

## PS-1. GPI Stimulation Induced Gait Disturbance Mimicking Parkinsonism

**Eeu Young Kim, Uhn Lee**

*Department of Neurosurgery, Gachon University Gil Hospital, Gachon University College of Medicine, Incheon, Korea*

**Objective:** Authors are going to present patients with gait disturbance after GPI DBS, to investigate the mechanism of gait disturbance induced by stimulation of GPi and to discuss the management.

**Methods:** present 2 cases

Case 1. 73 year-old male patient diagnosed with generalized dystonia

Case 2. 63 year-old female patient diagnosed with generalized dystonia

**Conclusion:** GPi DBS may induce hypokinetic gait disturbance. It tends to be correlated to high voltage amplitude. When it occurs, the optimization of stimulator could improve the gait disturbance.

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## PS-2. Adult Patients with Congenital Muscular Torticollis Treated with Bipolar Release: Report of 31 Cases

부산가톨릭의료원 메리놀병원 신경외과

**이건상, 이명기, 김우재, 총배기, 김정호, 김호상, 김윤석**

**Objective:** We assessed the surgical results of bipolar release in 31 adult patients with neglected congenital muscular torticollis (CMT) and more than 12 months of follow-up.

**Methods:** Thirty-one patients underwent a bipolar release of the sternocleidomastoid muscle (SCM) and were retrospectively analyzed. The mean follow-up period was 14.9 months (range, 12–30). The mean age at time of surgery was 30.3 years (range, 20–54). Patients were evaluated with a modified Lee's scoring system, cervicomandibular angle (CMA) measurement, and a global satisfaction rating scale using patient self-reporting.

**Results:** The modified Lee's scoring system indicated excellent results in 4 (12.9%) patients, good in 18 (58.1%), and fair in 9 (29.0%) at the last follow-up after surgery. The improvements in neck movement and head tilt were statistically significant ( $p < 0.05$ ). The preoperative mean CMA was  $15.4^\circ$  (range, 5.4–29.0), which was reduced to a mean of CMA of  $6.3^\circ$  (range, 0–25) after surgery ( $p < 0.05$ ). The global satisfaction rating scale was 93.7% (range, 90–100). A transient sensory deficit on the ipsilateral lower ear lobe was noted in three cases. No significant permanent complications occurred.

**Conclusion:** Bipolar release of the SCM is a safe and reliable technique for the treatment of CMT in adults.

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## PS-3. Pediatric Atlantoaxial Rotatory Displacement Presenting with Torticollis: A Case Report

부산가톨릭의료원 메리놀병원 신경외과

김우재, 총배기, 이건상, 이명기, 김정호, 김호상, 김윤석

**Objective:** Atlantoaxial rotatory displacement (AARD) may lead to torticollis in children. The diagnosis is often missed and delayed. We report one case of AARD with torticollis 2 months.

**Methods:** A 8 year old boy attended our hospital complaining of developed head tilt with neck pain for 2 months. Conservative treatments including physical exercising, botox treatment were done at other hospitals. But he continued to hold the fixed head tilt with neck pain. We performed cervical spine CT and confirmed anterior atlantoaxial interval was increased to 9 mm and lateral atlantoaxial interval gap was 5 mm, and no fracture was identified. Halo-vest application was performed after the reduction of the cervical displacement using Halo skull traction under general anesthesia. Reduction was confirmed by CT. The patient remained Halo-vest for 4 months before being mobilized in a soft neck collar.

**Results:** His head kept normal posture without neck pain. There is no neurologic sequelae until now. But follow-up cervical spine CT and MRI showed increased anterior atlantoaxial interval was 5 to 6 mm and partial tear of left transverse ligament.

**Conclusion:** Fixed torticollis with sudden onset in children should be considered the possibility of AARD. Early recognition of AARD will enable appropriate management options.

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## PS-4. Botulinum Toxin A in Primary Cervical Dystonia: Outcome According to Time Course

부산가톨릭의료원 메리놀병원 신경외과

김우재, 이명기, 이건설, 총배기, 김호상, 김정호, 김윤석

**Objective:** To analyze the relationship between outcome and time course effect of Botulinum toxin A (BoNT-A) in treatment of primary cervical dystonia (CD).

**Methods:** Thirty-six patients who underwent injection of BoNT-A for primary CD were analyzed retrospectively. Their last injections were required to be a minimum of 16 weeks before entry in the study. There were 14 males and 22 females, ranging in age from 18 to 65 years (mean, 46.2 years). The Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) and the subjective Clinical Global Improvement (CGI) scale were assessed at baseline and at 4, 8, and 12 weeks.

**Results:** Of the patients, 55.6% had rotatory torticollis, 16.7% had retrocollis, 8.3% had laterocollis, and 19.4% had combined type. The mean BoNT-A dose was  $160.5 \pm 40.5$  units (range, 100-200 units). The mean total TWSTRS scores improved by 45.8%, 51.0%, and 46.9% at 4, 8, and 12 weeks, respectively, after injection of BoNT-A. Statistically significant improvements in the TWSTRS total and sub-scores were observed at 4, 8, and 12 weeks from baseline ( $p < 0.05$ ). The mean satisfactory response (very much or much improved) on the subjective CGI was 60.2% of patients. There was transitory muscular weakness in the neck in 8.3% of patients and transitory mild dysphagia in 5.6%.

**Conclusion:** BoNT-A therapy can significantly sustain the improvement of primary CD at 4, 8, and 12 weeks compared to baseline, without serious complications. It is concluded that BoNT-A injection is an effective and safe treatment for CD despite the complex presentation of this disease.

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## PS-5. Enhancing Therapeutic Efficacy in Stem Cell Transplantation by Pulsed Focused Ultrasound

**Byeong-Wook Song<sup>1</sup>, Yu Jin Jung<sup>2</sup>, Ju Hyung Lee<sup>2</sup>, Hyunki Hong<sup>2</sup>, Bong Soo Kim<sup>1</sup>, Moon-Seo Park<sup>1</sup>, Ki-Chul Hwang<sup>3</sup>**

*EIT/LOFUS R&D Center, Institute for Integrative Medicine, Catholic Kwandong University International St. Mary's Hospital, Incheon; bMS Life Science Corporation, Incheon; cInstitute for Bio-Medical Convergence, College of Medicine, Catholic Kwandong University, Gangneung, Korea*

**Objective:** Bone marrow mesenchymal stem cells (MSCs) have shown considerable promise in the treatment of disease. The secreted trophic and immunomodulatory cytokines derived from MSCs, i.e. MSC secretome, have been used as regenerative medicine. However their therapeutic efficacy is often limited by the insufficient homing of systemically administered cells or undesirable side effects at sites. For stem cell therapy to be considered for clinical use of neurodegenerative disease, MSCs need to be functional improvement. We focused on MSC regulation for therapeutic efficacy and its mediators by modulating pulsed focused ultrasound (pFUS).

**Methods:** Bone marrow MSCs were isolated from rat femur and tibial bones. The characteristics of MSCs were demonstrated by immunophenotyping. MSCs were plated in 24-well plate at  $2 \times 10^4$  cells, and then we operated the in vitro scratch assay, mimicking the effects of cell-matrix and cell-cell interactions on cell migration. The pFUS parameters were: 0-20 W acoustic powers, 30 kHz frequency, burst modulation for 2 min, and 5% duty cycle. To analyze the change of cytokines in MSCs, we used cytokine array kit.

**Results:** The cultured MSCs expressed CD71, CD90, CD105, CD106, and ICAM. They expressed neither the hematopoietic marker CD34 nor CD14. The cell migratory effect of pFUS groups (10-50% acoustic power) was increased as determined by the in vitro scratch assay, compared to pFUS non-treated group. However, there was no effect on cell death (apoptotic or necrotic cell death). The pFUS also increased expression of several cytokines related to cell homing or adhesion).

**Conclusions:** pFUS could potentially enhance therapeutic efficacy of MSCs to target homing by establishing local chemoattractant and trophic factors of cells toward local tissue of brain. This may ultimately improve viability and flexibility of stem cell local therapy for neurodegenerative disease. This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (NRF-2015R1C1A1A02037693).



## PS-6. Relation Between Cognition and Neural Connection from Injured Cingulum to Brainstem Cholinergic Nuclei in Chronic Patients with Traumatic Brain Injury

**Jae Ho Lee, Jin Sun Yoo, Sung Ho Jang, Seong Ho Kim**

*Department of Neurosurgery, Yeungnam University College of Medicine, Daegu, Korea*

**Objective:** This study investigated the relation between cognition and the neural connection from injured cingulum to brainstem cholinergic nuclei in patients with traumatic brain injury (TBI), using diffusion tensor tractography (DTT).

**Methods:** Among 353 patients with TBI, 20 chronic patients who showed discontinuation of both anterior cingulums from the basal forebrain on DTT were recruited for this study. The Wechsler Intelligence Scale and the Memory Assessment Scale (MAS; short-term, verbal, visual and total memory) were used for assessment of cognition. Patients were divided into two groups according to the presence of a neural connection between injured cingulum and brainstem cholinergic nuclei.

**Results:** Eight patients who had a neural connection between injured cingulum and brainstem cholinergic nuclei showed better short-term memory on MAS than 12 patients who did not ( $p < 0.05$ ). However, other results of neuropsychological testing showed no significant difference ( $p > 0.05$ ).

**Conclusion:** Better short-term memory in patients who had the neural connection between injured cingulum and brainstem cholinergic nuclei appears to have been attributed to the presence of cholinergic innervation to the cerebral cortex through the neural connection instead of the injured anterior cingulum. The neural connection appears to compensate for the injured anterior cingulum in obtaining cholinergic innervation.

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## PS-7. Non-invasive Intracranial Mesenchymal Stem Cell Transplantation with Low Intensity Focused Ultrasound: Preliminary Results of Energy Dependent Transplantation Efficiency

**Jihyeon Lee<sup>1,2</sup>, Jaewoo Shin<sup>1,2</sup>, Chanho Kong<sup>1</sup>, Byeong-Wook Song<sup>4,5</sup>, Oh Rum Cha<sup>3</sup>, Bong-Soo Kim<sup>4,5</sup>, Won Seok Chang<sup>1</sup>, Jongbum Seo<sup>3</sup>, Jin Woo Chang<sup>1,2</sup>**

<sup>1</sup>Department of Neurosurgery, Yonsei University College of Medicine, Seoul;

<sup>2</sup>Brain Korea 21 PLUS Project for Medical Science & Brain Research Institute, Yonsei University College of Medicine, Seoul;

<sup>3</sup>Department of Biomedical Engineering, Yonsei University, Wonju;

<sup>4</sup>EIT/LOFUS R&D Center, Institute for Integrative Medicine, Catholic Kwandong University College of Medicine, Gangwon;

<sup>5</sup>Catholic Kwandong University International St. Mary's Hospital, Incheon, Korea

**Objective:** Stem cell therapy for neurodegenerative diseases has been reported with promising results through neuronal differentiation or control of microenvironment. However, the surgical transplant methods such as parenchymal or intravenous injection has limitations of secondary injury, infection and low survival rate of stem cell in the target site. Therefore, this study investigates a possibility of focused ultrasound for targeted non-invasive stem cell transplantation into the brain.

**Methods:** In this study, Male Sprague-Dawley rats (300-350 g) and bone marrow-derived MSC (5p) were used. Experimental groups consist of low intensity FUS+MSC, MSC-only and low intensity FUS+dye (Evans blue or Light green). All rats were anesthetized with ketamine cocktail, and low intensity focused ultrasound was applied with parameters of 1 Mpa, 300 s (AP+0.7, ML+2, DV-5.5). Three hours after sonication, BM-MSC (4×10<sup>6</sup>/200 uL) was injected into the tail vein.

**Results:** First, the position of BBB opening was confirmed by the FUS+dye group. Comparing FUS+MSC and MSC-only group, it was confirmed that LoFUS increase BM-MSC homing to the sonicated brain tissue. Also, we found that location stained with Evans blue, a dye with large molecular weight, had higher efficacy of stem cell homing compared to the location stained with Light green, a dye with smaller molecular weight. On the other hand, BM-MSC was not shown in group of MSC-only.

**Conclusion:** As a result, we confirmed MSC can be delivered into the brain by LoFUS. And the efficiency of stem cell delivery may be positively correlated to the ultrasonic energy. This study can contribute to determination of optimal energy for repetitive LoFUS to cell transplantation without tissue damage in neurodegenerative diseases. Further study about function of stem cell transplanted in brain and mechanisms of stem cell homing by low intensity focused ultrasound is needed.



## PS-8. Placenta-derived Mesenchymal Stem Cells Facilitate Neuroprotective Effects in Dementia Rat Models: A Comparison Study Between Cell Injection Methods

**Jae Sung Cho<sup>1</sup>, Jihyeon Lee<sup>2</sup>, Da Un Jeong<sup>1</sup>, Han Wool Kim<sup>3</sup>,  
Won Seok Chang<sup>1</sup>, Jisook Moon<sup>3,4</sup>, Jin Woo Chang<sup>1,2</sup>**

<sup>1</sup>*Department of Neurosurgery, Yonsei University College of Medicine, Seoul;*

<sup>2</sup>*Brain Korea 21 PLUS Project for Medical Science and Brain Research Institute, Yonsei University College of Medicine, Seoul;*

<sup>3</sup>*General Research Institute, Gangnam CHA General Hospital, Seoul;*

<sup>4</sup>*Department of Bioengineering, College of Life Science, CHA University, Seoul, Korea*

**Objective:** Therapeutic potential of mesenchymal stem cell (MSC) against neurodegenerative diseases have been reported. While MSCs derived from bone marrow, adipose tissue and umbilical cord were frequently used for such therapeutic research, effects of human placenta-derived MSC (pMSC) on dementia is lesser known. In this study, we evaluated the effect of pMSC on dementia rat models on behavioral and molecular levels. We then compared therapeutic effectiveness between intracerebroventricular (ICV) and intravenous (IV) stem cell injection methods, and also compared their effects with standard treatment for dementia.

**Methods:** Four experimental groups (lesion, intracerebroventricular, intravenous, and donepezil) and a control group were used. Dementia rat models were induced by basal forebrain cholinergic neuronal damage using 192 IgG-saporin. One week after administration of 192 IgG-saporin, pMSC was injected into the treatment groups either intraventricularly (ICV,  $1.2 \times 10^6$  cells/8  $\mu$ L or intravenously (IV,  $5 \times 10^6$  cells/200  $\mu$ L). In order to prevent immune reaction by innate immunity, cyclosporine (an immunosuppressant drug) was administrated daily into the peritoneal cavity of the rats for 5 weeks. A certain portion of rats from both groups were treated with donepezil, a standard treatment for dementia. Five weeks after stem cell transplantation, all animals were tested by Morris water maze test. Neuronal activity markers, neurogenesis markers, and stem cell markers were also compared among the five groups.

**Results:** In the Morris water maze test, pMSC-treated group and donepezil group recovered spatial memory to levels similar to the normal rats and significantly superior to the lesioned rats. The improvement was more marked in the IV group compared to the ICV group. Acetylcholinesterase (AChE)



activities in the hippocampus of the two groups were recovered to levels similar to normal rats. DCX and BDNF (neurogenesis markers) expressions in ICV and donepezil groups did not significantly recover from that of the lesion group, but the expression increased in the IV group to a level similar to the normal group. Immunohistochemistry showed more stem cell transplantation into the hippocampus in the IV group compared to the ICV group. Microglia count was lower in the IV group compared to the ICV group, and was similar between ICV group and the lesion group.

**Conclusion:** Our results suggest that pMSC transplantation effectively helps recovery of spatial memory in dementia rat models through promotion of neurogenesis and recovery of AChE activity. Microglial activity also seems to take part in such improvement. Stem cells, however, do not seem to directly differentiate to neuronal cells. In addition, IV injection showed higher efficacy compared to ICV injection in terms of cognitive function improvement, and its effect was similar to that of donepezil. Further investigation seems necessary for clarification of cognitive recovery mechanism and absolute optimization of stem cell transplantation methodology.

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## PS-9. Occipital Nerve Stimulation in a Patient with an Intractable Cluster Headache

**Ji Hun Han, Hyuk Jai Choi , Yong Jun Cho, Suk Hyung Kang,  
Jin Pyeong Jeon, Jin Seo Yang**

*Department of Neurosurgery, Chuncheon Sacred Heart Hospital, Hallym University School of Medicine,  
Chuncheon, Korea*

**Objective:** Cluster headache is thought to be the most common primary trigeminal autonomic headache, although it is a rare disabling medical condition. The brief duration and intensity of the attacks command the use of rapid-acting pain relievers. Inhalation of oxygen and subcutaneous sumatriptan are the two most effective acute therapeutic options for cluster headache. Several preventive medication are also available. However, in some patients, these treatments are not effective, especially in those who develop chronic cluster headache. Here, we report a case of occipital nerve stimulation in a patient with an intractable cluster headache.

**Methods:** A 38-year-old man presented with a 5-year history of severe headache at left occipital and parietal area (VAS score 8). Until he visited our pain clinic, the patient had been receiving medications, oxygen therapy and various interventions including cervical dorsal root ganglion block, occipital nerve block, radiofrequency ablation in other clinics. However, previous treatments were not effective. Despite various treatments, headache was worsened, the patient has developed needle phobia, panic disorder and could not do work.

**Results:** We performed occipital nerve stimulation (ONS). In general, ONS is performed under local anesthesia, because stimulation test is necessary for to find an appropriate stimulation program and lead location. But, in this case, we could not perform ONS under local anesthesia, carried out under general anesthesia because the patient has needle phobia and panic disorder. The trials of ONS were carried with the midline incision C1-2 level, inserted two 8 pole electrical leads (Dual lead trials) subcutaneously (to avoid muscle spasm) to oblique and cephalic direction (target to greater occipital nerve) and to oblique and caudal direction (target to lesser occipital nerve and posterior auricular nerve). When the patient woke up from under general anesthesia, the stimulation test was performed and the patient was satisfied with the stimulation program. After surgery, the patient's VAS score became 1-2 except operation site pain. After 1 week trial period, we performed the permanent implantation of occipital nerve stimulator. No serious complications were detected.



**Conclusion:** Cluster headache maybe be relieved by conservative treatment, but when the quality of life chronic headache patients is considered, we should consider aggressive treatments like ONS. ONS needs stimulation test under local anesthesia because to find an appropriate stimulation program and lead location, But in some cases we can not do a stimulation test in local anesthesia, then we should consider dual lead trials.

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## PS-10. A Case of Parasellar Meningioma

**Donguk Lee, Jun Cho**

*Department of Neurosurgery, Konkuk University Medical Center, Konkuk University College of Medicine, Seoul, Korea*

**Objective:** A clinical course of a patient with parasellar meningioma managed with GKS after surgery.

**Methods:** 52 years old female had Rt. parasellar meningioma treated with GKS. We followed this case for 18 months after initial diagnosis.

**Results:** In this study, we evaluated the outcome of parasellar meningioma managed with Gamma Knife Radiosurgery (GKRS) as an adjunct to microsurgical removal.

**Conclusion:** Gamma Knife radiosurgery offers a fabulous tumor control for patient with parasellar meningioma.

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## PS-11. Treatment Effect of Gamma Knife Radiosurgery for Germinomas in Pineal Gland

**Won Hee Lee, In Cheol Seo, So Young Ha, Gee Chang Lee, Young Seo Lee, Seong Tae Kim, Kun Soo Lee, Sung Hwa Paeng, Se Young Pyo, Young Gyun Jeong, Yong Tae Jung, Moo Seong Kim**

*Department of Neurosurgery, Busan Paik Hospital, Inje University College of Medicine, Pusan, Korea*

**Objective:** Germinomas in pineal gland is uncommon, so radiation therapy is generally accepted of primary treatment of choice, but there is controversy of optimal treatment strategy for pineal germinomas. We assessed treatment effect of Gamma Knife Radiosurgery (GKS) for germinomas in pineal region.

**Methods:** Between October, 1994 and December 2013, 18 patients with pineal germinomas were treated with GKS. 13 cases were treated with combined GKS and booster whole brain radiotherapy (70 Gy), while 5 cases were treated using GKS only. The mean radiosurgical tumor volume was 4.6 mL (range 0.5-36 mL). The mean dose delivered to the tumor center was 25.6 Gy (range 20-45) and to the tumor margin was 14.6 Gy (10-22.5 Gy).

**Results:** All patients underwent serial MRI scanning and mean duration of imaging follow-up was 40.6 months (range 23-148). Among 18 patients, 14 patients underwent shunts or external ventricular drainages (EVD) and biopsies were performed in all patients. Follow-up MR images were revealed complete response in 8 patients and partial response in 5 patients, while in 5 patients, it initially showed a partial response followed by no response after 8.3 months. Clinical outcome was showed better their symptoms in 13 patients and stable in 5 patients.

**Conclusion:** GKS is safe and effective treatment of pineal germinomas, and treatment combining radiosurgery with booster radiotherapy showed better results than the radiosurgery only treatment.

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## PS-12. Operant Conditioning in Rats Through Medial Forebrain Bundle (MFB) Stimulation

**Chanho Kong<sup>1</sup>, Jaewoo Shin<sup>1,2</sup>, Yena Lee<sup>3</sup>, Yoon Kyung Cho<sup>3</sup>, Soonyoung Kim<sup>3</sup>,  
Jaesung Cho<sup>1</sup>, Hyun Ho Jung<sup>1,2</sup>, Sang Beom Jun<sup>3,4</sup>, Jin Woo Chang<sup>1,2</sup>**

*<sup>1</sup>Department of Neurosurgery, Yonsei University College of Medicine, Seoul,*

*<sup>2</sup>Brain Korea <sup>21</sup>PLUS Project for Medical Science and Brain Research Institute, Yonsei University College of Medicine, Seoul,*

*<sup>3</sup>Department of electronics Engineering, College of Engineering, Ewha Womans University, Seoul,*

*<sup>4</sup>Department of Brain and Cognitive Sciences, Ewha Womans University, Seoul, Korea*

Medial forebrain bundle (MFB) is a part of the reward system, involved in the integration of pleasure and reward. Previous studies used various stimulation parameter values for operant conditioning, but the effectiveness of each parameter value has not been systematically studied. Our study investigated the optimal parameter value for operant conditioning.

Electrodes were implanted in the MFB region (AP:-2.3 mm, ML: 1.8 mm DV: 8.6 mm) of Male Sprague-Dawley rats (n=9, 250-300 g). Tungsten array electrodes were for the MFB stimulation. After implantation, we conducted a self-training experiment where an electrical stimulation is sent to the MFB region via the implanted electrodes upon pressing of a lever in the Skinner box. Magnitude of the electrical stimulation was gradually increased from 50  $\mu$ A to 350  $\mu$ A. Individuals that pressed the lever more than 30 times per minute were used for the maze experiment.

Individuals pressed the lever most frequently when magnitude of the stimulation was 200  $\mu$ A-280  $\mu$ A. Also, we were able to successfully control one individual's direction by using MFB stimulations in the maze experiment.

Our results showed positive prospects in behavioral control of rats via MFB stimulation in range of 200  $\mu$ A-280  $\mu$ A. Based on our results, we anticipate that more efficient training for operant conditioning could be possible using optimal parameters.

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## PS-13. Analysis of Factors for Improvement of Symptoms Related to Trigeminal Schwannoma Treated by Gamma Knife Radiosurgery

**Chang Kyu Park, Na Young Jung, Min Soo Kim, Won Seok Chang,  
Hyun Ho Jung, Jin Woo Chang, Yong Gou Park**

*Department of Neurosurgery, Yonsei University College of Medicine, Seoul, Korea*

**Objective:** The patients with symptomatic trigeminal schwannoma (TS) desire to effective treatment. Traditionally TS have been treated microsurgery. However, complete resection is not guarantee complete remission of symptoms and other complications may be occurred. Gamma Knife radiosurgery (GKRS) offers a minimally invasive alternate in treating TS. A number of studies were reported for effectiveness of treatment. The aim of the present study was to evaluate the clinical outcome and to investigate the prognostic factors in a series of patients in whom GKRS used to treat symptomatic TS.

**Methods:** We performed a retrospective analysis of 66 patients who underwent GKRS to treat TS. We excluded patients who were had no symptoms related to TS. After excluding ineligible patients, 34 qualified for this study and were included in the analysis. The mean age was 48.8 years (range: 18-78). The mean follow-up period was 85.3 months (range: 6-216). Twenty-three patients presented facial pain; 7 patients complaint facial hypoesthesia; diplopia were presented in 4 patients. The following parameters were analyzed as prognostic factors for improvement of symptoms: age, sex, target volume, prescription dose, and tumor enhancement pattern. The tumor enhancement pattern was divided into two groups: group A (homogeneous enhancement) and group B (heterogeneous or rim enhancement).

**Results:** Of 34 patients, 16 (47%) improved the symptoms. In types of symptoms, thirteen patients (56.5%) experienced pain relief in 23 patients with facial pain; two patients (28.5%) improved facial hypoesthesia in seven patients; one patient (25%) presented betterment of diplopia in four patients. Almost improvement of symptoms was observed within three years after GKRS. No significant association was observed between any of the parameters investigated and the improvement of symptoms, with the exception of prescription dose. Prescription dose exhibited a statistically significant difference by univariate analysis ( $p=0.022$ ); this difference was also significant by multivariate analysis ( $p=0.042$ ). The interesting thing is, although there was no statistical significance, the patients of group B presented faster improvements of symptoms than group A.



**Conclusion:** According to the studies, GKRS is effective and safe treatment for tumor control of TS. However, a number of studies for effectiveness of symptoms are being progress. In the present study, we suggested that appropriate prescription dose would help to relief of symptoms and the patient with heterogeneous tumor enhance pattern might be expected for rapid symptom improvement.

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## PS-14. The Study of Inappropriate Locations of Teflon Pledget through MRI Findings in Patients with a Failed Prior Microvascular Decompression for Hemifacial Spasm

**Chang Kyu Park, Na Young Jung, Min Soo Kim, Won Seok Chang,  
Hyun Ho Jung, Jin Woo Chang**

*Department of Neurosurgery, Yonsei University College of Medicine, Seoul, Korea*

**Objective:** Microvascular decompression (MVD) is treatment choice for hemifacial spasm (HFS) due to its high rate of complete resolution. However, some patients still suffer from persistence after prior MVD. The aim of this study was to determine whether MR imaging could identify unaddressed neurovascular contact in patients with ongoing HFS despite prior MVD and to report the frequency and locations of Teflon pledget which was inserted at prior MVD.

**Methods:** Between January 2000 and December 2015, we retrospective analyzed for 16 patients who underwent repeat MVD for persistent symptom after prior MVD. All patients underwent MRI which included thin section axial T2 images and time of flight images. Their images were used to evaluate the presence of persistent vascular compression and location of the point of contact relative to the existing surgical Teflon pledget.

**Results:** Neurovascular contacts were revealed in all patients. The locations of prior inserted Teflon pledget were as following: anterior lateral portion from root exit zone (REZ) in 7 cases; anterior medial area was 4 cases; posterior lateral and medial portion were 2 cases, respectively. The Teflon pledget was not observed in one patient. Un-decompressed REZs were confirmed in operational field. Successful microvascular decompressions were performed. The all surgeries were completed without any complications. All patients experienced relief of symptoms within one year after MVD.

**Conclusion:** Although MVD is successful treatment for HFS, inappropriate decompression does not relieve the symptom. It is important that establishing the sufficient knowledge and understanding of REZ of facial nerve and its surrounding neurovascular structure is contributing to improve surgical outcome.

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