

Department of Neurosurgery

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General Summary

The research studies in our department, examining such topics as syringomyelia, endovascular surgery, mechanism of head injury, and pediatric neurosurgery, made good progress in the past year. Research in these areas is performed to international standards. Clinical research on brain tumors, hypothalamic disorders, and spine and spinal cord diseases has also continued.

Research Activities

Cerebrovascular diseases / Endovascular surgeries

1. Analysis on the natural history of unruptured intracranial aneurysms
 Since 2003, more than 5,000 intracranial aneurysm patients have been visited our department. As a leading aneurysm treatment center in the world, we have placed a great value on a precise real-time data base of the aneurysms patients. We focused on the analysis of 1) natural history of the unruptured aneurysms, 2) risk factors *Associate* with the rupture of aneurysms, and 3) risk factors *Associate* with treatment.

2. Analysis of bio-fluid mechanics on human intracranial aneurysms using a computational fluid dynamics (CFD)

The main topics of our current study include 1) development of novel parameters, 2) elucidation of relationship between the hemodynamic patterns vs. rupture risk, 3) Development of a novel CFD software dedicated to the image workstation for angio machines.

3. Newly development technique of neuroradiological imaging — 4DDSA, Neuro PBV, Metal artifact removal —

In addition to three-dimensional aneurysm analysis using 3D DSA, 4DDSA made it possible to evaluate the three-dimensional state of blood flow over time. It is used to help analyze blood flow of cerebral arteriovenous malformation, dural arteriovenous fistula, cerebral aneurysm. Neuro PBV, iFlow is a technique for evaluating cerebral blood flow using a cerebral angiography device. It is applied to stroke disease and it is possible to evaluate cerebral blood flow before treatment, treatment, and evaluation of cerebral blood flow after treatment with only cerebral angiography apparatus. By comparing with conventional cerebral blood flow test, its usefulness is judged. Metal artifact removal is a

new technique for improving the accuracy of postoperative evaluation during operation of coil embolization by reducing metal artifact. We conduct these clinical studies as collaborative research with Siemens.

4. Development of a novel intracranial stent device for the treatment of brain aneurysms

A novel intracranial stent device for the treatment of brain aneurysm is currently under development.

A preclinical animal study is ongoing. This project is supported by the Ministry of Economy, Trade and Industry under a research grant. We are now in the final stage of consecutive experiments, and the results will be reported to the Ministry of Economy, Trade and Industry in 2016.

5. Development of new therapy for ischemic stroke using small animal cerebral infarction model

Using a cerebral angiography device for animals and MRI, we developed a highly reproducible small animal cerebral infarction model. Using this, new research has begun on researches on cerebral circulation metabolism and drug discovery.

6. Establishment of a tele-medicine network utilizing a novel software for smartphones

Recently tele-medicine software “Join” is available for any smartphone users. The application allows every medical staff to have instant access to the PACS system in the Jikei university hospital, and allows each member to communicate using an online bulletin board system. The application is released under the collaboration with NTT Docomo, which is the Japan’s largest mobile service provider, serving more than 60 million customers

Brain tumor

1. Immunotherapy against malignant glioma-

We started a clinical trial of “Immunotherapy with fusions of glioma cells, glioma initiating cells, and dendritic cells (DCs)”. Although several cell types have the ability to induce antitumor immune response, this function is performed most efficiently by professional antigen presenting cells, of which DCs are the most potent. We had earlier shown that immunotherapy with fusion cells (FC) of DCs and glioma cells induces safe, tumor specific immune responses in glioma patients. In the recent study, we found that transfection of Poly(I:C) and IL-10-siRNA in FCs accelerated endogenous IL-12 secretion. The IL-12-secreting FCs induced potent antitumor immune response. So now, we are using the Poly(I:C)/IL-10-siRNA transfected FCs as a tumor vaccine in the present clinical trial.

2. Analysis of gene mutation *Associated* neo-antigens using next generation sequencer

We previously reported that FC immunotherapy, a vaccination with fusions of autologous DCs and tumor cells, provided significant prolongation of progression free survival (PFS) and overall survival (OS) in patients with malignant gliomas (MGs). The gene expression of the MG cells used for the generation of the dendritic/tumor fusion vaccine was investigated to identify genes *Associated* with the clinical responses. The number of candidate neo-antigen peptides binding to human leukocyte antigen (HLA)-A*24:02 in the MG cells was not significantly different between the effective and ineffective groups. Although twelve types of common neo-antigen peptide were identified in the MG cells from the effective group, they were also expressed in the MG cells from the ineffective group.

3. Study of intra operative imaging using C-arm CT

We use a C-arm CT, syngo DynaCT system (SIEMENS), as well as an image analyzing software for metal-artifact reduction in surgical resection of brain tumors. An intra operative imaging by this system supports to increase the resection ratio of tumors, with a surgical navigation system and a photo-dynamic diagnosis by 5-ALA. This study is aimed at establishing safe technical innovations in the operation of brain tumors.

Neurotrauma

Few institutions have performed research in neurotraumatology. A unique aspect of our department is that we have undertaken 3 major studies in this area of research. We examined the prevalence of sports-related head injury in collaboration with the Japan Society of Clinical Sports Medicine and the Japan Society of Neurotraumatology. We have also examined sports-related concussion and performed mechanical studies of head injury through simulations.

Spine and Syringomyelia

About 30 patients with syringomyelia are treated surgically in our department each year. By evaluating cerebrospinal fluid (CSF) obstruction at the craniovertebral junction in patients with syringomyelia related to Chiari malformation, the relation between CSF circulation blockage and cavitation of the spinal cord has been clarified. Therefore, improving the CSF circulation becomes the goal of surgical treatment. However, the mechanism of cavitation of the spinal cord is not fully understood. In patients with Chiari malformation, the cerebellar tonsils and the ventral vector (i.e., dens) compress the spinal cord and restrict CSF circulation. We examined whether these 2 factors influence the effects of foramen magnum decompression.

We also developed an implant for cervical laminoplasty. This corresponds to various surgical methods and its initial fixation power increased. Furthermore, we performed spinal surgery in Hybrid OR as a global pioneer, making it safer and more reliable for patients.

Division of Pediatric Neurosurgery

In division of pediatric neurosurgery, we offer many patients with spina-bifida, hydrocephalus, cranial facial anomaly, and brain tumor, etc, gentle and minimally invasive operations. We also follow not only post-operative patients but inoperative patients with disease to check their development and conditions for long periods in outpatient clinic.

There have been more than 2,000 new cases in various entities over the 15 years. We currently consist of a consultant, a division staff, and a resident, promoting clinical research through various clinical activities.

As for spina-bifida, we are currently examining the prognosis of neurological functions by operating under neuro-monitoring, and the early detecting system for occult spina bifida through the type of skin stigmata.

We are also developing operative procedures and instruments for hydrocephalus, intracranial cysts and brain tumor by neuroendoscopic maneuvering, and proposing the usage of navigation systems.

In the craniofacial surgical field, we proposed the age related operative method and won

awards in Japan and international society of pediatric neurosurgery.

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