Obsessive-compulsive disorder is a psychiatric condition associated with anxiety and ritualistic behaviors. Although medical management and psychiatric therapy are effective for many patients, severe and extreme cases may prove refractory to these approaches. The authors evaluated their experience with Gamma Knife (GK) capsulotomy in treating patients with severe OCD.

Methods. A retrospective review of an institutional review board–approved prospective clinical GK database was conducted for patients treated for severe OCD. All patients were evaluated preoperatively by at least one psychiatrist, and their condition was deemed refractory to pharmacological and psychiatric therapy.

Results. Five patients were identified. Gamma Knife surgery with the GK Perfexion unit was used to target the anterior limb of the internal capsule bilaterally. A single 4-mm isocenter was used; maximum radiation doses of 140–160 Gy were delivered. All 5 patients were preoperatively and postoperatively assessed for clinical response by using both subjective and objective metrics, including the Yale-Brown Obsessive Compulsive Scale (YBOCS); 4 of the 5 patients had postoperative radiological follow-up. The median clinical follow-up was 24 months (range 6–33 months). At the time of radiosurgery, all patients had YBOCS scores in the severe or extreme range (median 32, range 31–34). At the last follow-up, 4 (80%) of the 5 patients showed marked clinical improvement; in the remaining patient (20%), mild improvement was seen. The median YBOCS score was 13 (range 12–31) at the last follow-up. Neuroimaging studies at 6 months after GK treatment demonstrated a small area of enhancement corresponding to the site of the isocenter and some mild T2 signal changes in the internal capsule. No adverse clinical effects were noted from the radiosurgery.

Conclusions. For patients with severe OCD refractory to medications and psychiatric therapy, GK capsulotomy afforded clinical improvement. Further study of this approach seems warranted.

Key Words • radiosurgery • Gamma Knife • obsessive-compulsive disorder • functional neurosurgery • stereotactic radiosurgery

Abbreviations used in this paper: DBS = deep brain stimulation; GK = Gamma Knife; GKS = GK surgery; OCD = obsessive-compulsive disorder; SRS = stereotactic radiosurgery; SSRI = selective serotonin reuptake inhibitor; UVA = University of Virginia; YBOCS = Yale-Brown Obsessive Compulsive Scale.

This article contains some figures that are displayed in color online but in black-and-white in the print edition.
Radiotherapy for obsessive-compulsive disorder

Methods

All patients undergoing GKs at UVA are followed in a prospectively collected database approved by the institutional review board. From this database, we identified all patients who had been treated for severe OCD refractory to pharmacological and psychiatric therapy over a 3-year period from August 2009 to August 2010 and retrospectively reviewed their cases.

Patient Selection and Attributes

Gamma Knife surgery is considered in the context of a multidisciplinary evaluation (for example, psychiatry and neurosurgery) for patients with OCD. Patients with OCD were evaluated as candidates for GKs if they had severe OCD with a YBOCS score ≥ 24 and if the treating psychiatrist indicated that the patient had exhausted all reasonable nonoperative treatments. Patients were required to have pre-GKS brain MRI showing no evidence of structural abnormalities such as tumor, stroke, or vascular malformation. If there was any ambiguity on the part of the local psychiatrist about other nonsurgical options for the patient, a second opinion was obtained from a psychiatrist on staff at UVA. A patient was only considered for GKs if all psychiatrists evaluating that particular patient agreed that meaningful OCD treatment via nonoperative means had been exhausted. In addition, before the option of GKs was presented, patients had been offered the option of DBS but had refused this approach.

Radiotherapy Technique

Radiotherapy was delivered using the Gamma Knife Perfexion unit (Elekta AB). Thin-sliced (1.3 mm), volumetric T1-weighted MR images were obtained throughout the entire head, and T2-weighted images were obtained in the region of the anterior limb of the internal capsule. One 4-mm isocenter was targeted to the anterior limb of the internal capsule on each side. Using stereotactic T1- and T2-weighted MRI, we located the isocenter at the midputaminal point of the anterior limb of the capsule. The base of the isocenter (as defined by the 50% isodose line) was positioned near the ventral portion of the internal capsule. A maximum radiation dose of 140–160 Gy was delivered to each isocenter.

After a brief period of postprocedural observation, patients were discharged from the hospital on the same day as their radiotherapy.

Patient Follow-Up

After GKs, patients were assessed by their treating psychiatrist at routine intervals. Records were obtained from each patient’s local physician. Whenever possible, patients were assessed in the neurosurgical clinic at UVA and with a follow-up MRI study 6 months after GKs. If the patient was unable to return to the UVA neurosurgery clinic, he or she underwent MRI locally and had the images sent to UVA for review. The treating neurosurgeon (J.P.S.) and a neuroradiologist at UVA reviewed the MR images.

Finally, clinicians in the GK center periodically contacted patients by phone to follow their clinical progress and to assist with their care. The YBOCS scores were recorded at the last follow-up.

Results

Five patients with OCD refractory to medical and psychiatric treatment were identified and retrospectively reviewed (Table 1). Of these 5 patients, 3 were male and 2 were female. The mean age at the time of GKs was 37.8 years (range 29–49 years). The median follow-up was 24 months (range 6–33 months). At the time of radiotherapy, all patients had YBOCS scores in the severe or extreme range (median 32, range 31–34; Fig. 1). At the last follow-up, 4 (80%) of the 5 patients showed marked clinical improvement; in the remaining patient (20%), mild improvement was seen. The median YBOCS score was 13 (range 12–31) at the last follow-up. Neuroimaging studies at 6 months after GK treatment demonstrated a small area of enhancement corresponding to the site of the isocenter and some mild T2 signal changes in the internal capsule. No adverse clinical effects were noted from the radiotherapy.

Illustrative Cases

Case 1

History and Examination. This patient described her situation as “just simply awful.” She was hospitalized at the age of 17 years for extreme dysfunction and a reclusive nature. She refused to leave the house even to empty the trash. While all her friends were excited to drive a car, she was unable to drive or maintain employment. She also exhibited obsessive thoughts of cleanliness. She believed that if she did not wash her hands before handling objects, especially money, she would harm others through pathogen contamination or poisoning when those objects were handed over. Her hand-washing events reached 45 times a day with the classic presentation of dry, red, cracked, and bleeding hands. She obsessively checked doors to make sure that dogs would not attack her cat. She would also check the coffee pot and stove many times per day to confirm that the appliances were off.

She tried medical therapy including Seroquel, Zyprexa, Tranxene, Ativan, Xanax, Paxil, Zoloft, Effexor, Cymbalta, Prozac, Celexa, Geodon, clomipramine, and olanzapine. Unfortunately, these medications did not relieve her condition. Psychiatric treatment did not afford her stability, much less improvement. Her father, a physician, contacted our institution, and a second opinion was arranged with a professor of psychiatry at UVA. The second opinion confirmed that all reasonable nonoperative interventions had been tried and failed. Prior to GKs, her YBOCS score was 31 of 40.

Operation. At the age of 47 years, she underwent GKs, with bilateral anterior capsulotomies performed using a single 4-mm isocenter per side and a maximum radiation dose of 140 Gy. Figure 2A and B depict the GK dose plan. The treatment was delivered without difficulty.

Postoperative Course. Within 2 months of GKs, the
patient’s father noted, “[she’s] back.” Her behaviors dramatically improved. Hand washing decreased to 10 times a day and centered mostly on money handling. She obtained a part-time job with a construction firm. She now drives to and from work and appointments, although she admits, “I am somewhat anxious driving and feel better when others ride with me.” She is no longer concerned about poisoning. Her social life has also improved, and she is “getting more friends.”

Six months after GKS, she underwent surveillance MRI, which revealed T2-weighted changes within the anterior internal capsule and around the site of the isocenter as well as a focal ring of enhancement corresponding to the location of the isocenters (Fig. 2C–E). The T2 changes also appeared to involve the region of the nucleus accumbens. Fifteen months after GKS, she continued to improve according to her local psychiatrist and her family. Her YBOCS score at the last follow-up was 12.

Case 2

History and Examination. This patient’s OCD symptoms started at age 19 years. Initially his symptoms included excessive hand washing. He also had intrusive musical and sexual thoughts. The “music” in his head was so loud at times that it became a distraction.

His OCD became severe approximately 6 years prior to his radiosurgery. Eventually the sexual thoughts led to the termination of a romantic relationship as well as most friendships. The thoughts and compulsions eventually drove him into reclusion and disability. A psychiatrist unsuccessfully treated him with multiple pharmacotherapies, including 5 different SSRIs, antidepressants, 7 different mood stabilizers, second-generation antipsychotics, and benzodiazepines, as well as electroconvulsive therapy. Individual psychotherapy failed as well, and he was unable to tolerate cognitive behavior therapy. His preoperative YBOCS score was 34 of 40.

Operation. At age 31 years, he underwent GKS with bilateral anterior capsulotomies. He received a maximum radiation dose of 140 Gy to each side.

Postoperative Course. Six months following GKS, his YBOCS score was 13 and no adverse effects from the radiosurgery were observed. He reported that his obsessive sexual and music thoughts diminished by more than 90%. He has begun to develop new relationships. No follow-up imaging was available on this patient.

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**Table 1: Summary of patient attributes and radiosurgical parameters**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age at Time of Diagnosis (yrs)</th>
<th>Age at Time of GKS (yrs)</th>
<th>Maximum GK Dose (Gy)</th>
<th>Follow-Up (mos)</th>
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<th>Last YBOCS Score</th>
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**Fig. 1.** The YBOCS scores of the 5 patients at the time of GKS and the last follow-up. GKRS = Gamma Knife radiosurgery.
Radiosurgery for obsessive-compulsive disorder

**Case 3**

*History and Examination.* Obsessive-compulsive disorder was diagnosed in this patient when he was 17 years old. At that time, he was described as having racing thoughts, panic attacks, anxiety, and intrusive thoughts. A job and relationship had become unobtainable.

Multiple drug trials of SSRIs, tricyclic antidepressants, anxiolytics, antipsychotics, and mood stabilizers had failed in this patient. Cognitive therapy and psychotherapy also failed, and 3 “courses” of electroconvulsive therapy were of “no long-term benefit.” The treating psychiatrist indicated that the patient had exhausted all nonoperative treatments, and thus the patient was referred for GKS. His preradiosurgical YBOCS score was 33 of 40.

*Operation.* At age 44 years, the patient underwent GKS. He received a maximum radiation dose of 140 Gy delivered in a 4-mm isocenter to each anterior limb of the internal capsule.

*Postoperative Course.* Follow-up MRI performed 6 months after GKS showed radiographic changes similar to those seen in the patient in Case 1.

In the months that followed, the patient showed no appreciable change in his OCD symptoms but also no side effects attributable to the GKS. At 24 months post-radiosurgery, his YBOCS score was 31 of 40. He continued to demonstrate no appreciable improvement in his symptoms. He is unable to maintain a relationship or a job. He is currently exploring options for a clinical trial at the National Institutes of Mental Health.

**Case 4**

*History and Examination.* Obsessive-compulsive disorder was diagnosed in this patient when he was 13 years old. He experienced many of the common themes of OCD, such as a fear of contamination from germs, which affected both his professional and personal relationships. He engaged in cleaning and washing compulsions; for example, he would head to the shower immediately after work to remove germs and then clean his steps into the house where he had tracked the germs into the house. He indicated that he was washing his hands “hundreds” of times a day. He was also described as having compulsions to frequently check the stove or door lock. These symptoms and the accompanying stress led to depressive symptoms.

**Fig. 2.** Case 1. The GK dose plan depicts placement of the isocenters in the axial (A) and coronal (B) views. Each side was treated with a single 4-mm isocenter (*yellow sphere*) located in the anterior internal capsule; a maximum radiation dose of 140 Gy was applied to each isocenter. Images 6 months post-GKS: axial T2-weighted (C), postcontrast T1-weighted (D), and coronal postcontrast T1-weighted (E) MR images showing T2-weighted changes within the anterior internal capsule and around the site of the isocenter as well as a focal ring of enhancement corresponding to the location of each isocenter. The patient showed marked clinical improvement when these images were obtained.
with intermittent suicidal ideation. He reported very limited contact with peers. He followed a path similar to that of other patients, with trials of multiple medications and psychiatric therapy. Unfortunately, none of these therapies yielded success. His preoperative YBOCS score was 34 of 40.

**Operation.** At age 26 years, he underwent GKS. He was treated with bilateral anterior capsulotomies using a maximum radiation dose of 160 Gy.

**Postoperative Course.** Within 3 months of the radiosurgery, his OCD symptoms began to diminish. Magnetic resonance imaging performed 6 months after GKS showed small ring-enhancing lesions in the bilateral anterior internal capsules and mild T2-weighted changes around the region of enhancement. At the last follow-up, the hand-washing compulsions were completely eliminated. The compulsive behavior of checking the door now occurs only once in the morning while leaving and once before retiring for the night. He routinely leaves the house to participate in a regular exercise program. His social anxiety remains, but he is working with a psychologist in the more intensive therapies that were previously intolerable, such as guided imagery and meditation. He now works part-time in a parcel delivery job and part-time with his father. At 33 months post-GKS, his YBOCS score was 13. He and his local psychiatrist have noted no adverse effects from the GKS.

**Case 5**

**History and Examination.** Obsessive-compulsive disorder was diagnosed in this patient when she was 18 years old. She presented with multiple comorbidities: depression and anorexia in addition to a severe case of OCD. She has had multiple hospitalizations with suicidal “gestures” from cutting herself with a knife to overdosing on prescription medication. Multiple pharmacological agents were tried with little to no success. Intensive psychiatric therapy offered no appreciable improvement in her condition. She described herself as anxious, nervous, and “worrying all the time.” Her preradiosurgical YBOCS score was 31 of 40.

**Operation.** At 36 years of age, she underwent GKS with a maximal radiation dose of 160 Gy to each target in the anterior internal capsule.

**Postoperative Course.** Within months of radiosurgery, she was better able to cope with day to day stressors and her anxiety level decreased substantially. Follow-up brain MRI 6 months after GKS demonstrated changes similar to those seen with the preceding patients, that is, T2-weighted changes within the anterior internal capsule and a focal ring of enhancement corresponding to the location of the isocenters.

Under the guidance of her psychiatrist, her daily psychiatric medications have been reduced from 5 different ones to 3; she remains on Pristiq, Clozaril, and Klonopin. At the last follow-up 33 months after GKS, her YBOCS score was 12. She and her family have noted no adverse effects since her radiosurgery.

**Discussion**

Obsessive-compulsive disorder is a type of anxiety disorder. Its lifetime prevalence in the US is 1.6%.

Those afflicted with it have undesired and repetitious ideas, feelings, sensations, and behaviors that they feel forced to do, and ritualistic behaviors are often commonplace. Symptoms are usually exhibited by the age of 30 years. The YBOCS is the most frequently used tool to assess and track the progress of patients with OCD. The scale is subdivided based on severity of the disease: 1) subclinical OCD = 0–7; 2) mild = 8–15; 3) moderate = 16–23; 4) severe = 24–31; and 5) extreme = 32–40. First-line treatment for OCD includes psychotherapy and medications. Selective serotonin reuptake inhibitors, such as fluoxetine (Prozac) and sertraline (Zoloft), are frequently prescribed. If these drugs do not prove effective, tricyclic antidepressants, such as clomipramine, have been used. Low doses of antipsychotics and benzodiazepines can be added to the medical regimen as necessary.

While many patients improve with treatment, some demonstrate symptoms that are both refractory to medical therapy and severely debilitating. Early work by psychiatrist P. Mindus and colleagues at the Karolinska Institute explored the safety and efficacy of stereotactic capsulotomy in treating patients with severe OCD. In a cohort of 24 consecutively treated patients, Mindus and Nyman reported significant symptomatic relief in 80% of the cases. They also noted correlations between changes in brain metabolism on PET and changes in personality scores. Side effects, including a decline in executive function, were generally tolerable and slowly improved with time. Despite this promising early work in Sweden, few centers in the US embraced GKS for OCD. The stigma attached to psychosurgery remains, and partnerships between neurosurgeons and psychiatrists are not commonplace in the US.

In 2009, the US FDA approved DBS for OCD under the Humanitarian Device Exemption program. Deep brain stimulation targets for OCD have varied: nucleus accumbens, nucleus caudalis, subthalamic nucleus, ventral internal capsule/ventral striatum, and anterior internal capsule. In 25 studies including 130 patients, DBS has shown promise, with recent results demonstrating a 50% reduction in OCD scores. Stimulation-induced side effects have included hypomania in several patients, and 3 patients have suffered intracerebral hemorrhage. While DBS has the advantages of reversibility and mobilization of stimulation over time, radiosurgical lesioning also has certain advantages, which include the fact that the lesion is permanent and does not require adjustment with time. Radiosurgery also avoids the expense and morbidity (lead breakage, infection, and stroke) associated with an implant such as the deep brain stimulator. Thus, some have used GK to make lesions similar to those described early on by Mindus and Nyman.

In one report of 25 OCD patients undergoing capsulotomy, 9 underwent lesioning via the GK at doses as high as 200 Gy (Table 2). For the entire cohort, the mean preoperative YBOCS score was 34, and it improved to 18 at the last follow-up. Ten patients experienced various...
degrees of adverse events including apathy, decline in executive function, and disinhibition. In another case series, Kondziolka et al. noted significant functional improvement and a reduction in OCD behavior in 3 patients. In that same study, no adverse effects from the GK capsulotomy were noted.

The precise volume appropriate for a GK capsulotomy remains the subject of debate. In the original study by the Karolinska Institute group, single-isocenter lesioning in each capsule was generally performed. A double-isocenter lesion has been proposed by the group at Brown University (G. Noren, paper presented at the 2002 annual meeting of the American Association of Neurological Surgeons, http://www.aans.org/Media/Article.aspx?ArticleId=12171). After using this approach, this group observed a clinical improvement of at least 35% in the YBOCS score in at least 59% of patients 1 year and in 69% of patients 2 years after radiosurgery. Kondziolka et al. also used a double-isocenter lesioning technique. Lopes et al. demonstrated clinical improvement in 3 of 5 patients treated with GK capsulotomy using a double-isocenter technique.

In our series, we used the single-isocenter technique and performed bilateral lesioning. Our choice of a single isocenter was based in part on personal experiences described by Dr. Ladislau Steiner (L. Steiner, personal communications, 2007). We began with a lower dose of 140 Gy given our concerns for possible side effects with such a high dose relative to the doses commonly used for brain tumors, arteriovenous malformations, and even trigeminal neuralgia. However, we have since adopted a dose of 160 Gy with the single-isocenter approach to produce a sufficient lesioning effect despite some ambiguity to the optimal target. Although our technique warrants further study, perhaps the position of the isocenter inferior enough to produce a lesioning effect in the nucleus accumbens is, in fact, critical to achieving a beneficial effect for patients with OCD. The therapeutic value in lesioning the superior portion of the capsule seems less certain. With maximum doses of 140–180 Gy, it is important to note that the T2-weighted signal changes seen on postoperative MRI extend beyond the 4-mm planned treatment volume (Fig. 2C).

The current study showed appreciable clinical improvement in 80% of the patients treated. No side effects were noted, albeit ours was a small group of patients with limited follow-up. This group had refused DBS, underscoring the fact that some patients do not find this approach as appealing as a GK capsulotomy. Although our results seem promising, the approach warrants further study. We acknowledge that this study is limited by a small number of patients and a uniform but rigorous selection process. The study lacks sufficient statistical power or a control arm to compare this approach with either medical therapy or DBS. Nevertheless, a larger study with a longer follow-up does seem warranted. In particular, future studies must help to better define the radiosurgical technique (that is, the target and volume) and the criteria for patient selection.

Conclusions

The management of patients with severe OCD is challenging. Medications and other nonoperative thera-
pies prove inadequate for some patients. In those with severe OCD refractory to polypharmacy regimens and psychiatric therapy, neurosurgical intervention may be warranted. Select patients with severe OCD appear to benefit from GKS capsulotomy. This promising approach warrants further study.

Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Sheehan. Acquisition of data: Sheehan, Patterson, Schlesinger. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Sheehan.

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