



## Influencing Factors on Hard-to-Treat Trigeminal Neuralgia Treated with Multiple Gamma Knife

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**Objectives:** Trigeminal neuralgia (TN) is a well-known facial pain disease that has been shown to have difficult control with high recurrence rates after medication, surgical decompression (MVD) and ablation. Gamma Knife Radiosurgery (GKRS) is a treatment modality where a focused high-dose radiation is delivered to the trigeminal nerve. It has become the best treatment alternative after MVD for uncontrollable pain and the main option after failure or recurrence. It has a response rate of 76-92%, with a durability that can reach 4.9 years, with recurrence rate of 30 to 40%. We present the result of a 24-years' experience with repeated GKRS for hard-to-treat TN.

**Methods:** A single-institution retrospective analysis, from 1998 to 2023, of TN cases treated with GKRS and their need for re-treatments for pain control. Indications for re-treatment were uncontrolled pain; controlled pain with medication but intolerable side-effects; recurrence after initial response; no pain improvement after treatment; patient choice of GKRS over other treatment modalities. All patients were evaluated on BNI pain scale prior and after each treatment, pain characterization between typical and atypical, evaluation of TN type, time interval between treatments, prescription dose and reported side-effects. Cohen's Kappa, Pearson and point bi-serial correlation were used to analyzed anatomical and dose impact on re-treatment.

**Results:** Of the 206 patients treated with GKRS, 51 (24.8%) needed additional GKRS, of those, 8 (15.7%) needed 3 treatments for pain control. No patients were treated more than 3 times. Of the retreated patients, 20 were Type II, 10 related to MS and the others, to tumor compression. One patient with MS and 1 with tumor compression needed 3 GKRS. Only 2 patients initially presented with atypical pain but 7 changed into atypical after the first GKRS and 8 after the second. No patients presented this change after the third procedure. The time interval between the first and second treatment had a median of 3 years and between the second and third of 6 years. After the first and second treatment, BNI improved from a median of 4 to 3b. After the third, it improved from 4 to 2. Initial BNI had poor correlation with number of treatments required ( $rpb=.12$ ,  $p=0.08$ ). The median doses to the nerve were 72Gy, 66.5Gy and 70Gy respectively. No adverse radiation effects were reported. Nerve visualization had poor negative correlation with the need for a 2nd and 3rd re-treatments ( $K=-.12$ ,  $p=0.26$  and  $K=-.1$ ,  $p=0.3$  respectively). Sub-visualization of the nerve had poor positive correlation with the need to re-treat ( $K=.18$ ,  $p=0.08$ ) and no impact on the number of re-treatments ( $rpb=-.2$ ). Mean variation of the nerve length between treatments was 10mm and had no correlation with the need for a 3rd treatment ( $rpb=.02$ ). Mean dose to REZ was 13.5Gy with no impact on re-treatment or number of treatments



( $r_{pb} = -.02$  and  $r = -.02$  respectively) but it did lead to improvement of the BNI ( $r = .39$ ,  $p = 0.006$ ). . No adverse radiation effects were observed in this cohort.

**Conclusion(s):** GKRS has been used for TN since its development and has had its use increased as a primary or secondary procedure option for uncontrolled pain. We report a 24-year experience of a single high-volume center that shows the visibility, efficiency, and safety of repeating GKRS for hard-to-treat TN. Nerve's visibility, length change after first treatment and REZ dose showed no impact on the need for or quantity of re-treatments. Dose to REZ lead to improvement of BNI without increase of adverse radiation effect to the brain stem, which can influence on the isocenter placement. Although not reviewed in this study, based on our finding of dose impact on BNI improvement, the correction for BED is expected to improve outcomes.

