

BF-1. Spatial Errors of Stereotactic MRIs: Clinical Consideration during Stereotactic Surgery

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Objective: The aim of this study is to identify the effects of frequency encoding direction during planning for gamma knife radiosurgery using 1.5-tesla MRI.

Methods: We retrospectively reviewed imaging data of 57 patients treated with gamma knife radiosurgery from September 2014 to December 2014. In all patients, two frequency encoding direction (right to left and anterior to posterior) images with gadolinium-enhanced T1-weighted MRIs were obtained. Spatial errors were evaluated by comparing the difference of marginal radiation dose for lesion between right to left and anterior to posterior frequency encoding direction images in each patient.

Results: Among 57 patients, two patients were treated with AVMs, 28 patients with meningioma, 26 with metastatic brain tumor, and one with vestibular schwannoma. The mean distances from center of the frame to center of lesion were as follows; 24.2 mm (± 16.1) for X-axis, 32.1 mm (± 18.2) for y-axis, 38.4 mm (± 25.9) for z-axis, and 62.1 mm (± 22.0) for actual. The mean difference of minimum marginal radiation dose for lesions was 0.56 Gy (± 0.79) and the mean difference of maximum marginal dose to normal brain was 1.37 Gy (± 1.41) between each frequency encoding direction images. The z-axis and actual distances from center of frame to center of lesion had statistical significance for mean difference of minimum marginal radiation dose for lesions between each frequency encoding direction images.

Conclusions: This retrospective study showed spatial errors of stereotactic MRIs for gamma knife radiosurgery. Although there is no definitive way to eliminate these errors, we must consider that there could be spatial error during radiosurgery resulting in inadvertent treatment failure.

MEMO



BF-2. Optogenetic Inhibition of Subthalamic Nucleus Alleviates Levodopa-induced Dyskinesias in a Rat Model of Parkinson's Disease

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Background: The inhibition of neuronal activity by electrical deep brain stimulation is one of the mechanisms explaining the amelioration of levodopa-induced dyskinesia. However, electrical deep brain stimulation cannot specifically activate or inactivate selected types of neurons.

Objective: We applied optogenetics as an alternative treatment to deep brain stimulation for levodopa-induced dyskinesia, and also to confirm that the mechanism of levodopa-induced dyskinesia amelioration by subthalamic nucleus deep brain stimulation is mediated through neuronal inhibition.

Methods: 6-hydroxydopamine induced hemiparkinsonian rats received injections of hSynapsin1-NpHR-YFP AAV or hSynapsin1-YFP AAV. Two weeks after viral injections, all rats were treated with daily injections of levodopa. Then, the optic fiber was implanted into the ipsilateral subthalamic nucleus. We performed various behavioral tests to evaluate the changes in levodopa-induced dyskinesias after optogenetic expression and illumination in the subthalamic nucleus.

Results: The behavioral tests revealed that optical inhibition of the subthalamic nucleus significantly ameliorated levodopa-induced dyskinesia by reducing the duration of the dyskinesias as well as the severity of axial dyskinesia.

Conclusion: These findings will provide a useful foundation for the future development of optogenetic modulation systems that may replace electrical deep brain stimulation treatment in Parkinson's disease.

MEMO



BF-3. Injury of the Lower Ascending Reticular Activating System in Patients with Hypoxic-ischemic Brain Injury: Diffusion Tensor Imaging Study

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Objective: Many studies have reported on vulnerable areas and neural tracts of the brain after hypoxic-ischemic brain injury (HI-BI). However, little is known about injury of the ascending reticular activating system (ARAS). We attempted to investigate on injury of the lower portion of the ARAS in patients with HI-BI using diffusion tensor tractography (DTT).

Methods: Fourteen consecutive patients with HI-BI and 10 control subjects were recruited for this study. We classified the patients into two subgroups according to the preservation of arousal: subgroup A (eight patients)-intact arousal and subgroup B (six patients)-impaired arousal. The lower portion of the ARAS between the pontine reticular formation and the thalamus was reconstructed using the probabilistic tractography method. Fractional anisotropy (FA), mean diffusivity (MD), and tract volume (TV) were measured.

Results: The FA value and TV were decreased in subgroup B compared with those of the control group, although no difference was observed in the MD value ($p < 0.05$). However, for all DTT parameters, no difference was observed between subgroup A and the control group and between subgroup A and subgroup B ($p > 0.05$).

Conclusion: Injury of the lower portion of the ARAS was found between the pontine reticular formation and the thalamus in patients with impaired arousal after HI-BI. We believe that analysis using DTT could be helpful in the evaluation of patients with impaired arousal after HI-BI.

MEMO



BF-4. White Matter Fiber Tractography: DTI (Diffusion-based Tractography Imaging) and TDI (Track-density Imaging)

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Objective: Neuroimaging advances have given rise to major progress in neurosciences and neurology, as ever more subtle and specific imaging methods reveal new aspects of the brain. Diffusion tensor imaging (DTI) that the majority of white matter fiber tractography software packages currently available to clinicians rely on a fundamentally flawed framework to generate fiber orientations from diffusion-weighted data. But One major limitation of current methods is the spatial scale of the information available. Spatial resolution using post-processing methods based on diffusion MRI fiber-tracking, to reveal structures beyond the resolution of the acquired imaging voxel: term such a method as super-resolution track-density imaging (TDI). We were compared to TDI and DTI image.

Methods: Diffusor tensor imaging (DTI) and Track-density imaging (TDI) were acquired in 10 cases with hemorrhage strokes, Tumor, Diffusion axonal injury (DAI). We classified there with the tracts as good, displaced, compressed, partial cut off, poor and compared these with the clinical symptoms, and then we compared the DTI and TDI image.

Results: The patients with partial cut off, poor of corticospinal tracts in DTI image (But tract were being maintained in TDI image) had good recovery.

Discussion: The TDI technique not only has a role in structural delineation of brain features (due to its high anatomical contrast), but can also play a very important complementary role in tractography studies. This approach constitutes a major new advance in technology for the study of white matter in the human brain and its role in human diseases. Not only does TDI provide super-resolution anatomical data, but it can also be a very valuable complementary tool for white matter fiber-tracking study. TDI image can express much tract than DTI image and the result of We think that TDI image was supplements the DTI image



BF-5. Stem Cell Biology and Therapeutic Implications for Neurodegenerative Disease - An Efficient Way forward in Mesenchymal Stem Cell Therapy of Parkinson's Disease

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Objective: Neurodegenerative diseases, include Alzheimer's disease (AD), Parkinson's disease (PD), multiple sclerosis (MS), and etc., are characterized by the loss of neurons, and have effects on cellular and molecular changes at different levels. Stem cells have been used as an attractive candidate to treat these diseases; however their therapeutic efficacy is often limited by the insufficient delivery of systemically administered cells or undesirable side effects at sites. We focused on the therapeutic application of mesenchymal stem cells (MSCs) by modulating pathophysiological functions in an animal model of PD.

Methods: Bone marrow MSCs were isolated from rat femur and tibial bones. To transplant effectively MSCs, we used low intensity focused ultrasound (LIFUS). LIFUS was delivered with 0.2-1.0 KPa to stimulate with 3.5 W/cm^2 of acoustic intensity.

Results: We induced primed-neurospheres (pNS) derived from microRNA (miR)-treated MSCs. We selected three miRs, which are involved in the proliferation and differentiation by regulation of hypoxia inducible factor (HIF)-1 α . MiR complex induced neural differentiation from MSCs, expressing early neuronal proteins. The efficiency of MSC and pNS delivery was validated in 6-hydroxydopamine (6-OHDA)-lesioned rat model of Parkinson's disease (PD).

Conclusions: LIFUS can offer effective delivery, and promote therapeutic efficacy for non-invasive stem cell therapy to clinical PD.



BF-6. The Effects of different Anesthetic Methods on Neuronal Activity and Movement Symptoms of Parkinson's Disease

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Objective: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is widely used in the treatment of Parkinson's disease. DBS surgery is usually performed with the patient under local anesthesia (LA) however many patients required surgery under sedation because they do not tolerate LA. We evaluated whether the differences in anesthetic methods affect STN single-unit activity, MER and symptoms of Parkinson's disease.

Methods: We analyzed 8 patients with Parkinson's disease, underwent bilateral STN DBS with MER. The left sides were done under awake with LA and then their right sides were done with monitored anesthesia care (MAC). The electrode position was evaluated by preoperative MRI and postoperative CT. The clinical outcomes were assessed at six months after surgery. We compared STN single-unit activity as well as movement symptoms of Parkinson's disease.

Results: The primary results revealed no significant difference in the mean firing rate of STN single-unit activity under LA (38.7 ± 16.8 spikes/sec, $n=78$) and MAC (35.5 ± 17.2 spikes/sec, $n=66$). However, there were differences in the spike characteristics and firing patterns of STN activity between the two methods. All the electrode position were within the STNs on both sides locations in postoperative fusion images. On both sides and the off-time Unified Parkinson's Disease Rating Scale part III scores at six months after surgery decreased.

Conclusion: Continuous infusion of propofol and fentanyl neither interfered with MER to achieve a precise electrode location nor affected the clinical outcome.

MEMO



BF-7. Monitored Sleep-awake Anesthesia with Dexmedetomidine and Propofol for the Deep Brain Stimulation Surgery

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Objectives: The preferred choice of anesthesia for the DBS has been local in many centers due to the need of patient's cooperation during the procedure. Another reason of using local anesthesia is a concern of interfering effect of sedatives on microelectrode recording (MER) results. However, using local anesthetics during the whole DBS procedure may not be possible in some patients due to severe anxiety, fear, delirium or exhaustion. We used 'asleep-awake' technique using dexmedetomidine (Dex) based monitored anesthesia during DBS for three different subcortical nuclei.

Methods: A data from 13 different subcortical nuclei from eight consecutive patients underwent DBS were retrospectively reviewed. We used continuous dexmedetomidine (Dex) and intermittent small boluses of propofol during the painful invasive procedure with continuous intraoperative monitorings. Bispectral index (BIS), intraoperative EEG and modified observer's assessment of sedation (MOAA/S) were used to estimate the level of consciousness. Microelectrode recordings were performed on four subthalamic nucleus (STN), six globus pallidus internus (GPi) and three thalamic nuclei.

Results: Overall, all patients were satisfactorily sedated using continuous infusion of low dose dexmedetomidine and intermittent boluses of propofol. After the discontinuation of anesthetics, the time to full awake were various among subjects. MER results showed some differences according to the level of patient's consciousness, but the localizing value was good enough to decide the target in all target nuclei. Respiratory functions and hemodynamics were well maintained without any intraoperative complication.

Conclusion: We concluded that Dex-based monitored anesthesia is a safe and good alternative of local anesthesia for MER during the DBS.

MEMO



BF-8. Bilateral Deep Brain Stimulation of the Subthalamic Nucleus under Sedation with Propofol and Fentanyl

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Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is helpful in the advanced PD patients with motor fluctuation and levodopa-induced dyskinesia. The precise contact of electrodes is very important to achieve best clinical outcome and avoid various complications from stimulation of surrounding structures. Most surgeon simulated targeting with brain MRI, approached the STN with MER, and then checked the improvements and complications with intraoperative macrostimulation. However, intraoperative awakening is very stressful to patients. The current study was aimed to assess the influence on MER signals and their applicability for the STN DBS surgery even when the sedation with the propofol and fentanyl was applied to both sides. Intraoperative MER data were analyzed for both sides of all 16 patients. The MER signals of bilateral STNs under propofol were slightly attenuated. However, the changes of MER signals did not deserve to interfere with targeting good locations in postoperative fusion images. Additionally, all the included patients were improved clinically without remarkable complications. In conclusion, propofol and fentanyl can be used safely for bilateral STN-DBS surgery on advanced PD and the clinical outcomes also were improved without burdened experiences of the patients.

MEMO

