Brain Retraction and Thickness of Cerebral Neocortex: An Automated Technique for Detecting Retraction-Induced Anatomic Changes Using Magnetic Resonance Imaging

BACKGROUND: Treating deep-seated cerebral lesions often requires retracting the brain. Retraction, however, causes clinically significant postoperative neurological deficits in 3% to 9% of intracranial cases.

OBJECTIVE: This pilot study used automated analysis of postoperative magnetic resonance images (MRIs) to determine whether brain retraction caused local anatomic changes to the cerebral neocortex and whether such changes represented sensitive markers for detecting brain retraction injury.

METHODS: Pre- and postoperative maps of whole-brain cortical thickness were generated from 3-dimensional MRIs of 6 patients who underwent selective amygdalohippocampectomy for temporal lobe epilepsy (5 left hemispheres, 1 right hemisphere). Mean cortical thickness was determined in the inferior temporal gyrus (ITG test), where a retractor was placed during surgery, and in 2 control gyri—the posterior portion of the inferior temporal gyrus (ITG control) and motor cortex control. Regions of cortical thinning were also compared with signs of retraction injury on early postoperative MRIs.

RESULTS: Postoperative maps of cortical thickness showed thinning in the inferior temporal gyrus where the retractor was placed in 5 patients. Postoperatively, mean cortical thickness declined from 4.1 ± 0.4 mm to 2.9 ± 0.9 mm in ITG test (P = .03) and was unchanged in the control regions. Anatomically, the region of neocortical thinning correlated with postoperative edema on MRIs obtained within 48 hours of surgery.

CONCLUSION: Postoperative MRIs can be successfully interrogated for information on cortical thickness. Brain retraction is associated with chronic local thinning of the neocortex. This automated technique may be sensitive enough to detect regions at risk for functional impairment during craniotomy that cannot be easily detected on postoperative structural imaging.

KEY WORDS: Amygdalohippocampectomy, Brain retraction injury, Cortical thickness, FreeSurfer

TECHNIQUE ASSESSMENT

Treating deep-seated cerebral lesions often requires retracting the brain. Retraction, however, causes clinically significant postoperative neurological deficits in 3% to 9% of intracranial cases. The local pressure on the brain surface deforms the brain, causing ischemia by compromising perforating arteries. The extent of injury depends on the pressure exerted by the retractor, the geometry of the retractor, and the duration of retraction. To date, characterization of the functional and anatomic consequences of brain retraction has been limited to a description of the obvious postoperative patient deficits and obvious regions of brain injury. A technique that more precisely, sensitively, and quantitatively detects brain regions at risk from retraction would facilitate future studies designed to optimize surgical technique and improve patient outcome.

A change in the composition of the cerebral neocortex is a sensitive indicator of brain pathol-
ogy. Cortical thinning is associated with dementia in Alzheimer’s disease, disability from multiple sclerosis, treatment of medulloblastomas, and a prolonged history of seizure.\(^5\)-\(^8\) A freely available, quantitative, automated algorithm has been developed to reliably interrogate in vivo cortical thickness on high-resolution magnetic resonance images (MRIs).\(^9\),\(^10\) This technology can be used to evaluate whole-brain cortical thickness. We hypothesized that this technology could be applied to elucidate the anatomic consequences of brain retraction. The goals of this pilot study were (1) to investigate the feasibility of applying the cortical thickness algorithm to postoperative MRIs, (2) to describe the chronic imaging findings associated with brain retraction, and (3) to evaluate whether measurements of cortical thickness can be useful in screening for evidence of brain retraction injury.

**PATIENTS AND METHODS**

**Study Cohort**

We identified patients with unilateral temporal lobe epilepsy who had undergone uncomplicated selective amygdalohippocampectomy between 2005 and 2007 (Table 1). These patients were participants in an epilepsy outcomes project at our institution. They were selected from the research cohort because of the availability of high-resolution imaging. The diagnosis of unilateral temporal lobe epilepsy was confirmed by ictal or interictal medial temporal lobe epileptiform activity demonstrated on video-electroencephalography. All patients had mesial temporal sclerosis demonstrated by imaging or pathology. The protocol was approved by the St. Joseph’s Hospital and Medical Center Institutional Review Board.

**Surgical Technique**

Complete selective amygdalohippocampectomy was performed in all patients by a subtemporal technique previously described.\(^11\) In brief, mesial temporal lobe was resected through a keyhole craniotomy based on the temporal floor. The temporal lobe was elevated using a brain retractor, and a corticectomy was made in the fusiform gyrus to gain access to the amygdala and hippocampus. To elevate the temporal lobe, a malleable self-retaining retractor was placed on the inferior temporal gyrus (Figure 1). The cross-sectional area of the retractor in contact with the brain was about 3 cm.\(^2\) The retractor was applied, with occasional adjustments, for 1 to 2 hours. The amount of pressure applied did not cause a direct brain contusion that was visible during surgery. The mesial temporal lobe structures were resected using a subpial technique.

**MRI Acquisition**

Imaging was performed at St. Joseph’s Hospital and Medical Center on a General Electric Signa 3T scanner. Image acquisitions included a 3-plane localizer, calibration scan, and a T1-weighted volume acquisition pulse sequence. Axial fluid-attenuated inversion recovery, coronal T2-weighted, and diffusion-weighted sequences were also obtained. The 3-dimensional T1-weighted spoiled gradient recalled acquisition (SPGR) sequence was obtained with the following parameters: TE, 2 milliseconds; TR, 5 milliseconds; flip angle, 12 degrees; matrix size, 256 × 256; and slice thickness, 1 mm. Images were transferred to a Unix workstation for analysis utilizing FreeSurfer (version 4.3.1; http://surfer.nmr.mgh.harvard.edu/) to determine cortical thickness. Preoperative imaging was obtained within 1 week of surgery. Postoperative imaging was obtained 24 to 48 hours after surgery and then 7 to 12 months after surgery. A neuroradiology fellow (L.H.) reviewed the postoperative images for obvious signs of retraction effect (ie, hyperintensity suggestive of edema on T2-weighted and fluid-attenuated inversion recovery images) and for postoperative complications such as hematoma or infarcts.

**Cortical Thickness Determinations**

The procedure for generating cortical surface models from T1-weighted volumetric MRIs required 4 steps: segmentation of white matter, determination of gray and white matter and pial boundaries using tessellation, inflation of the resulting surface, and correction for topological defects.\(^9\),\(^10\) Cortical thickness was estimated by measuring the shortest distance from each point on the white matter surface to the pial surface, and the shortest distance from each point on the pial surface to the white matter surface. Cortical thickness at each vertex was calculated as the means of surface-to-pial and pial-to-surface measurements.

Cortical thickness averages were computed for 3 gyral-based regions of interest (ROIs) on preoperative and late postoperative (obtained 6-12 months after surgery) MRIs (Figure 2). The test region (inferior temporal gyrus [ITG] test), a 1-cm\(^2\) area on the midpoint of the inferior temporal gyrus, correlated with the center of the operative field where the

---

**TABLE 1. Characteristics of Patient Population**

| Patient No. | Age, y/SEX | Operated Hemisphere | Seizure Outcome\(^a\) |
|-------------|------------|---------------------|-----------------------|
| 1           | 22/F       | R                   | I                     |
| 2           | 30/F       | L                   | I                     |
| 3           | 32/F       | L                   | I                     |
| 4           | 38/F       | L                   | I                     |
| 5           | 40/M       | L                   | I                     |
| 6           | 47/F       | L                   | I                     |

\(^a\) Engel score at 1 year.\(^12\)

---

**FIGURE 1. Illustration of the position of the self-retaining retractor placed on the inferior temporal gyrus (ITG)** used to elevate the temporal lobe during selective amygdalohippocampectomy. The operative view for a left-sided approach is shown. The operative corridor is between the base of the temporal lobe and the base of the temporal floor. An incision is made in the fusiform gyrus (*), followed by subpial resection of the amygdala and hippocampus. MTG, middle temporal gyrus; STG, superior temporal gyrus. Used with permission from Barrow Neurological Institute.
retractor blade was placed. The 2 control regions were 1-cm² areas located on the ipsilateral ITG control 2.5 cm posterior to the ITG test region (ie, not in the operative field) and an area of the most inferiorly located portion of the motor cortex (MC) control. The ITG control was chosen to account for any changes in cortical thickness that might result from hippocampal resection and disruption of the axons to the basal temporal lobe. The MC control was selected as a second control outside the operative field and not at risk for denervation after hippocampal resection. This control tested the validity of measuring cortical thickness on postoperative specimens. ROIs were assigned jointly by a senior neurosurgery resident (A.S.L.) and research associate (S.L.).

Statistical Analysis

Paired single-tailed t tests were used to evaluate changes in the average cortical thickness of the ROIs. A single-tailed distribution was selected because it was reasonable to assume that cortical thickness was only likely to decrease after surgery.

RESULTS

Patient Characteristics

Six patients were included in the study (Table 1). Their mean age was 35 years (range, 22-47 year). One patient underwent right-sided surgery and 5 underwent left-sided surgery. There were no perioperative complications. At their 1-year follow-up examination, all patients were free of seizures and auras (Engel Class I).12

Early MRI Findings Associated With Brain Retraction

Acute retraction injury was evaluated by reviewing MRIs obtained within 48 hours of surgery. Coronal T2-weighted fast spin-echo sequences showed hyperintense signal suggestive of edema from brain retraction within the inferior temporal gyrus in all specimens (Figure 3). Four patients also had edema within the fusiform gyrus. Imaging showed no effect from retraction in either the middle or superior temporal gyri in any specimen. The location of this postoperative edema correlated with the region of the brain that was retracted during surgery. There were no cases of vein of Labbé infarct, hemorrhage, or arterial infarct.

Changes in Cortical Thickness Caused by Brain Retraction

Postoperative MRIs obtained between 7 and 12 months (median, 10 months) after surgery were compared with preoperative studies (Figure 4). To validate that the computational algorithm had correctly interpreted the postoperative specimens, we compared the whole-brain topographical maps of the postoperative specimens to the preoperative specimens gyrus by gyrus. Cortical topography was similar across most of the cortex with the expected loss of morphology in the surgical region. For a more detailed analysis, we compared the average cortical thicknesses for the 2 control ROIs (ie, ITG control and MC control) and determined that there was no significant difference between the preoperative and postoperative thickness of the brains (P = .40 and I = .42, respectively) (Table 2). As a third method of validating our results, we compared the thickness of the occipital cortex in our specimens with previously published results and found no substantial differences (data not shown).9

Whole-brain cortical thickness topographical maps showed substantial thinning of the midportion of the inferior temporal gyrus in 5 of 6 specimens. The region of cortical thinning correlated anatomically with the site of retractor placement and with the location of the edema on immediate postoperative MRIs. Cortical thickness declined in this region (ITG test) from a mean of 4.1 ± 0.4 mm before surgery to 2.9 ± 0.9 mm after surgery (P = .03) (Table 2). This subtle neocortical thinning noted on the cor-
FIGURE 4. Cortical thickness determination for patient 1. A, topographical cortical thickness maps showing thinning of inferior temporal gyrus cortex (arrow). Basal views of temporal lobe from before and 7 months after surgery are presented. Circle denotes the amygdalohippocampectomy. Color scale: Gray represents thickness <3 mm. Red to yellow represents thicknesses of 3 to 5 mm. Bright yellow represents thicknesses greater than 5 mm.

B, representative spoiled gradient recalled acquisition (SPGR) sequence from which the cortical thickness maps were created demonstrating the difficulty of detecting subtle neocortical changes by casual inspection of postoperative images. These differences were obvious after the automated technique was applied. Used with permission from Barrow Neurological Institute.

tical thickness maps was difficult to visualize on the MRIs before the automated analysis was performed (Figure 4).

DISCUSSION

Previous methodologies used to quantify the extent of retraction injury on postoperative imaging have relied on gross descriptions of the regions involved or on simple measurements of the maximum diameter of edema. For example, Chi et al14 investigated retraction-related edema after bifrontal craniotomy for midline meningiomas. They used a 3-tier grading system based on the involvement of the gyrus rectus.

Helmstaedter et al13 measured the diameter of T2-weighted hyperintensity in the perisylvian region on perioperative MRIs after amygdalohippocampectomy. We supplemented these previous observations by investigating the more subtle anatomic consequences of brain retraction. We applied a reliable, automated computational algorithm to interrogate in vivo cortical thickness using high-resolution MRIs.14 Our results demonstrate that not only is it feasible to measure cortical thickness in postoperative specimens, but also the methodology may be a sensitive technique for detecting permanent anatomic changes caused by brain retraction. This technique was able to document a 1-mm change in cortical thickness not easily visualized on routine postoperative imaging (Figure 4). This anatomic change persisted after the acute signs of injury had faded.

Previous studies have shown that cortical thinning is likely the result of neuronal loss. For example, children demonstrate age- and region-specific cortical changes as a result of neuronal pruning.15,16 We hypothesize that cortical thinning in the context of brain retraction is a result of neuronal loss from ischemia of the cell bodies and axons. During vascular neurosurgery, for example, retraction limits perfusion of perforating vessels.17 However, even though neocortical atrophy is a sensitive measure of brain pathology, it is not specific for a cause. In our model, retraction seems the most likely cause of neuronal loss given that the thinning occurred where the retractor was placed during surgery and that there was no imaging evidence of other insults, such as hematoma formation or infarct, to account for the change.

Study Design

Several aspects of the study design warrant further discussion. First, we selected retraction during amygdalohippocampectomy as our model system because of the availability of pre- and postoperative 3-dimensional T1-weighted SPGR studies and because the surgical target was deep-seated. Furthermore, the procedure was performed in a standardized fashion. The retractor was always placed on the inferior temporal gyrus and a similar amount of mesial temporal lobe was resected in each patient. The patients were available for long-term follow-up and harbored a relatively stable pathological entity.

A disadvantage of our model system was that the mesial temporal lobe was removed as the goal of surgery. Some of the axons that communicate between the mesial temporal lobe and inferior temporal gyrus may have been transected as part of the procedure. We attempted to control for this by measuring the cortical thickness of the portion of the inferior temporal gyrus that was outside the operative field (ITG control). That we detected no change in the control region after surgery suggests that the thinning observed in the test region was a result of retraction rather than disconnection. Furthermore, because patients with mesial temporal sclerosis have preexisting temporal cortical thinning, we hypothesize that resection of a diseased hippocampus would likely result in less neocortical thinning.
due to disconnection than resection of a healthy hippocampus with robust cortical projections.6

Future enhancements to the study design include documenting the pressure applied by retraction and the length of retraction to better determine the influence of the magnitude of the insult on cortical thickness.18-20 These measurements may help clarify why cortical thinning was detected in only 5 of 6 specimens even though the retractor was used in all cases. We hope to expand the study to a cohort of patients who have undergone a cranial surgery that does not involve brain resection, such as aneurysm clipping, to determine whether this technique can be applied more broadly. A second future modification is to perform susceptibility imaging on the postoperative brains to determine the impact hemosiderin might have on the cortical thickness measurements. Susceptibility sequences will allow us to study the degree of effect, if any, postsurgical changes have on these measurements.

**Future Directions**

We hope that measuring cortical thickness will improve understanding of the effects of brain retraction, promote the development of tasks to evaluate the significance of such injuries, and improve surgical technique. The consequences of brain retraction depend on the eloquence of the underlying brain. This preliminary study indicated that the inferior temporal gyrus is an area of interest for future study. Our approach to investigating the clinical significance of this finding is to apply functional MRI and neurocognitive testing to detect whether this subtle retraction injury results in cognitive changes. This line of inquiry might be able to establish a link between the regional metabolic and structural consequences of retraction and patient outcomes.

**CONCLUSIONS**

In this pilot study, we demonstrated that measuring cortical thickness on postoperative MRIs is a sensitive method for examining the effects of brain retraction. Areas of chronic cortical thinning were consistent with the site of retractor placement during surgery and with the location of acute retraction injury. A better understanding of the anatomic changes after brain retraction may provide insight into its functional consequences. Cortical thickness techniques may be useful for directing future studies designed to investigate causes of subtle functional and neurocognitive impairment after surgery.

**DISCLOSURE**

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

**REFERENCES**

1. Spetzler RF, Daspit CP, Pappas CT. The combined supratentorial and infratentorial approach for lesions of the petrous and clival regions: experience with 46 cases. *J Neurosurg*. 1992;76(4):588-599.
2. Andrews RJ, Bringas JR. A review of brain retraction and recommendations for minimizing intraoperative brain injury. *Neurosurgery*. 1993;33(6):1052-1063; discussion 1063-1064.
3. Zhong J, Dujovny M, Perlin AR, Perez-Arjona E, Park HK, Diaz FG. Brain retraction injury. *Neurourol. Urodyn.* 2003;22(8):831-838.
4. Chi JH, Parsa AT, Berger MS, Kunwar S, McDermott MW. Extended bifrontal craniotomy for midline anterior fossa meningiomas: minimization of retraction-related edema and surgical outcomes. *Neurosurgery*. 2006;59(4 suppl 2):ONS426-ONS433; discussion ONS433-ONS434.
5. Liu AK, Marcus KJ, Fischl B et al. Changes in cerebral cortex of children treated for medulloblastoma. *Int J Radiat Oncol Biol Phys*. 2007;68(4):992-998.
6. Lin JJ, Salamon N, Lee AD, et al. Reduced neocortical thickness and complexity mapped in mesial temporal lobe epilepsy with hippocampal sclerosis. *Cereb Cortex*. 2007;17(9):2007-2018.
7. Du AT, Schuff N, Kramer JH, et al. Different regional patterns of cortical thinning in Alzheimer’s disease and frontotemporal dementia. *Brain*. 2007;130(pt 4):1159-1166.
8. Sailer M, Fischl B, Salar D, et al. Focal thinning of the cerebral cortex in multiple sclerosis. *Brain*. 2003;126(pt 8):1734-1744.
9. Fischl B, Dale AM. Measuring the thickness of the human cerebral cortex from magnetic resonance images. *Proc Natl Acad Sci USA*. 2000;97(20):11050-11055.
10. Dale AM, Fischl B, Sereno MI. Cortical surface-based analysis: I. Segmentation and surface reconstruction. *Neuroimage*. 1999;9(2):179-194.
11. Little AS, Smith KA, Kürlin K, et al. Modifications to the subtemporal selective amygdalohippocampectomy using a minimal-access technique: seizure and neuropsychological outcomes. *J Neurosurg*. 2009;111(6):1263-1274.
12. Engel J Jr. *Surgical Treatment of the Epilepsies*. New York, NY: Raven Press; 1993.
13. Helmstaedter C, Van Roost D, Clusmann H, Urbach H, Elger CE, Schramm J. Collateral brain damage, a potential source of cognitive impairment after selective
provides a clear view of the actual effect of surgery on the brain. Changes on the brain can be identified in the immediate postoperative period, and long-term effects are easily detectable.

Little et al provide an elegant and thoughtful anatomical and magnetic resonance imaging (MRI) correlation of the effects of brain retractor pressure in patients undergoing a temporal lobectomy for seizure disorders. The study is a good initial step toward the documentation of the effects of pressure on cerebral tissue. The study provides an anatomical and imaging correlation, but does not provide a direct demonstration of the effect of pressure changes on brain tissue, in a very small group of 6 patients.

This study could be further enhanced by adding tonometric measurements of brain tissue pressure under the retractor blade, which can be correlated with a true analysis of the retractor blade surface area. This could be further complemented with an evaluation of cerebral blood flow, and correlated with PET (Positron emission tomography) studies evaluating changes in cerebral blood flow, oxygen consumption, and cerebral metabolic rate for oxygen.

The study provides a description of a reduction of the thickness of the cerebral cortex under the retractor blade, and extrapolates that observation to a reduction on the neuronal bodies and axons. The authors are wise to indicate that the reduction on the neuronal population may be the direct result of the surgical resection, and not totally the result of retractor pressure. A study similar to the present one could be conducted on patients who have elective aneurysm surgery, without brain tissue resection, to determine whether there is, in fact, a loss of tissue under the retractor site. Measurements of the brain retractor pressure on the brain could then also be done, and correlated with cerebral blood flow and PET studies to complete the evaluation.

I congratulate the authors for an interesting and provocative study, and urge them to continue their pursuit of this interesting project.

Fernando G. Diaz
Royal Oak, Michigan