Department of Neurosurgery

Yuichi Murayama, *Professor and Chairperson*
Takaaki Yanagisawa, *Professor*
Yasuharu Akasaki, *Associate Professor*
Ichiro Yuki, *Associate Professor*
Hiroyuki Takao, *Associate Professor*
Nobuyoshi Kaito, *Assistant Professor*
Toshihide Tanaka, *Assistant Professor*
Toru Terao, *Assistant Professor*
Yuichiro Nonaka, *Assistant Professor*
Hiroki Ohashi, *Assistant Professor*
Ryosuke Mori, *Assistant Professor*
Satoshi Tani, *Professor*
Yuzuru Hasegawa, *Associate Professor*
Toshihiro Ishibashi, *Associate Professor*
Yudo Ishii, *Associate Professor*
Masayoshi Matsumoto, *Assistant Professor*
Hiroyasu Nagashima, *Assistant Professor*
Akira Isoshima, *Assistant Professor*
Hideki Arakawa, *Assistant Professor*
Koreaki Irie, *Assistant Professor*
Shougo Kaku, *Assistant Professor*
Naoki Kato, *Assistant Professor*

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 of the natural history of unruptured intracranial aneurysms

Since 2003, more than 5,000 patients with intracranial aneurysms have 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 patients with aneurysms. We focused on the analysis of (1) the natural history of unruptured aneurysms, (2) risk factors associated with the rupture of aneurysms, and (3) risk factors associated with treatment.

2. Analysis of biofluid mechanics on human intracranial aneurysms using computational fluid dynamics

The main topics of our current studies include (1) development of novel parameters, (2) clarifying the relationship of hemodynamic patterns with the risk of rupture, and (3) the development of a novel software program for computational fluid dynamics dedicated to the image workstation of angiographic machines.

3. Newly developed techniques of neuroradiological imaging

Although intra-arterial 3-dimensional digital subtraction angiography (3DDSA) using an angiographic C-arm system is still the gold standard for postoperative confirmation of surgical clipping of intracranial aneurysms, intra-arterial 3DDSA requires catheterization and intra-arterial injection of a contrast medium, which adds risks and time to the surgical procedure. We propose a less invasive acquisition of 3DDSA with intravenous injection in the hybrid operating room to confirm the results of surgical clipping immediately after surgery.

Neuro PBV and iFlow (Siemens Healthcare GmbH, Erlangen, Germany) are software applications for evaluating cerebral blood flow with a cerebral angiography device. These applications are usedin patients who have had a stroke to evaluate cerebral blood flow with only a cerebral angiography apparatus before, during, and after treatment. By comparing results with those of conventional cerebral blood flow tests, the usefulness of Neuro PBV and iFlow can be assessed. Metal artifact removal is a new technique for improving the accuracy of postoperative evaluation during surgery for coil embolization by reducing metal artifact. We conduct these clinical studies in collaboration with Siemens Healthcare.

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 a research grant from the Ministry of Economy, Trade and Industry. We are now in the final stage of consecutive experiments, and the results will be reported to the Ministry in 2016.

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

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

6. Establishment of a telemedicine network utilizing a novel software program for smartphones

The telemedicine software application “Join” has recently become available for any smartphone users. This application allows every member of the medical staff to have instant access to the picture archiving and communication system in The Jikei University Hospital and to communicate with an online bulletin-board system. The application is released in collaboration with NTT Docomo, which is Japan’s largest mobile service provider, serving more than 60 million customers.

Brain tumor

1. Immunotherapy against malignant glioma

We have started a clinical trial of immunotherapy with fusions of glioma cells, glioma-initiating cells, and dendritic cells. Although several cell types can induce an antitumor immune response, this function is performed most efficiently by professional antigen-presenting cells, of which dendritic cells are the most potent. We have earlier shown that immunotherapy with fusion cells made of dendritic cells and glioma cells induces safe, tumor-specific immune responses in patients with glioma. In our recent study, we have found that transfection of Poly(I:C) and interleukin (IL)-10-small interfering (si) RNA in fusion cells accelerates endogenous IL-12 secretion. The IL-12-secretory fusion cells induced a potent antitumor immune response. Therefore, we are now using Poly(I:C)/IL-10-siRNA transfected fusion cells as a tumor vaccine in clinical trial.

2. Analysis of gene mutation-associated neoantigens via a next-generation sequencer

We have previously reported that fusion cell immunotherapy, a vaccination with fusions of autologous dendritic cells and tumor cells, significantly prolongs progression-free sur-

vival and overall survival in patients with malignant gliomas. The gene expression of the malignant glioma cells used to generate a dendritic/tumor fusion vaccine was investigated to identify genes associated with the clinical responses. The number of candidate neoantigen peptides binding to HLA-A*24:02 in malignant glioma cells did not differ significantly between the effective and ineffective groups. Although 12 types of common neoantigen peptide were identified in the malignant glioma cells from the effective group, they were also expressed in the malignant glioma cells from the ineffective group.

3. Study of intraoperative imaging with C-arm computed tomography

We use a C-arm computed tomographic scanner, the *syngo* DynaCT system (Siemens Healthcare), and an image-analyzing software program to reduce metallic artifacts during the surgical resection of brain tumors. Intraoperative imaging with this system increases the resection ratio of tumors, with a surgical navigation system and a photodynamic diagnosis by 5-aminolevulinic acid. This study is aimed at establishing safe technical innovations in the surgical treatment 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 concussions and performed mechanical studies of head injuries through simulations. We work with Hosei University for studies of American football, with the Japan Football Association for studies of football, and the Japan Boxing Commission for studies of boxing.

Spine and Syringomyelia

Each year approximately 30 patients with syringomyelia are treated surgically in our department. To date, we have treated more than 750 patients with syringomyelia. By evaluating cerebrospinal fluid (CSF) obstruction at the craniovertebral junction in patients with syringomyelia related to Chiari malformation, the relation of CSF circulation blockage to cavitation of the spinal cord has been clarified. Therefore, improving 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. The use of this implant corresponds with various surgical methods, and its initial fixation power has increased. Furthermore, we have performed spinal surgery in a hybrid operating room as a global pioneer, making the procedure safer and more reliable for patients.

We have presented these research results at the Neurospinal Society of Japan, the Japan Neurosurgical Society, and the Global Spine Congress.

Division of Pediatric Neurosurgery

In the division of pediatric neurosurgery, we offer gentle and minimally invasive operations to many patients with spina bifida, hydrocephalus, cranial facial anomaly, and brain tumor. We also follow-up postoperative patients and inoperative patients with diseases to assess their development and conditions for long periods of treatment in the outpatient clinic.

Over the past 15 years, new cases in various entities number more than 2,000. This division currently consists 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 neuromonitoring and examining an early detection 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 are proposing the usage of navigation systems.

We have proposed an age-related operative method for craniofacial surgery and have won awards in Japan and international societies of pediatric neurosurgery.

Publications

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