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Radiobiological Assessment of Pain Relief and Sensory Dysfunctions Outcomes Following CyberKnife Treatment for Trigeminal Neuralgia: An International Multicenter Retrospective Study

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Abstract

Objectives: Evaluate the effectiveness of CyberKnife radiosurgery (CKRS) in the management of TN, examine the variability in treatment delivery times, and explore the relationship between delivery time, and clinical outcomes.

Methods: Demographic, clinical and treatment data of patients who underwent CKRS for TN were retrospectively reviewed. Treatment duration and planning parameters were extracted from xml files stored by the system after each procedure. For each case, time-resolved dose and dose-rate distributions were computed on a beam-by-beam basis for every voxel within the target using a raytracing dose calculation algorithm. Biological effective dose (BED) distributions accounting for sublethal repair were calculated using an a/b ratio of 2.47 Gy. Follow-up data were obtained from medical records and supplemented with telephone interviews. Pain intensity and sensory dysfunction were assessed using the modified Barrow Neurological Institute (BNI) Pain Scale and the BNI Facial Numbness Scale, respectively. Recurrence was defined as a bothering and prolonged worsening of pain relative to the maximum level of response. Analyzed variables included target volume, prescription dose and isodose line, beam-on-time (BOT), treatment duration, target dose and BED metrics, integral dose (ID) and integral BED (IBED) to the target, pain relief latency, pain score, and facial numbness at the last follow-up.

Results: A total of 608 patients were included (median age 68 years, range: 25–100); 59% were female. TN was right sided in 56%. Prior to CKRS, 89% presented with BNI grade IV-V pain; 87% reported no facial numbness, 12% mild non-bothersome numbness, and 1% bothersome numbness. Treatments were delivered using CyberKnife systems operating at 800 or 1000 MU/min. Median target volume was 25 mm^3 (range: 4–125), with a marginal dose of 60 Gy (range: 50–72), and median maximum dose of 75 Gy (range: 52–90); median ID was 1.7 mJ (range: 0.2–8.1). All treatment plans used the 5-mm fixed collimator. A median of 117 beams (range: 72–267) delivered 22,868 MUs (range: 13,950–40,219), with a median BOT of 26 min (range: 14-54) and treatment time of 44 min (median, range: 27–114). Median maximum and mean BED to the target were 1,610 Gy2.47 (range: 1,024–2,214) and 1,318 Gy2.47 (range: 609–1,832), respectively; median IBED was 33 mJ2.47 (range: 4–152). Over a median follow-up time of 48 months (range: 3–175), initial pain relief (BNI I–IIIa) was achieved in 91% of patients, after a median latency of 12 weeks (range: 0–76). At the last follow-up, overall pain control was maintained in 71% of patients, with a median time to recurrence of 34 months (range: 1–163). Onset of grade III-IV BNI facial numbness occurred in 8% of patients. Univariate Cox proportional hazards analysis showed that pain relief duration correlated with target volume, prescription isodose line, maximum dose, ID, BOT, IBED, vessel contact, and pain relief latency. Probit univariate analysis indicated that onset of grade IV BNI facial numbness was associated with lower prescription isodose, larger target volume, higher ID and IBED, and pain relief latency < 4 weeks.

Conclusion(s): CKRS is a safe and effective treatment option for TN, achieving initial pain relief in over 90% of patients with a median onset of 12 weeks. The median time to pain recurrence was 34 months. Besides

clinical and treatment planning parameters, the clinical outcome and the toxicity profile were associated with factors related to treatment delivery duration.