Epilepsy and radiosurgery

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Usami and colleagues4 from the University of Tokyo provide data on 7 patients who underwent Gamma Knife surgery (GKS) for mesial temporal lobe epilepsy (MTLE) between 1996 and 1999. Five of the 7 patients received a maximum radiosurgery dose of 50 Gy, which led to significant reduction in seizures in all 4 patients who underwent follow-up. However, 2 had signs of adverse radiation effects, and resection was later performed 5 and 10 years later. The authors caution, “…the risk of [symptomatic radiation necrosis] should be considered when the clinical significance of this treatment is evaluated.”

Currently, there is interest in epilepsy radiosurgery as an alternative to microsurgical resection for MTLE. A multicenter randomized trial, in which I am a participating investigator, comparing radiosurgery with resection is being performed under the leadership of Drs. Nicholas Barbaro and Mark Quigg.

First, it is interesting that these cases were even performed by Usami and colleagues in the way in which they were. Epilepsy radiosurgery was still being performed in animal models in the 1990s and even into the early part of the past decade.2,3 Results on the biology of these radiosurgical effects were still coming out prior to the first National Institutes of Health–sponsored trial in the US, which was completed just a few years ago.1 As the authors describe, radiation injury is related to numerous factors, of which dose and volume (in addition to location and other patient characteristics) are paramount. To summarize, the patients underwent early generation dose planning using the Kula system for which image integration was not possible and had rather excessive target volumes, and large collimators (18 mm) were used. Dose planning without image integration (the isodose lines were not directly shown on a brain image) was performed in Cases 1–4 and with image integration in Cases 5–7. It is important to note that in the National Institutes of Health–sponsored trial,7 all centers had to create a target volume between 5.5 and 7.5 cm³. The target volumes in this experience in Cases 3, 4, and 5 were 12, 7.8, and 8.3 ml, respectively.

Within the protocol of the ongoing Radiosurgery or Open Surgery for Epilepsy (ROSE) trial, dose planning is challenging even with sophisticated software. Multiple iso-

Disclosure

Dr. Kondziolka is a consultant for Elekta.

References

Response

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We appreciate the comments by Dr. Kondziolka, which may help clarify some points related to our paper. Our study addresses a long-term effect, particularly focusing on the associated complications, with our preliminary radiosurgical protocol for MTLE, which had started more than 10 years ago. When we initially designed our clinical study, available information about stereotactic radiosurgery (SRS) for MTLE was quite limited. Thus, we decided to deliver a relatively low radiosurgical dose to the possibly affected areas, which eventually turned out to be safe but not effective. Those patients underwent anterior temporal lobectomy later, and the pathological evaluation revealed subtle histological change with small necrotic focus only in 1 patient. Based on these experiences, we revised our protocol and adopted a higher radiosurgical dose to more extensive areas, which turned out to be effective in most of the patients but was simultaneously associated with serious radiation-induced complications over a long period of time. In the patient in Case 4 (Fig. 3 of our paper), Dr. Kondziolka asked us to explain the diagnosis of “cavernous malformation.” Nowadays, MRI offers the most sensitive means of suspecting a diagnosis of cavernous malformation. In Fig. 3, MRI revealed a smoothly circumscribed, well-delineated complex lesion with a low signal intensity hemosiderin rim, which is a typical radiographic finding of cavernous malformation. Also, the eventual pathological specimen showed histological evidence of fragments of cavernous malformation.

What we learned from our experience is that high-dose radiosurgery can be a double-edged sword for patients with MTLE. Its efficacy largely depends on the irradiated dose and volume, but, on the other hand, the same factors (and probably homogeneity in dose distribution too) may also be associated with the risk of long-term radiation-induced complications in turn. To achieve the ideal goals, that is, sufficient seizure control with an acceptable risk of complications, the equilibrium points concerning the dose, volume, and dose distribution, are not easy to determine. As Dr. Kondziolka indicates, thanks to the recent technological progress, accuracy of SRS has greatly improved not only in terms of dose planning and its assessment but also irradiation technology itself. In combination with accumulated knowledge about “success” and “failure” of MTLE radiosurgery in the last decade,1–4 it seems that the protocol of the ongoing ROSE trial is quite reasonable using a relatively high dose with homogeneous dose distribution delivered to the restricted areas responsible for the pathology. Now, we are looking forward to the final results of this study with the state-of-the-art radiosurgical technology.

It is evident that there is a big gap between the radiosurgical technique applied more than 10 years ago in this study and the one in 2012. Therefore, the results of SRS for MTLE will be quite different from our study. However, even if the outcome of SRS for MTLE is equivalent to that of resection, we think that resection will continue to be a first choice of treatment for patients with MTLE. In the patients with medically intractable MTLE, delay of achievement in seizure control sometimes can be fatal. While the quality of life in patients with MTLE is threatened by those seizure attacks itself, furthermore, gnawing apprehension about unanticipated complex partial seizure in the daily life also restricts their activities and significantly continues to affect their quality of life. Therefore, early symptom remission is one of the highest priorities in the treatment. In this light, resection is the most ideal option, which can achieve immediate seizure freedom with an acceptable risk of craniotomy. It is true that the associated risks of SRS for MTLE in short-term periods seem to be quite minimal, but they may well be cumulative and can be significant during the long-term follow-up periods. In general clinical cases (that is, in patients with arteriovenous malformation with lower Spetzler-Martin grades, benign tumor, or trigeminal neuralgia), when differences of treatment-related complications between surgery and SRS are discussed, we usually explain to patients that resection has an immediate but single-phase risk, and SRS has a long-lasting and undetermined risk. If the single-phase risk is acceptably small for each patient, it will be preferable to the vague risk with an unknown end point.

Stereotactic radiosurgery is a “new hope” for patients suffering MTLE. However, as long-term outcomes remain unclear, continual follow-up for elucidation of decisive therapeutic results is inevitable, even after complete seizure remission has been achieved. From the standpoint of sufficient long-term outcomes, a long journey remains ahead. We hope that SRS can be a “chosen one” that will bring balance to the treatment of MTLE in future.

References


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