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Radiobiological Evaluation of Pain Relief and Sensory Dysfunctions in CyberKnife Trigeminal Neuralgia Applications: Preliminary Results from an International Multicentric Retrospective Study

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Published 03/05/2025

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Categories: Medical Physics, Radiation Oncology
Keywords: cyberknife, trigeminal neuralgia

How to cite this abstract
Pantelis E, Moutsatsos A, STERGIOULA A, et al. (March 05, 2025) Radiobiological Evaluation of Pain Relief and Sensory Dysfunctions in CyberKnife Trigeminal Neuralgia Applications: Preliminary Results from an International Multicentric Retrospective Study. Cureus 17(3): a1481

Abstract

Objectives:

Stereotactic radiosurgery (SRS) is an effective treatment of trigeminal neuralgia (TN). Factors associated with a higher probability of pain relief include no prior surgery, SRS within 3 years of pain onset. A higher incidence of facial numbness is associated with targeting the root entry zone and using maximum doses higher than 90 Gy. In Gamma Knife radiosurgery the time required to deliver the SRS treatment has been found to affect local control and toxicity profile. In this study we aimed to quantify the range of treatment delivery times in CyberKnife (CK) radiosurgery (CKRS) for TN and investigate its impact on pain relief and development of new facial numbness.

Methods:

Demographic, clinical and treatment details of patients who underwent CKRS for TN were exported from the CK database and reviewed retrospectively. The duration of treatment delivery and treatment planning details were extracted from the xml treatment files stored by the system at the end of each patient's treatment. For each TN case, time-resolved dose and dose-rate distributions were derived on a beam-by-beam basis for every voxel within the target and brainstem using a raytracing-based dose calculation algorithm developed in-house [1]. Biological effective dose (BED) distributions accounting for sublethal repair effects (BEDSRE), were calculated using the Millan and Canney formula [2], as revised by Pop et al [3] and employing an a/b ratio of 2.47 Gy. Patient follow-up data were collected from medical records available at each clinic and supplemented by telephone interviews. Pain intensity was assessed using the Barrow Neurological Institute Pain Scale, while facial numbness was evaluated using the BNI Numbness Scale. Recurrence was defined as any worsening of pain from the maximum level of response. The variables examined included target volume, prescription dose, maximum, minimum, average and integral doses to the target, maximum, minimum, average and integral BEDSRE to the target, pain score, and facial numbness at the last follow-up.

Results:

This study aims to include over 400 patients. The results from an interim statistical analysis of 130 patients with complete treatment and follow-up data are presented in Table 1. The median age of the analyzed cohort is 66 years (range: 31 – 85). Fifty-four percent (54%) of the patients are male, while 46% are female. Fifty-five percent (55%) of the patients had right trigeminal neuralgia, and 45% left trigeminal neuralgia. Pain intensity was scored as grade IV and V in 83% of the cases, and IIIb in 17%, according to the BNI pain scoring system. Prior to CKRS, 88% of the patients had no facial numbness, whereas 12% experienced mild non-bothersome numbness. Treatment was applied using a variety of CK systems equipped with linear

accelerators (LINACs) that had output rates of 800 Monitor Unit (MU) per min and 1000 MU/min. The median delineated nerve volume was 39 mm3 (range: 12 – 125). A median dose of 60 Gy (range: 50 – 60) was prescribed at the periphery of the delineated target volume. The median maximum and minimum dose values were 75 Gy (range: 63 – 86) and 56 Gy (range: 50 – 58), respectively. The median integral dose was found to be 2.6 mJ (range: 0.8 - 14.6). All treatment plans used a 5 mm fixed cone. The “Full path” was used in 46% of the cases, whereas the rest 54% employed the “trigeminal_path”. Treatment planning was performed using the Ray Tracing dose calculation algorithm in all cases. A total of 135 beams (median; range: 56 - 267) were used, resulting in a median total MUs of 22,120 (range: 13,950 - 40,219) and a median treatment delivery time of 43 min (range: 28 - 80). The median maximum and minimum BEDSER values to the target were 1,725 Gy (range: 1,129 - 2,113) and 939 Gy (range: 796 – 1,031), respectively. With a median follow-up of 38 months (range: 2 - 120), pain relief classified as grade I to III on the BNI scoring system was achieved in 97 patients (74%). Onset of facial numbness occurred in 10 cases (8%). Despite the wide range of treatment delivery times and BEDSRE values, no statistically significant correlation between clinical outcomes and BEDSRE was found, probably due to the small size of the cohort in this interim analysis.

Conclusion(s):

The probability of pain control in the analyzed patient cohort was consistent with findings from the literature. Treatment delivery times varied significantly among the different plans, ranging from approximately 0.5 h to nearly 1.5 h for the same physical dose of 60 Gy. This variation correspondingly affected the BEDSRE delivered to the target by a factor of 2. The small size of the analyzed cohort limited the ability to correlate BEDSRE with clinical outcomes.

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