagged using 2D region growing. This is repeated for each slice and is effective for separating brain from head tissues in most slices. The absence of inhomogeneities and shading artifacts of SPGR allow use of a constant threshold for the seeding operation, though we have found that median filtering of the image data can aid the segmentation and subsequent contour following operation.. In those sections where there are connections between brain and scalp tissues, the bridging tissues are removed by painting a gap using the mouse cursor before executing the region growing method.

The brain cerebellar hemispheres, brain stem and cranial nerves are edited from the image by deleting the active pixels using the mouse cursor as an eraser. This procedure results in a dataset of approximately 80 image frames and requires about 50 minutes for a trained operator.

2.3 Cortical area contour determination

Contour determination is carried out using a 2D contour following program. The input to the program is the segmented brain cortex dataset, the output of the program is a contour file describing each 2D contour as a list of coordinates in three dimensions. Because the cortex is a complex structure with closely adjacent surfaces at sulcal boundaries, a generic contour following algorithm is unable to accurately penetrate many of the deep sulcal regions of the brain. To deal with this problem, the segmented dataset is first thresholded to remove voxels on the outer surface of the gray matter / CSF boundary. Because of partial volume effects, the MRI signal intensity is slightly less than that of pure gray matter at this boundary. Therefore, a simple thresholding operation is usually sufficient to define and segment away the outer "skin" of gray matter voxels. In some cases, however, the facing sulcal surfaces are so close that gray matter/CSF partial volume effects are small, and the thresholding operation does not create a gap between all facing sulcal surfaces. Here, morphological operations, such as erosion and open operations can be used to create a gap between facing sulcal surfaces [12]. Alternately, a higher threshold may be chosen that creates an isocontour somewhere between the grey and white matter boundaries. The effect of different threshold choices are discussed later in this paper.

Once the data have been suitably thresholded and/or processed using the morphological operators, a generic 2D contour following algorithm is used to obtain isocontours representing the cortical and ventricle boundaries. Each contour is recorded as a set of voxel positions in a 3D dataset. On each data slice, many contours can be formed, these contours are classified into inner and outer regions so that subsequent surface area and volume calculations are correct. The contours are post processed as follows:

(a) The contours are smoothed to eliminate abrupt changes due to the discrete voxel locations, thus producing simpler, smoothly varying contours more representative of the true brain boundary. For the original contours, each vertex is located in the center of a pixel coordinate and the adjacent vertices are at a distance of 1 or 1.414, and angled at either 0, 45 or 90 degrees. Obviously, the true cortical surface does not follow this voxelized constraint. A cubic B-Spline algorithm is used to produce smoothly varying contours from the voxel-centered contour data.

(b) After smoothing, a compensation can be applied for the effects of the previously applied erosion operations. The contours are dilated or shrunk depending on whether the contour is inside or outside. Contours are dilated a distance equal to the erosion size. The dilation procedure is halted in regions of sharp contour curvature where two dilated contours would intersect. This ensures that the deep contour valleys between sulci are retained.

(c) Finally, the resulting dilated contours are simplified using an algorithm which removes nearly co-linear vertices. The simplified contours retain the shape of the original contour, yet subsequent contour calculations are easier to carry out.

In practice, the contours are overlaid on the original gray level images for visual verification of their accuracy.

2.4 3D cortical surface area reconstruction and subsequent calculations

The 3D brain surface is constructed by tiling together the 2D cortex contours into a closed triangular mesh. We used the NUAGE algorithm [13] to obtain this surface. The algorithm is based on a Delaunay triangulation of each 2D contour from which an exterior triangular surface is derived. Typical brain surfaces analyzed in this paper are composed of some 50,000 - 75,000 triangles formed from roughly 500 - 1000 2D contours. To facilitate manipulations of the polyhedral surface model, the list of triangles is organized in a data structure known as a winged edge structure [14]. This structure stores adjacency information between faces, vertices and edges.

Once a surface model of the cortex has been obtained, brain surface area is computed by summing all triangles in the polyhedral surface mesh. Likewise, brain volume can be computed by calculating the interior volume of the surface model. For a polyhedron formed of triangular faces like this cortex surface model, volume can be computed as [15]:

$$\sum_n (v_{0x}^n v_{1y}^n v_{2z}^n + v_{0z}^n v_{1x}^n v_{2y}^n + v_{0y}^n v_{1z}^n v_{2x}^n - v_{0y}^n v_{1x}^n v_{2z}^n - v_{0z}^n v_{1y}^n v_{2x}^n - v_{0x}^n v_{1z}^n v_{2y}^n)$$

where N is the total number of triangular faces, and $(v_{0x}^n v_{0y}^n v_{0z}^n), (v_{1x}^n v_{1y}^n v_{1z}^n), (v_{2x}^n v_{2y}^n v_{2z}^n)$ are the vertices of the nth face. The whole brain volume is formed by tiling all the edge data around the cortex regions including both the C_{out} and C_{in}. Because the contouring methodology as described will define inner contours around the ventricles of the brain, calculated brain volume will exclude the volume of the ventricles. The surface of the ventricles will, however, be included in the total surface area. For estimates of cortical surface area only, the contours overlying the ventricle boundaries can be quickly selected and deleted in VIDA's region-of-interest user interface. Surface area calculations can then be made of this modified contour set. Alternately, the ventricle voxels can be segmented to a higher voxel value before the contour following step, and thus will not contribute to the surface model. Using the same region growing interface as was used for segmenting the brain from the head, our users can segment the voxels corresponding to the ventricles in about 10 minutes.

3. RESULTS

Two types of results are presented in this paper. First a basic validation of the technique is demonstrated using a simple mathematical phantom and a MRI spherical phantom. This was done to verify that the automatically detected contours and subsequently tiled surfaces give accurate surface and volume estimates for simple structures, such as the outer exposed surface of the cortex. Second, the algorithm is applied to three human brain datasets to investigate the sensitivity of the volume and surface area calculations to thresholding and other parameters. These latter studies indicate how well the algorithm follows the complex shape of the cortical boundaries, and how reliably the calculated measures may be interpreted. Resulting 2D contours were also displayed as overlays on the image data as an additional validity check by visually noting the correspondence of computed contours to cerebrum gray-level images.

3.1 Validation

A mathematical phantom simulating a simplified cortex structure (Figure 1) was generated to validate the algorithm's per-

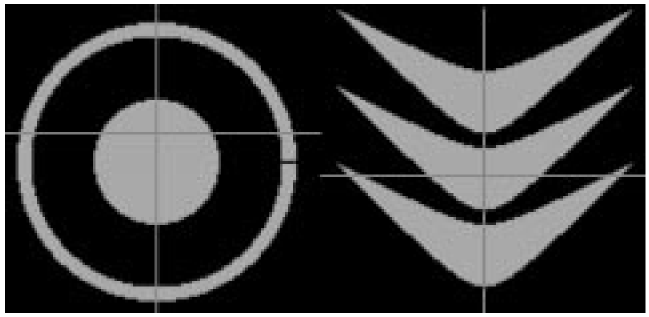


Figure 1. Mathematical Phantom. Two cross sections through the mathematical phantom used to validate the contour following algorithm.

formance. This phantom tests the ability of the 2D contour-following and surface reconstruction programs to deal with nested 2D contours and narrow image gaps, yet the phantom is simple enough that surface area and volume can be calculated analytically. This "cone tree" is a dataset of 128 x 128 x 240 voxels, with voxel size 1 x 1 x 0.5 mm. The second dataset was obtained from a spherical phantom scanned using MRI. The phantom was a 171 mm diameter hollow spherical vessel filled with $CuSO_4$ doped water, and imaged on the 1.5 T Signa system using a protocol similar to that of patient acquisitions. The resulting 256 x 256 x 96 voxel dataset was automatically segmented using a single thresholding operation.

Table 1 shows the results of the contour following technique verses analytical calculations. It is seen that for both datasets, the surface area and volume calculations are within 2% of the true value, and for the case of the sphere, the accuracy is within one voxel distance (1 mm) in the direction normal to the surface. Note that the surface area of the sphere is slightly overestimated by the contour following technique. This is probably due to small nonuniformities in the surface, which would slightly increase the surface area without dramatically increasing the total volume of the object.

Table 1: Phantom Validation Results

Technique	Cone Phantom	Sphere Phantom
Analytical Volume (cm^3)	334	2618 (r=8.55 cm)
Measured Volume (cm^3)	328	2625 (r=8.56 cm)
Analytical Surf. Area (cm^2)	886	919 (r=8.55 cm)
Measured Surf. Area (cm^2)	875	928 (r=8.59 cm)

3.2 Sensitivity Analysis

Sensitivity of the algorithm was investigated with respect to three different aspects: the chosen threshold level, the degree of contour smoothing, and the effects of image smoothing. Of these, the threshold level chosen before contour following is the most critical. Figure 2 shows the gray level histogram of a typical MRI cortex dataset. Two distinct peaks can be seen in the data. The grey matter distribution corresponds to the lower valued peak, white matter corresponds to the higher peak. To investigate the effect of different threshold levels, the algorithm was run for a range of threshold choices spanning the values of the gray and white matter histogram distributions for the human brain datasets. Figure 3 shows the calculated surface area and volume as the threshold parameter varies for one of the human datasets. It is seen that the surface area reaches a distinct peak for a threshold somewhere between the gray and white matter histogram peaks. Volume, on the other hand, slowly decreases with increasing threshold. Similar curves were seen for the other two human brain datasets. A look at the detected contours on a representative slice for the different thresholds (Figure 4) explains this phenomenon. Too low a threshold prevents the algorithm from detecting surface boundaries at deep sulcal locations. Therefore, though the volume at this threshold is greatest, the

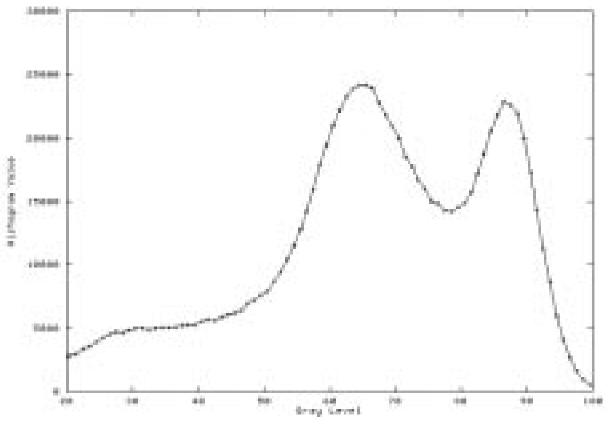


Figure 2. Gray Level Histogram for MRI Brain Dataset. Two peaks are seen; one due to cortical gray matter, the other due to cortical white matter.

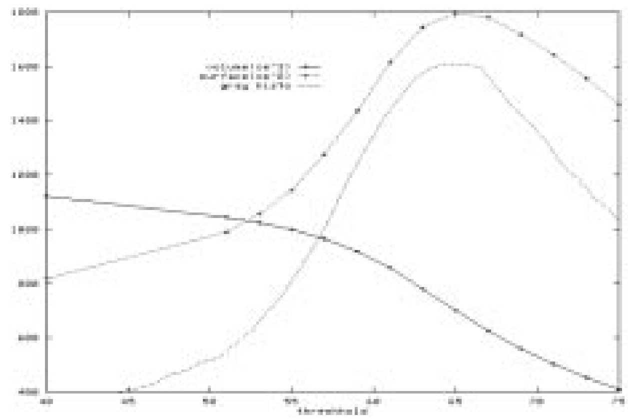


Figure 3. Surface Area and Volume Verses Threshold. Surface area increases to a peak as the threshold varies. Volume monotonically decreases.

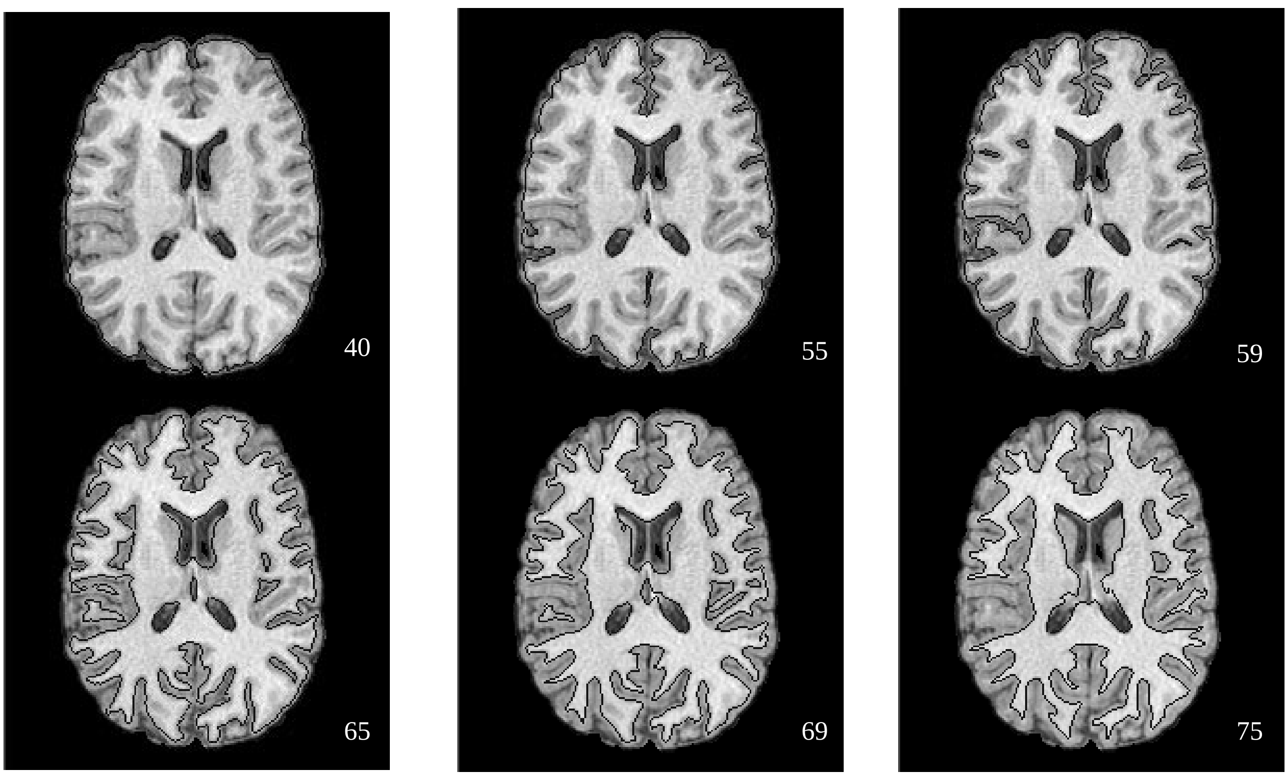
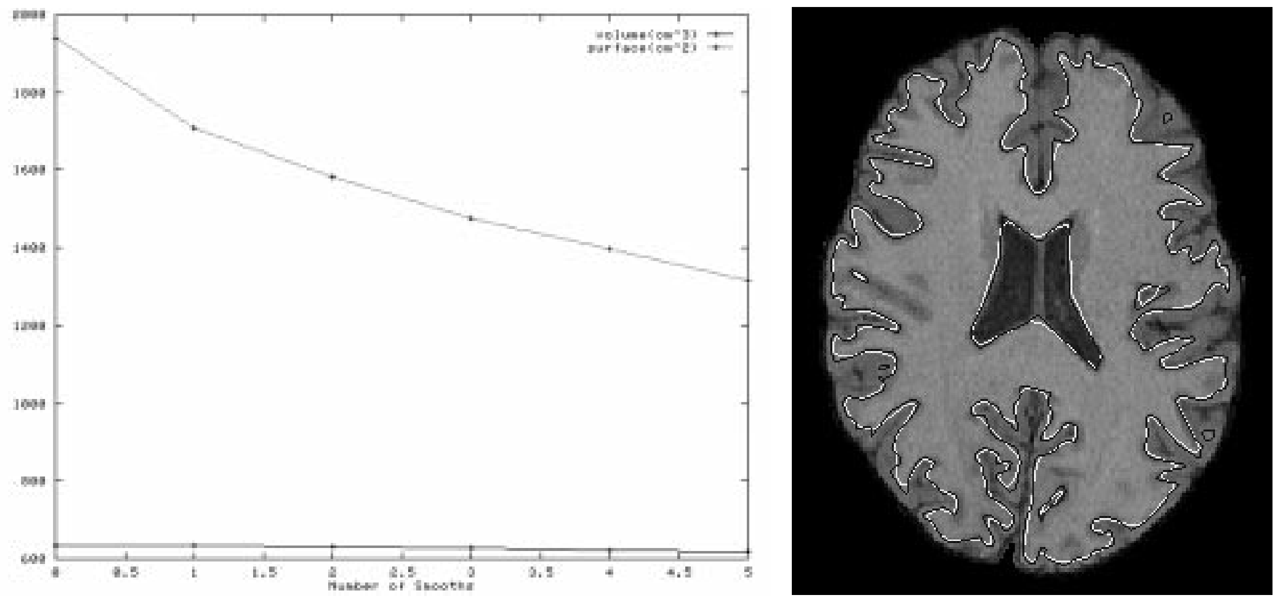


Figure 4. Detected Contours Verses Threshold. A threshold greater than the value for CSF is necessary for contours to follow the inner suclal folds. Thresholds used for contour following are indicated on each image.

surface area is severely underestimated because the surface area of most inner sulci is neglected. A higher threshold defines an isosurface inside the CSF/gray matter boundary, somewhere near the grey matter/white matter interface. Here, even though some of the outer voxels are shaved away, and the total estimated volume decreases, more of the inner cortical surfaces are detected so the surface area estimate increases. Finally, at very high threshold values, no “new” sulcal surfaces are detected, and surface area decreases due to the shrinking interior of the detected isocontour, now well within the cortical white matter.

The degree of contour smoothing can also have a significant effect on estimated surface area. As previously described in the methods section, a B-spline smoothing is applied to the contours to remove the voxelized constraint of the contour point

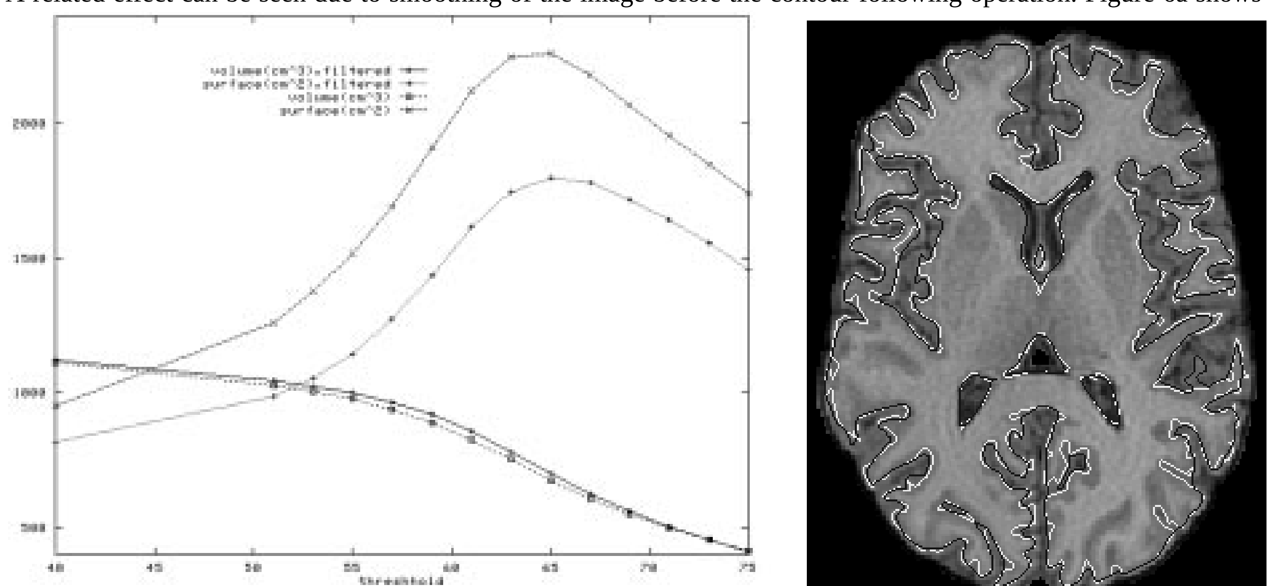


(a) (b)

Figure 5. Effects of Contour Smoothing. Slightly smoothing contours dramatically reduces calculated surface area, whereas volume is affected little (a). An overlay of contours after one and three smooths show little difference (b), yet the surface area estimate differs by over 15%. Here the unsmoothed contours are shown in black; the smooth contours are white.

positions immediately after the contour following procedure. This procedure may be carried out successively to increasingly smooth the 2D contours. A plot of the surface area and volume verses number of smooths is seen in Figure 5. The detected contours after the first and third smoothing operation are displayed in Figure 5b. It is seen that though the contours appear very similar, the surface area varies considerable between these five estimates. As the contours become more smooth, area of the reconstructed triangle meshes decreases. The volume estimate, on the other hand is relatively stable.

A related effect can be seen due to smoothing of the image before the contour following operation. Figure 6a shows the



(a) (b)

Figure 6. Effects of Image Smoothing. Though the contours found on the unsmoothed and smooth images look quite similar (b), the estimated surface area can vary considerably (a). Contours produced by the unsmoothed images are shown in white, contours produced by the median filtered image are shown in black.

surface area verses threshold for a dataset calculated before and after median filtering. Examination of the contours detected on each dataset (Figure 6b) reveal that the greater surface area of the noisier, non-filtered image is caused by contours slightly more jagged than those produced by the filtered dataset.

4. DISCUSSION

This work proposes a methodology for measuring surface areas and volumes of the whole human brain using MRI data which are isotropic in resolution at the 1 mm level, and analyzes the robustness of the method. Among the applications of these types of measurements are evaluations of natural changes of brain size with growth and aging, and neurodegeneration disorders. Given the considerable differences in the surface area and volume estimates that were seen in the sensitivity analysis section, two obvious questions that arise are: 1.)what are the best choices for thresholding and smoothing parameters, and 2.)given these choices, are the estimates reliable enough for comparing different brains. To answer these questions, one needs to consider possible errors in the methodology. At least four classes of errors can exist with the proposed algorithm:

- missed "deep" sulcal surfaces
- segmentation errors due to incorrect thresholding
- false holes due to image noise
- tiling artifacts.

The plots of surface area and volume verses threshold indicates that the most important error which can bias surface and volume estimates is the missed detection of inner sulcal surfaces. For the case shown in Figure 3, the surface area calculated at the lowest threshold represents approximately the surface area of only the exposed surfaces of the cortex. This value is less than half the surface area calculated for higher thresholds, which better approximates the surface area for deep sulci. In fact, since the higher thresholds define an isosurface close to the gray matter/white matter boundary (i.e. the subcortical, or white matter surface), the actual surface area of the outer cortex is likely to be greater than the highest value shown in the graph, assuming gray matter is homogeneous. Considering both the curves of Figure 3 and the accompanying pictures in Figure 4, it is difficult to decide which threshold best detects the deep sulci without shaving away too much gray matter. Further, it would be difficult to define a criteria for threshold choice that would allow meaningful comparisons of brain data from different subjects. Therefore, the detection of the gray matter/white matter boundary and calculation of the surface area of this boundary may be a better goal. A contour following algorithm can easily navigate the large gaps between the sulci along this isosurface. Choosing the threshold that maximizes surface area would most likely give a robust estimate of the white matter surface, since this value detects nearly all the deep sulci, but does not erode away the white matter too drastically. Also, since gray matter thickness is fairly constant, the subcortical surface area should be closely correlated to the actual outer cortical surface area at the gray matter/CSF boundary. For cortical *volume* estimates, on the other hand, it makes more sense to use the low thresholds that draw a contour on only the exposed cortical surfaces. Here the small spaces between the deep sulci do not contribute appreciably to the cortical volume, and a higher threshold would only unnecessarily exclude grey matter voxels. Indeed, a simple summing of total nonzero voxels in the cortical segmentation is probably sufficient to obtain reasonable volume estimates without resorting to mathematics on the surface model.

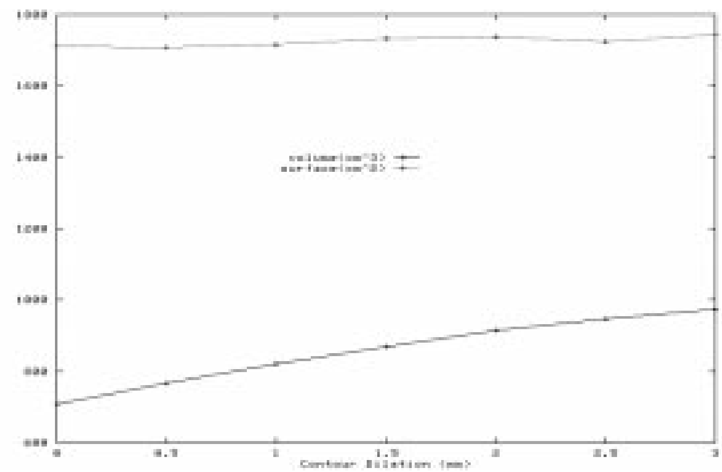


Figure 7. Effects of Segmentation Errors. Small dilations of the brain surface to not greatly increase surface area. The effect of segmenation errors on calculated surface area may therefore be small.

Once all sulcal surfaces have been identified, the effect on surface area and volume of shaving off too many or too few voxels from this surface is probably secondary. To demonstrate this, surface area and volume are calculated for a brain dataset where the surface has been dilated by 0.5, 1.0, 1.5, 2.0, 2.5 and 3.0 mm in directions normal to the 2D contour, thus simulating various degrees of segmentation error. For these brain surface area calculations, a threshold was chosen so that the initial surface was located close to the gray matter/white matter interface. Because of the complicated shape of the cortical surface, the surface and volume ratio changes for a change in radius, d, will not follow the relations $\frac{S_{r+d}}{S_r} = \frac{(r+d)^2}{r^2}$, and $\frac{V_{r+d}}{V_r} = \frac{(r+d)^3}{r^3}$,where S_r and V_r are the surface area and volumes for a sphere of radius r. Instead, surface area is usually decreased in the sulcal regions and increased in the gyral regions, and in general, volume grows with dilation. Further, the rate of surface area increase is less than the volume increase with radius increase. For these reasons, it is seen in Figure 7 that surface area of the cortex remains fairly stable as the surface is dilated. The results indicate that the surface area of the white matter may be a close estimate of the grey matter surface area

False contours around noisy image "holes" are errors caused when the thresholding or morphological operations do not work perfectly to isolate the cortical or subcortical surface. Occasionally, these operations create small holes within noisy portions of contiguous gray or white matter. An accurate quantification of the effect of the false contours would be hard to calculate, since manual editing of the datasets is required, and often hard to judge in noisy regions. Visual verification of false contours for the brain datasets showed that for thresholds chosen to isolate the white matter surface, only a small number of these contours were formed. In our experiences, manual deletion of these contours resulted in negligible surface area and volume changes.

Errors due to modeling a smooth surface with a triangular mesh is another possible source for errors. It is likely that in the absence of any other errors, the surface area is slightly overestimated when applying the polyhedral model. Indeed, as Koenderink showed, the surface area of a cylinder is the limes inferior of the surface area derived from a number of different triangular mesh approximations to that cylinder [16]. This led him to suggests: "*you should be suspicious of any method that proposes to make use of surface area of a polyhedral model*." As demonstrated by the accuracy of the cone and spherical phantom results, this can be a small effect for these simple objects. However, the marked difference in surface area of the cortex after different degrees of contour smoothing lead one to believe that this may be a more problematic error for complicated structures like the brain. Relating surface areas from different brains may only be possible when using identical smoothing procedures on contours obtained from volumes of identical voxel size.

Using the peak surface area over all thresholds as the "true" brain surface area, and a low threshold to obtain a contour around the exterior cortical surface to estimate brain volume, our results are in reasonable agreement with previously published values which employed different methods (Table 2). The method we propose has numerous advantages over other meth-

Table 2: Published Brain Surface and Volume Estimates

Research Group & Year	Surface Area (cm^2)	Volume (cm^3)
Hennenberg, 1910	1500 - 2000	NA
Blinkov & Glezer, 1968	1468 - 1670	460-1122
Elias & Schwartz, 1969	1715 - 3031	1198
Sisodiya, 1996	1626	NA
Loftus, 1995	1610	NA
Hofman, 1985	2430	1167
Joandet et. al., 1989	1511 - 1846	NA
Griffin, 1994	2238	NA
current paper (case A)	1686	1048
current paper (case B)	1796	1121
current paper (case C)	1774	1081

ods. *Ex vivo* techniques [1], [2], [3], [17], [9] all suffer from the same recognized problem of the shape changes of the cerebrum when it is removed from the support of CSF pool and the vascular pressure system upon extraction. The shrinkage of brain volume has been reported to be of 37-40% when the brain is embedded in paraffin wax[2]. When the cortex is finely sectioned with a microtome as a part of the surface area calculation, considerable deformations of each slice can contribute to surface area and volume errors. Two dimensional slice techniques which rely on perimeter measurements to obtain surface are also plagued by the fact that the true surface is rarely perpendicular to the slicing plane, consequently, errors are introduced as the slope of the surface with respect to the cutting plane increases. For example, using simple arguments from the Pythagorean theorem, a 2D based estimate of our cone phantom which has surface slopes of 26 and 45 degrees would be underestimated by a factor between 2.23 and 1.41 (i.e. the ratio of the hypotenuse to the height in a right triangle with angles of 26 and 45 degrees respectively). Thus this frequently used technique of adding the perimeter length times slice thickness to obtain surface area can induce unnecessary error. The *in-vivo* technique using a well calibrated MRI scanning system avoids the problems of data shrinkage and deformation, and our 3D surface based calculation reduces errors due to surface curvature.

Other techniques for obtaining surface models of the cortex have made use of parametric cortical surface models obtained by fitting a sphere topology with an active contour warping method to best match a segmented cortical dataset [18],[10],[19]. The resulting surfaces can in many cases produce accurate renderings and are useful for matching similar datasets, however, the active deformable surface algorithms have limitations in following surfaces which have high curvature. These algorithms do not sufficiently warp the sphere topology into sulcal regions of the cerebrum. Consequently, though the surfaces corresponding to the outer gyri are well-matched, these algorithms do not adequately follow the entire cortical surface well enough for accurate surface area calculations. Another widely used 3D surface technique is the marching cubes algorithm [20]. This technique can be thought of as the 3D extension to the 2D contour-following algorithm used in this paper. The technique directly builds a triangular mesh surface model from a discrete volume isosurface. It is expected that similar results would be obtained if the marching cubes technique were used for the surface construction instead of the 2D contour detection and subsequent Delaunay-based tiling. However, the 2D method has the advantages that performance is often better when voxel size is non-isotropic, and resulting surfaces are more compactly represented than when using the Marching Cubes algorithm [21].

5. SUMMARY

We have presented a methodology for obtaining *in vivo* surface area and volume measurements of the human cortex from MRI data. Mathematical and imaged phantom studies as well as MRI scans from three normal subjects were used to obtain a sensitivity analysis of these measurements. The phantoms were used to establish the accuracy of the measurements for known objects. Brain datasets were used to investigate the range of computed surface area and volume as various thresholding and morphological image processing parameters were varied. Visual verification of 2D contours on the image slices was also used to evaluate algorithm accuracy. The sensitivity analysis indicate that a technique for defining the outer cortex boundary in a comparable manner for different brain datasets is a problem not yet adequately solved. This is due to the fact that inner sulcal surfaces are nearly touching, and surface detection algorithms face difficulty in precisely locating *all* inner surfaces. Calculation of the white matter surface area may be a preferable measurement to obtain, since the white matter surface is far easier to locate, and since white and grey matter surface areas are very likely to be correlated. The results also pointed out the fact that calculations of surface area based on a polyhedral surface model can be quite sensitive to image and surface post-processing techniques, such as smoothing, or other noise suppression methods. For comparisons of parameters between different datasets, it is therefore important that they be acquired and processed in a similar manner.

6. ACKNOWLEDGEMENTS

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