Results Following Gamma Knife Radiosurgical Anterior Capsulotomies for Obsessive Compulsive Disorder

BACKGROUND: Obsessive compulsive disorder (OCD), in its severe form, can cause tremendous disability for affected patients. 

OBJECTIVE: To evaluate the results following bilateral radiosurgical anterior capsulotomy for severe medically refractory OCD.

METHODS: We performed gamma knife anterior capsulotomy (GKAC) on 3 patients with extreme, medically intractable OCD. According to our protocol, all patients were evaluated by at least 2 psychiatrists who recommended surgery. The patient had to request the procedure, and had to have severe OCD according to the Yale-Brown Obsessive Compulsive Scale (YBOCS). Patient ages were 37, 55, and 40 years, and pre-radiosurgery YBOCS scores were 34/40, 39/40, and 39/40. Bilateral lesions were created with 2 4-mm isocenters to create an oval volume in the ventral internal capsule at the putaminal midpoint. A maximum dose of 140 or 150 Gy was used.

RESULTS: There was no morbidity after the procedure, and all patients returned immediately to baseline function. All patients noted significant functional improvements, and reduction in OCD behavior. Follow-up was at 55, 42, and 28 months. The first patient reduced her YBOCS score from 34 to 24. One patient with compulsive skin picking and an open wound had later healing of the chronic wound and a reduction in the YBOCS score from 39 to 8. At 28 months, the third patient is living and working independently, and her YBOCS score is 18.

CONCLUSION: Within a strict protocol, gamma knife radiosurgery provided improvement of OCD behavior with no adverse effects. This technique should be evaluated further in patients with severe and disabling behavioral disorders.

KEY WORDS: Capsulotomy, Obsessive compulsive disorder, Radiosurgery
biological effect of radiosurgery is permanent and not adjustable. DBS recently was approved for use in OCD by the United States Food and Drug Administration (FDA). With DBS, pulse generators must be replaced, and there is a risk of failure with sudden behavioral decline. Radiosurgery, on the other hand, is always “on.” The benefit of DBS or radiosurgery over the long term and in large numbers of patients is not known; therefore, one can only speculate as to which procedure may be optimal. DBS is more costly, and requires complex programming of the device tailored to improve the behavioral disability, whereas radiosurgery requires no such programming. In this report, we describe the indications for and results of bilateral radiosurgical anterior capsulotomies for patients with OCD.

Clinical Material and Methods

This report was approved by the University of Pittsburgh Institutional Review Board. GKAC was recommended in all patients by 2 independent psychiatrists who closely evaluated the patients. The patient had to request surgery on his or her own and had to understand the alternatives and risks of the procedure after meeting with a neurosurgeon and radiation oncologist. The Yale-Brown Obsessive Compulsive Score (YBOCS) had to be at the severe or extreme level (0-7 = subclinical OCD; 8-15 = mild; 16-23 = moderate; 24-31 = severe; 32-40 = extreme.) Scores were stable over the months before radiosurgery. Finally, the patient had to have a normal MRI scan of the brain. GKAC was performed using 2 4-mm isocenters targeted to the anterior limb of the internal capsule at the mid-putaminal point along the length of the capsule, using stereotactic MRI. The isocenters were spaced in a superior-inferior configuration to create an oval plan where the base was at the ventral portion of the capsule. A maximum dose of 140 or 150 Gy was delivered to an average target volume of 48 mm$^3$. The patient was discharged from the hospital the same day.

RESULTS

Case 1

The first patient was a 37-year-old woman who had had OCD since the age of 12, and had a history of approximately 40 hospitalizations, 5 of them in state facilities. She left school at the age of 13, obsessed with her academic performance but unable to perform. Cleanliness and hygiene-related activities took hours, and it was common for her to awaken at 2:00 AM to prepare for school. In the year before surgery, she had not left her house. Medications included chlomipramine, fluvoxamine, ziprasidone, and clonazepam. Obsessions included contamination, religious thoughts, and symmetry. Compulsive behavior included cleaning, checking, counting, and arranging. She had prior suicidal and cutting behaviors. Her YBOCS score before radiosurgery was 34. The time from the first neurosurgical assessment to the procedure was 5 months. After 140-Gy GKAC, MR imaging at 6 months showed regions of contrast enhancement and signal change at the target volume. The dose plan is shown in Figure 1.

At 30 months follow-up, time required for bathing and hair care had been reduced from 4 to 2 hours. The patient had thrown away things that she had kept since the age of 18. She was now leaving the house to go shopping and to keep appointments and was staying up for longer periods of time. She had left the house to visit friends, began dating, and attended classes at a local college. Cutting behavior and suicidal thoughts have stopped, and there have been no further hospitalizations. She remains on chlomipramine, fluvoxamine, lithium, and clonazepam. Her YBOCS score at 55 months was 24. She describes her life now as “stabilized.” Figure 2 shows a segment of a letter she provided at last follow-up.
Case 2

The second patient was a 55-year-old engineer who underwent GKAC for compulsive skin picking related to OCD. He had undergone high-dose medical therapy and behavioral therapy, had sustained 4 skin grafts and multiple blood transfusions, and had used scissors and other instruments to cut and gouge his skin. The entire anterior neck had been grafted, and he was brought to our care with severe skin picking of a large proportion of his upper back. Prior to his request for the procedure, a second psychiatric assessment requested a 12-week trial of high-dose chlorimipramine and olanzapine. The time elapsed from the first neurosurgical test to the procedure was 14 months. His YBOCS score was 39 out of 40. Gamma knife radiosurgery was performed as for Case 1 using a maximum dose of 140 Gy. Figure 3 shows his MRI results.

At 3 months, his wife noted that her husband was much more agreeable and appreciative, was sitting down with the family for meals, and was much less argumentative regarding his care. He was no longer apathetic, but had become more interactive. By 7 months, medications seemed to work better. He was driving his daughter to school and was interested in family activities at home, with lessening of ritualistic behavior. His YBOCS score had been reduced to 32, and by 17 months it had fallen to 8. Neuro-psychological testing performed at 14 months and compared to his pre-radiosurgery baseline showed that he was performing at or above his baseline level, especially in psychomotor speed. He had normal frontal lobe performance, although behaviorally he showed some impulsivity and perseveration. At 18 months, his wound had healed, and by 30 months, the area had been grafted. The YBOCS scores at 30 and 42 months were 4 and 7. At approximately 36 months, because he felt well and wanted to reduce fatigue, he secretly stopped taking fluvoxamine and reduced his quetiapine. This was associated with return to picking of a small area behind his right ear, above the prior site. His symptoms improved after medication was reinstituted. In a separate report, we show images of his wound healing.8

Case 3

The third patient was a 39-year-old woman with OCD behavior beginning at the age of 6. She had had numerous hospitalizations at centers across the country. Her obsessions included cleanliness, straightening, and bad luck or scary thoughts, and included thoughts such as “is my life real.” Compulsions included writing, counting, avoidance, grooming, and other rituals. Her medication therapy included fluvoxamine, quetiapine, escitalopram, and lorazepam. Her YBOCS score was 39. GKAC was performed to a maximum dose of 150 Gy. At 28 months follow-up her YBOCS score had been reduced to 18. She had been living and working independently since month 4 after the procedure. She described her OCD as “manageable,” and stated that it caused significantly less interference in her daily life. She remains on lorazepam (2 mg/day), quetiapine (200 mg/day), fluvoxamine (300 mg/day), and pregabalin (150 mg/day). There were no adverse effects from the procedure. Line plots of the OCD scores for all three patients are shown in Figure 4.

DISCUSSION

Imaging studies in obsessive compulsive disorder note hypermetabolic changes in the orbital frontal cortex, the anterior cingulate region, the caudate nucleus, and the thalamus. Current studies support models of cortico-striato-thalamo-cortical dysfunction, providing a basis for modulation or effects on this circuitry.6 The ventral anterior internal capsule should be an appropriate target for such modulation.

The utility of radiosurgery in the anterior limb of the internal capsule has been described in older studies from the Karolinska Institut showing target effects, but without details on clinical outcomes.9-11 A recent report on 25 patients who underwent capsulotomy with either gamma knife radiosurgery (n = 9), bilateral radiofrequency lesioning (n = 12), or unilateral radiofrequency lesioning (n = 4) was published in 2008.12 The mean YBOCS score was 34 before surgery and 18 at long-term follow-up, and response rates did not differ between surgical methods. However, 10 patients had adverse events (eg, apathy, disinhibition, or problems in executive functioning) and in some these were attributed to large lesion volumes. Six of these 10 patients received high radiation doses (200 Gy with 3 isocenters) or underwent multiple surgeries.

Studies at Brown University showed efficacy using conservative response criteria, achieving a 35% reduction in the YBOCS score in approximately half of patients with intractable OCD. The gamma knife radiosurgery procedure was well tolerated. The initial results using single isocenter lesions were not successful, and thus a larger oval-shaped radiosurgical volume with two 4-mm isocenters was recommended.1 A recent report from Lopes et al3 used this technique in 5 patients (maximum dose, 180 Gy), with 3 of those patients meeting response criteria 3 years later. The mean YBOCS score dropped from 32.2 to 20.2. Adverse events appeared to be minor and included short-term headache, light-headedness, weight changes, and episodic nausea. The oval shape of this radiosurgical volume may mimic the stimulation volume with a DBS electrode. Typically, the radiosurgery effect develops over several months, and tissue necrosis at the target

FIGURE 2. Portion of a letter from Patient 1 55 months after radiosurgery.
should occur by 2 to 4 months. All of our patients began to describe or exhibit improved behavior by 2 months after radiosurgery. The percentage response in our 3 patients was 24%, 90%, and 54% with follow-up greater than 2 years in all (Table).

Recently, the FDA approved bilateral anterior internal capsule DBS for the management of OCD. Although there may be benefits to placement of DBS systems, including reversibility and adjustability, there have been reports of significant problems associated with battery failure, since current use typically is high. Ideally, a procedure that would be long-lasting and not reliant on the function of implanted hardware might be a better solution. The comparative costs of DBS or radiosurgery should be studied as well. With the creation of a lesion either by radiosurgical or radiofrequency technique, the effect is permanent, but is not adjustable. The success rate of lesioning has not been studied in large numbers of patients. However, for a patient with compulsive skin picking, the placement of DBS electrodes, cables, and pulse generators was contraindicated. There have been no clinical studies that compare the safety and efficacy of DBS to radiosurgery. Our radiosurgery target was slightly more superior and more anterior than the ventral striatum DBS target. It is not known whether radiosurgery at the junction of the anterior commissure and the internal capsule would be even more efficacious.

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*OCD, obsessive compulsive disorder; YBOCS, Yale-Brown Obsessive Compulsive Scale.
Our patient with compulsive skin picking represented an unusual manifestation of OCD not suitable for DBS. Pathological skin picking is classified as an Impulse Control Disorder Not Otherwise Specified in the current edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). It is a repetitive, body-focused disorder that can have considerable overlap and show features of other psychiatric illnesses, such as obsessive compulsive disorder, body dysmorphic disorder, and trichotillomania.\textsuperscript{14-19} The medical morbidity of this condition can be significant, with such complications as scarring and dermatologic infections. Management of patients with severe skin picking or self-mutilation typically includes medical therapy consistent with OCD-related illness such as medications and behavioral therapy.\textsuperscript{16,20} In rare instances, intractable OCD may be treated with surgery such as limbic leucotomy.\textsuperscript{21} Skin picking is not covered under the recent humanitarian device exemption given by the FDA for ventral striatum DBS, which is not surprising, given that wound healing could be a major problem.

OCD remains a challenging behavioral disorder that can be refractory to multimodal pharmacologic and other psychiatric therapies. Continued use of medications is imperative, and symptoms may worsen if medications are terminated or reduced without proper psychiatric supervision. It is not known whether improvement is related to a synergistic effect of medication and surgery, or to surgery alone, although we suspect the latter, because patients’ conditions had been medication refractory. Our study is limited by small sample size, and by the diversity of OCD within our group. Detailed neurocognitive testing was conducted in only 1 of the 3 patients. It would be very useful to obtain such testing in all patients following this procedure. Nevertheless, we found that radiosurgical anterior capsulotomies can provide benefit in patients with extreme obsessive compulsive disorder. Such benefits lead to improvement in social and thought behaviors as well as in physical manifestations of the disease. No adverse events were identified in this small series. Appropriate patients should be selected cautiously and judiciously according to set criteria. Studies that directly compare DBS to stereotactic radiosurgery are warranted.

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

REFERENCES

COMMENTS
The authors describe the outcome of bilateral gamma knife anterior capsulotomy (GKAC) on 3 patients with extreme, treatment-refractory OCD, as measured by YBOCS scores pre- and post-treatment. The study design was a retrospective, unblinded case series. Follow-up in these patients ranged from 28 to 55 months. No adverse effects were noted, and all patients improved on YBOCS (24-90%) to a degree not seen with medical or cognitive therapy in this difficult patient population. This is a timely study, given the recent US Food and Drug Administration approval for deep brain stimulation of the ventral capsule/ventral striatum (VC/VS) in the treatment of OCD, on a humanitarian device exemption basis (HDE# H050003; February 2009). The authors’ description of their technique for GKAC is clear and nicely detailed.

The treatment of OCD with gamma knife capsulotomy is not novel, as the authors point out in their discussion. Furthermore, the authors have previously reported preliminary results for 1 of the 3 patients described in the current study. Kondziolka et al point out that their study was notable for the lack of adverse effects compared to other studies, and ascribe this finding to the lower radiation dose they used. However, the assertion that there was no morbidity following the procedure must be tempered with the observation that detailed neuropsychological testing...
was performed in only 1 patient. The authors correctly point out that their study is limited by the “small sample size and diversity of OCD” represented.

It must be emphasized that skin picking may represent a very different pathophysiology from OCD. Although there is overlap, many people with skin picking do not have OCD. It is worth reiterating the authors’ point that skin picking is not covered by the recent humanitarian device exemption accorded to VC/VS DBS for the treatment of OCD.

No head-to-head comparison between VC/VS DBS and GKAC has yet been performed, and for neither of these therapies has the optimal location or patient subpopulation been confirmed.

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This is a fascinating paper. Previous reports of gamma knife radiosurgery for this disease were disappointing. Of special concern was a rather unpredictable lesion size. Kondziolka and colleagues report a new technique, using 2-4 mm collimator shots, designed to mimic the shape of a radiofrequency lesion. All 3 patients in this report were completely disabled by OCD preoperatively and experienced very well documented, objective improvements postoperatively. Deep brain stimulation is the current rage for OCD, but battery changes, thus far, appear to be needed much more frequently than previously experienced with motor disorder treatment—The therapeutic effect appears to require much more current (a bigger area of stimulation). If further studies of radiosurgical lesioning compare well with DBS, it could become the favored treatment.

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The International Bureau of Weights and is an international standards organization, one of three such organizations established to maintain the International System of Units (SI) under the terms of the Metre Convention (Convention du Mètre). The organization is usually referred to by its French initials, BIPM. The BIPM was created on May 20, 1875, following the signing of the Metre Convention, a treaty among 51 nations. Under the authority of the Metric Convention, the BIPM helps to ensure uniformity of SI weights and measures around the world. It does so through a series of consultative committees, whose members are the national metrology laboratories of the Convention’s member states, and through its own laboratory work.