Hospital

Preface

The National Cancer Center Hospital (NCCH) provides the highest level of standard care with its missions to research and develop the whole area of cancer from novel diagnosis and treatment, palliative care, to patient support.

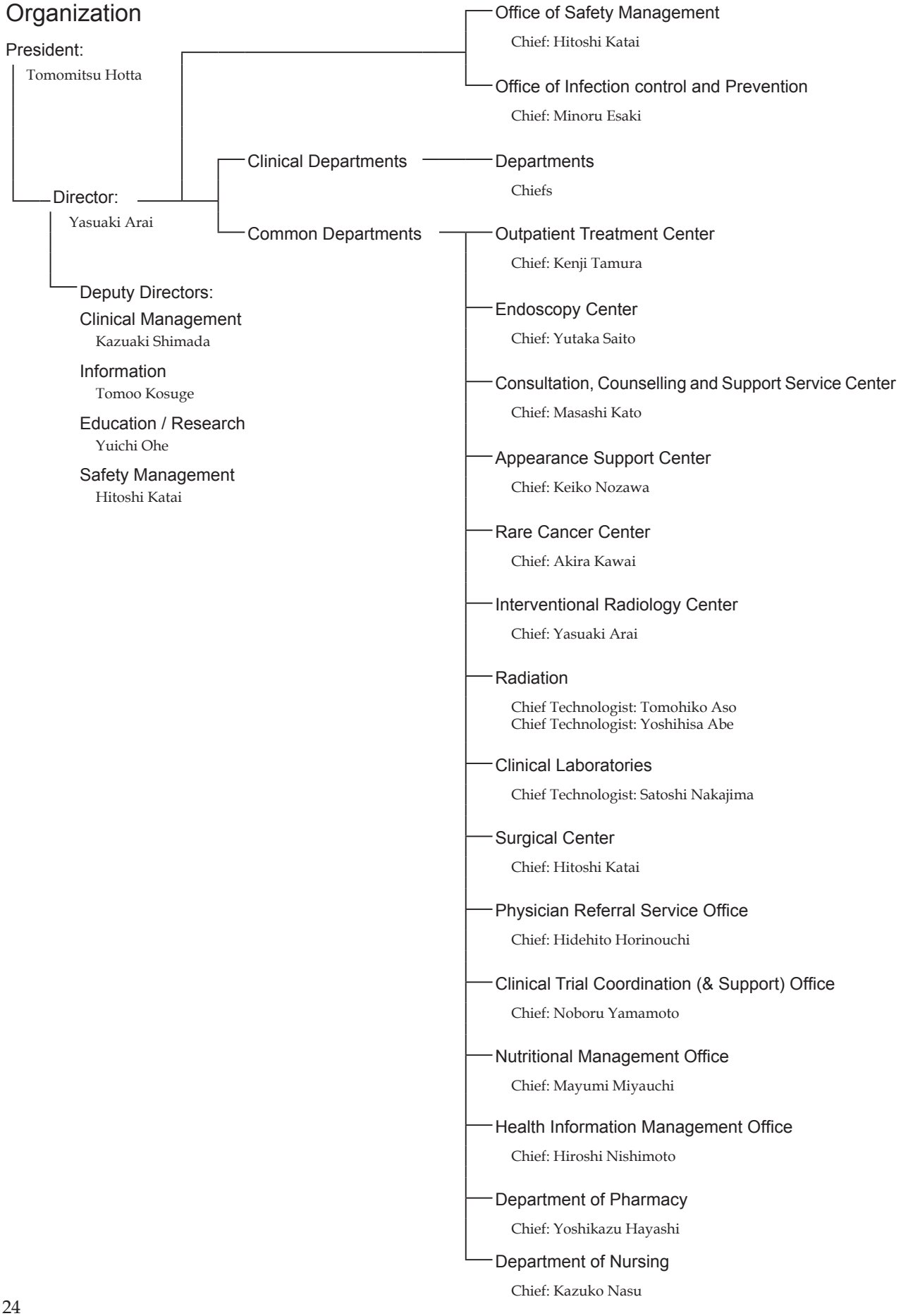
Following to the major reorganization to 14 common departments and 30 clinical departments in 2013, we newly set up two departments: the Interventional Radiology (IR) Center with a hotline which accepts patients requiring for difficult IR treatments; and the Second Outpatient Treatment Center with 62 beds where facilities area available for conducting pharmacokinetic analysis and coping with emergent issues in clinical trials. The Outpatient Treatment Center aims to provide better outpatient treatment and extend outpatient clinics for clinical studies at an early phase. Moreover, we reorganized research facilities to improve the effectiveness of system for translational research with the NCC Research Institute and the Exploratory Oncology Research & Clinical Trial Center (EPOC).

To strengthen the system to care patients with complications, the NCCH concluded a comprehensive cooperation agreement with the Jikei University School of Medicine and prepared for concluding a clinical cooperation agreement with Saiseikai Central Hospital. In addition, we established the medical care ethics committee in collaboration with the NCCH East, and two innovative treatments were started at patients' own expense after their deliberation. For a better supportive care, the Patient Support Center (tentative) is planned to be open. We continue to work for a better hospital management through enhancing staff members' awareness of management improvement.

In this year, we have completed in improving clinical and research as well as management systems and promoting collaboration with other institutes for expansion of clinical practices.

Yasuaki Arai, MD
Director of the Hospital
National Cancer Center

Organization



Clinical Departments

Director:
Yasuaki Arai

Deputy Directors:

Clinical Management
Kazuaki Shimada

Information
Tomoo Kosuge

Education/Research
Yuichiro Ohe

Safety Management
Hitoshi Katai

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  Chief: Yoshitaka Narita
- Department of Ophthalmic Oncology
  Chief: Shigenobu Suzuki
- Department of Head and Neck Surgery
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- Department of Plastic and Reconstructive Surgery
  Chief: Shimpei Miyamoto
- Department of Breast Surgery
  Chief: Takayuki Kinoshita
- Department of Breast and Medical Oncology
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  Chief: Kensei Tobinai
- Department of Hematopoietic Stem Cell Transplantation
  Chief: Takahiro Fukuda
- Department of Blood Transfusion and Cellular Therapy
  Chief: Ryuji Tanosaki
- Department of Pediatric Oncology
  Chief: Chitose Ogawa
- Department of General Internal Medicine, Dentistry, Oncologic Emergencies
  Chief: Ken Ohashi
- Department of Anesthesia and Intensive Care
  Chief: Tetsufumi Sato
- Department of Palliative Care
  Chief: Eriko Satomi
- Department of Psycho-Oncology
  Chief: Ken Shimizu
- Department of Diagnostic Radiology
  Chief: Yasuaki Arai
- Department of Radiation Oncology
  Chief: Jun Itami
- Department of Pathology and Clinical Laboratories
  Chief: Nobuyoshi Hiraoka

Activities of the Departments

Department of Neurosurgery and Neuro-Oncology

Yoshitaka Narita, Yasuji Miyakita, Makoto Ohno, Masamichi Takahashi, Hideyuki Arita, Takahiro Ogawa, Motoki Yonezawa, Sakura Kuzuoka

Introduction

Patients with primary and metastatic brain tumors are treated by 4 neurosurgeons and 1 senior resident in the Department of Neurosurgery and Neuro-Oncology. 317 patients were admitted and 96 craniotomies for tumor removal were carried out in 2014 including 34 gliomas, 42 brain metastases, 5 primary CNS lymphomas, and 7 meningiomas (Table 1). The site of the craniotomy and the extent of tumor removal were visualized on the intraoperative MRI in real time, contributing to safer and more precise surgery. Intraoperative monitoring with motor- and sensory evoked potential (MEP and SEP) recording as well as preoperative functional MRI and MR tractography were also used to preserve patient neurological function. 12 awake surgeries were also performed, particularly for removal of gliomas near the speech center. Patients with malignant brain tumors were treated with postoperative radiotherapy and chemotherapy. In order to design a more effective chemotherapy regimen, molecular biological studies for drug resistance, growth factors, cell kinetic studies on individual tumors and several clinical trials are ongoing.

Routine activities

A weekly conference of treatment of patients with brain tumors is held with doctors of the Department of Radiation Oncology on diagnosis and the Division of Brain Tumor Translational Research. Usually 20 patients are hospitalized and 2 or 3 of them undergo surgical treatment every week. The patients with malignant brain tumors receive postoperative radiotherapy and chemotherapy. Statistical analysis revealed that surgical removal of as much of the tumor as possible yielded better survival rates even for the most malignant glioblastomas, which usually recur soon after the surgery without radiotherapy. Concomitant use of chemotherapy is considered to enhance the anti-tumor effect of radiotherapy. Temozolomide has been given to all malignant glioma patients during radiotherapy and repeated every month for 2 years. The 5-year survival rates of the patients with anaplastic astrocytomas and glioblastomas were 66.1% and 10.1%, respectively, which were better than those recorded in the Brain Tumor Registry of Japan (BTRJ). High dose methotrexate is administered to the patients with primary CNS lymphoma before radiotherapy.

The decision on the indication for surgery of metastatic brain tumors is not simple. Multiplicity of brain metastasis, the stage of the primary malignancy and the patient performance status should be taken into careful consideration.

Research activities

Patients with brain tumors have been registered in the BTRJ since 1969. More than 100,000 patients have been registered and followed up. The Department of Neurosurgery and Neuro-Oncology, the National Cancer Center Hospital, contributes as a managing office of the BTRJ and established on-line registration using the University Hospital Medical Information Network (UMIN) system in 2009. Clinical data during 2001 and 2004 were collected and the report will be published in 2014 as a supplement of the official journal of the Japan Neurosurgical Society.

An analysis of gene expression profiles in malignant gliomas is being carried out in order to determine specific genes that have an influence on the effects of chemotherapy and radiation therapy in cooperation with the Division of Brain Tumor Translational Research, the National Cancer Center Research Institute. The determination of the methylation status of O6-methylguanine-DNA methyltransferase (MGMT) and the mutation of IDH1/2 and TERT are also carried out to predict the prognosis of the patients with malignant gliomas.

Clinical trials

The Japan Clinical Oncology Group (JCOG)-Brain Tumor Study Group was organized in 2002 and a multi-institutional randomized controlled trial is performed. "A randomized controlled phase II/III study of chemoradiotherapy using ACNU versus procarbazine and ACNU for astrocytoma grade 3 and 4 (JCOG0305)" was published. "A multicenter randomized phase II trial of Interferon-beta and Temozolomide combination chemoradiotherapy for newly diagnosed glioblastomas (JCOG 0911)" and "A Randomized phase III trial of postoperative whole brain radiation therapy compared with salvage stereotactic radiosurgery in patients with one to four brain metastasis (JCOG 0504)" was finished.

These studies, under the surveillance of JCOG, aim to set a standard protocol for treating malignant brain tumor patients. Moreover, a proper methodology for performing randomized studies will be established in the field of neuro-oncology. "Phase III randomized Study in patients with anaplastic glioma of radiotherapy with versus nimustine hydrochloride (ACNU) followed by temozolomide (JCOG1016)," "Phase III Study of High-dose Methotrexate and Whole Brain Radiotherapy With or Without Concomitant and Adjuvant Temozolomide in Patients with Primary CNS Lymphoma (JCGO1114)," "Randomized phase III study for unresectable WHO Grade II astrocytoma with radiotherapy alone or chemoradiotherapy with temozolomide (JCOG1303)," and "a multicenter randomized phase III study for recurrent glioblastoma comparing bevacizumab alone with dose-dense temozolomide followed by bevacizumab" are now ongoing.

Education

Our Department plays roles as an office of general secretary of JCOG-Brain tumor study group and brain tumor registry of Japan, we conducted many clinical trials and brain tumor registry. We educate many neurosurgeons and oncologist about surgical techniques of awake craniotomy and intraoperative MRI and the effective usage and adverse effects of many chemotherapeutic agents about malignant brain tumors.

Future Prospects

Malignant brain tumors, especially glioblastoma have still worse prognosis among cancers. We always make an effort to conquer these brain cancers through various clinical works and research.

Table 1. Number of patients

	2010	2011	2012	2013	2014
Surgeries	145	123	132	140	128
Craniotomy	115	92	98	106	96
Glioma	51	35	47	39	34
Brain metastases	42	39	33	40	42
Meningioma	9	5	7	12	7
Lymphoma	4	6	4	7	5
Spinal tumors			2	4	1
Others	4	7	5	8	7
Neuroendoscope, shunt	30	31	34	34	32

List of papers published in 2014

Journal

1. Narita Y, Tsukagoshi S, Suzuki M, Miyakita Y, Ohno M, Arita H, Saito Y, Kokojima Y, Watanabe N, Moriyama N, Shibui S. Usefulness of a glass-free medical threedimensional autostereoscopic display in neurosurgery. Int J Comput Assist Radiol Surg, 9:905-911, 2014
2. Committee of Brain Tumor Registry of Japan. REPORT OF BRAIN TUMOR REGISTRY OF JAPAN (2001-2004) 13th Edition. Neurol Med Chir (Tokyo), 54:1-102, 2014
3. Arita H, Narita Y, Miyakita Y, Ohno M, Sumi M, Shibui S. Risk factors for early death after surgery in patients with brain metastases: reevaluation of the indications for and role of surgery. J Neurooncol, 116:145-152, 2014
4. Fukushima S, Yoshida A, Honda K, Maeshima AM, Narita Y, Yamada T, Shibui S, Tsuda H. Immunohistochemical actinin-4 expression in infiltrating gliomas: association with WHO grade and differentiation. Brain Tumor Pathol, 31:11-16, 2014
5. Fukushima S, Otsuka A, Suzuki T, Yanagisawa T, Mishima K, Mukasa A, Saito N, Kumabe T, Kanamori M, Tominaga T, Narita Y, Shibui S, Kato M, Shibata T, Matsutani M, Nishikawa R, Ichimura K. Mutually exclusive mutations of KIT and RAS are associated with KIT mRNA expression and chromosomal instability in primary intracranial pure germinomas. Acta Neuropathol, 127:911-925, 2014
6. Fukushima S, Narita Y, Yonezawa M, Ohno M, Arita H, Miyakita Y, Ichimura K, Yoshida A, Shibui S. Short communication: sclerosing meningioma in the deep sylvian fissure. Brain Tumor Pathol, 31:289-292, 2014
7. Saito K, Mukasa A, Narita Y, Tabei Y, Shinoura N, Shibui S, Saito N. Toxicity and outcome of radiotherapy with concomitant and adjuvant temozolomide in elderly patients with glioblastoma: a retrospective study. Neurol Med Chir (Tokyo), 54:272-279, 2014
8. Sato A, Okada M, Shibuya K, Watanabe E, Seino S, Narita Y, Shibui S, Kayama T, Kitanaka C. Pivotal role for ROS activation of p38 MAPK in the control of differentiation and tumor-initiating capacity of glioma-initiating cells. Stem Cell Res, 12:119-131, 2014
9. Okada M, Sato A, Shibuya K, Watanabe E, Seino S, Suzuki S, Seino M, Narita Y, Shibui S, Kayama T, Kitanaka C. JNK contributes to temozolomide resistance of stem-like glioblastoma cells via regulation of MGMT expression. Int J Oncol, 44:591-599, 2014
10. Kinoshita M, Sasayama T, Narita Y, Yamashita F, Kawaguchi A, Chiba Y, Kagawa N, Tanaka K, Kohmura E, Arita H, Okita Y, Ohno M, Miyakita Y, Shibui S, Hashimoto N, Yoshimine T. Different spatial distribution between germinal center B and non-germinal center B primary central nervous system lymphoma revealed by magnetic resonance group analysis. Neuro Oncol, 16:728-734, 2014
11. Aihara K, Mukasa A, Gotoh K, Saito K, Nagae G, Tsuji S, Tatsuno K, Yamamoto S, Takayanagi S, Narita Y, Shibui S, Aburatani H, Saito N. H3F3A K27M mutations in thalamic gliomas from young adult patients. Neuro Oncol, 16:140-146, 2014
12. Yoshida A, Tsuta K, Ohno M, Yoshida M, Narita Y, Kawai A, Asamura H, Kushima R. STAT6 immunohistochemistry is helpful in the diagnosis of solitary fibrous tumors. Am J Surg Pathol, 38:552-559, 2014

Department of Ophthalmic Oncology

Shigenobu Suzuki, Yukiko Aihara, Shuichi Sano

Introduction

Our Department is one of the rare groups specializing in ocular tumors, especially intraocular tumors. Recently, more than 70% of patients nationwide with retinoblastoma, which is the most frequent intraocular malignancy in childhood, and more than 50% of patients with choroidal melanoma, which is the most frequent primary intraocular malignancy in adults, have been referred to our Department.

Routine activities

Our outpatient service is open for four days a week. Every week, seven operations under general anesthesia and minor surgeries under local anesthesia are performed in our department. Our treatment strategies for ocular tumors are as follows:

1) Retinoblastoma

Unless the patient's family has anxiety about preserving the affected eye, if the eye has already suffered from complication such as secondary glaucoma or severe hemorrhage, or if extraocular extension of the retinoblastoma is strongly suspected, we can offer the family eye-preserving treatment. Initial systemic chemotherapy and additional local therapies, called "chemoreduction therapy", comprise the main strategy. If the tumor is localized in the peripheral retina, plaque radiotherapy using ruthenium-106 is also available. Transpupillary thermotherapy or cryotherapy is also used in cases with localized small tumors. Patients with extraocular extension, recurrence or metastasis who need systemic chemotherapy are treated with dedicated support from the Department of Pediatric Oncology.

2) Choroidal melanoma

Choroidal melanoma is a rare disease in Asians. Recent reports from Western countries have demonstrated that the prognosis of eye-preserving treatment with plaque radiotherapy is equivalent to that of enucleation (COMS, medium-sized tumor study). For localized tumors up to 5 mm thick, ruthenium-106 plaque radiotherapy is the first choice. In Japan, plaque radiotherapy is only available in our institute. Patients with much larger tumors are referred to the National Institute of Radiological Science, Research Center for Charged Particle Therapy, for carbon ion therapy. Choroidal melanomas often metastasize to the liver and this is invariably fatal. Life-long follow-up with liver imaging is routinely conducted for our patients. Patients with liver and systemic metastases are treated by the Department of Dermatologic Oncology.

3) Orbital tumors

Whereas most orbital tumors in childhood are benign, rhabdomyosarcoma is a malignant tumor that requires systemic chemotherapy and radiation after biopsy. The most common orbital tumors in adults include cavernous hemangioma, lacrimal gland tumor, lymphoma, metastatic tumor, and orbital inflammatory disease. Patients with a biopsy-confirmed orbital lymphoma are referred to the Department of Hematology, and Hematopoietic Stem Cell Transplantation. Total resection by orbitotomy, or sometimes orbital exenteration, is used for lacrimal gland tumors. Recurrent lacrimal gland cancers are referred to the National Institute of Radiological Science, Research Center for Charged Particle Therapy, for carbon ion therapy.

4) Eyelid tumors

The most common malignant eyelid tumors include basal cell carcinoma, sebaceous carcinoma, and squamous cell carcinoma. They are treated by excisional resection with reconstruction. Radiotherapy using electrons is another strategy. Orbital exenteration is selected in cases of orbital invasion.

5) Conjunctival tumors

Conjunctival malignant tumors are treated by excisional resection with a safety margin combined with cryotherapy at the resection margin. Diffuse conjunctival tumors or tumors with orbital invasion are treaded with orbital exenteration.

Research activities

One of the unique techniques in our department is local chemotherapy for retinoblastoma via selective ophthalmic artery infusion using a balloon catheter. This procedure was developed in our hospital from 1987, and has been modified and performed after 2009 in more than 20 countries. We are planning the clinical trial on selective ophthalmic artery injection therapy for initial treatment methods.

Direct injection of diluted melphalan into the vitreous cavity is performed for retinoblastoma eyes with vitreous seeding. Vitreous seeding can be cured for eyes with vitreous seeds after other treatment modalities, and about 65% eyes were rescued using this strategy.

The National Registry of Retinoblastoma in Japan was organized in 1975, and more than 3,000 patients are registered. We contribute to this registry as an administrator of personal data, and checking overlapping. This registry covers almost all patients in Japan now, and providing epidemiological data.

Clinical study concerning about the development of retinoblastoma patients with visual disturbance, and maternal psychological burden, is now ongoing. The result will be helpful for social and psychological approach to retinoblastoma patients and their families.

We are now investigating the specific marker or genetic change for eye tumors, especially retinoblastoma, choroidal melanoma, and ciliary tumors.

We also contribute to the international registry system, as AJCC Ophthalmic Expert Panel, to advise and reflect the Asian data to TNM system.

Ocular adverse events by anti-cancer drugs used for systemic disease are recently recognized, and ocular examinations are included in clinical trials, especially for molecular targeted drugs. Serous retinal detachment (SRD), retinal vein occlusion (RVO), and ocular surface complications are major adverse events by kinase inhibitor drugs, stenosis or occlusion of lacrimal drainage systems are common events by S-1, and cystoid macular edema (CME) by some drugs. We examine and follow these adverse events, with or without additional treatment, to support clinical studies, to contribute establishing protocols, and to enlighten these events to general ophthalmologist.

Future Prospects

We should establish the multicenter study group for eye tumors to employ clinical studies, confirm the diagnostic criteria and guidelines, and clarify the carcinogenesis for eye tumors.

Table 1. Number of patients for each primary site (surgical case only)

Retinoblastoma	53
Choroidal melanoma	15
Other intraocular tumors	25
Eyelid tumor	18
Conjunctival tumor	10
Orbital tumor	21
Ocular adnexal lymphoma	11
Other	23
Total	176

Table 2. Type of procedure

Retinoblastoma	
Selective ophthalmic arterial injection	117
Laser and/or vitreous injection	131
Ruthenium brachytherapy	7
Enucleation	19
Examination under general anesthesia	5
Choroidal melanoma	
Ruthenium brachytherapy	8
Enucleation	3
Resection of ciliary body tumor	2
Resection of eyelid tumor	6
Resection of conjunctival tumor	8
Resection of orbital tumor	16
Total	322

List of papers published in 2014

Journal

1. Harada K, Murakami N, Kitaguchi M, Sekii, S, Takahashi K, Yoshio K, Inaba K, Morota, M, Ito Y, Sumi M, Suzuki S, Tobinai K, Uno, T, Itami J. Localized ocular adnexal mucosaassociated lymphoid tissue lymphoma treated with radiation therapy: a long-term outcome in 86 patients with 104 treated eyes. Int J Radiat Oncol Biol Phys, 88:650-654, 2014

Department of Head and Neck Oncology

Seiichi Yoshimoto, Fumihiko Matsumoto, Kenya Kobayashi, Daisuke Maki, Sadahiro Kishishita

Introduction

The treatment strategy for head and neck cancer is to improve the survival rates while preserving the significant functions including speech, mastication, swallowing and cosmetic appearance. In order to achieve this strategy, our Department has tried to select the best treatment modality and devise new surgical procedure based on the clinic-pathological findings and our large database of the patients with head and neck cancer.

Our Department has developed and performed original surgical procedure of partial laryngectomy for newly-diagnosed and radiation-failed early glottic cancer, partial pharyngectomy for early hypopharyngeal cancer and total glossectomy for advanced tongue cancer. These surgical approaches can be performed without sacrificing the larynx. Compared with the results of conventional surgery, there are apparently fewer wound complications. Patients can resume social activities more easily when they maintain their ability to communicate vocally.

Routine activities

The Department of Head and Neck Oncology at NCCH consists of 5 head and neck surgeons. Many operations are performed under general and local anesthesia with or without microsurgical reconstructive surgery. In addition to radiotherapy, concurrent chemo-radiotherapy is performed with the Department of Radiation Oncology.

In 2014, 345 patients with head and neck tumor underwent surgery under local or general anesthesia; 91 and 254, respectively, including 57 patients with major ablation and reconstructive surgery. Table 1 shows the number of surgical cases with each primary site. Table 2 shows the number of each surgical procedure.

Research activities

We have been taking part in multi-institutional studies of sentinel lymph node navigation surgery for oral cavity cancer using RI and laryngopharyngeal cancer using ICG. We are also taking part in multi-institutional study of intra-arterial chemo-radiotherapy for maxillary cancer.

Education

We provide plenty of educational opportunities for resident doctors, especially focusing on acquiring operative technique. They can learn everything about perioperative management, such as physical examination, image diagnosis, informed consent, preoperative preparation and postoperative management.

Future Prospects

We recently have started trans-oral resection for superficial laryngo-pharyngeal cancer. Trans-oral resection will be indicated for more patients. Cetuximab is used for many patients with recurrent or metastatic tumor. We will be able to get useful information about the response rate of Cetuximab for Japanese patients.

Table 1. Number of patients for each primary site (surgical case only)

Tongue	38
Oral Cavity (without tongue)	56
Nasal and paranasal cavity	16
Nasopharynx	6
Oropharynx	35
Hypopharynx	53
Cervical esophagus	9
Larynx	29
Salivary Gland	20
Thyroid	34
Parathyroid	0
Neck	43
Others	6
Total	345

Table 2. Type of procedure

Skull base (+reconstruction)	4(3)
Maxillectomy (+reconstruction)	11(3)
Glossectomy (+reconstruction)	35(7)
Resection of Oral Cavity (+reconstruction)	46(11)
Nasopharyngectomy	5(2)
Oropharyngectomy (+reconstruction)	27(7)
Endoscopic resection of hypopharynx	24
Trans-oral resection of hypopharynx	4
Partial pharyngectomy (+reconstruction)	5(5)
Total laryngopharyngectomy (+recon.)	15(14)
Trans-oral resection of larynx	5
Partial laryngectomy	4
Total laryngectomy (+reconstruction)	6
Thyroidecotmy	26(1)
Parotidectomy	10
Neck dissection (+reconstruction)	28(1)
Resection of parapharyngeal tumor	3
Voice prosthesis	9
Lymphadenectomy	48
Others (+reconstruction)	30(3)
Total	345(57)

List of papers published in 2014

Journal

1. Yoshimoto S, Nakashima T, Fujii T, Matsuura K, Otsuki N, Asakage T, Fujimoto Y, Hanai N, Homma A, Monden N, Okami K, Sugasawa M, Hasegawa Y, Nibu K, Kamata S, Kishimoto S, Kohno N, Fukuda S, Hisa Y. Japanese Board Certification System for head and neck surgeons. Auris Nasus Larynx, 41:327-330, 2014
2. Fukunaga Y, Sakuraba M, Miyamoto S, Kayano S, Kurosawa K, Fujiki M, Sakisaka M, Yoshimoto S. One-stage reconstruction of a tracheal defect with a free radial forearm flap and free costal cartilage grafts. J Plast Reconstr Aesthet Surg, 67:857-859, 2014
3. Watabe Y, Mori T, Yoshimoto S, Nomura T, Shibahara T, Yamada T, Honda K. Copy number increase of ACTN4 is a prognostic indicator in salivary gland carcinoma. Cancer Med, 3:613-622, 2014
4. Murakami N, Mori T, Yoshimoto S, Ito Y, Kobayashi K, Ken H, Kitaguchi M, Sekii S, Takahashi K, Yoshio K, Inaba K, Morota M, Sumi M, Itami J. Expression of EpCAM and prognosis in early-stage glottic cancer treated by radiotherapy. Laryngoscope, 124:E431-436, 2014

Department of Plastic and Reconstructive Surgery

Shimpei Miyamoto, Masahide Fujiki, Masaki Arikawa

Introduction

Department of Plastic and Reconstructive Surgery has mainly focused on surgical reconstruction after cancer ablation. In our institution, reconstructive procedures using free flap transfer with microvascular anastomosis are the most important operations. In addition, several methods such as tissue transfer with pedicled flap, local flap, skin graft etc are used for reconstructive surgery. The objectives of reconstructive surgery are not only the morphological reconstruction, but also the restoration of postoperative function after ablative surgery. The quality of life (QOL) of the patient can be improved by the functional and morphological reconstruction.

Routine activities

Two plastic surgeons cover reconstructive operations. Every week five to ten reconstructive operations are performed. These reconstructive surgeries are performed in cooperation with the surgeons of another division of hospital, such as Head and Neck Surgery, Breast Surgery, Orthopedic Surgery, Esophageal Surgery, and Dermatology etc. The number of the patients who receive immediate breast reconstruction is increasing. Most patients undergo breast reconstruction with a silicone implant. Limb reconstruction after limb preservation surgery has increased.

Research activities

Multi-institutional analysis of postoperative function after microvascular tongue reconstruction is now going on. Also, laboratory research of flow-through flap using a rat model is now going on.

Table 1. Reconstructive procedures

Free flap	131
DIEP	34
ALT	35
Jejunum	26
LD (or TAP)	17
RAMC	10
Fibula	3
Scapula	5
Dorsalis Pedis	1
Other microsurgical procedures	15
Supercharge	3
Extremity revascularization	3
Hepatic artery	3
Others	6
Total (Microsurgery)	146
Pedicled flap	39
LD (or TAP)	12
Pectoralis Major	7
ALT	6
RAMC	4
Others	10

Table 2. Breast reconstruction

Tissue expander	56
Silicone implant	29
DIEP	30
LD	5

List of papers published in 2014

Journal

1. Miyamoto S, Fukunaga Y, Shinozaki T, Yasunaga Y, Hayashi R, Sakuraba M. T-shaped Pectoralis Major Musculocutaneous Flap for Reconstruction of an Extensive Circumferential Pharyngeal Defect. Plast Reconstr Surg Glob Open, 2:e129, 2014
2. Miyamoto S, Kayano S, Fujiki M, Chuman H, Kawai A, Sakuraba M. Early Mobilization after Free-flap Transfer to the Lower Extremities: Preferential Use of Flow-through Anastomosis. Plast Reconstr Surg Glob Open, 2:e127, 2014
3. Miyamoto S, Kayano S, Fujiki M, Sakuraba M. Combined use of the cephalic vein and pectoralis major muscle flap for secondary esophageal reconstruction. Microsurgery, 34:319-323, 2014
4. Miyamoto S, Kayano S, Kamizono K, Fukunaga Y, Nakao J, Nakatani F, Kobayashi E, Sakuraba M. Pedicled superficial femoral artery perforator flaps for reconstruction of large groin defects. Microsurgery, 34:470-474, 2014
5. Miyamoto S, Kayano S, Umezawa H, Fujiki M, Nakao J, Sakuraba M. Efficient design of a latissimus dorsi musculocutaneous flap to repair large skin defects of the upper back. Microsurgery, 34:20-22, 2014

Department of Breast Surgery

Takayuki Kinoshita, Takashi Hojo, Sota Asaga, Kenjiro Jimbo, Eriko Iwamoto, Kanae Taruno, Takuya Ogura

Introduction

The Department of Breast Surgery deals with treatment of breast cancer thorough surgeries, as well as diagnosis of breast diseases and assessment of lymph nodes in the axillary and clavicular regions which are suspected harboring metastases. The trend of surgical procedure has been changing year by year. Although breast-conserving therapy (BCT) has accounted for 43% of the total surgeries in our Department in 2014, BCT are on the decline in recent years. One of the reasons is increasing needs of immediate reconstruction surgeries. In 2010, immediate breast reconstruction became one of the choices for these patients in whom breast preservation was impossible, and a total of 75 immediate breast reconstructions were performed in 2014, comprising more than 14% of all the cases. The number of cases of immediate breast reconstruction has gradually increased year by year to match the increase needs of patients. Sentinel lymph node (SLN) biopsies (SLNB) were performed in 67% of the cases. Following SLNB, the axillary lymph node dissection (ALND) could be avoided when the SLNB was negative. One-step nucleic acid amplification (OSNA) assay, that quantitatively measures CK19 mRNA detects sentinel lymph node metastases even in molecular levels, in conjunction with this assay and conventional microscopic method, we began to be able to evaluate the SLN more precisely. Further, by comparing the OSNA results with that of conventional histological diagnosis, we try to search the possibility of omitting axillary lymph node dissection by using two methods. Thus, to meet the diverse needs of breast cancer patients, we are striving continuously.

Routine activities

Our Department comprised of four staff surgeons, one chief resident, and three or four rotating residents. From 7:20 every morning, all the staff and the residents perform in patient rounds together. Journal club and research conference are scheduled on every Tuesday morning after rounds. Weekly conferences are held on Monday and Wednesday from 17:00 to 18:00 for shared discussions with surgeons, medical oncologists, radiologists, and radiology and sonography technicians. The diagnostic images of pre-operative patients are reviewed and compared to pathological reports in every postoperative patient. A breast pathology/imaging conference is held on the second Wednesday of each month from 19:00 to 20:00 to discuss problems with diagnostic imaging, and with pathologically interesting cases. A conference about studies, institutional treatment guidelines and recent topics regarding breast cancer is held on last Wednesday of each month by a multidisciplinary team. Treatment Guidelines for primary and metastatic breast cancer have been updated regularly through this multidisciplinary discussion since 2003.

Surgery

We perform surgeries from Monday to Friday, regularly 10 to 12 cases of breast cancer in a week.

Table 1 showed a total number of patients with primary breast cancer (including breast primary sarcoma) and other breast disease. The types and number of operative procedures are shown in Table 2. The rate of mastectomy was 51% (262/514), including 75 cases of immediate reconstruction. SLNB was performed in 331 patients, and 251 patients were spared from ALND.

Research activities and Clinical trials

1) Radiofrequency ablation therapy for early breast cancer as local therapy (RAFAELO study)

Trial of image-guided radiofrequency ablation (non-surgical therapy) has accomplished for early-stage breast carcinomas of less than 1.0

cm in diameter (Phase I/II study; Kinoshita et al.). After these years of trial, indication has just been expanded up to 1.5 cm in diameter and this technique is certified as an advanced medical treatment by Ministry of Health, Labour and Welfare. Our secondary goals are to determine the size, configuration and pathological features of acute RFA treatment of breast cancers, and have been conducted clinical study to evaluate the oncologic safety of RFA in terms of local recurrence.

2) Intensive vs. standard post-operative surveillance in high risk breast cancer patients (JCOG1204, INSPIRE Trial)

This is a multi-center randomized phase 3 trial which started in 2012. This clinical trial is to prove the hypothesis that postoperative intensive follow-up of patients with breast cancer is good for a standard follow-up.

3) Denosumab adjuvant treatment (D-CARE)

This phase 3 multi-center, randomized, double blind, placebo controlled study has continued, designed to compare the treatment effect of denosumab with that of a placebo on prolonging bone metastasis-free survival in subjects with early-stage breast cancer at high risk of disease recurrence.

4) Scalp-cooling device during chemotherapy

A feasibility study to test the use of a scalp-cooling device that breast cancer patients will wear while undergoing chemotherapy treatment has started and continued in order to slow or halt hair loss during chemotherapy.

5) Postoperative Therapy with Endocrine and TS-1 (POTENT study)

This multi-center randomized trial continued from 2012. This study compares invasive disease-free survival in patients with or without TS-1 administration together with adjuvant endocrine therapy in hormone positive and HER2 negative high recurrence risk patients.

6) Registration Data-base System of the breast cancer patient who carried out the lymph node metastasis diagnosis by the OSNA® method (LynoLog Data-base)

The aim of this study is to accumulate the administrative data of case with OSNA method in common database LynoLog and to evaluate the clinical significance of intraoperative SLN metastases detected by OSNA.

7) Olaparib as Adjuvant Treatment in Patients With Germline BRCA Mutated High Risk HER2 Negative Primary Breast Cancer (OlympiA)

A randomised, double-blind, parallel group, placebo-controlled multi-centre phase III study has started in 2014. The aim of study is to assess the efficacy and safety of olaparib versus placebo as adjuvant treatment in patients with germline BRCA1/2 mutations and high risk HER2 negative primary breast cancer who have completed definitive local treatment and neoadjuvant or adjuvant chemotherapy.

Table 1. Number of patients

		2012	2013	2014
Primary breast cancer (or sarcoma)		494	555	514
cStage	0	76	99	106
	II	199	215	184
	II	194	203	189
	III	17	33	27
	IV	8	5	3
unknown		2	0	6

16 and 11 case were bilateral breast cancer in 2013 and 2014.

Table 2. Type of procedure

	2011		2012		2013		2014	
Total number of operations	576		581		613		566	
Total number of Primary breast cancer	525		494		555		514	
Mastectomy (%)	250	(48)	234	(45)	263	(47)	262	(51)
Breast-conserving surgery (%)	269	(51)	275	(53)	283	(51)	222	(43)
Radiofrequency ablation (%)	6	(1)	6	(1)	9	(2)	30	(6)
Axillary lymph node dissection (ALND) (%)	205	(42)	188	(38)	93	(18)	83	(17)
Sentinel lymph node biopsy (SLNB) (%)	402	(81)	409	(83)	347	(66)	331	(67)
ALND after SLNB (%)	113	(23)	103	(21)	83	(16)	80	(16)
Immediate breast reconstruction (%)	74	(14)	62	(13)	65	(12)	75	(14)
Neoadjuvant therapy	57	(11)	45	(8)	38	(7)	36	(7)

Table 3. Survival (2006.1-2007.12)

		No. of patients	5-yr survival (%)
Total			92
stage	0	150	100
	I	303	95
	II	381	93
	III	28	73

List of papers published in 2014

Journal

1. Shien T, Iwata H, Fukutomi T, Inoue K, Aogi K, Kinoshita T, Ando J, Takashima S, Nakamura K, Shibata T, Fukuda H. Tamoxifen plus tegafur-uracil (TUFT) versus tamoxifen plus Adriamycin (doxorubicin) and cyclophosphamide (ACT) as adjuvant therapy to treat node-positive premenopausal breast cancer (PreMBC): results of Japan Clinical Oncology Group Study 9404. Cancer Chemother Pharmacol, 74:603-609, 2014
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6. Shien T, Iwata H, Aogi K, Fukutomi T, Inoue K, Kinoshita T, Takahashi M, Matsui A, Shibata T, Fukuda H. Tamoxifen versus tamoxifen plus doxorubicin and cyclophosphamide as adjuvant therapy for node-positive postmenopausal breast cancer: results of a Japan Clinical Oncology Group Study (JCOG9401). Int J Clin Oncol, 19:982-988, 2014

Department of Breast and Medical Oncology

Kenji Tamura, Yasuhiro Fujiwara , Chikako Shimizu, Kan Yonemori, Mayu Yunokawa, Harukaze Yamamoto, Makoto Kodaira, Jun Hashimoto

Introduction

The Department of Breast and Medical Oncology provides the most effective treatment by the use of chemotherapy, and also works on the establishment of new standard care for adult malignancies including breast cancer, gynecologic cancer, soft-tissue sarcoma, extragonadal germ cell tumor, primary unknown tumors and other rare types of solid tumors.

We envisage becoming a premier medical oncology department which leads cancer care in Japan and in the world. Our mission is to provide patient-centered, state-of-the-art medical care to cancer patients, to develop new effective cancer treatment through clinical and translational research, and to nurture medical oncologist. An evidence-based, research-oriented and multi-disciplinary approach is the core value of our practice.

Clinical activities

1. Setup

Our Division consists of eight full-time attending physicians, four chief residents (fellows) and one to three clinical residents. We also provide educational opportunities to short-term (a half year) residents. Full-time attending physicians are on duty at the outpatient clinic two to three days per week. The management of hospitalized patients is undertaken by clinical teams consisting of attending physicians and residents. A Grand Round is scheduled on every Wednesday and Friday.

2. Performance

There were a total of 898 first visits of new patients in 2014 (Table 1). Approximately two-thirds of the new patients were referred from other departments of the National Cancer Center Hospital (NCCH). About a half of new patients are breast cancer patients, but it is noteworthy that there was approximately 50% increase in patients with adult sarcoma this year as a result of our devotion to the Rare Cancer Center. The number of outpatient chemotherapy delivered by our Division were 9,662, which accounts for 37% of the total number and rank first of the number of treatments delivered at of the Outpatient Treatment Center.

We have approximately 27 (range 22-33) inpatients daily. Terminally-ill patients are transferred to palliative care units or in-home care clinics outside the NCCH, whereas 24 patients of our Division passed away in the NCCH in 2014. Autopsy was undertaken in five patients.

3. Conference

The one-hour briefing medical conference is held every morning to discuss the evidenced-based care for individual patients. Basic and translational research conference is held on Tuesday, a journal club on Wednesday, a clinical trial conference on Thursday, and a weekend and outpatient follow-up conference on Friday. A Multidisciplinary Case Conferences with diagnostic radiologists, surgeons, and pathologists is held with members of Department of Breast Surgery, Gynecology, Musculoskeletal Oncology and Rehabilitation, Radiation Oncology and Pathology, once or twice (Breast) per week, respectively. We also participate in Exploratory Oncology Research and Clinical Trial Center Conference (Phase 1 team) twice per week as its active members.

Monthly Breast Cancer Conference is held with the participation of the multidisciplinary specialists to discuss recent topics in breast oncology and to update institutional treatment guidelines. This year, we published "Nyugan-shinnryou Application Notebook" from Nankodo based on this guideline, which reflects the consensus of breast team on the body of evidence on breast cancer management.

4. Coordination of care

Three board-certified Breast Cancer Specialist Nurses help providing seamless and comprehensive care to breast cancer patients. Group-assigned pharmacists support patients in the ward and in the clinic. Most patients are supported by the Consultation, Counseling and Support Service Center for coordination of care. Post-operative breast cancer patients without disease recurrence are referred to local breast cancer specialists participating in Tokyo Breast Consortium network (http://breastcons.com/).

Research activities

Our research interest extends across xtends across a wide range of topics related to treatment and clinical program development. Many of our researches are secured by public and consignment research grants. In 2014, we conducted ten research programs as primary investigator and also participated in additional nine programs as co-investigator in research programs secured by competitive research funds.

In 2014, we actively enrolled patients in phase I studies (including first in human or global) as well as national and international phase II and III studies (Table 2). Of note, we launched pharmacokinetic and dose-finding study of eribulin/olaparib, and phase II study of eribulin in neoadjuvant setting in triple negative breast cancer as our fourth and fifth investigator-initiated clinical trial (IIT* in Table 2). New molecular imaging studies are launched in cooperation with the Research Institutes. We also conducted many type of prospective cohort translational studies to find novel biomarker.

We value cancer survivorship as a research theme in order to develop a patient-centered comprehensive care program. In 2014, we published a guideline on fertility and fertility preservation for young breast cancer patients in cooperation with gynecologist and reproductive specialists. Also, we took the lead of a multidisciplinary collaborative study group on End-of-life decision support for patients with advanced cancer.

Education

We provide rich educational opportunities to both residents and chief residents through clinical experience as well as research activities. Residents are encouraged to make presentation at local and national conferences. We vigorously support basic, clinical, or translational researches conducted by postgraduate students.

Future prospects

We will continue to establish new standard treatments and propose a near-future model of clinical management of adult solid tumor, including breast cancer, gynecologic cancer. And we also aim to build a comprehensive program which includes tumor registry, translational research, clinical trials and patient care in rare adult tumors based on our rich clinical experience. We would also like to improve the efficiency of anti-cancer drug development by coordinating basic and translational researches in early-phase clinical trials survivorship research and care in Japan, we are going to develop activities in cooperation with domestic and international researchers and practitioners.

Table 1. Demographics of Patients at their 1st Visit to the Clinic of the Breast and Medical Oncology Division (Jan - Dec, 2014)

Number of new patients	n	%
Total	898	
Breast	410	45.6
GYN	160	17.8
Sarcoma	121	13.4
Cancer of primary unknown	110	12.2
Others	97	10.8
Reason for visits of new patients		
2nd opinion	58	6.4
Treatment at NCCH	300	33.4
Referrals from other hospitals	55	6.1
Referrals from other divisions in NCCH	481	53.5 (100)
Breast surgery	310	(64.4)
GYN	68	(14.1)
Urology	26	(5.4)
Orthopedics	20	(4.1)
Others	57	(11.8)
Others	4	0.4

Table 2. Active Clinical Trials (Jan. 2014-Dec. 2014)

Disease	Clinical setting	Phase	Protocol	Regimen	Status
Breast	Neo-adjuvant	II (IIT*)	Neo-Eribulin (TNBC)	Eribulin followed by FEC	Active
	Follow up	III	JCOG1204	Intensive follow up vs standard follow up	Active
	Adjuvant	III	BEATRICE (TNBC)	CTx vs CTx + Bevacizumab	Active, not recruiting
		III	ALTTO (HER2)	Lapatinib vs HCN vs Lapa/HCN	Active, not recruiting
		III	CREATE-X (JBCRG04)	Capecitabine vs none post-NAC	Active, not recruiting
		III	D-CARE	Denosumab vs placebo	Active, not recruiting
		III	APHINITY (HER2)	CTx+HCN/placebo vs CTx/HCN/Pertuzumab	Active
		III	POTENT	HTx+S1 vs HTx alone	Active
		III	KAITLIN (HER2)	Taxane/Trastuzumab/Pertuzumab vs. T-DM1/Pertuzumab	Active
	Metastatic	III	JCOG1017	Surgery vs no surgery for primary Stage IV BC	Active
		III	MARIANNE (HER2)	RO5304020+/- RO4368451 vs HCN/PTX	Active
		III	NK105	NK105 vs Paclitaxel	Active, not recruiting
		III	PALOMA-2 (HR+)	Letrozole +/- PD0332991	Active
		III	ELTOP (WJOG)	Lapa/Capecitabine vs HCN/Capecitabine	Active
		III	OlympAD (BRCA+)	Olaparib vs TPC	Active
		II	CAPTURE (HR+)	Paclitaxel/Bevacizumab vs maintenance endocrine therapy	Active
		II	BEECH	AZD5363+PTX	Active
		II	TARGET (HR+)	Tamoxifen vs high-dose Tamoxifen /CIP2D6	Active
		II	lapaHER (HER2)	Lapatinib/HCN	Active
		II	CBDCA/S1 (TNBC)	CBDCA/S1	Active
		I/II	CAPIRI	Capecitabine/CPT-11	Active
		I/II	S1/docetaxel	S1/docetaxel	Active
		I/II	Lapa/eriburin (HER2)	Lapatinib/eriburin	Active
		I/II (*IIT)	EO (TNBC)	Eribulin/AZD2281	Active
		I/II	PD0332991	Letrozole +PD0332991	Active
		I (exp)	AZD5363 (AKT+ or PIK3CA+)	AZD5363	Active
		PK/PD/PGx	Eriburin PK	Eriburin	Active
Ovary	Adjuvant	III	AZD2281	Chemotherapy+/-Olaparib	Active, not recruiting
	Advanced	III	JCOG0602	Primary surgery vs NAC	Active
		III	JGOG3017	TC vs. CDDP/CPT-11	Active
		III	GOG213	TC +/- bevacizumab	Active
		III	GOG218	TC +/- bevacizumab	Active, not recruiting
		III	AMG386	PTX+/-AMG386	Active, not recruiting
		III	GW786034	Pazopanib	Active, not recruiting
		II	GOG268	TC+Temsirolimus	Active
Cervical cancer	Advanced	I	S1/CDDP	S1/CDDP chemoradiation	Active
Ovary/Endometrial/Cervical		II	Perifosine (PIK3CA+)	Perifosine	Active
Primary unknown cancer		II	CBDCA/S1	CBDCA/S1	Active
PNET/Ewing's sarcoma		II	CDDP/CPT-11 for refractory PNET	CDDP/CPT-11	Active
Solid tumor		I	AZD2281	Olaparib	Active
		I	AZD1208 (global FIH))	AZD1208	Active
		I	AZD5363	AZD5363	Active, not recruiting
		I	PD0332991	PD0332991	Active
		I	Veriparib (BRCA+)	Veriparib	Active
		I	BAY1179470 (FGFR+)	BAY1179470	Active
		I	MK3475 (PDL1+)	MK3475	Active
		I	GDC0032	GDC0032	Active
		I	Ds5573a (FIH)	Ds5573a	Active
Soft tissue sarcoma		II	ET-743	ET-743	Active
CIPN SNPs		TR	Paclitaxel induced peripheral neuropathy	Paclitaxel	Active
Molecular Imaging		TR	Cu64-trastuzumab/PET	Nano-dose, radio-labeled trastuzumab as PET probe	Active
		TR	Cu64- cetuximab/PET	Nano-dose, radio-labeled trastuzumab as PET probe	Active
		TR	MAS- imaging	MAS-imaging for solid tumor	Active
Liquid Biopsy		TR	CTC	CTC/breast, gynecologic (blood)	Active
		TR	ADCC	Quantitative ADCC (blood)	Active
		TR	miRNA in exosome	miRNA in exosome (blood)	Active
Genomic test		TR	TOP-GEAR (NGS)	Genome screening for phase I	Active
(NGS, Sequencing at hot spots, Whole Exon Sequence)		TR	HER-Antibody induced heart failure	HER-Antibody	Active
		TR	Sequencing	Methylation of promoter BRCA	Active, not recruiting
		TR	Sequencing	Methylation of promoter TERT	Active
		TR	Sequencing	AKT1P, PIK3CA	Active

*IIT; investigator-initiated clinical trial, TNBC; triple negative breast cancer, CTx; chemotherapy, HTx; hormonal therapy, HR; hormone receptor, TPC; therapy of physician's choice, TR; translational, NGS; next generation sequence

List of papers published in 2014

Journal

1. Ando M, Yamauchi H, Aogi K, Shimizu S, Iwata H, Masuda N, Yamamoto N, Inoue K, Ohono S, Kuroi K, Hamano T, Sukigara T, Fujiwara Y. Randomized phase II study of weekly paclitaxel with and without carboplatin followed by cyclophosphamide/epirubicin/5-fluorouracil as neoadjuvant chemotherapy for stage II/IIIA breast cancer without HER2 overexpression. Breast Cancer Res Treat, 145:401-409, 2014
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Department of Thoracic Surgery

Shun-ichi Watanabe, Hiroyuki Sakurai, Kazuo Nakagawa, Keisuke Asakura, Kyohei Masai

Introduction

The Department of Thoracic Surgery deals with various kinds of neoplasms and allied diseases in the thorax, with the exception of the esophagus. These include both primary and metastatic lung tumors, mediastinal tumors, pleural tumors (mesotheliomas), and chest wall tumors. The surgical management of lung cancer patients has been the main clinical activity of the Department, as well as the subject of most of its research activities. In addition to continuing to improve procedures, such as the combined resection of neighboring vital structures and minimally invasive techniques (video-assisted thoracic surgery, VATS), it has become increasingly important to define the role of surgery in multimodality treatment for patients with a poor prognosis.

Routine activities

The Department has 4 attending surgeons. Attending surgeons and residents perform all of the inpatient care, operations, examinations, and outpatient care. In 2014, we performed a total of 667 operations; for lung cancer in 485 patients, metastatic tumor in 80, mediastinal tumor in 18, and others in 84.

The treatment strategy for patients with lung cancer is based on tumor histology (non-small cell vs. small cell), extent of disease (clinical Stage), and physical status of the patient. In lung cancer patients, surgical resection is usually indicated for clinical Stages I, II, and some IIIA with non-small cell histology and clinical Stages I with small cell histology. However, to improve the poor prognosis of patients with clinically and histologically proven mediastinal lymph node metastasis or with invasion to the neighboring vital structures, optimal treatment modalities are sought in a clinical trial setting. Recently, adjuvant chemotherapy is often given to the patient with advanced lung cancer even after complete pulmonary resection.

For metastatic lung tumors, resection has been attempted on the basis of Thomford's criteria: eligible patients are those who are at good risk, with no extrathoracic disease, with the primary site in control, and with completely resectable lung disease. Metastasis from colorectal carcinomas is the most common disease.

For mediastinal tumors, thymic epithelial tumors are most commonly encountered for resection. In the mediastinum, where a variety of tumor histologies can arise, the treatment must be carefully determined by the cytologic/histologic diagnosis before surgery. For this purpose, CT-guided needle biopsy is replacing the formerly common biopsy under X-ray fluoroscopy. For patients with thymoma, we have already adopted video-assisted resection (VATS) of the tumor. VATS resection of mediastinal tumor is indicated exclusively for small thymomas.

As for meetings, there are 2 department meetings. One is for the preoperative evaluation and postoperative inpatient review on Friday and the other is for the journal club on Tuesday. In addition, the chest group has a plenary meeting to share basic information about the current issues for diagnosis and treatment of patients with lung malignancy on Thursday

Research activities

We started a new modality, radiofrequency ablation (RFA), for malignant tumors of the lung in 2007. This modality should be effective for patients in whom it would be difficult to perform surgical resection, radiotherapy, or chemotherapy because of their poor risk. We have conducted a clinical trial to evaluate the feasibility of RFA for poor-risk patients with malignant tumors of the lung. The accrual for the RFA trial has been closed in 2013. The results will be announced in a little while.

Lymph node dissection for lung cancer has been a major issue in lung cancer treatment, and has been extensively studied in our Department. We continue to improve the surgical technique of dissection based on oncological and surgical considerations: a more effective and less invasive lymph node dissection called "selective mediastinal/hilar dissection" according to the location of the primary tumor by the lobe.

Minimally invasive surgery with the thoracoscope for thoracic malignancies is also an important challenge in our Department. In particular, the indications and surgical techniques of video-assisted surgery for early lung cancer are of special interest because of the increased incidence of such minute tumors due to improvements in CT devices and CT screening.

Clinical trials

Due to the advent of new technologies in CT scanning, small-sized lung cancers are being found in a screening setting and also by chance. They usually present as "ground-glass opacity (GGO)" on CT, and pathologically they are considered early adenocarcinoma. The surgical management of such GGO-type lung cancer remains undetermined in terms of the extent of pulmonary parenchymal resection and lymph node dissection. Some cases might be followed up with careful monitoring by CT, since indolent tumors are known to exist. We are seeking the appropriate way to manage these patients. A clinical trial to determine the appropriateness of limited resection for early adenocarcinoma had been planned in the Japan Clinical Oncology Group (JCOG)- Lung Cancer Study Group, and 2 clinical trials (a phase III trial, JCOG 0802; a phase II trial, JCOG 0804) have been conducted since the end of 2009. In addition, another phase II trial (JCOG1211), a confirmatory trial of segmentectomy for clinical T1N0 lung cancer dominant with GGO, was started in 2013. The accrual for JCOG 0804 trial has been already closed. The accrual for JCOG0802 has been closed in 2014. 37 cases have been registered for JCOG 1211 from our Department.

As for postoperative adjuvant therapy, a phase III clinical trial to compare the effectiveness of UFT with that of TS-1 for Stage IA more than 2 cm and IB NSCLC planned in JCOG (JCOG 0707) has been conducted since 2008. This trial completed the full accrual of 960 patients in 2013. A phase III clinical trial (JCOG 1205) to compare Irinotecan/Cisplatin with Etoposide/Cisplatin for adjuvant chemotherapy of resected pulmonary high-grade neuroendocrine carcinoma has been started in 2013.

Table 1. Number of patients for each primary site (surgical case only)

Primary lung cancer	485
Metastatic lung tumor	80
Mediastinal tumor	18
Pleural disease	19
Chest wall tumor	13
Benign lung nodule	37
Others	15
Total	667

Table 2. Type of procedure in 2014

Lung resection	588
Lobectomy	363
Pneumonectomy	16
Segmentectomy	74
Wedge resection	135
Tracheal resection	0
Surgery for mediastinal tumors	19
Surgery for pleural tumors	24
Surgery for chest wall tumors	13
Others	23
Total	667

Table 3. Survival rates for primary lung cancer patients after surgery

Pathological stage (TNM-7)	No. of pts	5-yr survival (%)
IA	1,902	94.2
IB	556	83.5
IIA	320	71.7
IIB	208	64.4
IIIA	453	48.3
IIIB	82	34.9
IV	30	26.8
Operation period: 2003.1-2011.12	Total 3,551	

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Journal

1. Watanabe S. Lymph node dissection for lung cancer: past, present, and future. Gen Thorac Cardiovasc Surg, 62:407-414, 2014
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Department of Thoracic Oncology

Yuichiro Ohe, Noboru Yamamoto, Hiroshi Nokihara, Yutaka Fujiwara, Hidehito Horinouchi, Shintaro Kanda, Yasushi Goto, Kuniko Sunami, Tetsuhiko Asao, Shinsuke Kitahara

Introduction

Lung cancer is the leading cause of cancer death in Japan and worldwide. The incidence of lung cancer in Japan is still increasing, especially in elderly populations. The Department of Thoracic Oncology provides care for patients with primary lung cancer, mediastinal tumors, and pleural tumors. The goals of the Department are to provide the highest quality treatment and establish new effective treatments against lung cancer and other thoracic malignancies through innovative clinical and translational research. To provide assistance to our patients through multidisciplinary care, the staff members of the department work closely with thoracic surgeons, radiation oncologists, pharmacists, clinical research coordinators, and psychiatrists who have expertise in these areas. The Department includes 7 staff physicians. Moreover, residents and trainees from other institutions have joined the Thoracic Oncology Program.

Routine activities

The staff physicians attend outpatient services for thoracic diseases, and the Department has approximately 60 beds in the hospital. Inpatient care is carried out by five teams. Each team consists of one staff physician and one or two residents and/or trainee doctors. Protocol and case conferences are scheduled every Monday morning and afternoon, respectively. The journal club is scheduled on Thursday mornings.

A total of 332 new patients were admitted in 2014, and the backgrounds and initial treatments of these patients are shown in Table 1 and 2. The initial treatments were chemotherapy in 169, adjuvant chemotherapy after surgery in 53, chemoradiotherapy in 52, curative radiotherapy in 5, and supportive care including palliative radiotherapy in 31. Survival of lung cancer patients treated in 2005-2009 is shown in Table 3.

Research activities

Research activities of the department can be classified into four categories: (1) multi-institutional phase III studies to establish new standard treatments against lung cancer; (2) phase I and phase II studies to evaluate new anticancer drugs, (3) pharmacokinetic and pharmacodynamic (PK/PD) studies to investigate interpatient variability, optimal administration schedules and drug-drug interactions; and (4) translational research using clinical samples from bench to bed-side or from bed-side to bench for the development of innovative treatment strategies.

Clinical trials

The Department is currently conducting and participating in multi-institutional phase III studies to establish new standard treatments against lung cancer such as the Japan Clinical Oncology Group (JCOG) trials and global trials conducted by pharmaceutical companies. Three JCOG phase III studies, JCOG1201 for elderly ED-SCLC, JCOG1206 for high grade neuroendocrine carcinoma and JCOG1210/WJOG7813L for elderly non-squamous NSCLC are ongoing. The Department is also participating nationwide screening project of lung cancer with rare driver mutation (LC-SCRUM) and phase II studies targeting rare driver mutation. The department carried out many clinical trials using 3rd generation EGFR-TKIs, anti-PD-1Ab, anti-PD-L1Ab.

Education

In 2014, three chief residents, 19 residents and one research resident are joined the Department. Monthly research conference is held to discuss about clinical and translational research conducted by young doctors.

Future Prospects

Recent progression of lung cancer treatment is very rapid. Driver gene alteration targeted therapy such as EGFR-TKIs and ALK inhibitors are already established as a standard treatment for lung cancer patients with EGFR mutation and ALK fusion gene. Other rare driver gene alterations such as ROS1 fusion, RET fusion, BRAF mutation will be able to good targets for treatment of lung cancer. Immunotherapy using anti-PD-1Ab and anti-PD-L1Ab will also be established as a standard treatment of lung cancer in near future. These immunotherapies could provide durable response for some lung cancer patients. Establishment of good biomarkers to identify the patients who respond the immunotherapy is very important.

Table 1. Number of new inpatients in 2014

Thoracic malignancies total	328
NSCLC	274
Adenocarcinoma	192
Squamous cell carcinoma	52
Others	30
SCLC	38
Mesothelioma	5
Thymic cancer	8
Thymoma	3

Table 2. Initial treatments for new inpatients with lung cancer in 2014

Chemotherapy	169
Chemoradiotherapy	52
Adjuvant chemotherapy after surgery	53
Chemoradiotherapy followed by surgery	2
Curative radiotherapy	5
Supportive care including palliative radiotherapy	31

Table 3. Survival of lung cancer patients treated in 2005-2009

Disease	Stage	Treatment	N	Survival rate (%)				
				1y	2y	3y	4y	5y
NSCLC	52	chemotherapy	654	63	38	21	12	8
NSCLC	53	chemoradiotherapy	178	80	55	38	29	26
SCLC	2	chemotherapy	128	55	17	5	5	4
SCLC	5	chemoradiotherapy	68	91	69	45	35	29

List of papers published in 2014

Journal

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Department of Esophageal Surgery

Yuji Tachimori, Hiroyasu Igaki, Kazuo Koyanagi, Hidetsugu Nakazato, Jun Iwabu

Introduction

More than 300 new patients with esophageal tumors are admitted to the National Cancer Center Hospital (NCCH) every year. The multidisciplinary treatment plans are determined by the stage of the tumor in close cooperation with other teams. The Department of Esophageal Surgery particularly cooperates with the Department of Gastrointestinal Medical Oncology and the Department of Radiation Oncology for preoperative chemotherapy and chemoradiotherapy and salvage surgery after definitive chemoradiotherapy, and the Department of Endoscopy for diagnosis and endoscopic resection. We also maintain close cooperation with the Department of Head and Neck Surgery for cervical esophageal carcinomas and with the Department of Gastric Surgery for adenocarcinomas in the esophagogastric junction. Patients who required laryngectomy for resection of cervical esophageal cancer were operated in the Department of Head and Neck Surgery. In our department, squamous cell carcinomas still constitute the largest proportion of esophageal tumors, and only three patients with adenocarcinomas of esophagogastric junction underwent esophagectomy in 2014. Most patients with Siewert Type II and III adenocarcinoma were operated in the Department of Gastric Surgery.

Routine activities

The Department of Esophageal Surgery consists of three staff surgeons, one chief resident and 1-2 rotating senior residents. A multidisciplinary conference (Esophageal Tumor Board) is held weekly in which surgeons, medical oncologists, radiation oncologists, endoscopists, radiologists, and pathologists who are involved in the treatment of esophageal diseases meet and discuss the diagnosis, staging, and treatment plans for patients with esophageal tumors. Every week, 2-3 patients with esophageal cancer undergo surgery. One hundred and five patients underwent esophagectomy including 4 patients with cervical esophageal cancer, three with carcinosarcoma, two with malignant melanoma, and one with neuroendocrine tumor. Four patients with gastric cancer after esophagectomy, a patient with cervical squamous cell carcinoma after esophagectomy, and a patient with cervical adenocarcinoma after esophagectomy underwent surgery. Preoperative chemotherapy was recommended for 52 patients and preoperative chemoradiotherapy was recommended for 8 patients with resectable Stage II-IV esophageal squamous cell cancer. A three-field dissection, including the whole upper mediastinum and supraclavicular area in addition to the lower mediastinum and abdomen, was performed in 74 patients as our standard procedure. Video-assisted thoracic surgery was introduced for esophagectomy as minimally invasive surgery in 42 patients. Two hospital deaths occurred due to postoperative complication including pneumonia after salvage esophagectomy and bronchial necrosis after salvage esophagectomy.

In a paradigm shift toward organ-sparing therapy, the number of patients who receive definitive chemoradiotherapy as their primary treatment for resectable tumor, especially Stage I squamous cell carcinoma, is increasing. However, the number of patients who accept minimally invasive esophagectomy also increased. Persistent or recurrent loco-regional disease is not infrequent after chemoradiotherapy. Eleven patients underwent salvage esophagectomy after the failure of definitive chemoradiotherapy in 2014. A three-field dissection is avoided for salvage esophagectomy.

Research activities

Several translational studies are being carried out in cooperation with the National Cancer Center Research Institute. A study of DNA methylation in biopsied specimens is also ongoing to estimate the efficacy of preoperative chemotherapy in patients with advanced esophageal cancer.

Clinical trials

A multi-institutional randomized controlled trial comparing standard preoperative chemotherapy (5FU and cisplatin), an intensive one (5FU and cisplatin plus docetaxel), and preoperative chemoradiotherapy (5FU and cisplatin plus 41.4 Gy irradiation) for Stage II-III esophageal cancer (JCOG1109) is ongoing. A Phase II trial for definitive chemoradiotherapy with or without salvage esophagectomy (JCOG0909) has finished registration. A new Phase II trial for tri-modality strategy with docetaxel plus 5FU and cisplatin (DCF) induction chemotherapy for locally advanced unresectable esophageal cancer followed by conversion surgery for responders and chemoradiotherapy for non-responders (COSMOS) launched in 2013 and is ongoing. A new multi-institutional randomized controlled trial comparing minimally invasive esophagectomy versus open thoracic esophagectomy (JCOG1409) starts registration in 2015.

Education

We accepted many surgeons from foreign countries, especially from Asia. A dramatic increase in the incidence of adenocarcinoma has been seen in Western patients. However, in Asian patients, including Japanese patients, squamous cell carcinoma remains the predominant type of esophageal cancer. Japanese strategies and surgical techniques for esophageal squamous cell carcinoma are instructive for Asian surgeons.

Table 1. Number of patients

Thoracic esophageal squamous cell carcinoma	94
Adenocarcinoma of esophagogastric junction	3
Cervical esophageal squamous cell carcinoma	3
Cervical Barrett adenocarcinoma after esophagectomy	1
Carcinosarcoma	3
Malignant melanoma	2
Neuroendocrine tumor	1
Large leiomyoma	1
Gastric cancer after esophagectomy	4
Esophago-pulmonary fistula	1

Table 2. Type of surgical procedure

Open thoracic esophagectomy	57
Video-assisted esophagectomy	42
Transhiatal esophagectomy	2
Cervical esophagectomy	4
Gastrectomy for esophagogastric junction cancer	3
Gastrectomy for gastric cancer after esophagectomy	4
Esophageal bypass	1
Esophageal reconstruction after conduit necrosis	1
Esophageal reconstruction for anastomotic stenosis	1
Salvage lymph node dissection after definitive chemoradiotherapy	8
Cervical esophagostomy	1

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Journal

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Department of Gastric Surgery

Hitoshi Katai, Takeo Fukagawa, Shinji Morita, Hisataka Fujiwara, Takeyuki Wada

Introduction

This Department treats not only gastric adenocarcinoma but also sarcomas of gastric origin, such as malignant lymphomas or gastrointestinal stromal tumors (GISTs). Principally, we treat tumors of the esophagogastric junction.

Routine activities

The Department includes four staff surgeons, two chief residents and three or four rotating residents at any given time. Nine to eleven patients are operated upon every week. The Department shares a ward with the Department of Gastrointestinal Medical Oncology, so that specialists from both departments can treat patients with gastric cancer. Patients with Stage I disease are followed-up without adjuvant chemotherapy. Adjuvant S-1 chemotherapy is used for patients with Stage II and III disease. Neoadjuvant chemotherapy is frequently used for patients with locally advanced tumor.

Patients with a superficial well-differentiated adenocarcinoma lesion are treated with endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). Some undergo subsequent surgery based on the histological findings of the resected specimen. Every Tuesday from 6:15 to 7:00 P.M., a clinical conference is held for surgeons, a medical oncologist and endoscopists. All patients with gastric malignancies in the ward or on the waiting list for admission are briefly reviewed and those whose treatment is controversial are discussed in detail. Every Friday between 7:15 and 8:30 A.M., another clinical conference is held, in which endoscopists, radiologists, and pathologists present all candidates for surgical and endoscopic treatment for the following week, and the treatment strategy for each case is discussed in detail. These conferences are held in English whenever a foreign guest doctor is present.

We consider the education of foreign surgeons is to be an important function. In 2014, more than 20 surgeons from various countries visited this department for 1 week to 3 months to learn about the management of gastric cancer patients, especially surgical techniques for lymph node dissection and postoperative care. All staff surgeons have sufficient experience in teaching in English.

Research activities

Several translational studies are being carried out in cooperation with the National Cancer Center Research Institute. Genomic scanning in gastric cancer is being carried out. DNA methylation as a gastric cancer metastasis risk factor has been investigated. A mini-chip assay of peritoneal washings for prediction of gastric cancer recurrence is being developed. Research on the detection of small amounts of cancer cells in peripheral blood and bone marrow of gastric cancer patients is being carried out in cooperation with Kyusyu University and Hamburg-Eppendorf University.

Clinical trials

Our Department has been playing a central role in conducting multi-institutional clinical trials. H. Katai is a representative of the Gastric Cancer Surgical Study Group of the Japan Clinical Oncology Group (JCOG). Patients with gastric cancer are, when eligible, invited to participate in one of the ongoing clinical trials mentioned below. Randomized controlled trials are currently underway in a multi-institutional setting. The JCOG 0501 phase III trial to evaluate the effect of neo-adjuvant (S-1 and CDDP) and adjuvant chemotherapy (S-1) for large type III and type

IV tumors has been completed for accrual. JCOG 1001 is designed to evaluate the significance of bursectomy for advanced cancer. This trial includes the evaluation of long-term survival, postoperative morbidity, and mortality. The JCOG 0912 phase III trial to prove the non-inferiority of laparoscopic gastrectomy over its open counterpart for patients with clinical stage IA and IB gastric cancer has also been completed for accrual. The JCOG1002, phase II study of systemic chemotherapy with Docetaxel, CDDP, and S-1 followed by surgery in advanced cancer with extensive lymph node metastasis has been completed for accrual. JCOG1302-A is a study to evaluate accuracy of pre-operative staging for advanced tumor. Phase II study to check feasibility of Oxaliplatin, and S-1 neoadjuvant chemotherapy for Stage III disease was carried out. Now, we designed a new phase II trial to prove feasibility of laparoscopic total and proximal gastrectomy for Stage IA and IB gastric cancer (JCOG1401).

Education

The education of surgical operation has been introduced for chief and rotating residents throughout perioperative management of more than 400 gastric cancer patients.

Future prospects

D2 gastrectomy is considered the standard surgical treatment for advanced gastric cancer but multi-modality treatments combined with surgery will further improve survival. However, the results of this gastrectomy are not sufficient stage III disease. We plan new clinical trial to evaluate D2 gastrectomy plus duplet chemotherapy including neoadjuvant chemotherapy. There are several surgical options for early gastric cancer depending on the risk of nodal metastasis. The efficacy of laparoscopic surgery for early gastric cancer has to be being assessed.

Table 1. Number of Patients

Adenocarcinoma	400
GIST	10
Others	27
Total	437

Table 2. Operative morbidity and mortality after gastrectomy

	Number of patients	%
Major complications	31	9.9
Minor complications	47	15.1
Postoperative hospital deaths	0	0
Total	312	

Gastrectomy includes total, proximal, distal, and pylorus-preserving gastrectomy.
Major complications include pancreatic fistulae, leakage, and intra-abdominal abscesses
Minor complications include wound infection, urinary tract infection, line infection, etc.

Table 3. Operative Procedures

Distal gastrectomy	111
Total gastrectomy	85
Completion gastrectomy	8
Pylorus-preserving gastrectomy	32
Proximal gastrectomy	24
Wedge resection	10
Laparoscopic total gastrectomy	1
Laparoscopic distal gastrectomy	25
Laparoscopic pylorus preserving gastrectomy	26
Other (bypass, exploration, etc.)	115
Total	437

Table 4. Survival Rates

Stage	No. of patients	5-yr survival
IA	1,920	94.8%
IB	396	92.6%
IIA	348	84.8%
IIB	316	78.6%
IIIA	242	64.0%
IIIB	214	57.7%
IIIC	195	38.6%
IV	644	11.9%
Total	4,275	78.6%

Stage: Japanese classification (14th ed.)
Period: 2000-2007

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Journal

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Department of Colorectal Surgery

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Introduction

The Department of Colorectal Surgery deals with colorectal cancer and allied malignancies in the colon and rectum. Liver metastasis from colorectal cancer is treated in cooperation with the Department of Hepatobiliary and Pancreatic Surgery. Lung metastasis from colorectal cancer is also treated in cooperation with the Department of Thoracic Surgery. Although surgery is still the main treatment modality for colorectal cancer, multi-disciplinary treatments including radiotherapy and chemotherapy are important in advanced cancer. We have multi-disciplinary meetings with the Department of Gastrointestinal Oncology, the Department of Digestive Endoscopy, the Department of Diagnostic Radiology and the Department of Pathology and Clinical Laboratories every week, and decide treatment strategy by a multi-disciplinary team (MDT) before treatment is held.

Routine activities

There are four staff surgeons, one chief resident, and three or four rotating residents. Every morning (7:30-8:30), we have a morning conference and rounds in wards 15A and B. A multidisciplinary team (MDT) meeting is held for cancer patients as a form of institutionalised communication every Tuesday morning (7:15-8:00), and a conference is held for the diagnosis of colorectal cancer: colorectal surgeons, endoscopists, and radiologists discuss the diagnosis for preoperative patients every Tuesday evening (18:30-19:30). Every Wednesday morning (7:00-7:30), a conference is held for the treatment of colorectal cancer: colorectal surgeons discuss treatments for preoperative and postoperative patients. Ten to twelve operations are performed a week in our Department. Thus, we operate upon about 500 patients with colorectal cancers and allied diseases annually.

Patients with clinical stage I colon and rectal cancers mainly undergo laparoscopic surgery. Patients with clinical stage II or III colon cancer are treated with laparoscopic or conventional surgery. Other patients with T3 or T4 colon cancers are treated with conventional techniques or the no-touch isolation technique as part of a clinical trial (JCOG1006 study). Patients with advanced rectal cancers are treated with conventional surgery. Adjuvant chemotherapy is being used in Stage III colorectal cancer patients in a clinical setting. Although preoperative radiotherapy is not performed routinely for advanced rectal cancer, patients with T4b rectal cancers or rectal cancers with multiple lymph node metastases are treated with preoperative chemoradiotherapy and surgery. Patients with symptoms caused by unresectable tumors are treated with palliative surgery including palliative resection, bypass, and stoma before chemotherapy. To evaluate the survival benefit and safety of primary resection plus chemotherapy compared to chemotherapy alone in asymptomatic Stage IV colorectal cancer with synchronous unresectable metastatic disease, a randomized controlled trial comparing resection of primary tumor plus chemotherapy with chemotherapy alone in incurable Stage IV colorectal cancer is ongoing (JCOG1007, iPACS). Another randomized controlled trial is ongoing to evaluate the non-inferiority of overall survival of laparoscopic surgery to open surgery for palliative resection of primary tumor in incurable Stage IV colorectal cancer (JCOG1107, ENCORE). Symptomatic, Stage IV colorectal cancer patients with non-curable metastasis are pre-operatively randomized to either open or laparoscopic colorectal resection. Patients with resectable liver metastasis are treated in cooperation with the Department of Hepatobiliary and Pancreatic Surgery and adjuvant chemotherapy

regimens are being evaluated in a clinical trial (JCOG0603 study).

Research activities

As described in "Routine Activities", clinical trials are integrated into our routine work. Many clinical trials are underway, and the details are described in "Clinical Trials". Long-term clinical outcomes from a randomized controlled trial to evaluate laparoscopic versus open complete mesocolic excision (CME) for Stage II, III colorectal cancer: Japan Clinical Oncology Group Study JCOG0404 (NCT00147134) was out. A total of 1,057 patients were randomized (OP: 528, LAP: 529) between October 2004 and March 2009. 5-years' OS is 90.4% (87.5-92.6%) in OP, and 91.8% (89.1-93.8%) in LAP. 5-years' RFS is 79.7% (76.0-82.9%) in OP, and 79.3% (75.6-82.6%) in LAP. The non-inferiority of laparoscopic CME in OS was not demonstrated (1.056; 0.790-1.413, p=0.0732).

We are evaluating new surgical procedures, including intersphincteric resection (ISR) for very low rectal cancer, laparoscopic surgery, and surgery for pelvic recurrence of rectal cancer. We also carry out basic research in cooperation with scientists at the National Cancer Center Research Institute and the identification of a suitable treatment based on such a prediction is one of our important goals.

Clinical trials

Our Department plays a central role in conducting multi-institutional clinical trials in Japan. Y. Shimada is a representative of the Colorectal Cancer Group of the Japan Clinical Oncology Group (JCOG). Our Department is participating in six phase III JCOG studies.

1. JCOG0212: A randomized study that compares mesorectal excision (ME) to ME with pelvic lateral lymph node dissection for clinical stage II or stage III lower rectal cancer patients. Seven hundred and one eligible patients were enrolled and recruitment is complete. Follow-up is on-going.
2. JCOG0603: A randomized study that compares adjuvant modified FOLFOX (5-FU + l-LV +Oxaliplatin) to surgery alone after hepatic resection for liver metastasis from colorectal cancer. One hundred and seventy patients have been enrolled and recruitment continues.
3. JCOG1006: A randomized study that compares conventional techniques to the no-touch isolation technique for clinical T3 or T4 colon cancer. Five hundred and seventy patients have been enrolled and recruitment continues.
4. JCOG1007: A randomized controlled trial comparing resection of primary tumor plus chemotherapy with chemotherapy alone in incurable Stage IV colorectal cancer is ongoing.
5. JCOG1018: A randomized phase III study of mFOLFOX7 or CAPOX plus bevacizumab versus 5-Fluorouracil/leucovorin or capecitabine plus bevacizumab as first-line treatment in elderly patients with metastatic colorectal cancer is ongoing.
6. JCOG1107: A randomized controlled trial comparing laparoscopic surgery with open surgery in palliative resection of primary tumor in incurable Stage IV colorectal cancer is ongoing.

Table 1. Operative Procedures

	Number of patients	
	Open	Laparoscopic
Colectomy	94	107
High anterior resection	9	15
Low anterior resection	51	21
Abdomino-perineal resection	11	3
Hartmann's operation	3	
Intersphincteric resection	10	7
Robot-assisted suregery		18
Total extirpation of large intestine	0	0
Total pelvic exenteration	2	
Total pelvic exenteration with sacrectomy	1	
Bypass	4	
Colostomy or ileostomy	48	
Local excision	1	
Other	35	

List of papers published in 2014

Journal

1. Shimada Y, Hamaguchi T, Mizusawa J, Saito N, Kanemitsu Y, Takiguchi N, Ohue M, Kato T, Takii Y, Sato T, Tomita N, Yamaguchi S, Akaike M, Mishima H, Kubo Y, Nakamura K, Fukuda H, Moriya Y. Randomised phase III trial of adjuvant chemotherapy with oral uracil and tegafur plus leucovorin versus intravenous fluorouracil and levofolinate in patients with stage III colorectal cancer who have undergone Japanese D2/D3 lymph node dissection: final results of JCOG0205. Eur J Cancer, 50:2231-2240, 2014
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Department of Gastrointestinal Medical Oncology

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Introduction

The Department of Gastrointestinal Medical Oncology focuses on the development of new drugs and standard chemotherapy combined with or without surgery and radiation therapy for advanced colorectal, gastric and esophageal cancer, gastrointestinal stromal tumor and other gastrointestinal (GI) malignancies.

Over recent years, new therapeutic agents have been developed. The highlights include the development of a molecular-targeted antibody, bevacizumab (BV), directed against vascular endothelial growth factor (VEGF) and the finding that it causes changes in the microenvironment of the tumor by inhibiting angiogenesis. Other two molecular target drugs are the anti-epidermal growth factor receptor (EGFR) antibodies, cetuximab and panitumumab, which were approved in 2008 and 2010 for metastatic colorectal cancer. For gastric cancer, an anti-HER2 monoclonal antibody, trastuzumab, was also approved in 2011. Moreover, for colorectal cancer, multi-kinase inhibitor regorafenib was approved in 2013, and a new cytotoxic agent, TPI/FTD (TAS-102) was also approved in March 2014. In near future, new anti-VEGF agent, ramucirumab will be also approved for gastric cancer and colorectal cancer based on the results of randomized controlled trials. On the other hand, in recent years, the efficacy of the immune-checkpoint inhibitor is also being evaluated for GI malignancies.

We expect to identify other novel agents for the treatment of metastatic GI cancers that inhibit intracellular signal transduction and cellular interactions. However, many unique adverse effects and a marked increase in medical cost have led to extensive discussion on more optimal targeting of the population using biomarkers. Although the response rates of these molecular-targeted drugs up to now have not been high (about 5% to 20%) when used broadly to a large population of patients, there are a few new candidate biomarkers that may be useful for identifying patients for whom these molecular-targeted drugs will be effective. For example, RAS mutation in tumor tissue is one of negative predictive factors for lack in the efficacy of cetuximab/panitumumab. Accordingly, the identification of molecular markers that can be used to predict tumor shrinkage and prognosis will be critical for the identification of possible new targets and for tailored treatments based on tumor genotype or marker expression.

Routine activities

The staff of the Department consists of 8 medical oncologists, 3 senior residents, and 3 or 4 residents. We hold a daily case conference together at 8 am before the morning rounds. Intergroup meetings with surgical departments (Colorectal, Gastric, and Esophageal Surgery departments) and the Department of Radiation Oncology are held weekly to decide treatment strategies for each individual case or to discuss future treatment strategies for the disease. Palliative care considering the physical and psychological aspects of each case is another important issue to be discussed with co-medical staff. The palliative care team and psycho-oncologists advise us on how to minimize patient discomfort and anxiety throughout end-of-life care. In 2014, we treated 1,869 hospitalized patients (576 of whom were newly diagnosed). Of these patients, 154 were entered in protocol studies.

Research activities

An endoscopic biopsy and blood sampling before and after chemotherapy provide an excellent opportunity to study biomarkers related to the efficacy of each treatment. We are collecting these fresh samples from patients with gastric cancer to evaluate the correlations between gene expression profiles and patients' outcome by using genome sequencing, microarray or real time (RT) -PCR techniques.

We also have measured the gene expressions of possible predictive biomarkers by using paraffin-

embedded GI cancer specimens obtained from surgical resection or endoscopic biopsy, and investigated the correlation between enzymes related to anti-cancer drug metabolism and clinical outcomes. Some of these results on the correlation between gene mutation profile and cancer outcomes led to propose novel molecular targeted drugs, for example an anti-FGF (fibroblast growth factor) antibody or FGF kinase inhibitor for gastric cancer.

These studies are being performed in collaboration with the Center for Medical Genomics, National Cancer Center Research Institute, or other institutions.

Clinical trials

We carried out several clinical trials in collaboration with the surgery and radiation oncology departments in our hospital and other institutes. Details of clinical trials are summarized in the Table. Some trials are conducted in collaboration with JCOG (Japan Clinical Oncology Group).

1. Colorectal and Anal Canal Cancer

In first-line treatment, we established the combination chemotherapy regimens based on the oral fluoropyrimidine, S-1 (S-1/oxaliplatin/BV [SOXB], S-1/irinotecan/BV [SIRB]). A combination treatment with oral fluoropyrimidines is an important treatment option to improve patient QOL, medical cost and medical staff burden. From the result of SOFT trial, non-inferiority of SOXB to FOLFOX(5-FU/l-LV/oxaliplatin) plus BV has been demonstrated (Yamada Y et al. Lancet Oncol. 2014). We also investigated whether SIRB regimen is non-inferior to XELOX (capecitabine/oxaliplatin) plus BV in a multicenter phase III trial (TRICOLORE), and finished patient accrual on schedule. A randomized trial to investigate the superiority of fluoropyrimidine/oxaliplatin/BV to fluoropyrimidine/BV targeted at frail or elderly patients (JCOG1018) is also ongoing.

In second-line treatment, we are investigating the non-inferiority of XELIRI (capecitabine/irinotecan) to FOLFIRI (5-FU/l-LV/irinotecan) for patients who failed in first-line treatment with FOLFOX or XELOX plus BV in a multicenter phase III trial conducted in Asian countries (AXEPT).

In salvage-line treatment, TAS-102 (Lonsurf®) was approved in Japan on March 2014 for patients' who failed to respond to standard treatment based on the results of a randomized phase II trial in Japan (J003-10040030) and global phase III trial (RECOURSE). TAS-102 is an oral combination drug of trifluridine (FTD) and tipiracil hydrochloride (TPI). FTD is an antineoplastic nucleoside analog, which is incorporated directly into DNA, thereby interfering with the function of DNA. The blood concentration of FTD is maintained via TPI, which is an inhibitor of the FTD-degrading enzyme, thymidine phosphorylase. Moreover, a randomized trial to investigate the efficacy of the peptide therapeutic vaccine (OCV-C02) compared with best supportive care (BSC) was also carried out.

As an adjuvant treatment, JCOG0910, comparing S-1 with capecitabine, finished patients recruitment in 2013 on schedule, and the result was shown in ASCO 2015. A randomized trial comparing adjuvant mFOLFOX6 with observation after complete resection of liver metastasis from colorectal cancer, JCOG0603 is going.

The phase II part of JCOG0903, a phase I/II trial of definitive chemoradiotherapy with S-1/MMC for locally advanced anal canal squamous cell carcinoma, will complete recruitment soon.

2. Gastric cancer

In a first-line treatment, a new pivotal phase III trial comparing S-1/CDDP (CS) to S-1/CDDP/Docetaxel (DCS) has been started from April, 2012, and progressing as expected. A phase II/III study, comparing FLTAX with 5FU alone for patients who are unfit for CDDP usage due to severe peritoneal dissemination is also ongoing. From the result of G-SOX trial comparing SOX with CS at first-line, non-inferiority of SOX to CS has been demonstrated. Therefore, in 2014, oxaliplatin was approved for unresectable or metastatic gastric cancer in Japan.

In second-line treatment, molecular-targeted drugs for advanced gastric cancer as well as colorectal cancer have been investigated. For HER2 negative gastric cancer, a phase III trial which evaluate the additional effect of nimotuzumab, anti-EGFR antibodies, combined with irinotecan in a second-line chemotherapy (ENRICH) started as targeted on patients with high expression of EGFR. Two phase III trials which evaluate the additional effect of (i) olaparib (PARP inhibitor), (ii) BBI608 (an inhibitor targeted at cancer stem cell), combined with paclitaxel

in a second-line treatment are also ongoing. For HER2 positive gastric cancer, we finished a phase III trial which evaluate the additional effect of pertuzumab with capecitabine and cisplatin plus trastuzumab in a first-line treatment (JACOB), and a phase II/III trial comparing TDM-1, ado-trastuzumab emtansine, with paclitaxel in second-line treatment (GATSBY).

In salvage-line treatment, a randomized trial to investigate the efficacy of ONO-4538, anti-programed cell death 1 (PD-1) immune-checkpoint inhibitor antibody, compared with best supportive care (BSC) is ongoing.

3. Esophageal Cancer

Based on the results of JCOG9907 trial, the standard care for stage IB/II/III esophageal cancer is preoperative 5-FU plus CDDP (CF) followed by surgery in Japan. The large pivotal trial JCOG1109 which compared DCF (Docetaxel plus CF) and CF plus radiotherapy (CF-RT, 41.4Gy) with standard preoperative CF in stage IB/II/III esophageal cancer started from 2012, and progressing on schedule. A phase II study, JCOG0909 investigating the efficacy of CF-RT (50.4 Gy) regimen followed by salvage surgery or endoscopic resection in stage IB/II/III esophageal cancer, completed accrual in 2014.

In first-line treatment for advanced esophageal cancer, a phase I/II study, JCOG0807 demonstrated the promising efficacy and feasibility of bi-weekly DCF regimen. According to this precedent, a phase III trial comparing biweekly DCF with standard CF regimen has started from September 2014 in JCOG.

In salvage-line treatment, two phase II studies (i) ONO-4538, PD-1 immune-checkpoint inhibitor, (ii) Sym004, a mixture of two synergistic full-length anti-EGFR antibodies, which bind to two separate non-overlapping epitopes on EGFR, were conducted to investigate the efficacy and safety.

4. Other

For metastatic neuroendocrine carcinoma (NEC) in GI-tract or hepato-billiary-Pancreatic field, a phase III trial comparing irinotecan plus CDDP with etoposide plus CDDP at first-line treatment started in JCOG from August 2014. Several phase I studies have also been conducted as shown in Table.

Table 1. Number of Patients Treated

Number of Patients Treated	Total no. of hospitalized pts	No. of newly diagnosed pts	No. of pts. enrolled protocol
1) Esophageal cancer	646	189	
CF-RT±salvage surgery JCOG0909 (phase II)			3
neoCF vs neoDCF vs neo CF-RT NExT study JCOG1109 (phase III)			10
CF vs biweekly-DCF MIRACLE study JCOG1314 (phase III)			2
Induction-DCF + conversion surgery or CF-RT COSMOS (phase II)			3
Sym004 (phase II)			7
ONO4538 (phase II)			16
IMRT for Ce-esophageal cancer (phase II)			2
2) Gastric cancer	628	121	
CS vs DCS JCOG1013 (phase III)			25
XP+Tmab±Pertuzumab for HER2+ pts JACOB (phase III)			1
CPT-11±Nimotuzmab for EGFR++ pts ENRICH (phase III)			12
FL vs FLTAX for ascites++ pts JCOG1108 (phase II/III)			2
weely-nabPTX vs triweekly-nabPTX vs wPTX (phase III)			15
TDM-1 vs wPTX for HER2+ pts GATSBY (phase II)			2
wPTX±Olaparib (phase III)			3
wPTX±BBI068 (phase III)			3
ONO4538 vs BSC (phase III)			6
CS for elderly patients (phase II)			18
3) Colorectal cancer	472	225	
FOLFOX/CAPOX+BV vs S-1+CPT-11+BV TRICOLORE (phase III)			10
mFOLFOX7/CAPOX+BV vs FL/Cape＋BV for eldery pts JCOG1018 (phase III)			9
XELIRI±BV vs FOLFIRI±BV AXEPT (phaseIII)			12
Anal canal cancer S-1/MMC-RT JCOG0903 (phase I/II)			3
Cetuximab+LGX818±BYL719 for BRAF-MT (phase II)			6
OCV-C02 vs BSC (phase III)			3
CPT-11 + Cmab + Bmab (phase I)			4
Regorafenib (Observational study)			8
4) Others	123	41	
EP vs IP for GI & HBP-NEC TOPIC-NEC JCOG1213 (phase III)			1
BYL719 (phase I)			0
Neo-adjuvant imatinib for GIST (phase II)			1
High risk GIST (Observational study)			2
Oranzapin (phase II)			37
5) Translational research			
Biomarker for Gastric Cancer			22
CTC			22
Immune monitoring			42
Fibrin degradation product			40
GI-SCREEN			35
Total	1,869	576	387

List of papers published in 2014

Journal

1. Koyama N, Saito K, Nishioka Y, Yusa W, Yamamoto N, Yamada Y, Nokihara H, Koizumi F, Nishio K, Tamura T. Pharmacodynamic change in plasma angiogenic proteins: a doseescalation phase 1 study of the multi-kinase inhibitor lenvatinib. BMC Cancer, 14:530-537, 2014
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5. Shimada Y, Hamaguchi T, Mizusawa J, Saito N, Kanemitsu Y, Takiguchi N, Ohue M, Kato T, Takii Y, Sato T, Tomita N, Yamaguchi S, Akaike M, Mishima H, Kubo Y, Nakamura K, Fukuda H, Moriya Y. Randomised phase III trial of adjuvant chemotherapy with oral uracil and tegafur plus leucovorin versus intravenous fluorouracil and levofolinate in patients with stage III colorectal cancer who have undergone Japanese D2/D3 lymph node dissection: final results of JCOG0205. Eur J Cancer, 50:2231-2240, 2014
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Department of Endoscopy, Gastrointestinal Endoscopy Division

Yutaka Saito, Takahisa Matsuda, Ichiro Oda, Yasuo Kakugawa, Takeshi Nakajima, Shigetaka Yoshinaga, Haruhisa Suzuki, Satoru Nonaka, Taku Sakamoto, Seichiro Abe and Minori Matsumoto (Gastrointestinal Endoscopy, National Cancer Center Hospital)
Yuji Matsumoto, Shinji Sasada, Takaaki Tsuchida and Takehiro Izumo (Bronchoscopy)

Introduction

Our Department of Endoscopy have moved to the New Endoscopy Center from 20th Jan. 2014 and we believe this is the biggest Endoscopy Center in Japan at this moment (15 Endoscopy Rooms (251.112 m^2) and 136.788 m^2 Recovery Rooms in two floors of 1949.554 m^2).

The total number of nursing staff is increased to 15 staff members and three endoscopy engineers are working with us.

The Gastrointestinal Endoscopy Division has 11 staff physicians in the National Cancer Center Hospital and in the Screening Technology and Development Division, four chief residents, 7 residents, two trainees and several rotating residents.

The Bronchoscopy Division has four staff members and one resident doctor and the total number of bronchoscopies and therapeutic procedures has been dramatically increased.

Dramatic developments have recently changed the operational mechanism and design of endoscopes along with a variety of accessory devices and instruments so clinical applications using the latest equipment are evolving on a continuous basis. In the Gastrointestinal Endoscopy Division, more advanced and technically difficult endoscopic treatments such as endoscopic submucosal dissection (ESD) are being used in place of conventional endoscopic mucosal resection (EMR) not only for early gastric cancer, but also for superficial esophageal and colorectal neoplasms. In addition, educational activities are an important part of our division's activities with many Japanese medical students, residents and staff physicians as well as approximately 100 overseas post-graduate physicians attending our training courses annually.

Routine Activities in GI Endoscopy

Various diagnostic techniques including chromoendoscopy, magnifying endoscopy and endoscopic ultrasonography (EUS) are used to detect and evaluate early malignant lesions. Capsule endoscopy also has been accepted as being far less invasive. In our facility, small intestine capsule endoscopy has been performed since 2005. In order to obtain more accurate endoscopic diagnosis of gastrointestinal disease, we routinely use the recently developed narrow-band imaging (NBI) system. A total of 11,481, 3,881, 496, 82, 175, 79 and 105 screening and/or diagnostic procedures by gastroscopy, colonoscopy, EUS, EUS-fine needle aspiration (EUS-FNA), endoscopic retrograde cholangiopancreatography (ERCP), capsule endoscopy and double balloon endoscopies, respectively, were performed in 2014 (Table 1).

Due to the increasing number of patients with superficial gastrointestinal neoplasms, the number of therapeutic endoscopy procedures is also increasing in this field. In 2014, 2,187 endoscopic resections were carried out (pharynx 23, esophagus 165, stomach 340 and colon 1,659). Among these, ESD, which was developed for large en-bloc resections with a low-risk of local recurrence, was performed for 100 superficial esophageal cancers, 340 early gastric cancers and 194 superficial colorectal neoplasms. For colorectal ESDs and some esophageal ESDs, the newly developed ball-tip bipolar needle knife (B-knife) and IT-knife nano were used together with CO_2 insufflation. Our colleagues originally developed these procedures and devices.

ESD achieves a higher en-bloc resection rate compared to the standard EMR technique and is less invasive than a surgical operation while EUS-FNA provides a less invasive procedure to improve diagnosis for patients with pancreatic tumors,

Table 1. Chronological Trend of Total number of Diagnostic and Therapeutic Gastrointestinal Endoscopic Procedures

Year	2007	2008	2009	2010	2011	2012	2013	2014
Upper GI Endoscopy	10,910	10,909	10,174	10,644	10,810	11,193	11,314	11,481
Colonoscopy	3,569	3,161	2,670	2,756	2,924	3,232	3,367	3,881
EUS	373	375	402	395	372	393	477	496
EUS-FNA	-	-	-	48	59	69	85	82
Total number of Therapeutic Procedures	1,854	1,848	1,849	1,756	1,984	2,077	2,146	2,164
Gastric EMR/ESD	24/410	19/397	36/375	23/334	23/343	361	375	340
Esophageal EMR/ESD	89/25	94/25	95/43	102/45	132/61	115/66	97/92	65/100
Colorectal EMR/ESD	1,212/97	1,216/97	1,177/123	1,132/120	1,210/125	1,402/133	1,398/184	1,465/194
Duodenal EMR	7	7	9	11	8	23	38	32
Pharyngeal EMR/ESD	18	7	8	9	20	24	34	23
DBE, Stent, etc.						29	91	105
ERCP, etc.					49	104	140	175
Capsule Endoscopy (Small bowel/colon)	25	30	25	22/-	37/44	43/21	45/0	60/19

lymph-node swelling, submucosal tumors of the GI tract, etc.

Image-reading conferences are held regularly and we attend all clinical conferences in the Surgery, Oncology, Radiology and Pathology Divisions to discuss and decide on treatment strategies.

Research Activities in GI Endoscopy (Figure 1)

Our efforts have been focused on new diagnostic and therapeutic strategies. For more accurate endoscopic diagnosis of gastrointestinal disease, we are utilizing the NBI system that enables us to narrow the spectral transmittance bandwidth of the optical filters used in the light source of electronic endoscope systems. In addition, we have conducted a trial study on an autofluorescence imaging (AFI) system. This system can identify lesions based on differences in tissue fluorescence properties and reveal gastrointestinal neoplasms that are not detectable with conventional endoscopy.

Gastric cancer is the second leading cause of cancer death worldwide. In order to improve the survival rate, early diagnosis is one of the optimal strategies, but it has been difficult to differentiate early gastric cancer from other non-neoplastic lesions using conventional WLE. We have conducted a multicenter prospective RCT and concluded that magnifying-NBI improved the diagnostic accuracy for discriminating gastric neoplasms from benign small depressed lesions. We reported this paper at a Plenary Session of the American Society for Gastrointestinal Endoscopy (ASGE) in 2011 and this study has been published in Gastroenterology in 2012.

Endoscopic submucosal dissection (ESD) is accepted as a minimally invasive treatment for early gastric cancer although not widely used in the colorectum because of increased technical difficulty. We have conducted a multicenter prospective study at 10 specialized institutions to examine the current status of colorectal ESDs at specialized endoscopic treatment institutions. Our conclusion was that ESD performed by experienced endoscopists is an effective alternative treatment to surgery providing high en-bloc and curative resection rates for large superficial colorectal tumors based on a prospective series of 1,111 cases.

We have also participated in a further multi-center prospective study on endoscopic treatment of large early colorectal neoplasia conducted by the Colorectal Endoscopic Resection Standardization Implementation Working Group of the Japanese Society for Cancer of the Colon and Rectum and the Japan Gastroenterological Endoscopy Society.

In a recent translational study, it was shown that *Helicobacter pylori* (*H. pylori*) infection induces methylation of CpG islands in non-cancerous mucosae and the methylation level in *H. pylori*-negative patients is closely associated with the risk of gastric cancer. Metachronous gastric cancer after EMR/ESD is now an issue of concern so we need to identify an appropriate biomarker. Based on our recent results, we started a multicenter

prospective observational study in 2008 to confirm the usefulness of the methylation level as a risk marker for metachronous gastric cancer after EMR/ESD. The recommended sample size is 1,000 and over 600 patients have already been enrolled in this particular study.

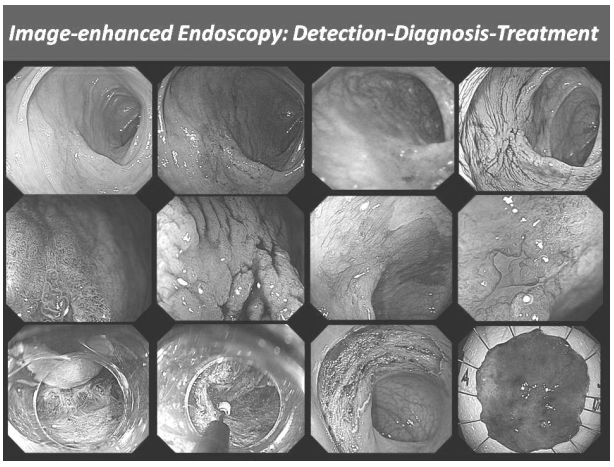

Figure 1. Endoscopic diagnosis using image-enhanced endoscopy (high-resolution endoscopy, narrow-band imaging and autofluorescence imaging) and endoscopic submucosal dissection (ESD) procedure for treating early colon cancer

Clinical Trials in GI Endoscopy

A multicenter clinical trial has been underway to identify the proper surveillance after EMR for superficial esophageal squamous cell carcinoma. Our division has cooperated as a participating institution in a Phase II study on the efficacy of EMR combined with chemo-radiotherapy for clinical stage I esophageal carcinoma (JCOG 0508).

A nationwide cancer registry system has been developed for early gastric cancer treated with EMR/ESD. A five-year multicenter prospective cohort study has been ongoing using this cancer registry system since 2010. Our division has also cooperated as a participating institution in a Phase II trial of endoscopic submucosal dissection to expand the indications for early gastric cancer (JCOG 0607).

RCTs concerning colorectal neoplasms are ongoing as well. The Japan Polyp Study (JPS) was started in February 2003. The JPS is a multicenter RCT designed to evaluate colorectal cancer surveillance strategies in patients who have undergone complete colonoscopies on two occasions with the removal of all detected neoplasia including flat and depressed lesions using a high-resolution colonoscope. Finally, about 4,000 patients have been enrolled in this study. This multicenter RCT is completed and analysis of data will help to develop future recommendations for surveillance guidelines in Japan after the excision of polyps including flat and depressed lesions.

Little is known about the long-term outcomes of patients with submucosal invasive colorectal cancer who undergo endoscopic or surgical resection. We performed a retrospective analysis of long-term outcomes of patients treated for submucosal colon and rectal cancer. We collected data from 549 patients with submucosal colon cancer and 209 with submucosal rectal cancer who underwent endoscopic or surgical resection at 6 institutions, over a median follow-up period of 60.5 months. We assessed recurrence rates, 5-year disease free survival, and 5-year overall survival. As a result, of patients treated with only endoscopic resection, the risk for local recurrence was significantly higher in high-risk patients with submucosal rectal cancer than patients with submucosal colon cancer. The addition of surgery is therefore recommended for patients with submucosal rectal cancer with pathology features indicating a high risk of tumor progression (Gastroenterology 2012). Considering this study result, we are now planning a prospective cohort study for the possibility of chemo-radiotherapy for high-risk rectal submucosal cancer after endoscopic resections.

A nationwide cancer registry system has been also developed for early colorectal cancer treated with ESD. A five-year multicenter prospective cohort study has been ongoing using this cancer registry system since 2013. A total of 2066 patients were enrolled to this multicenter cohort study and this should be the largest cohort study in colorectal ESD in the world.

Molecular imaging endoscopy is one of new era for very early cancer diagnosis and detection of metastasis. We have just started a collaborative

study between Endoscopy Division, Colorectal and Gastric Surgery Division, Pathology Division, Research Institute, Tokyo University and Jikei University.

We have also organized several multicenter study groups in order to evaluate the efficacy and clinical impact of newly developed endoscopies and medical devices prospectively.

We have been collaborating with the Japan Gastroenterological Endoscopy Society (JGES) in order to build All Japan Endoscopy Database (JED) of gastrointestinal endoscopies including not only therapeutic but also diagnostic procedures. This all Japan project is named as JED and have a potential to construct the largest and most precise database of all endoscopic procedures. Japanese endoscopists have been well known as most excellent endoscopists, therefore, we can create lots of evidences using this huge endoscopy database from now.

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Journal

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Department of Endoscopy, Respiratory Endoscopy Division

Takehiro Izumo, Yuji Matsumoto, Takaaki Tsuchida

Introduction

In the field of bronchoscopy, bronchoscopic treatments are coupled with computerized tomography (CT) for the treatment of airway stenosis, minute peripheral lung cancer, and so on. For respiratory diseases, we have focused on the accurate and less-invasive diagnosis of minute peripheral malignancies detected by CT, which can lead to earlier surgical treatment and less-invasive treatments including bronchoscopic therapies. This is facilitated by a multi-purpose bronchoscopy system consisting of a flat-panel fluoroscope, as well as with the patient's cooperation and appropriate support by medical personnel. Endobronchial malignancies are diagnosed with videobronchoscopy, together with an endobronchial ultrasound system, and a high-resolution flat-panel fluoroscope. In addition, imaging diagnosis, including that with high-resolution CT, is also a routine activity for bronchoscopy, which leads to more accurate and safer diagnoses and the earlier detection of tracheobronchial malignancies.

Routine activities

A weekly conference with CT imaging analysis and confirmation of the pathology results was held. Furthermore, we attended all clinical conferences in the Surgery, Oncology, Radiology and Pathology Divisions to discuss and decide upon treatment strategies. Endobronchial ultrasonography (EBUS) is used not only to evaluate mediastinal or hilar malignant lesions but also to evaluate whether the biopsy devices can be directed to the peripheral lung lesions. One-hundred seventy six cases of EBUS-TBNA (EBUS-trans bronchial needle aspiration) were performed as a less invasive procedure to improve the diagnosis for patients with mediastinal or hilar lymph node swelling. The EBUS-GS (guide sheath) method was performed in most of the peripheral pulmonary lesions.

Endobronchial stenosis patients were treated with airway stent placement, photodynamic therapy and endobronchial electrocautery ablation. Medical thoracoscopy under local anesthesia in the operation suite was performed in 17 cases with unknown pleural effusion or a pleural tumor. Some of these cases underwent an electrocautery (IT knife) pleural biopsy because of pleural thickening.

Research activities

We tried to improve the accuracy of a GGO (ground grass opacity) which had been impossible to visualize using a routine chest radiography or X-ray fluoroscopy. Radial endobronchial ultrasound (R-EBUS) is a useful tool for precise localisation of peripheral pulmonary lesions, but there have been no detailed reports about the use of R-EBUS images for ground-glass opacity (GGO). R-EBUS images of GGO were identified based on the internal structure of the lesion and classified into two groups. Blizzard showed an enlarged, diffuse hyperintense acoustic shadow. Mixed blizzard showed a combination of blizzard and some diffuse heterogeneity with several hyperechoic dots and vessels.

Endobronchial ultrasound elastography is a new technique for describing the stiffness of tissue during endobronchial ultrasound-guided transbronchial needle aspiration. In classifying Type 1 as ‘benign’ and Type 3 as ‘malignant,’ the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy rates were 100, 92.3, 94.6, 100 and 96.7%, respectively.

A new middle-range diameter bronchoscope with large channel combined with endobronchial ultrasound with a guide sheath can enhance the efficacy of transbronchial sampling to its maximal

potential to diagnose peripheral pulmonary lesions safely and accurately, particularly for patients who have tumors away from the visceral pleura.

Clinical trials

We conducted a multi-center prospective study for evaluation of photodynamic therapy for peripheral lung cancer.

Education

Flexible bronchoscope has a history that has been developed in this hospital for the first time in the world and a large number of residents and overseas doctors wish to be trained at our hospital. I was given the opportunity of writing papers and making conference presentations to many residents. Overseas training doctors included three from Philippines, one from Singapore, one from China, and three from India.

Future prospects

A multicenter trial of photodynamic therapy for peripheral lung cancer is expected to be carried out.

Table 1. Number of Patients Treated

Diagnostic bronchoscopy without X-ray	155
Diagnostic bronchoscopy under X-ray fluoroscopy	565
Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA)	176
Medical thoracoscopy	17
Tharapeutic bronchoscopy	4
Total	917

List of papers published in 2014

Journal

1. Takai M, Izumo T, Chavez C, Tsuchida T, Sasada S. Transbronchial needle aspiration through a guide sheath with endobronchial ultrasonography (GS-TBNA) for peripheral pulmonary lesions. Ann Thorac Cardiovasc Surg, 20:19-25, 2014
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Department of Hepatobiliary and Pancreatic Surgery

Kazuaki Shimada, Tomoo Kosuge, Minoru Esaki, Satoshi Nara, Yoji Kishi, Yasuhito Iwao, Hironobu Suto

Introduction

The Department of Hepatobiliary and Pancreatic (HBP) Surgery deals with malignant neoplasms arising from the liver, biliary tract and pancreas. We conduct aggressive surgical treatment and also multidisciplinary treatment in cooperation with the Departments of Diagnostic Radiology, HBP Oncology, and Pathology and Clinical Laboratories.

Routine activities

The Department of HBP Surgery consists of 5 staff surgeons and we perform around 300 surgeries each year, along with 1 chief resident and 3 or 4 residents. Occasionally, trainees from both Japan and overseas join our group.

Operation and perioperative care

Usually 5 to 7 major operations for hepatobiliary and pancreatic malignancies are performed every week. 1 staff surgeon and 1 resident are in charge of each patient, and conduct the operation and provide postoperative care. The chief resident attends all the operations, supervises the residents and manages the care of all inpatients.

Conferences

We have several clinical or educational conferences on the treatment of HBP malignancies. At the "Ward Conference", the clinical conditions of the perioperative patients and surgical strategies for preoperative cases are discussed. At "Cherry Conference," surgeons and radiologists discuss imaging studies of mainly the patients scheduled for surgery. An "HBP Case Conference" is held by surgeons and medical oncologists to discuss the clinical course of both surgical and medical patients as well as common issues among HBP malignancies. The "Micro Conference" is a pathological conference on postoperative cases, where surgeons, radiologists, and pathologists participate in the discussion. In the "Research conference", which is held every 3 months, progress situation of academic studies including clinical research and paper writing are evaluated.

Surgical strategies for HBP malignancies

Hepatocellular carcinoma (HCC): Surgical treatment for HCC is always determined based on the balance between tumor condition and hepatic functional reserve. Surgical resection is usually indicated in patients with solitary or only a few tumors and with favorable hepatic function. Huge tumor or HCC with macroscopic vasculobiliary tumor thrombosis are also indicated for resection as long as sufficient hepatic function and remnant liver volume is expected. Alternative treatments other than hepatectomy are performed in cooperation with medical oncologists and radiologists.

Pancreatic cancer: The prognosis of patients with invasive ductal carcinoma is poor even with aggressive surgical resection. Multidisciplinary treatments with curative resection followed by adjuvant chemotherapy is the standard strategy for this potentially noncurative disease. Resection of borderline malignancies, such as pancreatic cystic neoplasms, neuroendocrine tumors (NETS) is performed aggressively, since a favorable prognosis can be expected with surgical resection.

Biliary cancer – cholangiocarcinoma & gall bladder cancer: Based on careful imaging evaluations of cancer extension, a wide variety of surgical resections can be applied to biliary cancer. Pancreatoduodenectomy is conducted for middle to distal bile duct cancer. Extended hemihepatectomy with caudate lobe and extrahepatic bile duct resection is considered as the first-line procedure for perihilar cholangiocarcinoma. When necessary, portal vein and/or hepatic artery resection and reconstruction is performed to achieve curative resection.

Research activities

Dr. Kosuge et al. reported the results of a multicenter controlled trial to evaluate the effect of adjuvant gemcitabine administration after curative resection in cases of pancreatic cancer (JSAP-02, Ueno, Kosuge et al. Br J Cancer 2009). They are now analyzing "Randomized phase III study of adjuvant chemotherapy with combination therapy of gemcitabine and S-1 vs. gemcitabine alone in patients with resected pancreatic cancer (JSAP-04)".

Dr. Shimada et al. conducted 3 prospective randomized trials to evaluate the efficacy of surgical devises in HBP surgery; 1) "Safety of stapler vs. non-stapler closure of the pancreatic remnant after distal pancreatectomy: a multicenter randomized controlled trial (SNS-RCT)," 2) "The impact of use of energy devise during parenchyma transection of the liver: a multicenter randomized controlled trial (EPL-RCT)," and 3) "Effect of stapled vs. hand-sewn duodenal reconstruction on delayed gastric emptying during pancreaticoduodenectomy: a dual-center randomized controlled trial (SH-RCT)". In all these studies, patients' recruit and registration have finished and the results of each study are being prepared for publication. Dr. Nara et al. has finished a study to evaluate the feasibility of laparoscopic hepatectomy in this hospital. Now Dr. Shimada and the colleagues plan to launch other new 3 randomized controlled trials.

All the studies above are supported by Grants-in-Aid for scientific research from the Ministry of Health, Labour and Welfare of Japan.

Table 1. Number of patients

Type of disease	n
Invasive pancreatic cancer	82
Other pancreatic neoplasms	46
Hepatocellular carcinoma	43
Hepatic metastases	61
Intrahepatic cholangiocarcinoma	2
Bile duct cancer	32
Gallbladder cancer	12
Ampullary cancer	5
Duodenal cancer	4
Others	34
Total	321

Education

During 3 to 6 months of trainee period, each resident attend 1 to 2 major HBP surgeries mainly as a first assistant every week. They also have chance to be an operator depending on their skill. For each case, they learn how to decide the indication and type of procedure. In the operation room, the residents learn not only each step of HBP surgery, but also the tips how to help safely proceed the surgery. Chief resident trains in two-year-program. In the first year, they devote to the management of all inpatients and attend basically every surgery. Depending on development of the skill, they have opportunity to be an operating surgeon for major HBP surgery. In the second year, chief resident works on research studies and publish several English papers.

Visitors both from domestic and foreign institutions are anytime welcome.

Future prospects

HBP malignancy often requires technically demanding surgical procedures, whereas the long-term prognosis so far is not satisfactory. Our most important mission is to establish safer and more feasible surgical techniques including perioperative patients' management, and to promote the survival outcomes by multidisciplinary approaches. For these objectives, we continue making efforts to create new skills and treatment strategies.

Table 2. Type of procedures

Procedure	n
Hepatectomy without biliary resection	106
Hepatectomy with biliary resection	17
Hemihepatectomy and pancreaticoduodenectomy (HPD)	2
Substomach preserving pancreaticoduodenectomy (SSPPD) or Classical Whipple (PD)	17
Pylorus-preserving pancreaticoduodenectomy (PPPD)	55
Distal pancreatectomy	38
Appleby operation	3
Medial pancreatectomy	4
Total pancreatectomy*	10
Extended cholecystectomy	16
Other resections	21
No resection	32
Total	321

*includes total resection of remnant pancreas

Table 3. Postoperative survival rates of the patients with a) pancreatic invasive ductal cancer (IDC) and b) hepatocellular carcinoma (HCC)

a) IDC (2002-2011)

Stages	n	3-year survival rate (%)	5-year survival rate (%)
I	12	57	57
II	7	83	63
III	106	61	47
IVa	269	41	26
IVb	122	27	14
Total	516	43	29

b) HCCJ (2002-2011)

Stages	n	3-year survival rate (%)	5-year survival rate (%)
I	35	88	74
II	139	88	82
III	196	72	58
IV	67	61	47
Total	437	77	66

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Department of Hepatobiliary and Pancreatic Oncology

Takuji Okusaka, Hideki Ueno, Chigusa Morizane, Shunsuke Kondo, Yasunari Sakamoto, Satoshi Shiba, Mitsuhito Sasaki

Introduction

The Department of Hepatobiliary and Pancreatic Oncology treats tumors originating from the liver, biliary system or pancreas, which include hepatocellular carcinoma (HCC), biliary tract cancer and pancreatic cancer. As part of the multi-disciplinary care given at the National Cancer Center Hospital (NCCH), we work closely with surgeons and radiologists who have special expertise in these areas. We also conduct research into the pathophysiology of hepatobiliary and pancreatic tumors and seek to develop new and more effective diagnostic methods and treatments.

Routine activities

The Department consists of 5 staff oncologists and 3 to 4 residents. In 1990, the Department began using percutaneous ethanol injection (PEI) to treat patients with small HCCs. In 1999, radiofrequency ablation therapy (RFA) was introduced clinically as an alternative to PEI. Based on long-term observations of PEI-treated patients, we have used percutaneous ablation therapy as a valuable alternative to surgery for most patients with 3 or fewer HCC nodules, all of which are smaller than 3 cm in diameter. We also perform transcatheter arterial chemoembolization (TACE), mainly in patients with multiple HCC nodules. Systemic or intra-arterial chemotherapeutic regimens are indicated in advanced HCC patients for whom locoregional intervention and surgery are unsuitable or had been unsuccessful. In patients with unresectable pancreatic cancer or biliary tract cancer, chemotherapy is performed in clinical practice or as a clinical trial to develop active treatment. Patients with locally advanced pancreatic cancer may receive chemoradiotherapy, which has shown some clinical benefits for symptom control and survival.

Case conferences are held weekly with surgeons and radiologists to determine treatment strategies for these patients. Rounds and conferences for patients admitted to the Department are made by all staff oncologists and residents every morning and evening.

Research activities

We carried out a phase II study to examine the efficacy and safety of FOLFIRINOX in chemotherapy-naïve Japanese patients with metastatic pancreatic cancer (Okusaka T, et al. Cancer Sci. 2014). The response rate was 38.9%; median overall survival, 10.7 months; and median progression-free survival, 5.6 months. There were no treatment-related deaths. FOLFIRINOX can be a standard regimen showing favorable efficacy and acceptable toxicity profile.

We analyzed the outcomes of systemic chemotherapy for advanced neuroendocrine carcinoma (NEC) of the digestive system (Yamaguchi T, et al. Cancer Sci. 2014). Clinical data from 258 patients with unresectable or recurrent NEC of the gastrointestinal tract (GI) or hepato-biliary-pancreatic system (HBP), who received chemotherapy, were collected from 23 Japanese institutions and analyzed retrospectively. HBP primary sites and elevated lactate dehydrogenase levels are unfavorable prognostic factors for survival.

We analyzed how specific end-of-life (EOL) care, especially anticancer therapies, selected by patients with pancreatic carcinoma affected their place of death (POD) in Japan (Kondo S, et al. BMJ Open. 2014). Certain factors such as gender, medical environment and EOL care selection might influence the POD. Patients who pursue aggressive anticancer therapies, such as CAM use, were possibly deprived of a chance of early reference to

a primary care unit (PCU).

We conducted a nationwide survey to examine the situation of patients with HCC treated with sorafenib who obtained a complete response (CR) (Shiba S, Hepatol Res. 2014). Significant factors in the CR group were a female sex, a low bodyweight (<59 kg), an early clinical stage and a small initial dose of sorafenib ($P < 0.05$). Specific adverse events (palmar-plantar erythrodysesthesia syndrome, hypertension, diarrhea, alopecia, fatigue, nausea and anorexia) were frequently observed in the CR group ($P < 0.05$).

Clinical trials

18 clinical trials are ongoing and 6 are in planning, including 12 phase I or I/II trials, 3 phase II or II/III trials, and 9 phase III trials such as adjuvant chemotherapy after resection versus resection alone for patients with resectable tumor, and chemotherapy with a new regimen versus standard therapy for patients with advanced tumor. Our studies are supported by the National Cancer Center Research and Development Fund (Grant No. 26-A-4), Health and Labour Sciences Research Grants (Grant No. H25-kakushintekiganippan-076, 081, 142) from the Ministry of Health, Labour, and Welfare of Japan.

Education

Our staff members are working with residents and chief residents closely to support their skill development and knowledge expansion in both clinical and research fields. We are conducting conferences dairy for clinical practice and weekly for research development. The residents in our department have published 5 papers as a first author in peer-reviewed journals in 2014, and are performing 8 ongoing studies as a leading researcher, with assistance from staff members.

Future prospects

Our Department strives to maintain provision of the best and latest diagnosis, treatment and supportive care, and to develop more effective methods and techniques for all patients with hepatobiliary and pancreatic cancer, not only in this country but also worldwide. Among these approaches, conducting clinical trials with novel promising agents for this disease is considered one of the most important tasks, and establishment of cutting-edge medical treatments in this field is the most significant mission for us. To achieve our aim, we are initiating screening for biliary cancer patients with gene-mutations in the Kanto area as a first step, and are going to expand it to a nation-wide program for accrual to clinical trials for new molecular targeted agents.

Table 1. Primary tumor

	No. of pts
Pancreatic cancer	
Invasive ductal	185
Neuroendocrine	20
Others	31
Biliary tract cancer	
Extrahepatic bile duct	22
Gallbladder	25
Papilla of Vater	4
Liver cancer	
Hepatocellular	187
Intrahepatic cholangio	23

Table 2. Treatment

	No. of pts
Pancreatic cancer	
Systemic chemotherapy	202
Chemoradiotherapy	2
Adjuvant	31
Biliary tract cancer and Intrahepatic cholangio carcinoma	
Systemic chemotherapy	71
Adjuvant	3
Hepatocellular carcinoma	
Ethanol injection	5
Radiofrequency ablation	48
Transcatheter arterial (chemo)embolization	97
Intra-arterial chemotherapy	19
Systemic chemotherapy	24
Radiotherapy	8

List of papers published in 2014

Journal

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Department of Urology

Hiroyuki Fujimoto, Motokiyo Komiyama, Takashi Kawahara, Tomohiko Hara, Yasuo Shinoda, Tsukasa Narukawa

Introduction

In the Department of Urology, all urogenital malignant diseases, including kidney cancer, urothelial cancer, prostate cancer, testicular germ cell tumors and retroperitoneal tumors, are the subject of diagnosis and treatment with comprehensive approaches, including radical surgery, irradiation, and chemotherapy.

Routine activities

The urology team consists of 5staff physicians and 1 resident. In addition, with the participation of a radiation oncologist, multi-disciplinary treatments for advanced disease including renal cancer, urothelial cancer, hormone-refractory prostate cancer and metastatic germ cell tumors, are performed. Every morning clinical rounds are started at 7:30 a.m., and a weekly conference to discuss inpatient management is held on Monday evenings.

Major urological malignant diseases are treated according to the following strategies:

(1) Renal cell carcinoma: M0, partial or radical nephrectomy; M1: chemotherapy with target drugs with TKI or mTOR with or without palliative nephrectomy.

(2) Bladder cancer. Carcinoma in situ: BCG instillation therapy. Ta, T1, transurethral resection of bladder cancer (TURBT), often combined with preoperative or postoperative BCG instillation. T2-T4, radical cystectomy with or without neoadjuvant chemotherapy with M-VAC/GC regimen. N+, systemic chemotherapy, radiation; sometimes urinary diversion alone. M+, chemotherapy with M-VAC or GC regimen.

(3) Prostate cancer. Organ-confined disease, active surveillance, robotic-assisted or open radical prostatectomy, irradiation, or endocrine therapy. Specimen-confined disease, extended radical prostatectomy without neoadjuvant endocrine therapy, radiation therapy with endocrine therapy, or endocrine therapy alone. M1 disease, endocrine therapy and palliative radiation if necessary. For castration refractory disease, DTX chemotherapy is indicated.

(4) Testicular germ cell tumor (GCT): Stage I, careful observation regardless of a pathological element. Stage II or higher, EP (etoposide + CDDP) or BEP (BLM + etoposide + CDDP) chemotherapy as the first line. In nonseminomatous cases, a salvage operation is performed after induction chemotherapy. In seminoma cases, careful observation rather than surgery is selected.

Research activities

We are constantly seeking ways to improve the treatment for malignant urological tumors.

1. Urothelial cancer: The effectiveness of a phase III study to confirm the efficacy of BCG instillation for high grade T1 bladder cancer (JCOG1019) is ongoing. For metastatic disease, a weekly CBDCA + PTX regimen has been indicated.
2. Prostate cancer: A phase II study to evaluate the efficacy of robotic assisted laparoscopic radical prostatectomy for low and intermediate risk prostate cancer is ongoing. A new operative method to achieve a complete surgical margin (extended radical prostatectomy) has been developed, and its efficacy in patients with specimen-confined disease has been evaluated without neoadjuvant endocrine therapy. To provide a more precise preoperative diagnosis, a new imaging strategy using 3.0 Tesla MRI has been developed. To identify the most effective treatment for the recurrence of PSA failure after radical prostatectomy, a phase III study to

evaluate the efficacy of salvage irradiation vs hormone ablation for postoperative PSA failure in T1c-T2 prostate cancer (JCOG0401) is under review. For DTX refractory prostate cancer, a study on a vaccine regime with IKT1 is ongoing.

3. Testicular germ cell tumors: Advanced and/or refractory cases: A so-called "desperate operation," which was designed for patients whose tumor markers do not normalize after induction chemotherapy, has been shown to be both efficacious and of clinical significance. For CDDP-refractory germ cell tumors, a second line TIP/TIN regimen has completed enrollment.

Clinical trials

We are actively involved in the following mainly ongoing protocol studies;

1. A phase III study: BCG instillation for high grade T1 bladder cancer (JCOG1019)
2. A phase II study: Robotic assisted laparoscopic prostatectomy for low and intermediate risk prostate cancer
3. A phase III study: Salvage radiation vs hormone ablation for postoperative PSA failure in T1c-T2 prostate cancer (JCOG0401)
4. A phase II study: IKT1 for chemo-refractory prostate cancer

Table 1. Patients stastistics: Major treatment

	2010	2011	2012	2013	2014
Radical/partial nephrectomy	35	30	46	39	33
Nephroureterectomy	15	12	17	8	10
Total cystectomy	31	24	25	24	17
TURBT	130	140	130	117	142
M-VAC	62	50	62	45	46
GC	71	84	83	70	83
Radical prostatectomy	98	111	87(RALP 2)	84(RALP32)	56(RALP 42)
Prostatic biopsy	168	175	151	128	144
High orchyectomy	12	8	6	6	5
Retroperitoneal lymphadenectomy	8	13	6	5	7
Chemotherapy for testicular cancer	14	30	35	7	3
Retroperitoneal tumor resection	15	10	18	13	32

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Journal

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Department of Gynecology

Tomoyasu Kato, Mitsuya Ishikawa, Shunichi Ikeda

Introduction

The Gynecologic Oncology Department deals with tumors originating from the female genital and reproductive organs. Surgery is the main treatment modality for most gynecologic cancers, but multidisciplinary treatments consisting of radiotherapy and chemotherapy are routinely considered in close cooperation with therapeutic radiation oncologists and medical oncologists. The incidences of 3 common gynecologic cancers, i.e., cervical, endometrial and ovarian cancer, are now on the rise in Japan.

Routine activities

1. The staff members of the Department of Gynecology comprise 3 gynecologic oncologists. In addition, our Division includes 3 residents in training. Current topics in the diagnosis and treatment of gynecologic malignancies are periodically discussed after the Monday general meeting. All patients under treatment are the subjects of presentation and discussion at the weekly joint conference on Wednesdays. A joint clinic pathological conference is held on the second Tuesday of each month.

2. Treatment strategy for uterine cervical cancer: Either conization or simple total hysterectomy is the treatment of choice for persistent CIN III, carcinoma in situ, or cervical cancer Stage Ia1. Patients with Stages Ia2 to IIb usually undergo radical hysterectomy and pelvic lymphadenectomy. Postoperative whole pelvic irradiation following radical hysterectomy is only considered for patients with metastasis to the pelvic nodes or parametrial tissue as confirmed by pathological examination. Furthermore, in 2012, intensity-modulated radiation therapy (IMRT) started to be employed for postoperative adjuvant radiotherapy. Thereafter none had radiation enterocolitis. Radiotherapy alone or concurrent chemo-radiotherapy is given to patients at any Stage. Chemotherapy is occasionally used for the treatment of distant metastasis.

3. Treatment strategy for endometrial cancer: The primary treatment choice is hysterectomy with bilateral salpingo-oophorectomy. Pelvic lymph node dissection is also performed for patients with a high risk of metastasis. Para-aortic node dissection is limited to those with biopsy proven nodal metastasis. Postoperative adjuvant chemotherapy is performed for patients with extra-uterine disease.

4. Treatment strategy for ovarian cancer: A simple total hysterectomy, bilateral salpingo-oophorectomy and omentectomy with or without combined resection of the involved intestine are the standard procedures for the treatment of ovarian cancer. When an intraperitoneal tumor can be optimally debulked and node metastasis is confirmed by pathologic sampling during the operation, combined pelvic and para-aortic lymph node dissection is indicated. For patients with advanced-stage cancer, surgery is followed by combination chemotherapy containing Carboplatin and Paclitaxel (TC or dose dense TC). Patients with more advanced Stage III and IV disease, who are unlikely to be optimally debulked, are treated with primary chemotherapy (NAC). After 3 of 4 courses of chemotherapy, an interval debulking surgery (IDS) is usually performed for 3 patients. Surgery alone can offer the chance of cure for patients with recurrence, but only when the disease is completely resectable. The type of patient number and surgical procedure are shown in Tables 1 and 2, respectively.

Research activities

A phase III study of dose dense TC chemotherapy (JCOG 1311) for patients with advanced or recurrent cervical cancer has approved. In addition, a nonrandomized confirmatory trial of post-operative irradiation using Intensity modulated radiotherapy (IMRT) for patients with cervical cancer who have undergone a radical hysterectomy (JCOG PC1402) and a randomized phase III study to verify treatment significance of para-aortic lymph node dissection for endometrial carcinoma with risk of lymph node metastasis (JCOG PC1412) are now being projected. Either project is expected to provide a higher evidence level of treatment modality.

We have been doing the translational research with research institute of NCC. We investigate the chemoresistance of ovarian clear cell adenocarcinoma of the ovary. Cancer stem cells (CSCs) are thought to be one of the causes of chemoresistance, Recently, human telomerase reverse transcriptase (hTERT) has been reported to promote CSC-like traits. We found that a mitotic inhibitor, eribulin mesylate (eribulin), effectively inhibited growth of platinum-resistant ovarian cancer cell lines. Eribulin-sensitive cells showed a higher efficiency for sphere formation, suggesting that these cells possess an enhanced CSC-like phenotype. Moreover, these cells expressed a higher level of hTERT, and suppression of hTERT expression by siRNA resulted in decreased sensitivity to eribulin, suggesting that hTERT may be a target for eribulin. Our article has published in Plos One.

Clinical trials

1. A phase III study to compare treatment starting with neoadjuvant chemotherapy and primary cytoreductive surgery followed by postsurgical chemotherapy for advanced ovarian cancer (JCOG 0602) had closed for enrollment.
2. A nonrandomized confirmatory trial of modified radical hysterectomy for patients with FIGO Stage Ib1 (< 2 cm) uterine cervical cancer (JCOG1101) is ongoing as planned.
3. A non-randomized verification study regarding selection of fertility-sparing surgery for patients with epithelial ovarian cancer (JCOG1203) has started.

Table 1. Number of patients

Primary site	number of patients
Cervix	39
Endometrium	69
Endomerium+Ovary	1
Ovary/tube/peritoneum	76
Vagina	1
Vulva	5
Benign or Others	38

Table 2. Type of procedure

Radical hysterectomy	24
Modified radical hysterectomy	4
TAH+/-BSO+/-omentectomy+Paraaortic lymphadenectomy	18
TAH+/-BSO+/-omentectomy+pelvic lymphadectomy	12
TAH+/-BSO+/-omentectomy+/-LAR	3
TAH+/-BSO+/- omentectomy+/-retroperitoneal lymphnode biopsy	121
Radical vulvectomy	1
Simple vulvectomy	3
Conization	9
Others	34

List of papers published in 2014

Journal

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5. Murakami N, Kasamatsu T, Sumi M, Yoshimura R, Harada K, Kitaguchi M, Sekii S, Takahashi K, Yoshio K, Inaba K, Morota M, Ito Y, Itami J. Vaginal tolerance of CT based image-guided high-dose rate interstitial brachytherapy for gynecological malignancies. Radiat Oncol, 9:31, 2014
6. Matsubara A, Sekine S, Ogawa R, Yoshida M, Kasamatsu T, Tsuda H, Kanai Y. Lobular endocervical glandular hyperplasia is a neoplastic entity with frequent activating GNAS mutations. Am J Surg Pathol, 38:370-376, 2014

Department of Musculoskeletal Oncology and Rehabilitation

Hirokazu Chuuman, Akira Kawai, Fumihiko Nakatani, Yoshikazu Tanzawa, Eisuke Kobayashi, Daisuke Kubota, Nokitaka Setsu, Kouki Shimizu, Yusuke Minami, KensakuYamaga

Introduction

Malignant tumors arising from connective tissue are extremely rare, estimated to account for only 0.01% of newly developed cancers. The rarity itself sometimes causes several problems in treating patients with bone and soft tissue tumors, including retardation of accurate diagnoses and a lack of understanding regarding standardized therapeutic approaches. Since 1962, the Orthopedic Surgery Division of the National Cancer Center Hospital (NCCH) has been accumulating a vast array of clinical knowledge regarding musculoskeletal tumors in collaboration with radiologists and pathologists specializing in sarcomas, which has enabled us to offer well-organized treatment strategies to patients with various types of bone and soft tissue tumors. We have also been conducting basic and clinical studies using accumulated clinical samples and information to establish novel diagnostic methods and therapeutic approaches for treating musculoskeletal tumors. In addition, we have given weight to clinical trials on three different but inseparable fields: surgery, chemotherapy and radiation therapy for bone and soft tissue tumors.

Routine activities

The musculoskeletal oncology division of the NCCH consists of 5 staff doctors (Drs. Hirokazu Chuuman, Akira Kawai, Fumihiko Nakatani, Yoshikazu Tanzawa and Eisuke Kobayashi), 4 residents and 2 physiotherapists, 1 occupational therapist and 1 speech therapist. Occasionally, several fellows from Japan and overseas join our group. Outpatient consultations are held every weekday. A constant number of about 28 patients are hospitalized for operation, chemotherapy or radiation therapy. Five or six major operations are routinely performed every week. In 2014, 320 operations were performed, including palliative operations for pathological fractures or spinal cord compression from metastatic bone and soft tissue tumors. Sarcomas in the trunk, including the 4 thoracic wall, 19 retroperitoneal space and 2 head and neck lesions were excised in cooperation with thoracic, general, urological or head-neck surgeons, respectively. A total of 58 reconstructive operations were conducted in collaboration with plastic surgeons to achieve adequate soft tissue coverage after the resection of malignant tumors of the trunk or limb-salvage operations for sarcomas of the extremities. As a result, almost 90% of the operations were performed with a limb-sparing approach. With regard to the patients' postoperative course, we have been collaborating with a physical therapist to rehabilitate the musculoskeletal system in cancer-bearing patients.

As for chemotherapy, we have been conducting neoadjuvant and adjuvant chemotherapy for high-grade bone and soft tissue tumors, palliative chemotherapy for metastatic bone and soft tissue sarcomas, where necessary in collaboration with medical oncologists. We have been collaborating with pediatric oncologists for chemotherapeutic treatment of children and adolescents with sarcomas.

Research activities

Since 2004, we have been collaborating with the NCC Research Institute to develop novel molecular target therapies or tailor-made treatments for sarcoma patients. With a genome-wide microarray system or a protein-wide two dimensional fluorescence difference gel electrophoresis (2D-DIGE) system, we have been analyzing the complete expression levels of mRNA and protein in the tumor samples from patients with Ewing's family tumors, osteosarcomas and soft tissue sarcomas. Combined with each patient's

clinical information, we have been establishing novel biomarkers for prediction of patients' prognoses or effects of the chemotherapeutic agents. Using the same method, we also have been searching for new genes or proteins for the molecular-targeted treatment approach. Since 2009, we have also been focusing on the aberrant microRNA expressions in Ewing's sarcoma and osteosarcoma with the aim of developing novel molecular targeted therapies or biomarkers.

Clinical trials

We also have been focusing on the standardization of adjuvant and second-line chemotherapy regimens for bone and soft tissue sarcomas. Three multi-institutional clinical trials are active as follows:

1. A multi-institutional phase III clinical trial of multidrugs adjuvant chemotherapy for osteosarcomas (JCOG 0905) since 2010.
2. A multi-institutional phase 3 study of trabectedin for advanced soft tissue sarcoma since 2012.
3. A multi-institutional phase II study of Eribulin (an inhibitor of microtubule dynamics) for advanced soft tissue sarcoma since 2011.
4. A multi-institutional phase III clinical trial of multidrugs adjuvant chemotherapy for highgrade soft tissue sarcomas (JCOG 1306) since 2014.

Education

Each resident performed 60-70 operations supervised by staff members one year, joined many domestic and international conferences and published several medical articles or reports during training courses. All staff member teach all clinical procedure or knowledge about oncological skills for bone and soft part sarcomas.

Future prospects

Our clinical divisions and translational study groups do many clinical trials of novel therapeutic innovations and promote clinical trials of novel drugs or targeted compounds for sarcomas and continue to make efforts in future.

Table 1. New patients (2013)

1	Soft tissue sarcomas	201
2	Bone sarcomas	25
3	Benign bone and soft tissue tumors	106
4	Spine or bone metastasis	26
Total		332

Table 2. Type of procedure

1	Soft tissue sarcomas	107
2	Bone sarcomas	34
3	Benign bone and soft tissue tumors	85
4	Spine or bone metastasis	14
5	biopsy	31
6	amputation	9
7	others	32
	Plastic surgery combined	58
	Reconstruction with prosthesis	18
	Spine surgery	6
Total		320

List of papers published in 2014

Journal

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12. Kataoka K, Tanaka K, Mizusawa J, Kimura A, Hiraga H, Kawai A, Matsunobu T, Matsumine A, Araki N, Oda Y, Fukuda H, Iwamoto Y. A randomized phase II/III trial of perioperative chemotherapy with adriamycin plus ifosfamide versus gemcitabine plus docetaxel for highgrade soft tissue sarcoma: Japan Clinical Oncology Group Study JCOG1306. Jpn J Clin Oncol, 44:765-769, 2014
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Department of Dermatologic Oncology

Naoya Yamazaki, Arata Tsutsumida, Akira Takahashi, Kenjiro Namikawa, Wataru Omata, Kohei Oashi, Kohei Nojima, Takehiro Onuma, Yoshio Nakamura, Saori Kan, Miki Sugiyama, Mika Hashimoto

Introduction

The Department of Dermatologic Oncology has consistently served as the core hospital for the establishment of treatment strategies for malignant skin tumors since the National Cancer Center opened in 1962, and over 2,000 cases of malignant melanoma have been accumulated thus far; an impressive number for a hospital or research institution in Japan. Today, patients are referred from throughout Japan. Of particular note, the number of patients with malignant melanoma was 206, which was approximately twice - the number 4 years ago. Most of the patients are examined and treated for skin cancer including malignant melanoma. Surgery is the main treatment modality for skin cancer, and multi-disciplinary treatments, consisting of chemotherapy, immunotherapy, and radiotherapy, are also routinely carried out. In addition, this Department plays an active role in multicenter trials for skin cancer all over Japan.

Routine activities

The Division has 4 staff dermatologic oncologists, 1 chief resident and 4 residents. We are also engaged in routine outpatient activities on Wednesdays and Thursdays in the National Cancer Center East.

Our Department is a high-volume center, where we have seen an average of more than 200 patients with malignant melanoma annually in the last 3 years. This is the result of creation of a national network to develop treatment for malignant skin tumors, and nivolumab, an anti-PD-1 antibody, was approved as a therapeutic agent for malignant melanoma in Japan for the first time in the world as a result of vigorous development of new drugs.

An expanded access program of a BRAF inhibitor, vemurafenib, was conducted through an investigator-initiated clinical trial.

About 20 patients are hospitalized to undergo surgery, chemotherapy, or radiation therapy. In 2013, 233 operations were performed including 115 operations under general anesthesia. Rounds are made and case presentations are held every morning. A Division conference is held every Monday to discuss the therapeutic principles for outpatients and inpatients. A clinicopathological conference that focuses on surgically removed skin specimens is held with pathologists once a month.

Besides, we have treated advanced cases of mucosal melanoma patients in the nasal cavity, genital lesions, perianal lesions, and uveal melanoma even if our origins are “dermatologic”.

Research activities

Malignant skin tumors are mainly treated by surgery (appended table). However, in recent years, several new drugs have been developed rapidly overseas for the treatment of malignant melanoma, and our Department is conducting many clinical studies and trials; the major ones are described below.

- A multicenter study for establishing the standard therapy for refractory malignancies
- A study on establishment of the early clinical development system of drugs for rare cancers and support for research
- Development of a system for boron neutron capture therapy (BNCT) using an accelerator installed at the hospital
- A study for developing guidelines to support the physical appearance of cancer patients
- A study on methods for assessing the skin changes associated with cancer treatment and establishment of standard care
- A study on the quantitative assessment of skin disorders associated with chemotherapy

using molecular-targeted agents and skin care
- A retrospective study to clarify the outcomes of conventional treatment for cutaneous angiosarcoma of the head and neck
- A retrospective study of factors affecting failure to identify sentinel lymph nodes in sentinel lymph node biopsy using the indocyanine green (ICG) fluorescence method in patients with cutaneous malignant melanoma
- A profiling study of genes related to the therapeutic effects and toxicity using clinical specimens from cancer patients (Cancer Gene Profiling Study)
- A retrospective study on the efficacy of multiagent chemotherapy (FECOM therapy) for metastatic extramammary Paget's disease
- A retrospective study on the outcomes of TACE therapy using cisplatin for liver metastasis from primary ocular malignant melanoma
- Diagnosis and study of familial and juvenile cancers and hereditary tumors
- A clinical study on BRAF V600 mutations in Japanese patients with malignant melanoma
- A phase I/II clinical trial of vemurafenib in patients with recurrent malignant melanoma harboring BRAF V600 mutations who are not suitable candidates for curative resection
- A phase I/II trial of combined dabrafenib and trametinib in patients with BRAF V600E or V600K mutation-positive advanced solid cancer (for phase I trial) or cutaneous malignant melanoma (for phase II trial)
- A randomized phase III trial comparing the efficacy of an MEK inhibitor, MEK162, with that of dacarbazine in patients with advanced unresectable or metastatic NRAS mutation-positive malignant melanoma
- A multicenter phase II trial on the effects of immune checkpoint inhibitors, such as nivolumab and ipilimumab, in patients with advanced malignant melanoma
- A multicenter, unblinded, uncontrolled phase I clinical trial of adjuvant therapy with PEG-modified IFNα-2b in patients with Stage II and III malignant melanoma
- An exploratory study on the usefulness of 18F-BPA PET/CT in diagnosing the Stage of malignancies
- Practical development of therapeutic agents for refractory skin cancer using innovative molecular-targeted agents inducing cancer-specific apoptosis through an investigator-initiated clinical trial

Clinical trials

Table2 shows our clinical trials.

Human resource development

Dr. Kenjiro Namikawa received the third 'My Oncology Dream' Award from the Japan Cancer Society and studied at MD Anderson Cancer Institute for a year.

Dr. Akira Takahashi has a doctorate in medicine.

Perspectives

We are attempting to eliminate drug lag, which seems to exist between Western countries and Japan, and our goal is to achieve this in 3 years. Furthermore, we think that we can develop treatment for rare cancers, such as Merkel cell carcinoma, by sharing the current research infrastructure.

Table 1. Number of New Patients

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Malignant melanoma	67	68	74	97	94	79	92	75	94	88	132	228	191	206
Squamous cell carcinoma	27	19	24	31	36	25	25	28	36	52	27	34	40	45
Basal cell carcinoma	40	29	31	47	33	23	25	33	31	28	28	33	38	37
Sweat gland carcinoma	3	10	7	8	10	17	6	10	10	9	9	8	7	16
Trichilemmal carcinoma	0	1	2	0	0	1	7	0	1	0	0	1	0	1
Paget's disease	10	16	13	12	18	16	19	20	21	19	22	18	16	22
Bowen's disease	16	8	7	12	9	8	4	2	10	3	9	5	14	11
Dermatofibrosarcoma protuberans	2	2	3	5	3	7	3	5	10	10	10	7	13	10
Angiosarcoma	7	5	3	3	5	9	6	12	9	9	9	6	10	11
Malignant fibrous histiocytoma	0	0	1	1	1	0	1	1	3	3	1	0	1	0
Epithelioid sarcoma	1	1	0	0	2	1	0	1	0	0	0	0	0	0
Malignant lymphoma	3	10	12	12	15	7	6	15	13	16	16	15	6	11
Merkel cell carcinoma	-	-	-	-	2	3	2	4	3	3	8	1	1	3
others	2	5	5	4	5	12	11	8	7	17	19	19	14	8
Total	178	175	182	232	233	208	207	204	248	257	290	375	327	381

Table 2. Operative Procedures (total number)

Wide local excision	148
Local excision	41
Sentinel node biopsy	44
Lymph node biopsy	10
Lymph node dissection	36
(neck)	6
(axilla)	11
(inguinal)	8
(groin)	9
(popliteal)	0
(epitrochlear)	1
Skin graft	44
Local flap	15
Free flap	1
Amputation	5
others (biopsy/debridement)	5

Table 3. New Agent Studies in 2014

Agent	Eligible Cancer Type	Trial Phase
Peg interferon alpha	Melanoma	I
MEK162	Melanoma	I
LGX818	Solid Tumors	I
Trametinib / Dabrafenib	Melanoma	I
MSB0010718C	Solid Tumors	I
ONO-4538	Melanoma	II
Vemurafenib	Melanoma	I / II
Trametinib / Dabrafenib	Melanoma	II
Ipilimumab+DTIC	Melanoma	II
ONO-4538	Melanoma	II
MEK162 / LGX818	Melanoma	III
Ipilimumab (3mg)	Melanoma	II
MEK162 / LGX818	Melanoma	III
MK-3475	Melanoma	I
HVJ-E	Melanoma	I

List of papers published in 2014

Journal

1. Gemma A, Kudoh S, Ando M, Ohe Y, Nakagawa K, Johkoh T, Yamazaki N, Arakawa H, Inoue Y, Ebina M, Kusumoto M, Kuwano K, Sakai F, Taniguchi H, Fukuda Y, Seki A, Ishii T, Fukuoka M. Final safety and efficacy of erlotinib in the phase 4 POLARSTAR surveillance study of 10 708 Japanese patients with non-small-cell lung cancer. Cancer Sci, 105:1584-1590, 2014
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Department of Hematology

Kensei Tobinai, Yukio Kobayashi, Dai Maruyama, Tatsuya Suzuki, Wataru Munakata, Suguru Fukuhara, Hideaki Kitahara, Shinichi Makita

Introduction

The Department of Hematology is united with the Department of Hematopoietic Stem Cell Transplantation (HSCT), and the research and clinical activities in the Department of Hematology are devoted to the diagnosis and treatment of hematological malignancies. In the past, our Department introduced novel disease entities, including adult T-cell leukemia-lymphoma (ATL) (J Clin Oncol 2009;27:453-9) and angioimmunoblastic T-cell lymphoma (Blood 1988;72:1000-6). This Department is one of the leading hematology-oncology centers in the world, especially for lymphoid malignancies.

Routine activities

The number of patients with newly diagnosed hematologic malignancies in the Division increased annually from 1997 to 2004, and then reached a plateau (Table 1). We hold a weekly case conference, where a summary of each hospitalized- or out-patient is presented. An educational cytology conference is held weekly for young doctors. Newly diagnosed lymphoma cases are presented at a weekly lymphoma case conference, where oncologists, pathologists, radiologists, and radiation oncologists discuss diagnosis and treatment plans. We also participate in weekly HSCT conferences, which deal with all HSCT cases.

In addition to patient care in the ward, our daily activities include management of hematology clinics and a diagnostic laboratory to perform bone marrow and peripheral blood microscopic examination, and flow cytometric and molecular-genetic analyses. Five staff physicians, two chief residents, and two to five rotating residents are involved in these activities.

Research activities

In addition to immunophenotypic analyses, molecular diagnosis is routinely performed, using polymerase chain reaction (PCR) and fluorescence in-situ hybridization (FISH) techniques for the detection of t(8;14), t(14;18), t(11;18), t(9;22), t(8;21), t(15;17), Flt3-ITD and so on. Our recent research has focused on indolent B-cell non-Hodgkin lymphoma (B-NHL). Clinical as well as molecular and cytogenetic analyses of ocular adnexal mucosa-associated lymphoid tissue (MALT) lymphoma cases led to the discovery of a new tumor suppressor gene deleted at 6q23; we identified A20 gene as a tumor suppressor gene in various B-cell malignancies (Nature 2009;459:712-6). The gene is involved in NFκB signaling and its status would be a biomarker for BCR inhibitors.

This year, we authored or coauthored 17 articles related to hematological malignancies including 3 editorials or review articles. We have constructed tumor sample banking system, collecting the rest of sample taken as routine diagnostic procedures. The samples' DNA and RNAs are extracted and reserved for future use.

Clinical trials

In 2014, we conducted 29 new-agent studies, including 8 international ones (Tables 2). The number is still increasing including domestic ones. Almost all the new agents that are developed against hematological malignancies in Japan have been evaluated in our Department, and many of them have been approved by the Ministry of Health, Labor and Welfare (MHLW).

A various phase I and II trials are ongoing on T cell malignancies. The agents include mogamulizumab, lenalidomide, romidepsin, forodesine, darinaparsin, chidamide and denileukin diftitox. Some of the agents are being evaluated

in international studies. For indolent ATL, we are evaluating interferon-alfa and AZT, as a phase III study (JCOG 1111).

With a completion of phase I study of oligopeptide vaccine OCV-501 against WT1 protein in AML cells to keep cases in complete remission, a randomized phase II trial is ongoing to evaluate the efficacy. The agent was developed in Japan, and is the first study against hematological malignancies aiming the approval by MHLW.

For treatment of B-cell malignancies, patient enrolment into a phase III trial for newly diagnosed, diffuse large B-cell lymphoma (JCOG 0601) was completed. In this trial, a dose-intense schedule of rituximab was compared with that of a standard 3-weekly regimen. We also completed patient enrolment into a phase II study of a rituximab-incorporating dose-intensified chemotherapy for high-risk, untreated DLBCL (JCOG 0908), using high-dose chemotherapy with autologous stem cell transplantation. For symptomatic multiple myeloma patients ineligible for transplantation, we are conducting a randomized phase II trial to find a more suitable combination regimen of bortezomib, melphalan and prednisolone (JCOG 1105).

Table 1. Newly diagnosed patients

Disease / Year	2006	2007	2008	2009	2010	2011	2012	2013	2014
Acute myelocytic leukemia (AML)	9	10	6	10	8	13	12	7	9
Acute lymphocytic leukemia (ALL)	4	9	8	2	2	1	1	6	3
Chronic myelocytic leukemia (CML)	10	11	3	3	2	2	2	2	3
Myelodysplastic syndrome (MDS)	3	9	8	20	9	3	3	6	3
Hodgkin lymphoma (HL)	21	11	12	7	11	16	15	13	9
Non-Hodgkin lymphoma (NHL)	265	210	208	151	185	243	172	193	151
Adult T-cell leukemia-lymphoma (ATL)	6	4	5	5	3	6	6	4	10
Chronic lymphocytic leukemia (CLL)	4	5	6	4	2	1	4	1	1
Multiple myeloma (MM)	9	8	10	12	9	10	7	8	3
Waldenström macroglobulinemia (WM)	0	2	3	1	2	2	1	0	0
Total	331	279	269	215	233	297	223	240	192

Table 2. Clinical trials for new agents

Disease	Agents	Phase	Enrolment in 2014	Total
CML	Nilotinib	III	0	1
	Bosutinib	I/II	0	3
	Ponatinib	I	0	3
MDS	Rigosertib	I	1	2
AML	WT1 (maintenance)	I	0	4
	Volasertib	I	0	6
	Volasertib		2	2
ALL	Inotuzumab ozogamicin	I	1	2
MM	Carfilzomib	I	0	1
	Carfilzomib	III	1	1
	Pomalidomaide	II	1	1
PTCL	Forodesine	I/II	4	6
	Romidepsin	I/II	4	10
	Pralatrexate	I	5	5
	Denileukin diftitox (E7777)	I	1	3
FL	Ofatumumab vs. Rituximab	III	5	40
	Ofatumumab + Bendamustine	III	0	4
	Obinutuzumab	III	0	16
	R-B +/- Ibrutinib	III	8	8
	Rituximab + Lenalidomide (RELEVANCE)		2	2
MCL	R-B +/- Ibrutinib	III	0	1
	VcR-CAP	III	0	2
DLBCL	Ofatumumab	III	0	3
	Everolimus	III	0	1
	Obinutuzumab	III	0	2
	Alisertib (MLN8237)	I	0	5
HL	SGN-35	I	1	3
B-NHL	Ibrutinib	I	0	7

PTCL, peripheral T-cell lymphoma; FL, follicular lymphoma; B-NHL, B-cell non-Hodgkin lymphoma; MCL, mantle cell lymphoma; DLBCL, diffuse large B-cell lymphoma; PSL, prednisolone; R-CVP, rituximab, cyclophosphamide, vincristine, PSL; R, rituximab

Table 3. Cooperative group studies

Disease / Protocol	Phase	Year	No. of pts (a)	%CR (b)	OS (b)
AML					
JALSG-AML 201	III	(02-06)	13	78%	57%(5-yr)
JALSG-APL 97	III	(98-02)	2	95%	86% (4-yr)
JALSG-APL 204	III	(04-11)	2	94.5%	89%(5-yr)
JALSG-AML209	IV	(11-)	11	NA	NA
JALSG-APL212	II	(13-)	1	NA	NA
ALL/Lymphoblastic lymphoma					
JALSG-ALL 97	II	(98-01)	8	74%	32% (5-yr)
JALSG-ALL 202	II	(03-10)	9	NA	NA
CML					
JALSG-CML 207	III	(08-10)	1	NA	NA
JALSG-CML 212	III	(13-)	3	NA	NA
Hodgkin lymphoma					
JCOG 9705	II	(98-00)	6	70%	81% (5-yr)
Aggressive NHL					
JCOG 9809	III	(99-02)	55	62%	56% (8-yr)
JCOG 0601	III	(08-14)	66	NA	NA
JCOG 0406	III	(08-13)	5	NA	NA
JCOG 0908	III	(08-)	21	NA	NA
Indolent B-cell lymphoma					
JCOG 0203	II/III	(02-07)	52	77%	88% (6-yr)
Adult T-cell leukemia-lymphoma					
JCOG 9801	III	(98-03)	6	33%	19% (3-yr)
JCOG 0907	II	(10-)	3	NA	NA
JCOG 1111	III	(13-)	4	NA	NA
Nasal NK/T-lymphoma					
JCOG 0211-DI	I/II	(03-07)	8	77%	78% (2-yr)
Multiple myeloma					
JCOG 0112	III	(02-05)	9	46% (d)	63% (2-yr)
JCOG 0904	II	(09-14)	7	NA	NA
JCOG 1105	III	(13-)	2	NA	NA

(a) the number of patients enrolled from our division; (b) As the number of enrolled patients in our division is relatively small, the %CR or OS for the entire enrolled patients in the JCOG or JALSG trials is shown here; (c) randomized phase II study; (d) CR + PR rate. Abbreviations: JCOG, Japan Clinical Oncology Group; JALSG, Japan Adult Leukemia Study Group; LSG, Lymphoma Study Group; OS, overall survival; NA, not available

List of papers published in 2014

Journal

1. Harada K, Murakami N, Kitaguchi M, Sekii S, Takahashi K, Yoshio K, Inaba K, Morota M, Ito Y, Sumi M, Suzuki S, Tobinai K, Uno T, Itami J. Localized ocular adnexal mucosaas-sociated lymphoid tissue lymphoma treated with radiation therapy: a long-term outcome in 86 patients with 104 treated eyes. Int J Radiat Oncol Biol Phys, 88:650-654, 2014
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Department of Hematopoietic Stem Cell Transplantation

Takahiro Fukuda, Takuya Yamashita, Sung-Won Kim, Saiko Kurosawa, Shigeo Fuji, Yoshihiro Inamoto, Yoshitaka Inoue, Reiko Ito, Takashi Tanaka

Introduction

At the National Cancer Center Hospital, the Department of Hematopoietic Stem Cell Transplantation (HSCT) specializes in patients who undergo allogeneic or autologous HSCT. 26 beds in ward 12B and an additional 3 beds on ward 11A, which are filtered by a central high-efficiency particulate air filtration system, are solely dedicated to our Transplant Unit.

Routine activities

6 staff physicians (Drs. Yamashita, Kim, Kurosawa, Fuji, Inamoto, and Fukuda) and 3 chief residents (Drs. Inoue, Ito, and Tanaka) participate in the transplant program. Children who have undergone HSCT are managed in collaboration with Dr. Ogawa, the chief of the Department of Pediatric Oncology, and transplant team. In 2014, a total of 103 transplantations were performed at the 12B and 12A transplant units. The numbers of each type of HCST and those who underwent HSCT between 2008 and 2014 are shown in Tables 1 and 2, respectively. At the weekly conference on Monday afternoons, in collaboration with doctors of the Department of Hematology, about 30 hospitalized HSCT patients and those who have been referred for HSCT, are reviewed for clinical management and a decision regarding their eligibility for HSCT. The transplant unit is staffed by 24 nurses trained in oncology and specialized supportive care for HSCT patients. The nursing unit has been assuming leadership in an effort to facilitate improved care for skin and gut graft-versus-host disease (GVHD), and establishment of a Long-term Follow-up Unit (LTFU) for the education of patients and their family members. In 2014, 342 patients visited our LTFU clinic. At the weekly 12B ward meeting on Friday afternoons, all HSCT patients are reviewed in detail by all transplant team members including doctors, nurses, pharmacists, the nutritional support team, clinical research coordinators, and the transplant coordinator.

Research activities and Clinical trials

Our transplant team has been focusing on the development of comprehensive cellular immunotherapy, including a reduced-intensity stem cell transplant for elderly patients. A clinical trial of post-transplant consolidation with the WT1 vaccine is also ongoing. A nationwide large survey of quality of life (QOL) in 576 patients with acute leukemia showed that the physical QOL in the allo-HCT patients without GVHD was comparable to that in the chemotherapy patients, and they experienced significantly better mental and general QOL than the chemotherapy patients. In 2014, we have published 23 articles in peer-reviewed international journals and 10 manuscripts have been accepted for E-pub before print or are in press for publication.

Table 1. Newly diagnosed patients

Year		2008	2009	2010	2011	2012	2013	2014
Allogeneic		77	93	90	76	72	87	93
Unrelated	BMT	48	59	60	54	46	53	52
	PBSCT	1	0	0	0	3	5	6
	CBT	1	5	1	4	8	8	9
Related	BMT	5	2	5	2	0	1	2
	PBSCT	22	27	24	16	15	20	24
Autologous		8	18	19	25	25	23	10
Total		85	111	109	101	97	110	103

Table 2. Number of patients who underwent HSCT between 2008 and 2014

Diagnosis	Allogeneic	Autologous
Acute myeloid leukemia	225	1
Myelodysplastic syndrome	45	0
Acute lymphocytic leukemia	86	0
Malignant Lymphoma (including ATL)	216	74
Multiple Myeloma	0	26
Solid tumors	3	27
Others	13	0
Total	588	128

List of papers published in 2014

Journal

1. Hiramoto N, Kurosawa S, Tajima K, Okinaka K, Tada K, Kobayashi Y, Shinohara A, Inoue Y, Ueda R, Tanaka T, Kim S-W, Yamashita T, Heike Y, Fukuda T. Positive impact of chronic graft-versus-host disease on the outcome of patients with de novo myelodysplastic syndrome after allogeneic hematopoietic cell transplantation: a single-center analysis of 115 patients. Eur J Haematol, 92:137-146, 2014
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Department of Blood Transfusion and Cellular Therapy

Ryuji Tanosaki

Introduction

The missions of the Department of Blood Transfusion and Cellular Therapy are management of in-hospital transfusion and a support for the hematopoietic stem cell transplantation team in respect of providing safe and secure cellular products. In common with the Department of Clinical Laboratories, our blood transfusion examination laboratory received ISO 15189 accreditation, which certifies the quality and competence of a medical laboratory with regard to quality management and technique, developed by the International Organization for Standardization Technical Committee 212 (ISO/TC 212). Our hospital is also accredited by the Japan Society of Transfusion Medicine and Cell Therapy (JSTMCT). The chief doctor (R.T.) also supervises the phlebotomy section of the outpatient clinics.

Routine activities

Currently, our staff members consist of 1 JSTMCT-accredited medical doctor and 6 specifically-engaged medical technologists (including 2 JSTMCT-accredited technologists) who come to us from the Department of Pathology and Clinical Laboratories. Most activities in our Department are undertaken in collaboration with the Department of Pathology and Clinical Laboratories.

The Transfusion Medicine Committee is held every month, the members of which consist of the deputy director in charge of safety management, chief doctors of our Department and clinical departments of surgery and internal medicine, chief of Department of Pharmacy, chief nurses of the Outpatient Treatment Center and the Hematopoietic Stem Cell Unit, and a secretary. An administrative meeting is also held weekly, the attendees consisting of 3 chief doctors and 2 head doctors of our Department and the Department of Pathology and Clinical Laboratories, and the head and vice-head medical technologists. All-staff meetings are held weekly in our Department and once a month in the Department of Clinical Laboratories, respectively.

As an in-hospital transfusion service section, we purchase blood products, which are required and ordered by clinicians, from the Red Cross, and examine and confirm the ABO blood type, and provide them for clinical use without any delay. In 2014, the total units of red cell concentrates (RCC), platelet concentrates (PC) and fresh frozen plasma (FFP), which were consumed in our hospital, were 10,667, 46,240 and 6,347, respectively, with wastage rate of 0.2% in total blood products. Thanks to the Tokyo Red Cross and the convenient location of our hospital, blood products are available within an hour almost every time when they are needed in an emergency.

We employ the Type & Screen and computer cross-match system, but a special attention is paid to blood typing, because about 100 cases of hematopoietic stem cell transplantation (SCT) are performed in our hospital every year including many ABO-mismatched donor-recipient pairs. To avoid any mistake of transfusions going to the incorrect recipients, we have established a firm safety system; a check sheet in which the appropriate or permissive ABO-blood types for the particular patient are described is always placed on the bedside of each patient undergoing allogeneic SCT, and the attending doctor, nurses and the patient double check this sheet with each other on every occasion of blood transfusion. When ordering blood products, protection is in place to prevent changing of the ABO-blood type, and some special process is required before any blood product of a type other than the patient's original blood type can be ordered. The unique computer program of the transfusion service section also protects

inappropriate blood type orders. Bar codes are used to match the patient and his or her designated blood product at each process during transfusion. Because the electronic medical record system was renewed since January 2014, the safety system for blood transfusion has also been strengthened and any case of incorrect blood transfusion has not been reported so far.

All transfusion procedures in our hospital are performed under a strict hemo-vigilant system which employs electronic medical records managed by the computer system at the blood transfusion service. Any adverse events must be recorded by the attending nurse at 5 min, 15 min, and at the end of transfusion and these data are gathered in the computer at the blood transfusion service. Adverse events are observed associated with transfusions, especially in the case of PC (about 5%). Reduction of supernatant from PC pack is performed in patients who have experienced repetitive or severe transfusion-associated reactions. Severe adverse events must be reported to the Red Cross and to the Ministry of Health, Labor and Welfare of Japan, and a further analysis of the causative agents is then performed by the Red Cross laboratory.

Hematopoietic stem cells which are to be transplanted to the SCT patients, i.e. grafts, are also subject to the same safety and bio-vigilant system as other blood products. The SCT grafts include fresh harvested bone marrow or peripheral blood stem cells (PBSC), and thawed PBSC or cord blood which have been cryopreserved in liquid nitrogen. Each graft is registered and allotted its unique code number, which is recognized as its bar code. This bio-vigilant system is important for analyzing and improving practical aspects of transplantation because the incidence of adverse reactions associated with graft infusion is significantly high; 10.4% in 652 cases between January 2008 and October 2013 in our hospital.

Since October 2014, we started the management of processing, storage, and quality control of hematopoietic stem cells used for transplantation as a routine activity, which were formerly conducted in the Department of Hematopoietic Stem Cell Transplantation. We also indicate and inform other SCT-team members including medical engineers of the optimal timing for peripheral blood stem cell harvest (PBSCH) by monitoring counts of chemotherapy/G-CSF-mobilized progenitor cells. The management meeting is held once a month, the members of which consist of staff from the Department of Hematopoietic Stem Cell Transplantation, Medical Engineer Section, the head of technologist, and our members of our Department.

The chief doctor is also involved in the management of transplant patients both as inpatients and in the outpatient clinic as a staff member of the hematopoietic stem cell transplantation team. He attends a daily morning round, a weekly transplantation conference, a weekend checkout meeting, and a weekly journal club. These activities facilitate and promote inter-departmental collaboration.

Research activities

One of the Department's research projects is to develop a new enumeration technique of hematopoietic stem cells using an automated hematology analyzer (designated as 'HPC'), which started in 2006, in collaboration with a medical diagnostic company. We conducted a multicenter prospective study for evaluation of HPC with the support of JSTMCT, analysis of which is now underway.

Another project is to establish the nation-wide infrastructure of processing and management of cellular products used for hematopoietic stem cell transplantation as a committee member of the corresponding academic societies with the support of Ministry of Health, Labor and Welfare. We also participated in multi-center evaluation studies for the standardization of CD34-positive cell enumeration.

The chief doctor also contributes to transplantation activities, especially for adult T-cell leukemia-lymphoma in collaboration with the Department of Hematopoietic Stem Cell Transplantation and members of the hematology/oncology group at the Institute of Medical Science, the University of Tokyo.

Education

The chief doctor supervises the education program of the Department of Clinical Laboratories for all medical technologists (MT). The education program consists of monthly educational meeting in which each MT gives presentations on his or her research, doctors' lectures, RCPC (twice a year). It also includes educational lectures concerning ISO 15189. We also support and facilitate academic presentations and publications by all the MT members.

Future prospects

Since April 2015, National Cancer Center will start its way as one of the National Research and Development Agencies. We will contribute to our mission by continuing the project of establishing the nation-wide infrastructure of processing and management of cellular products used for hematopoietic stem cell transplantation with the continuing support of the Ministry of Health, Labor and Welfare.

We are starting a modified Cell-Free and Concentrated Ascites Reinfusion Therapy (KM-CART), with which we are providing another tool for the management of refractory ascites in addition of an on-going phase III study evaluating the efficacy of peritoneo-venous shunting by the Department of Diagnostic Radiology.

List of papers published in 2014

Journal

1. Tanosaki R, Kumazawa T, Yoshida A, Oguni S, Nakano A, Yamagata S, Takahashi N, Kurosawa S, Kim SW, Yamashita T, Mori S, Heike Y, Fukuda T, Hamaguchi Y, Tsuda H. Novel and rapid enumeration method of peripheral blood stem cells using automated hematology analyzer. Int J Lab Hematol, 36:521-530, 2014

Department of Pediatric Oncology

Chitose Ogawa, Hiroshi Kawamoto, Naoko Yasui, Hide Kaneda, Ako Hosono

Introduction

Pediatric oncology includes a wide variety of malignancies in children and adolescents such as acute leukemia and malignant lymphoma, as well as solid tumors including osteosarcoma, soft tissue sarcoma, neuroblastoma, liver tumor and retinoblastoma. Many diseases are usually chemo-sensitive and curable with appropriate treatment. The common approach to these diseases is a "risk-adapted therapy" strategy considering long-term life expectancy. In the Department of Pediatric Oncology, patients with pediatric malignancies are managed by 4 pediatric oncologists and 1 pediatric surgeon. Although pediatric oncologists mainly treat and manage patients, a multidisciplinary team approach including radiation oncologists, orthopedic surgeons, ophthalmologic surgeons and others is incorporated for the treatment. To achieve treatment completion and optimal quality of hospital life for children, pediatric nurse specialists, teachers, child life specialists, psychologists and psychiatrists also join our team. For young patients, educational opportunities ranging from elementary school to high school are available in the pediatric ward, where 7 teachers work daily.

Routine activities

We deal with 60-80 new patients every year. Our daily activity in the pediatric outpatient clinic is to manage new patients, to treat patients with chemotherapy or blood transfusion and to provide follow-up care for patients who have completed intensive treatment. Patients receive multidisciplinary therapy, including surgical removal of the tumor, radiation therapy, chemotherapy, and sometimes SCT, as indicated.

A Pediatric Conference is held every morning, mainly to decide on individual treatment plans. The pediatric staff members and trainees discuss various issues regarding pediatric inpatients on daily rounds. Inter-department conferences in cooperation with orthopedics, radiation oncology, and palliative care are individually scheduled every 2 weeks.

Research activities

1. For newly diagnosed patients, we participate in several multicenter studies, including those by the Japan Ewing Sarcoma Study Group (JESS), Rhabdomyosarcoma Study Group (JRSG) and Japanese Pediatric Leukemia/Lymphoma Study Group (JPLSG). In addition, we also conduct our own clinical trials.
2. For relapsed patients, we are actively involved in the development of new drugs and treatments including off-label and unapproved medications.
3. For the patients with veno-occlusive disease in stem cell transplantation and the patients with delayed excretion of methotrexate, a phase I registration trial of defibrotide and a phase II registration trial of glucarpidase are ongoing.
4. For the establishment of standard therapy in Japanese nationwide study groups, we support infrastructure building with the National Center for Child Health and Development.

Clinical trials

In 2014, we conducted 16 trials, including early phase trials, an international study and cooperative studies. The 5 trials (3, 6, 8, 9, and 10) are investigator-initiated and 2 (15 and 16) are company sponsored registration-directed clinical trials conducted under the Pharmaceutical Affairs Law in Japan.

(1) A phase I-II trial of the combination of topotecan and ifosfamide for recurrent pediatric solid tumors.

(2) A randomized phase II study on two crossover sequences comprising vinorelbine /cyclophosphamide and temozolomide/ etoposide in the outpatient setting for relapsed or refractory solid tumors in children and young adults.
(3) A phase II trial of glucarpidase for patients who were treated with high-dose methotrexate resulting in delayed excretion.
(4) A phase Ib study of ^{131}I-metaiodobenzylguanidine (MIBG) therapy with valproic acid (VPA) for high risk or recurrent neuroblastoma.
(5) A phase Ib study of VPA and 13-cis-RA (isotretinoin) combination therapy for advanced and recurrent neuroblastoma.
(6) A feasibility trial of ch14.18 combined with IL-2 and various colony-stimulating factors for recurrent neuroblastoma.
(7) A phase I trial of immunotherapy using HLA-A2-and A24-restricted glypican-3 peptide vaccine for pediatric tumors.
(8) A phase I study of peptide cocktail vaccine for patients with refractory pediatric sarcoma.
(9) Efficacy and safety study of defibrotide (DF) for the treatment of veno-occlusive disease (VOD).
(10) Efficacy and safety study of defibrotide (DF) for the prophylaxis of veno-occlusive disease (VOD).
(11) Japanese Pediatric Leukemia/Lymphoma Study Group (JPLSG) ALL-T11 and Japan Adult Leukemia Study Group (JALSG) T-ALL-211-U ALL-T11: A Multi-Center Phase II Study in Children and Adolescence with Newly Diagnosed T-cell Acute Lymphoblastic Leukemia.
(12) Japanese Pediatric Leukemia/Lymphoma Study Group (JPLSG) ALL-B12: A Multi-Center Phase II/III Study in Children with Newly Diagnosed B-cell Precursor Acute Lymphoblastic Leukemia.
(13) An International Study for Treatment of Standard Risk Childhood Relapsed ALL 2010 (IntReALL SR 2010): A randomized Phase III Study Conducted by the Resistant Disease Committee of the International BFM Study Group.
(14) A Multi-Center Seamless Phase II-III Randomized Trial of High-dose Cytarabine in Initial Induction with Evaluation of Flow-cytometry-based Minimal Residual Disease for Children with de Novo Acute Myeloid Leukemia (AML-12).
(15) A phase I trial of YHI-1003 for patients with relapsed /refractory neuroblastom.
(16) A Multi-Center trial of ONO-7847 for prophylaxis of nausea and vomiting during chemothrapy.

Education

We provide personnel training and education for the skills of diagnosis for pediatric hematological malignancies and solid tumors. Residents also learn skills to treat not only newly diagnosed patients but also relapsed or refractory patients by the global standard therapy. In addition, senior residents acquire abilities to plan studies for new agents or new therapies, which we regard as an important role of this center.

Future prospects

We promote development of therapies for pediatric malignancies as a top priority. For this mission, we lead to plan clinical or registration trials in cooperation with domestic and international centers as a core institution in Japan.

Our other mission is to provide a progressive model for medical care environment for children. Through the appropriate use of medical and social resources, patients get to be able to live in their local communities as long as possible even during treatment as before.

Table 1. Number of patients

Acute lymphoblastic leukemia	3
Acute myeloid leukemia	2
Non-Hodgkin lymphoma	2
Hodgkin lymphoma	0
Other hematologic malignancies	1
Neuroblastoma	14
Retinoblastoma*	13*
Osteosarcoma	11
Ewing sarcoma family	7
Rhabdomyosarcoma	3
Other soft tissue tumors	1
Germ cell tumor	1
Other solid tumors	2
Total	61

*; advanced case only

Table 2. Type of procedure

Tumor resection	3
retroperitoneum	1
abdominal wall (Lap)	1
omentum	1
Lung resection (Lap assist)	8
Surgery for pleural tumor (Lap assist)	2
Soft tissue tumor resection	2
Lymph node dissection	2
retroperitoneum	1
pelvic	1
Lymph node biopsy	1
Central venous (CV) port / catheter	93
placement	50
cutdown	1
remove	42
Total	111

List of papers published in 2014

Journal

1. Kato M, Manabe A, Koh K, Inukai T, Kiyokawa N, Fukushima T, Goto H, Hasegawa D, Ogawa C, Koike K, Ota S, Noguchi Y, Kikuchi A, Tsuchida M, Ohara A. Treatment outcomes of adolescent acute lymphoblastic leukemia treated on Tokyo Children's Cancer Study Group (TCCSG) clinical trials. Int J Hematol, 100:180-187, 2014
2. Kobayashi S, Kikuta A, Ito M, Sano H, Mochizuki K, Akaihata M, Waragai T, Ohara Y, Ogawa C, Ono S, Ohto H, Hosoya M. Loss of mismatched HLA in myeloid/NK cell precursor acute leukemia relapse after T cellreplete haploidentical hematopoietic stem cell transplantation. Pediatr Blood Cancer, 61:1880-1882, 2014
3. Sekihara K, Okuma Y, Kawamoto H, Hosomi Y. Clinical outcome of thymic lymphoepitheliomalike carcinoma: Case report of a 14-year-old male. Oncol Lett, 8:2183-2186, 2014
4. Yasui N, Adachi N, Kato M, Koh K, Asanuma S, Sakata H, Hanada R. Cisplatin-induced hearing loss: the need for a long-term evaluating system. J Pediatr Hematol Oncol, 36:e241-245, 2014
5. Hoshino M, Sugito K, Kawashima H, Goto S, Kaneda H, Furuya T, Hosoda T, Masuko T, Ohashi K, Inoue M, Ikeda T, Tomita R, Koshinaga T. Prediction of contralateral inguinal hernias in children: a prospective study of 357 unilateral inguinal hernias. Hernia, 18:333-337, 2014
6. Araki Y, Kaneda H, Oashi K, Okada S, Tsutsumid A. Ovarian metastasis of malignant melanoma: The first pediatric case. J Pediatr Surg Case Rep, 2:473-475, 2014

Department of General Internal Medicine/Oncologic Emergencies

Ken Ohashi, Tomokazu Matsuura, Keiichiro Osame, Masaaki Shoji, Takeshi Iwasa, Kiyotaka Watanabe, Keiji Okinaka, Yukiko Okazaki

Introduction

The increasing numbers of cancer patients who visit the National Cancer Center Hospital have a wide range of non-cancer related medical problems such as diabetes, hypertension, heart diseases, and kidney diseases. Cancer or its treatment can aggravate the pre-existing medical conditions and sometimes can cause these problems. These medical issues must be addressed and managed along with the cancer itself so that our patients can go through optimal cancer therapies and have a better outcome. The Department of General Internal Medicine was reorganized in October 2010 to better serve these diverse needs of cancer patients and provide more comprehensive, patient-centered care. Our staff members have experience and expertise in their respective field and provide comprehensive management of these issues.

Routine activities

We see cancer patients on both an inpatient and outpatient basis in consultation upon the request of the NCCH cancer specialists. Reasons for consultation include preoperative assessment of surgical risks, assessment of ischemic heart disease, management of hyperglycemia, treatment of heart and renal failure, management of infections, and other medical disorders. When necessary, we also offer appropriate referral to other health care facilities for further evaluation or treatment. In addition, patients seen in consultation may be followed after discharge as outpatients for the duration of their care at the NCCH. Since April of 2011, we have expanded diabetes consultation service into the NCC Hospital East to improve the quality of diabetes care.

Cardiology:

Cardiologists take charge of ECG, echocardiography, in-hospital consultation, and outpatient clinic. Consultations include preoperative assessment of surgical risks, assessment of ischemic heart disease, management of arrhythmia, management of heart failure, and management of other cardiological problems. The number of consultations is about 2,000 a year. When emergency procedure is necessary, we consider transferring the patient to other facilities which have specialists. Recently, the number of clinical trials for cancer that require echocardiography assessment is increasing so that we make every effort to practice the test more efficiently.

Diabetology:

We have provided more than 600 diabetes consultations in 2014, which include perioperative management of diabetes, treatment of steroid-induced hyperglycemia during chemotherapy, and so on. In many cases, initiation of insulin is the treatment of choice. We also offer close follow-up on an outpatient basis for those who have diabetes during their cancer treatment at the NCCH.

Infectious diseases:

- Provide an infectious disease consultation service.
- Work with the infection control team.
- Investigated the cause of *Bacillus cereus* outbreak with a view to controlling and preventing further spreading.
- Analyzed the data obtained from the retrospective study of bacteremia among neutropenic cancer patients.
- Participated in the study of *Klebsiella pneumoniae* bacteremia, and provide information.
- Presented the cause and course of the *Bacillus cereus* outbreak at the 54th Interscience Conference on Antimicrobial Agents and Chemotherapy and the 30th Annual Meeting of Japanese Society for Infection Prevention and

Control.

- Presented the characteristics of bacteremia among neutropenic cancer patients at the 62nd Annual Meeting of the Japanese Society of Chemotherapy.
- Presented the lectures on infectious disease and infection control.
- Provided training programs for two trainee doctors of other facilities.
- Continue to work towards improvements in the quality of care
- Continue to provide training programs for trainee doctors

Department of Dentistry

Takao Ueno, Wakao Yatsuoka, Kyoko Miyamoto, Natsumi Nakamura, Mayuko Watari

Introduction

Oral complications are common in patients receiving chemotherapy or undergoing radiation therapy of the head and neck.

Oral complications during cancer treatment are directly linked to ingestion problems, and may even serve as a source of various infections such as aspiration pneumonia, thereby exacerbating systemic conditions, and sometimes preventing the completion of cancer treatment with negative effects on treatment prognoses. Oral health status of patients with cancer is associated with the incidence rate and the degree of severity of oral complications. Effective oral hygiene management before initiating cancer treatment will contribute to the reduction of oral complications such as mouth sores, oral mucositis, or dental infections, and provide important support to facilitate smooth cancer treatment.

Routine activities

To prevent or reduce oral complications, we check complication during cancer treatment oral conditions of the patients, identifying the patients at risk, start preventive measures before cancer therapy begins.

Our routine activities for cancer patient are below:

1) Management of oral complications of high-dose chemotherapy and/or stem cell transplant before treatment begins
2) Prevention and treatment of oral complications during chemotherapy and/or radiation therapy
3) Perioperative dental management for the prevention of postoperative pneumonia with oral, pharynx and esophageal surgery
4) Making prostheses for restoration of postoperative facial defects
5) Prevention and treatment of medication-associated osteonecrosis of the jaw (MRONJ)
6) Cooperation business of a medical department and dentistry for the solution to dental problem of the cancer patient

Education

The lecture and the practice concerning the oral health care were regularly held for nurses and residents.

Department of Genetic Counseling

Teruhiko Yoshida, Kokichi Sugano, Takeshi Nakajima

Introduction

Approximately 5% of all cancer cases are considered to be caused by a highly penetrant monogenic mutation. Major causative genes for major hereditary cancer syndromes were identified in the 1990s, and since then, genetic diagnosis has been introduced as the standard medical care for some of the tumors. The National Cancer Center Hospital (NCCH) launched the Outpatient Genetic Counseling Clinic in 1998 as a part of collaboration with the Research Institute. However, cancer medical genetics still has a number of issues to be addressed as shown in Figure 1, which is again shown this year with some modification from the last year, because it has been the basic set of the agenda of the Clinic.

Routine activities

As shown in the NCCH home page, the aim and mission of the clinical service of the Outpatient Genetic Counseling Clinic are:

#1/ to provide consultation and appropriate medical and genetic information (i.e., genetic counseling) to anyone who has a worry related to heredity of cancer.

#2/ to provide genetic testing when appropriate.

#3/ to support early diagnosis and treatment based on the family history and/or genetic test results.

In 2013, 113 patients and their relatives from 92 pedigrees visited the Clinic. In total, 1,242 clients from 834 families have visited the Clinic since its inception in 1998.

Research activities

Among the Figure 1 research agenda, the staff of the Outpatient Genetic Counseling Clinic has been playing a leading role to organize and maintain a multi-institute collaborative research group based on the National Cancer Center Research and Development Fund and its predecessor. The group will identify the cases with hereditary cancer syndromes such as multiple endocrine neoplasias, hereditary breast and ovarian cancer syndrome, Lynch syndrome, familial adenomatous polyposis, Peutz-Jeghers syndrome and retinoblastoma to provide genetic tests for the known causative genes. However, in general, sensitivity of the current standard genetic tests remains approximately 70-80% even for the cases well-matched to the clinical criteria for hereditary cancer syndromes. Thus, a new common protocol has been established to perform a germline clinical sequencing by the next generation sequencers for those with negative test results, who would represent a part of the Undiagnosed Disease Patients. As a test run, whole exome sequencing (WES) and target deep sequencing were carried out for several cases with familial pancreatic cancers, and WES for familial gastric cancers.

Clinical trials

The Outpatient Genetic Counseling Clinic has participated in a prospective clinical study to optimize BRCA1/2 genetic tests and clinical trials of PARP inhibitor for patients with ovarian or breast cancers both directed by the Departments of Breast and Medical Oncology and Breast Surgery.

Education

Attendees of genetic counseling in the clinic would be certified as the trainees fulfilling the eligibility required to take the examination for clinical geneticist acknowledged by the Japanese Society of Human Genetics and the Japanese

Society of Genetic Counseling. In 2014, 6 doctors were registered as the trainee for the clinical geneticist in the education committee of the clinical geneticists.

Future prospects

In Japan, most of the genetic tests are not covered by the mandatory health insurance, and the area clinical medical genetics has been in the transitional zone between the research and clinical practice. The well-publicized story by Ms. Angelina Jolie has increased the public awareness of the various issues on the hereditary cancer syndromes, as she disclosed in 2013 that she is a carrier of a pathogenic BRCA1 mutation with a family history of ovarian cancer and opted for Risk Reducing Mastectomy and Risk Reducing Salpingo-Oophorectomy. Moreover, on the technology side, the advent of the next generation sequencers has revolutionized medical sciences to herald the era of genomic medicine. Clinics of the hereditary cancer syndromes is expected to lead the germline part of the genomic medicine initiative in the oncology field, but the major agenda has been recognized already as Figure 1.

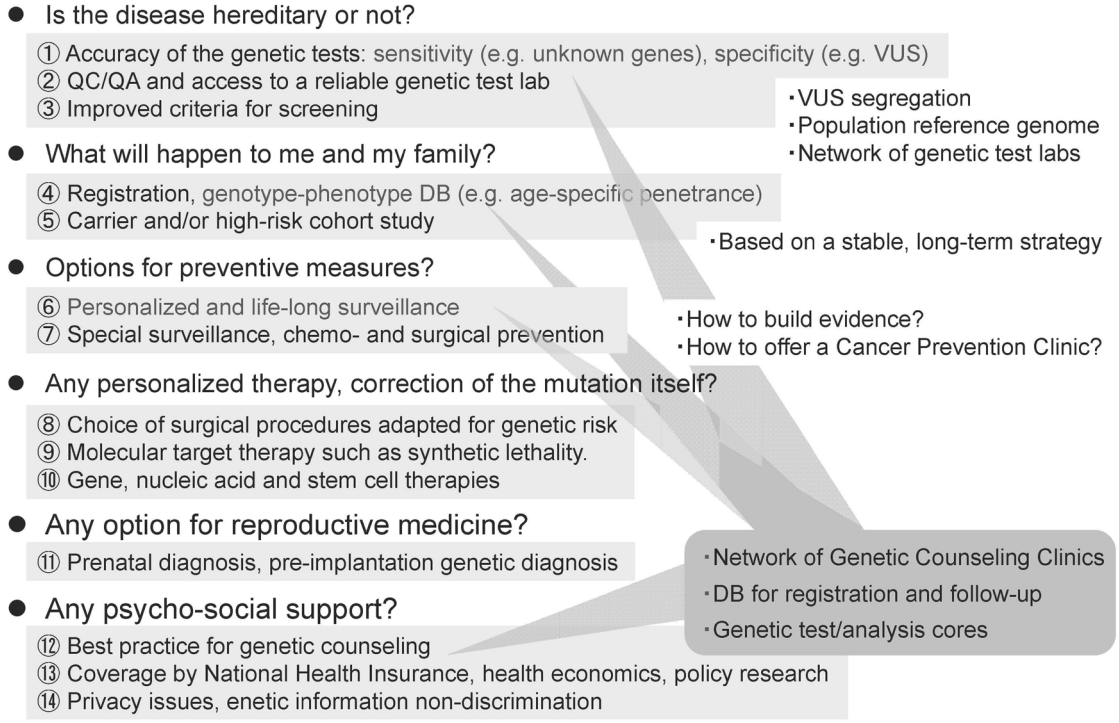

Figure 1. Major Questions by the Patients and Families with Hereditary Cancer Syndromes

Table 1. Number of clients

	Proband	Relative	Total
Lynch syndrome (Hereditary Non-Polyposis Colon Cancer; HNPCC)	11	4	15
Familial Adenomatous Polyposis (FAP)	4	3	7
Retinoblastoma	8	4	12
Hereditary Breast and Ovarian Cancer Syndrome (HBOC)	55	6	61
MEN I (Multiple Endocrine Neoplasia Type I)	0	0	0
Other diseases	14	4	18
Total	92	21	113

List of papers published in 2014

Journal

1. Yamada M, Fukagawa T, Nakajima T, Asada K, Sekine S, Yamashita S, Okochi-Takada E, Taniguchi H, Kushima R, Oda I, Saito Y, Ushijima T, Katai H. Hereditary diffuse gastric cancer in a Japanese family with a large deletion involving *CDH1*. Gastric Cancer, 17:750-756, 2014
2. Miyakura Y, Tahara M, Lefor AT, Yasuda Y, Sugano K. Haplotype defined by the MLH1-93G/A polymorphism is associated with MLH1 promoter hypermethylation in sporadic colorectal cancers. BMC Res Notes, 7:835, 2014
3. Tahara M, Inoue T, Sato F, Miyakura Y, Horie H, Yasuda Y, Fujii H, Kotake K, Sugano K. The use of Olaparib (AZD2281) potentiates SN-38 cytotoxicity in colon cancer cells by indirect inhibition of Rad51-mediated repair of DNA double-strand breaks. Mol Cancer Ther, 13:1170-1180, 2014

Department of Anesthesia and Intensive Care

Tetsufumi Sato, Yoko Kinoshita, Minako Arai, Jyunya Matsumi, Nobuko Yokokawa, Rie Suzuki, Yousuke Kawaguchi, Kazumasa Hiroi, Sayo Iwasaki, Kihoko Ichikawa, Rutesara Kyuragi

Introduction

Our Department provides anesthesia and intensive care. Anesthetic services are provided for 15 main operating theatres and sessions in endoscopy. There are about 4,000 operations per year. The Intensive Care Unit has 8 beds and provides care for all specialties including general medical and general surgical cases. There are over 500 admissions annually and the ICU is also responsible for resuscitation services within the hospital.

Routine activities

The department of anesthesia and intensive care at the National Cancer Research Center Central Hospital is comprised of 12 staff anesthetists who are involved in critical care, education and research. Our Department provides perioperative care to all the patients require general anesthesia and spinal analgesia (Table1). Our operation theater performs approximately 4,000 surgical procedures per year, which include neurosurgical, orthopedic, plastics, ophthalmologic, gynecologic, urologic, and general surgery. We also provide care to patients undergoing procedures in locations outside the main operating room such as sessions in endoscopy. In addition, many patients are seen in the Anesthesia Consult Clinic, which runs every weekday. Many staff also has other clinical appointments including attending in the ICU (the 8-bed Medical/Surgical Unit) and providing acute pain management. Some members of the Department are actively involved in research at the clinical levels and supervise post doctorate, doctorate, postgraduate and undergraduate students.

Our ICU is certificated by the Japanese Society of Intensive Care Medicine. It provides care for all specialties including general medical, general surgical and neurosurgical cases. It is managed as closed-system, supported by two certificated intensivists and trainee. There are 8 operational ICU beds and over 500 admissions annually (Table2). The ICU is also responsible for resuscitation services within the hospital.

Clinical trials

One of members is faculty of clinical trial group in Japanese society of Intensive care medicine. To understand the incidence and risk factors of severe adverse event in post-operative patients, epidemiological analyses were performed. To improve current care for perioperative patients, prospective studies are conducting.

Table 1. Number of Patients for anesthesia

General Anesthesia	1,957
General Anesthesia + Epidural Anesthesia	2301
Spinal Anesthesia + Epidural Anesthesia	4
Epidural Anesthesia	1
Spinal Anesthesia	59
Others	18
Total	4,340

Table 2. Number of patients admitted to the ICU

Esophageal Surgery	124
Neurosurgery	107
Hepatobiliary and Pancreatic Surgery	80
Head and Neck Surgery	63
Musculoskelertal Oncology	39
Gastric Surgery	33
Colorectal Surgery	33
Thoracic Surgery	31
Urology	18
Hematopoietic Stem Cell Transplantation	14
Gastrointestinal Medical Oncology	7
Gynecology	6
Hematology	5
Dermatorogic Oncology	4
Hpatobiliary and Pancreatic Oncology	3
Breast and Medical Oncology	2
Radiation Oncology	2
Ophthalmic Oncology	1
Thoracic Oncoogy	2
Pediatric Oncology	1
Breast Surgery	1
Total	576

Department of Palliative Care

Eriko Satomi

Introduction

Palliative care service has started as the palliative care team with multidiciplenary professionals (palliative care specialists, psyco-oncologists, certified nurses, pharmacists, psychologists) in the National Cancer Center Hospital (NCCH) since 1999 and the Department of Palliative Care and Psyco-oncology was established in 2010 when the reorganization of the NCCH. In 2013, the Department of palliative medicine has started. We provide palliative care to patients and families as members of palliative care team with primary doctors, nurses and other professionals to create an individualized palliative care plan. Our goals are:

- Relieve pain and other physical symptoms
- Focus patients' emotional and spiritual concerns, and those of their caregiver
- Coordinate patients' care
- Improve your quality of life with cancer
- Advance care planning

Routine activities

Our missions are:

- Manage cancer-related pain and symptoms
- Collaborate other medical professionals and plan care plan
- Support patients' decision making and advance care planning
- Educate basic skill of supportive and palliative medicine to resident doctors
- Research about new treatment of supportive and palliative medicine

1) for hospitalized patients

We work as the palliative care team and provide consulting and follow-up services to hospitalized patients throughout the NCCH. A consultation request is made by a physician (doctors in charge) or the medical staff. We provide support to the primary team. We follow up about 25~30 pts every day.

2) for outpatients

Our outpatient clinic of palliative medicine is open on Monday through Friday. We can possibly see patients on demand.

Research activities

We have just started to participate in some research groups for clinical trial about palliative care.

Education

We have 2 training courses which are for doctors who will be palliative care specialist and for residents to learn primary palliative care. All the residents of surgical medical oncologist in the NCCH need knowledge and skill about primary supportive and palliative care in Oncology. They participate in our team for 4 weeks and on the job training for palliative medicine. It includes an opportunity to attend home hospice round in corporation to Chuou-ku medical association. 20 residents have finished 4-week palliative medicine course in 2014.

Table 1. Number of patients for anesthesia

Cases		266	
male/female		139	127
age		55.6 (SD14.9)	
clinical stage			
	I		7
	II		5
	III		13
	IV		69
	reccurrence		136
	others		25
	unknown		11
primary site of cancer			
	brain ,eyes		0
	head and neck		9
	esophagus		11
	stomach		20
	colorectal		26
	hepatobiliary		3
	pancreas		7
	lung		40
	breast		25
	uterus,ovary		11
	prostate		3
	kidney,adrenal gland		5
	thyroid		0
	blood		42
	bone		2
	skin		23
	soft tissue, methotelioma		28
	unknown origin		7
	others		4
symptoms	pain		233
	breathlessness		63
	nausea/vomit		70
	fatigue		82

List of papers published in 2014

Journal

1. Kokubun H, Yoshimoto T, Hojo M, Fukumura K, Matoba M. Pharmacokinetics of oxycodone after intravenous and subcutaneous administration in Japanese patients with cancer pain. J Pain Palliat Care Pharmacother, 28:338-350, 2014
2. Sakai H, Sagara A, Matsumoto K, Jo A, Hirosaki A, Takase K, Sugiyama R, Sato K, Ikegami D, Horie S, Matoba M, Narita M. Neutrophil recruitment is critical for 5-fluorouracil-induced diarrhea and the decrease in aquaporins in the colon. Pharmacol Res, 87:71-79, 2014
3. Sakai H, Sagara A, Arakawa K, Sugiyama R, Hirosaki A, Takase K, Jo A, Sato K, Chiba Y, Yamazaki M, Matoba M, Narita M. Mechanisms of cisplatin-induced muscle atrophy. Toxicol Appl Pharmacol, 278:190-199, 2014
4. Kosugi T, Hamada S, Takigawa C, Shinozaki K, Kunikane H, Goto F, Tanda S, Shima Y, Yomiya K, Matoba M, Adachi I, Yoshimoto T, Eguchi K. A randomized, double-blind, placebo-controlled study of fentanyl buccal tablets for breakthrough pain: efficacy and safety in Japanese cancer patients. J Pain Symptom Manage, 47:990-1000, 2014

Department of Psycho-Oncology

Ken Shimizu, Rika Nakahara, Yoshio Oshima, Masashi Kato, Chikako Dotani, Hironobu Inoguchi, Saran Yoshida, Satomi Kojima, Mariko Kobayashi, Chisato Kobayashi

Introduction

The Department of Psycho-Oncology was reestablished in September 1995, together with establishment of the Psycho-Oncology Division, National Cancer Center Research Institute East (reorganized to the Division of Psycho-Oncology, Research Center for Innovative Oncology in 2005). One of the most important clinical activities of the Department is the management of cancer patients' behavioral and social problems as well as their psychological distress. Furthermore, this Department's aim is to alleviate distress of patients, patients' families and our staff. Research activity is focused on studying the psychosocial influence of cancer on the quality of life of patients, their families, and oncology staff.

Routine activities

The Department of Psycho-Oncology consists of four full-time staff psychiatrists, three full-time staff psychotherapists and three part-time psychotherapists. The department provides two major services; a clinic for outpatients (five days a week) and consultation for referred inpatients. The purpose of the psychiatric consultation is to diagnose and treat the mental distress and cancer related psychological problems of patients who have been referred by their attending physicians. Since 1999, the Department has played an active role as a member of the palliative care team. There is a palliative care team meeting with other members of the team every Tuesday. Additionally, a multicenter joint clinical teleconference to discuss difficult cases is held biweekly in Thursday evening with staff members from 6 cancer center hospitals and 4 university hospitals.

In 2014, a total of 827 patients were referred for psychiatric consultation (Table 1). The mean age was 50.7 years old and 17.3% percent of the referrals were outpatients. Three-hundred and forty three (41.5%) of the whole referred patients were males (Table 1). The most common cancer referrals were patients with sarcoma (17.4%), followed by hematological cancer (13.2%), breast cancer (10.2%), lung cancer (8.5%), and colorectal cancer (7.6%). The most common psychiatric diagnosis which is based on the DSM-IV criteria (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) was Delirium (22.9%), followed by Adjustment Disorders (22.1%), and major depressive disorder (12.8%), while 20.4% of the referrals had no psychiatric diagnosis. The three common mental disorders (delirium, adjustment disorders, and major depressive disorder) were responsible for half of the psychological problems.

Research activities

We are now developing the psychosocial intervention for allogenic hematopoietic stem cell transplant survivors, the purpose of which is to improve the quality of life. This year, we have planned an observational study to decide the intervention components.

We also explored the contents of "posttraumatic growth" in Japanese cancer patients. Posttraumatic Growth is a positive dimension of patients' psychological change aftermath of trauma. There has been known little about the process in Japanese cancer patients, and this result will provide precious information to develop intervention to support patients' psychological adaptation after cancer diagnosis.

Table 1. Psychiatric Consultation Data in 2014 (n=827)

	n	%
Age (years)	50.7	
Male	343	41.5
Inpatients	684	82.7
Top 5 of cancers by site		
Sarcoma	189	22.9
Hematological	183	22.1
Breast	84	10.2
Lung	70	8.5
Colorectal	63	7.6
Psychiatric diagnoses		
Delirium	189	22.9
Adjustment disorders	183	22.1
Major Depressive disorder	106	12.8
Others	180	21.8
No diagnosis	169	20.4

List of papers published in 2014

Journal

1. Yoshida S, Shimizu K, Kobayashi M, Inoguchi H, Oshima Y, Dotani C, Nakahara R, Takahashi T, Kato M., Barriers of healthcare providers against end-of-life discussions with pediatric cancer patients, Jpn J Clin Oncol, 44(8), 729-735, 2014

Book

1. Shimizu K, et al. Treatment of Anxiety and Stress-Related Disorders. Psychopharmacology in Oncology and Palliative Care, Springer, 129-144,2014

Department of Diagnostic Radiology

Yasuaki Arai, Ryutaro Kakinuma, Yasunori Mizuguchi, Gen Iinuma, Takashi Terauchi, Miyuki Sone, Hiroaki Kurihara, Nachiko Uchiyama, Hirokazu Watanabe, Minoru Machida, Seiko Kuroki, Mari Kikuchi, Tomoko Manabe, Mototaka Miyake, Hiroaki Ishii, Syunsuke Sugawara, Shinichi Morita, Masahiko Kusumoto, Yukio Muramatu

Introduction

The Department of Diagnostic Radiology provides a wide range of modalities, including interventional radiology (IR), general radiology, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, mammography and nuclear medicine. This year, we launched the Center for Interventional Radiology to facilitate widespread proliferation of IR in Japan and to provide various IR treatments for the patients referred from other hospitals or clinics. We seek individuals with outstanding leadership capabilities, proven academic and administrative experience, the vision to build and sustain programs at the forefront of imaging research, and a commitment to clinical experience.

Routine activities

Modality	Number of examinations
1 CT :	42,453
2 MRI:	8,248
3 IR:	4,508
4 RI:	4,363
5 Ultrasound:	14,156
6 Radiograph:	71,550
7 Gastrointestinal study:	1,888

Research activities

CT colonography (CTC) has been successfully introduced as an effective option for preoperative staging and colorectal screening in our center. Nearly 2000 patients and/or candidates have been examined with this modality in 2013. For the preparation of screening CTC, electronic cleansing with fecal barium tagging and automated CO_2 gas insufflation systems have been established in the formal National Cancer Center (NCC) collaboration studies with the associated companies. Furthermore, we are now developing computer-aided detection (CAD) for colorectal lesions, especially for flat lesions. The main purpose of our CTC research work is to conduct a multi-center trial to establish evidence regarding fully digitalized CTC for a colorectal screening system in Japan.

A multi tracer consisting of [18F]FDG, [18F] FBPA, [11C]choline, [11C] methionine and [64Cu]-DOTA-antibody PET imaging has been studied for cancer patients to improve the sensitivity and specificity of detecting tumor sites or tumor characteristics. [18F]-FDG dynamic PET sampling with Patrak-plot analysis allows us to calculate the glucose metabolic rate of the tumor site. [18F]-FBPA PET/CT has been conducted in 22 cancer patients in this year. [11C]-choline and [11C]-methionine PET/CT examinations have been scheduled routinely two days per week. As for [64Cu]-DOTA-antibody PET imaging, [64Cu]-DOTA-trastuzumab PET/CT has been conducted in HER-2 positive breast cancer patients. Respiratory-gated PET/CT was evaluated to reduce breathing-induced artifacts using a four-dimensional PET/CT protocol. It provided better localization and quantification of tumors around the lower thorax to the upper abdomen. For cancer treatment, internal radiotherapy was carried out in 20 thyroid cancer patients with use of radioactive iodine (I-131) chloride and 2 neuroblastoma patients with I-131 MIBG.

In accordance with the achievement of collaborative research with the associated company since 2009, digital breast tomosynthesis (DBT) has been introduced as an effective routine option for preoperative evaluation since March2014. Up to Dec 2014, 271 patients were examined.

A multicenter study has started to establish

the CT classification of lung adenocarcinomas corresponding to the new IASLC/ATS/ERS pathological classification and to build the database of small adenocarcinomas. Digital Imaging and Communications in Medicine (DICOM) data of resected lung cancers from each institute have been accumulated and evaluated in collaboration to the Japanese Society of Thoracic Radiology.

The Japan Response Evaluation Criteria in Solid Tumors (RECIST) working group has developed a tumor response evaluation computer system, which is capable of semiautomatic RECIST evaluation and is compliant with DICOM data.

Image guided preoperative Breast Marking using ultrasound alone or combined with mammography has been performed for partial mastectomy cases which are difficult to determine the spread of disease. This technique makes it possible to resect abnormal lesion more precisely and assists to prevent both re-operation and local recurrence. Total 57cases were performed since January 2014 to December 2014.

We evaluated the usefulness of MRI for differentiation between Type I and Type II endometrial cancer.

Clinical trials

A major departmental research theme is establishing an evidence base for interventional radiology. We have led a multi-institutional cooperative study group of interventional radiology (JIVROSG: Japan Interventional Radiology in Oncology Study Group) since 2002 as a steering organization of 90 participating domestic institutions. In this study group, we are investigating the efficacy of palliative interventional radiology in randomized controlled trials (RCTs) to compare it with other therapies. These palliative RCTs include: a phase III study evaluating the efficacy of peritoneo-venous shunting (JIVROSG-0803); a phase III study evaluating the efficacy of percutaneous vertebroplasty for painful bone metastases (JIVROSG-0804); a phase III study evaluating the efficacy of percutaneous trans-esophageal gastric tubing (JIVROSG-0805); a phase III study evaluating the efficacy of stenting for SVC/IVC syndrome (JIVROSG-0807) and JIVROSG-0807 completed patient enrollment in 2013. Other ongoing clinical trials are a phase I/II study of RFA for pelvic malignant tumors (JIVROSG-0204), a phase II study evaluating the efficacy of arterial infusion chemotherapy and radiotherapy for unresectable maxillary carcinoma (JIVROSG-0808) and a phase II study evaluating the efficacy and safety of n-butyl-2-cyanoacrylate (NBCA) in embolization (JIVROSG-0802).

Education

The clinical education and training of young radiologists is an important part of our department's activities. During 2014, 6 residents and 5 short-term residents were trained with our Department. The educational opportunities to 4 overseas physicians from Philippines, Taiwan, German and Italy, were also provided. We have several clinical or educational conferences. A daily clinical IR case conference, a weekly educational case conference on diagnostic radiology, and a monthly IR research conference, are held.

Future prospects

The Department of Radiology aims to strive for excellence in clinical care, education, and research. Our goal is to provide outstanding patient-centered radiology services and to establish evidence in this area. Future challenges include promoting the active role of the Center for Interventional Radiology opened this year and facilitating imaging as biomarkers for personalized cancer treatments such as molecular-targeted agents and boron neutron capture therapy.

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Department of Radiation Oncology

Jun Itami, Minako Sumi, Yoshinori Ito, Hiroshi Igaki, Madoka Morota, Naoya Murakami, Koichi Inaba, Kana Takahashi, Kotaro Yoshio, Shuhei Sekii, Hiroyuki Okamoto, Akihisa Wakita, Satoshi Nakamura

Introduction

The role of the Department is to provide the state-of-art radiation therapy to all relevant patients, to educate and develop the expertise of radiation oncologists, radiation technologists, and medical physicists, and to lead new developments in radiation oncology in Japan as well as worldwide. All departmental activities are dedicated to cancer patients. With a delay of as long as one-year, linear accelerator for the hospital-based boron neutron capture therapy (BNCT) was installed to the new facility and neutron beam will come in the summer of 2015. The Department will be fully involved in the development of BNCT.

Routine activities

The Department of Radiation Oncology of the National Cancer Center Hospital is one of the biggest radiation oncology departments in Japan. Five linear accelerators, CyberKnife, one X-ray simulator, three XCT-simulators, and 15 treatment planning computers are working together under on-line networks to provide a state-of-art precision external beam radiation therapy. In addition to the conventional X-ray and electron therapies, stereotactic irradiations of brain and body tumors and intensity-modulated radiation therapy (IMRT) are employed routinely. Stereotactic brain irradiation is performed with CyberKnife in the treatment of metastatic as well as primary brain tumors. Stereotactic body tumor irradiation is performed in lung and liver tumors under respiratory gating in linear accelerators or CyberKnife. Four out of the 5 linear accelerators have on-board kilovoltage CT imagers, which help to align patient and tumor coordinates precisely. These image guided radiation therapy (IGRT) facilities enable the precise delivery of IMRT in head and neck cancers, brain tumors, prostate cancers, and postoperative cervical cancers. Gold marker fiducials have been implanted to improve geometric precision of radiation field reproducibility.

Brachytherapy is also performed very intensively to improve local control and many patients are referred to from all over Japan. For brachytherapy the following modalities are being employed, an Ir-192 high dose rate (HDR) afterloading system including dedicated CT simulator and fluoroscopy, an I-125 seed implantation system, and other low dose rate (LDR) brachytherapy systems using Au grains, Ir-thin wires, and ruthenium eye plaques. The number of patients undergoing HDR brachytherapy continued to rise constantly. This Department is the only one institution in Tokyo, where HDR interstitial as well as intracavitary irradiations can be performed. The HDR interstitial radiation is performed mainly in gynecological, genitourinary, and head and neck tumors. Additionally, there are 2 beds in the shielded ward in Floor 13B. Ruthenium mold therapy is performed by ophthalmologists to treat retinoblastomas and choroidal melanomas. LDR interstitial implants are carried out by radiation oncologists using Au-198 grains and Ir-192 thin wires for the management of head and neck tumors and gynecological malignancies.

Research activities

Clinical research is an indispensable part of the daily activities of the Department. The primary interests of the research activities of the Department are 1) an optimal fractionation regimen for the pain palliation of bone metastasis; 2) the safety and feasibility of shortened fractionation regimen for various malignancies, especially for breast cancer and vocal cord cancer; 3) Image-guided HDR and LDR brachytherapy for genitourinary

and gynecologic cancers; 4) hypofractionated stereotactic irradiation of brain and body tumors; 5) adaptive radiation therapy in accordance with the intratherapeutic tumor and normal tissue change; and 6) development of accelerator based BNCT system.

Clinical trials

Brain tumors: A multicenter phase II/III trial on interferon-beta and temozolomide combination therapy for newly diagnosed glioblastomas.

Lung cancer: Phase II trial on high dose thorax irradiation excluding prophylactic mediastinal lymph node radiation concurrent with CDDP+VNL in unresectable stage III non-small-cell lung cancers (NSCLCs).

Lung cancer: Stereotactic radiation therapy for histologically non-verified lung tumors.

Pediatrics: Phase II clinical trial on multimodality therapy in localized Ewing sarcomas and related tumors (JESS 04).

Head and Neck cancers: Various JCOG studies including IMRT for nasopharyngeal and oropharyngeal cancers

Breast cancer: Phase II trial of SAVI applicator HDR brachytherapy after partial mastectomy.

Liver cancer: Phase I trial on stereotactic hypofractionated radiation to hepatocellular carcinoma.

F-BPA PET/CT: Feasibility study of F-BPA PET/CT in detecting malignancies with comparison to FDG PET/CT.

Development of an Adaptive Radiation Therapy System

Education

Five residents are trained in all fields of radiation oncology except particle beam therapy. Seminars about biology, physics, and clinical radiation oncology are regularly held in the evening time.

Future prospects

With the introduction of BNCT, a new manpower will be required and research perspectives will be very widened.

Table 1. Number of Patients

1) New patients referred to the Department	1,458
2) All patients undergoing radiation therapy	2,063
External Beam Radiation Therapy (EBRT)	
1) New patients undergoing EBRT	1,383
2) All patients undergoing EBRT	1,976
Brachytherapy (BT) and Radionuclide Therapy	
1) All patients undergoing intracavitary radiation	40
2) All patients undergoing interstitial radiation	78
3) All patients undergoing prostate permanent seed implantation	15
4) All patients undergoing I-131 therapy for thyroid cancer	22
5) All patients undergoing Sr-89 therapy for bone metastasis	2
Other Special Radiation Therapy	
1) All patients undergoing total body irradiation	68
2) All patients undergoing stereotactic brain radiation	247
3) All patients undergoing stereotactic body radiation	49
4) All patients undergoing intensity modulated radiation therapy	246

Table 2. Number of New Patients according to the Primary Site

1) CNS	48
2) Head and Neck	142
3) Esophagus	117
4) Intrathoracic	258
4)-a) Lung	136
5) Breast	296
6) Liver/Bile Duct/Pancreas	88
7) Digestive Tracts	252
8) GYN	80
9) GU	138
9)-a) Prostate	102
10) Hematopoietic/Lymphatic	88
11) Cutaneous/Bone/Soft Tissue	110
12) Other Malignancies	0
13) Benign	2
14) Child Aged less than 15 Years	19

Table 3. Radiation Therapy of Brain or Bone Metastasis

1) Brain metastasis	266
2) Bone metastasis	159

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Department of Pathology and Clinical Laboratories

Atsushi Ochiai, Nobuyoshi Hiraoka, Ryoji Kushima, Koji Tsuta, Shigeki Sekine, Koh Furuta, Akiko Maeshima, Taisuke Mori, Hirokazu Taniguchi, Masayuki Yoshida, Akihiko Yoshida, Hiroshi Yoshida, Yuko Sasajima, Akiko Matsubara, Yukinori Hattori, Aoi Sukeda, Takashi Yorozu, Junko Itoh, Taiki Hashimoto, Koko Mitsuma

Introduction

In the Department of Pathology , the practice, education and research of diagnostic and anatomic pathology were carried out. Diagnostic pathology practice comprised all issues on the processing of cell and tissue specimens obtained from patients, preparation of tissue blocks and pathology slides, and histological and cytopathological diagnoses of diseases. The practice of anatomic pathology consisted of the autopsy, post-mortem systemic gross and microscopic examination of patients. Case conferences with each clinical division were held periodically. Residents and trainees were accepted for training of diagnostic pathology on a rotating basis. To provide more accurate and informative diagnosis in future, the staff members conducted a basic, clinical, or translational research by themselves or in collaboration with other divisions or institutions.

The Clinical Laboratories Division provides an important service as an in-hospital diagnostic unit by examining laboratory specimens and screening for disorders. All laboratory data are provided for clinicians under the strict internal and external quality control. The laboratories in this Department have acquired the accreditation of ISO 15189, which certifies the quality and competence of a medical laboratory with regard to quality management and technique, developed by the International Organization for Standardization's Technical Committee 212 (ISO/TC 212). The staff of the Clinical Laboratories Division will continuously work to improve the quality and quantity of laboratory services.

Routine activities

Department of Pathology: In 2014, a total of 13 board-certified pathologists, 7 residents and 12 medical technologists, including 9 cytotechnologists, cooperatively performed routine histological and cytopathological diagnosis of specimens obtained from patients at the National Cancer Center Hospital (NCCH) and the Research Center for Cancer Prevention and Screening (RCCPS), and education of the residents. Twelve pathologists working exclusively in the NCCH also shared management of the Department. We provided a total of 20,894 histological diagnoses consisting of 17,216 biopsy specimens including 1,917 intraoperative frozen sections and 3,678 surgically resected specimens (Table 1), a total of cytopathological diagnoses of 12,656 patients including 446 for intraoperative diagnoses (Table 2), and a total of 20 autopsies (Table 3). We also provided a total of 200 pathological diagnoses for outpatient clinic for pathology consultation (second opinion).

Clinical Laboratories Division: 52 full-time and 9 part-time medical technologists, 2 photographer and 5 assistants provide services. These staff work in the sections of 1) general laboratory medicine and hematology, 2) biochemistry, 3) endocrinology, immunology, and tumor markers, 4) bacteriology, 5) genetic diagnostics, 6) transfusion, 7) phlebotomy, 8) physiological examination, and 9) pathology in the NCCH, and in the sections of phlebotomy and physiological examination in the RCCPS. The sections of 1) to 5) are to be supervised by Dr. Koh Furuta, 6) and 7) by Dr. Ryuji Tanozaki (Transfusion Therapy), 8) by Dr. Yasunori Mizuguchi (Diagnostic Radiology), Drs. Masaaki Syoji and Takeshi Iwasa (General Internal Medicine), and Dr. Eriko Iwamoto (Breast Surgery), and 9) by doctors in the Department of Pathology. The bacteriology staff are the members of the Infection Control Team and participate in the activities of infection

management. The actual number of laboratory tests performed in this Division in 2014 is shown in Table 4.

Research activities

1. Hepato-biliary pancreatic pathology

The gross appearance of pancreatic ductal adenocarcinoma, macroscopic necrosis and tube/branching structure were significantly correlated with patient outcome.

2. Gastrointestinal pathology

The roles of *GNAS* mutations in the tumorigenesis of gastrointestinal neoplasms were analyzed. HER2 expression was shown to be consistently absent in gastric neuroendocrine carcinomas, regardless of association with HER2-positive adenocarcinoma components.

3. Hematopathology

We reported prognostic significance of immunophenotypes and a nodular pattern in primary mediastinal large B-cell lymphoma and also case series of intrafollicular classical Hodgkin lymphoma mimicking nodular lymphocyte predominant Hodgkin lymphoma.

4. Pulmonary and mediastinal pathology

Clinical and molecular features of adenosquamous cell carcinoma, adenocarcinoma with morule-like components, or lung carcinoma with *RET* gene alterations were reported. Cytokeratin 19 or PAX8 expression was studied in lung carcinomas.

5. Bone and soft tissue pathology

We identified a unique and consistent mode of vascular involvement suggestive of an invasion-independent metastatic mechanism in alveolar soft part sarcomas. We demonstrated the utility of STAT6 immunohistochemistry for diagnosing solitary fibrous tumors and a value of SALL4 immunohistochemistry for differentiating malignant rhabdoid tumors from epithelioid sarcomas. Next generation sequencing of chondrogenic tumors identified recurrent mutations in *COL2A1* and other genes. We reported a benign metastasizing diffuse-type tenosynovial giant cell tumor.

6. Brain tumor pathology

We developed an optimal set of p53 immunohistochemistry interpretative criteria to predict *TP53* mutation in diffuse gliomas. We published a case of multinodular and vacuolating neuronal tumor of the cerebrum and a sclerosing variant of meningioma.

7. Breast and gynecological pathology

Wide local extension and higher proliferation indices were characteristic features of symptomatic lobular neoplasias and those with early invasive component. Lobular endocervical glandular hyperplasia was a neoplastic entity with frequent activating *GNAS* mutations.

8. Head and Neck pathology

A strong relationship between expression of CD326 and radiation response was demonstrated in early stage glottic cancer. We discovered a lack of SOX10 expression, high frequency of *BRAF* mutation and a lack of *GNAQ* or *GNA11* mutation in adenoma or adenocarcinoma of pigmented ciliary epithelium.

9. Clinical Laboratories

An in-hospital bio-bank has been maintained for use by various researchers, and more than 650,000 post-clinical-test blood samples have been stored at -20 °C as of the end of 2014. Three sections of hematology, biochemistry and endocrinology, immunology and tumor markers, participated in the external quality control program endorsed by the Japanese Society of Laboratory Medicine. Some Medical Technologists found interesting findings in their routine practice and made presentations at several domestic medical assemblies. At the molecular diagnostic section, mutation analyses of *EGFR*, *KRAS*, *NRAS*, and *BRAF* were provided as routine tests. At the cytogenetics section, using the Metafer system (an automated image analysis-assisted fluorescence *in situ hybridization* [FISH] system), the technique to evaluate the

FISH imaging of *HER2* gene amplification was established and maintained. These two sections provided data not only for clinical practices but also for research activities of doctors in the NCCH and/or the NCCRI.

Table 1. Numbers of Histopathological Specimens Diagnosed in the Department of Pathology in 2014

Field	Number of specimens Total
Gastrointestinal tracts	8,447
Breast	2,568
Respiratory organs	2,201
Hematology	1,422
Gynecology	1,294
Urology	785
Hepatobiliary and Pancreas	750
Head and Neck	941
Dermatology	639
Orthopedics	555
Others	342
Research Center for Cancer Prediction and Screening	570
Total	20,894

Table 2. Numbers of Cytopathological Specimens Diagnosed in the Department of Pathology in 2014

Field	Number of specimens Total
Gynecology	3,886
Urology	2,968
Respiratory organs	2,961
Gastrointestinal tracts	8,447
Breast	500
Hepatobiliary and Pancreas	544
Hematology	356
Head and Neck	274
Radiation Oncology	145
Others	196
Research Center for Cancer Prediction and Screening	0
Total	12,656

Table 3. Numbers of Autopsies Performed in the Department of Pathology in 2014

Deaprtment/Division	Number
Hematology and Hematopoietic Stem Cell Transplantation	6
Thoracic Oncology	6
Hepatobiliary and Pancreas	2
Oncology	
Dermatology	2
Gastrointestinal Oncology	1
Endoscopy, Respiratory	1
Endoscopy Division	
Esophageal Surgery	1
Colorectal Surgery	1
Total	20

Table 4. Number of laboratory tests examined in the Clinical Laboratories Division in 2014

Section	Number
General laboratory medicine	507,051
Hematology	1,308,384
Biochemistry	2,999,388
Endocrinology, immunology, and tumor markers	368,436
Bacteriology	49,126
Physiology	93,522
Genetic diagnostics	31981
Total	5,325,907

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Office of Infection Control and Prevention

Minoru Esaki, Keiji Okinaka, Noriko Wada, Keiichi Koido, Michi Shouji, Chiharu Miyamoto

Introduction

The Office of Infection Control and Prevention as a center of the infection control team consists of an infectious disease doctor (Infection Control Doctor), infection control nurse, board certified pharmacist in infection control, infection control microbiological technologist, office clerk, and director. The team works very closely with staff from all areas of the hospital to control and prevent infection. The annual activities of our team in 2014 were

- to announce the newest most up-to-date information and items for all clinical staff
- to reduce the risk of healthcare-associated infections among visitors, patients and staff by using the infection control management and workflow system "ICTweb"
- to collaborate with regional hospitals to keep cancer patient safe from healthcare-associated infections.
- to deliver the infection prevention education programs to all staff.

We hope to take on a role in improving the outcome of treatment for cancer patients through first class infection control and prevention.

Routine activities and Education

Our team provides

- Advice about the prevention and management of outbreaks, and delivering education programs to all staff including lectures by staff or regional hospital, basic study session for infection and hand hygiene training.
- Implementation of antimicrobials stewardship based on the newest data. We use high-quality evidenced-based policies, guidelines and protocols as a reference to ensure care.
- Monitoring of environmental cleanliness and provide providing advice about building and refurbishment projects in the hospital from the infection control aspect.

Research activities

1) In-Hospital Outbreaks of Bacillus cereus Bacteremia Associated with Reused Contaminated Bed Bath Towels (Washington DC)
2) The Efficacy of Certified Pharmacist in Infectious Diseases Region on Individualized Dosage Adjustment Concentrations of Vancomycin (in submission)

Outpatient Treatment Center

Kenji Tamura

Introduction

The Outpatients Treatment Center deals with all kinds of malignancies. Our mission is to provide safe, smooth and high quality of standard chemotherapies as outpatient style. There are 20 beds and 16 chairs (total 36) for chemotherapy. Several groups collaborate to ensure the best chemotherapies, consisting of medical oncologists, nurses, pharmacists, medical social workers (MSW) and clinical research coordinators (CRCs). Our visions are 1) to provide an evidence-based medicine, 2) to provide safe and efficient treatments, and 3) to keep quality of life of the patients.

Routine activities

From January to December in 2014, the Outpatients Treatment Center supported a total of 26,383 patients who received anticancer drug (Table 1), that means around 2,200 per month, or 105 per month. The breakdown by department was Breast and Medical Oncology (36.6%), Gasrointestinal Medical Oncology (22.8%), Hepatobiliary and Pancreatic Oncology (11.6%), Hematology (8.4%), Thoracic Oncology (6.9%), and other department (13.7%). General infusions, general intramuscular or subcutaneous injections, blood transfusions, bone marrow puncture, lumbar puncture, intraperitoneal or chest drainage, blood gas analyses were conducted in the Center.

Conference

The case conference is held on Tuesday biweekly with the participation of multidisciplinary specialists, including medical oncologists, nurses, and pharmacists. The monthly staff meeting is held on the second Tuesday every month with the participation of physicians and nurses who are the main members in the Center. The steering committee is held on the third Thursday every month.

Research activities

- Treatment of platinum containing regime in outpatient style.
- Efficacy of frozen globe against nail toxicities by docetaxel.
- Efficacy of frozen cap against alopecia by chemotherapy
- Protection of allergic reaction by Oxaliplatin in out-patients.
- Management of skin toxicities as adverse event of molecular-targeted drug.
- Cosmetic support for women cancer patients
- Support for continuing job and circumstance of working in outpatients.
- Telephone hotline for emergency for out-patients who receive chemotherapy.

Education

We provide educational opportunities for multidisciplinary specialists, including medical oncologists, nurses, and pharmacists. We also provide an educational program to hospitals outside the National Cancer Center, for medical oncologists, nurses, pharmacists and MSW in the designed hospital for cancer treatment in the each prefecture.

Future prospects

We continue to propose a near-future model of the more clinical trials in outpatient style (the Clinical Trial Center in outpatient style). We aim at

shortening of waiting time, smooth administration of novel molecular targeted drugs for outpatients, and putting into practice multidisciplinary care for cancer patients who received chemotherapy in the Outpatients Treatment Center. We plan to install the 2nd Outpatients Treatment Center adding chairs/beds from the current total of 36 to 62 at the beginning of 2015.

Table 1. Cumulative total number of patients who received anticancer drug by intravenous administration

Department	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Total
Breast and Medical Oncology	727	730	772	860	789	750	851	844	847	903	787	802	9,662
Gasrointestinal Medical Oncology	434	473	491	540	563	434	542	476	493	568	499	512	6,025
Hepatobiliary and Pancreatic Oncology	223	203	232	250	258	246	294	257	277	283	255	282	3,060
Hematology	168	190	173	200	184	162	218	170	190	200	167	185	2,207
Thoracic Oncology	169	153	159	144	139	105	160	158	138	170	140	182	1,817
Others	259	235	252	264	267	275	313	312	370	361	336	368	3,612
Total	1,980	1,984	2,079	2,258	2,200	1,972	2,378	2,217	2,315	2,485	2,184	2,331	2,6383

Consultation, Counseling and Support Service Center

Masashi Kato, Kayoko Miyata, Rieko Shimizu, Naoko Goto, Miho Koitabashi, Natsuko Moroi, Yasuko Arimoto, Mariko Tsuchiya, Megumi Osuga, Yukiko Higuchi, Haruhiko Saijo, Mayumi Miura, Yuko Itakura, Atsuko Kawami, Tomoko Asayama, Kim Hyeon Ok

Introduction

The staff members referred to as "Cancer Counseling and Support Specialists" work mainly at the Consultation, Counseling and Support Service Center of the National Cancer Center Hospital (NCCH). The staff copes with various problems of cancer patients and their families with the ultimate aim of helping patients feel relieved and to help them receive medical care. By putting ourselves in the patients' position, we can make real efforts to solve their problems.

Routine activities

1 Consultation, Counseling and Support Services
(1) Consultation and counseling face to face
(2) Consultation and counseling on the telephone

We provide consultation, counseling and support to help cancer patients, their families and ordinary citizens solve their psychosocial problems through various social work skills, social recourses and cancer information. Furthermore, we have begun to offer support for job seekers in closer coorperation

with a "Hello Work Navigator" and Social Insurance Labor Consultants. We also counsel on the telephone in the hope that patients can see the benefit of the information in the books and websites, and make use of this information by themselves.

2 Activities accompanying Consultation, Counseling and Support Services
(1) Administration of a group program for patients and their families
(2) Cooperation inside the hospital
(3) Cooperation with other hospitals and institutions

We hold the following support groups and programs for the patients and their families
- The pancreatic cancer and biliary tract cancer class
- The class for women before undergoing breast cancer surgery
- The support class for job seekers

In the hospital, we discuss the patients with the doctors and medical staff, and we cooperate with other hospitals and institutions so that cancer patients can live with as high a quality of life as possible. We rearranged community services where required and helped patients to change hospitals.

3 Activities of cooperation with other regional hospitals and institutions
(1) Support for holding information exchange meetings with regional hospitals and institutions
(2) Administration of a database on information about regional hospitals and institutions

4 Activities related to volunteers of the NCCH

5 Activities related to NCCH committees

6 Activities related to the education of NCCH staff

7 Administration of the patient library

Research activities

We analyze information and opinions obtained by counseling. In addition, we develop effective procedures about counseling and support for cancer patients and their families.

Education

We lecture and act as facilitators in seminars for education of Cancer Counseling and Support Specialists.

Table 1. Number of cases (January 2014 – December 2014)

1	Total	11,800
2	New cases	6,428
	New cases from NCCH	3,122
	New cases from other hospitals	3,306

Future prospects

We practice high quality cancer counseling and support, develop models and spread the results for the whole county.

Appearance Support Center

Keiko Nozawa, Naoya Yamazaki, Chikako Shimizu, Masahide Fujiki, Shoko Toma, Kazuko Aoki, Atsuko Ito, and Eriko Takahashi

Introduction

The Appearance Support Center aims to support patients to be able to 'live in society' and to 'live as a human' through clinical research and educational practices regarding patients' physical appearance.

Routine activities

Our team consists of two clinical psychologists (1 full-time and 1 part-time) specialized in cosmetics, and they consult both in- and out-patients as well as their families for questions and concerns regarding physical appearance. Examples of issues are side effects of chemotherapy and radiotherapy on skin, nails, and hair, scarring and epithesis from surgeries, and breast surgery. In order to expand our practice beyond solely consultation, we are currently developing a new team in collaboration with a dermatologist, plastic surgeon, medical oncologist, pharmacist, and nurses.

The outpatient space is open to the public from Monday to Thursday between 12 am and 1 pm during which patients can try on different products and consult staff. Despite limited hours for security reasons, we had 897 users from January to December. Additionally, we conduct a patient support program titled "Cosmetic Information" every Tuesday and Thursday from 2 pm. Its main aim is to provide information to patients through group sessions. We had 95 sessions in which 381 patients participated. Forty-nine men participated in "Men's Consultation Day" held on the fourth Wednesday of every month from 1 to 3 pm. In addition, we offered long-term inpatients a special program at the transplantation ward twice this year, and a total of 15 men and women participated. The program had a good reputation which will be held regularly (the third Wednesday of every odd month) next year.

As for individual consultations for new patients, there were a total of 1248 consultations offered to 253 in- and out- patients. Patients' main concerns were coping strategies with specific symptoms. Reasons for consultations also included seeking stress relief, concerns over significant life events such as the coming-of-age ceremony, weddings, and graduations, questions regarding mortuary makeup, and concerns from family members.

Research activities

One of the main purposes of this Center is information collection and active research due to lack of evidence regarding physical appearance. Current research projects are: the multi-faceted examination of the efficacy of support programs regarding physical appearance, the establishment of guidelines for support of cancer patients' appearance problems, the investigation and the development of the appearance-care educational training system, and the development of assessments and care methods for dermatological changes due to cancer treatment. In addition to examine the current situations and the issues of information for cancer patient regarding physical appearance, we found out that the appearance-related support program enhances psychological well-being of cancer patients. We also conducted research with business corporations and made the product called "wig na bousi (a cap looks like a wig)" based on patients' needs.

Education

In order to support medical staff to practice appearance-care, "The Educational Workshop Regarding Appearance Care for Cancer Patients"

was held three times in a year (210 participants) for medical staff working at designated regional cancer centers and hospitals. Additionally, we welcomed visitors of our hospital and held a special educational workshop to offer the same program conducted at Shikoku Cancer Center.

Future prospects

We anticipate emergence of new issues regarding physical appearance as the variety in treatment drugs increase, longer-survival rates increase, cosmetic surgeries develop, and cosmetic products continue innovations. Although responding to all patient needs is difficult as fulltime workers are scarce, we hope to expand human resources and develop this emerging field based on research.

Conferences

Sponsor:	The Appearance Support Center (Center Hospital)
Conference title:	The Educational Workshop on Appearance Care of Cancer Patients for Medical Staff: Basic course
	November 24th - December 21st, 2014
Location (prefecture):	Tokyo
Sponsor:	The Appearance Support Center (Center Hospital)
Conference title:	The Educational Workshop on Appearance Care of Cancer Patients for Medical Staff: Advanced course
Date:	Date: October 18th, 2014
Location (prefecture):	Tokyo

List of papers published in 2014

Journal

1. Boku N, Sugihara K, Kitagawa Y, Hatake K, Gemma A, Yamazaki N, Muro K, Hamaguchi T, Yoshino T, Yana I, Ueno H, Ohtsu A. Panitumumab in Japanese patients with unresectable colorectal cancer: a postmarketing surveillance study of 3085 patients. Jpn J Clin Oncol, 44:214-223, 2014
2. Namikawa K, Tsutsumida A, Tanaka R, Kato J, Yamazaki N. Limitation of indocyanine green fluorescence in identifying sentinel lymph node prior to skin incision in cutaneous melanoma. Int J Clin Oncol, 19:198-203, 2014

Rare Cancer Center

(NCCH) Akira Kawai, Hirokazu Chuuman, Eisuke Kobayashi, Yoshikazu Tanzawa, Seiichi Yoshimoto, Motokiyo Komiyama, Tomoyasu Kato, Makoto Kodaira, Mayu Yunokawa, Shunsuke Kondo, Chitose Ogawa, Miyuki Sone, Shunsuke Sugawara, Hiroshi Igaki, Kana Takahashi, Akihiko Yoshida, Takuro Sakurai, Yoshitaka Narita, Naoya Yamazaki, Arata Tsutsumida, Satoshi Takahashi, Shigenobu Suzuki, Yoshitaka Honma, Tadashi Kondo, Koichi Ichikawa, Naohiro Higashi, Makiko Murase, Yoko Kato,
(NCCHE) Fumihiko Nakatani, Naoto Gotohda, Toshihiko Doi, Yoichi Naito, Ako Hosono, Tetsuo Akimoto, Junya Ueno

Introduction

The Rare Cancer Center was launched in December 2013 and officially opened in June 2014 as a multidisciplinary team to take measures against the innate problems associated with rare cancers. In the past decades, major cancers such as gastric, breast and colorectal cancers have been a public health priority at the national and international level, but at the same time little attention has been paid to the issue of rare cancers. There is still no generally agreed definition of rare cancers in Japan. Rare diseases are often defined as those with a prevalence of < 50/100,000. According to the definition of Rare Cancers in Europe (RARECARE), rare cancers are those with an incidence < 6/100,000/year. Although each rare cancer is rare by itself, when the number of each rare cancer is combined, it corresponds to up to 15% of all new cancer diagnoses. Information on rare cancers is scarce. Rare cancers are often inadequately diagnosed and treated in relation both to lack of knowledge and clinical expertise. Patients with rare cancers face great difficulty in having their diseases treated adequately.

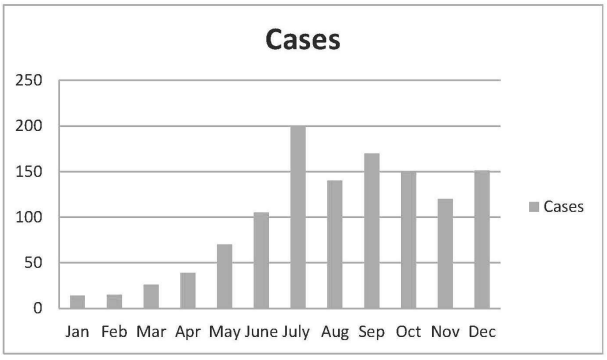

Figure 1. The Number of telephone call to Rare Cancer Hotline in 2014

Routine activities

The Rare Cancer Center plays a central role in the treating and managing of rare cancers in National Cancer Center (NCC).

The mission statements of the Rare Cancer Center are as follows.

I. Establishing a vital network of diagnosis and treatment for rare cancers in the NCC Hospital and Hospital East.

II. Reviewing the problems associated with rare cancers in Japan and making proposals and taking up the issues as medical professionals.

To enable the Center to play its role, a total of 35 doctors, nurses and researchers dealing with rare cancers have joined as members of the Center. Each staff member of the Rare Cancer Center provides specialized, high-quality medical care to patients with rare cancers in cooperation with his/her Department staff.

The Rare Cancer Center provides consultation to the patients and relatives with rare cancers on the telephone (Rare Cancer Hotline). The number of telephone call was 1,200 cases in 2014 (Figure 1). The Center also provides comprehensive, scientifically based, up-to-date unbiased information about rare cancers to all patients, families and health professionals fighting against rare cancers via website (Rare Cancer Center Homepage).

List of papers published in 2014

Journal

1. Fukushima S, Narita Y, Yonezawa M, Ohno M, Arita H, Miyakita Y, Ichimura K, Yoshida A, Shibui S. Short communication: sclerosing meningioma in the deep sylvian fissure. Brain Tumor Pathol, 31:289-292, 2014
2. Yoshida A, Tsuta K, Ohno M, Yoshida M, Narita Y, Kawai A, Asamura H, Kushima R. STAT6 immunohistochemistry is helpful in the diagnosis of solitary fibrous tumors. Am J Surg Pathol, 38:552-559, 2014
3. Miyamoto S, Kayano S, Fujiki M, Chuman H, Kawai A, Sakuraba M. Early Mobilization after Free-flap Transfer to the Lower Extremities: Preferential Use of Flow-through Anastomosis. Plast Reconstr Surg Glob Open, 2:e127, 2014
4. Miyamoto S, Kayano S, Kamizono K, Fukunaga Y, Nakao J, Nakatani F, Kobayashi E, Sakuraba M. Pedicled superficial femoral artery perforator flaps for reconstruction of large groin defects. Microsurgery, 34:470-474, 2014
5. Trautmann M, Sievers E, Aretz S, Kindler D, Michels S, Friedrichs N, Renner M, Kirfel J, Steiner S, Huss S, Koch A, Penzel R, Larsson O, Kawai A, Tanaka S, Sonobe H, Waha A, Schirmacher P, Mechtersheimer G, Wardelmann E, Buttner R, Hartmann W. SS18-SSX fusion protein-induced Wnt/ β -catenin signaling is a therapeutic target in synovial sarcoma. Oncogene, 33:5006-5016, 2014
6. Nakamura T, Matsumine A, Uchida A, Kawai A, Nishida Y, Kunisada T, Araki N, Sugiura H, Tomita M, Yokouchi M, Ueda T, Sudo A. Clinical outcomes of Kyocera Modular Limb Salvage system after resection of bone sarcoma of the distal part of the femur: the Japanese Musculoskeletal Oncology Group study. Int Orthop, 38:825-830, 2014
7. Yoneda Y, Kunisada T, Naka N, Nishida Y, Kawai A, Morii T, Takeda K, Hasei J, Yamakawa Y, Ozaki T. Favorable outcome after complete resection in elderly soft tissue sarcoma patients: Japanese Musculoskeletal Oncology Group study. Eur J Surg Oncol, 40:49-54, 2014
8. Iwata S, Ishii T, Kawai A, Hiruma T, Yonemoto T, Kamoda H, Asano N, Takeyama M. Prognostic factors in elderly osteosarcoma patients: a multi-institutional retrospective study of 86 cases. Ann Surg Oncol, 21:263-268, 2014
9. Asano N, Yoshida A, Kobayashi E, Yamaguchi T, Kawai A. Multiple metastases from histologically benign intraarticular diffuse-type tenosynovial giant cell tumor: a case report. Hum Pathol, 45:2355-2358, 2014
10. Fujiwara T, Katsuda T, Hagiwara K, Kosaka N, Yoshioka Y, Takahashi RU, Takeshita F, Kubota D, Kondo T, Ichikawa H, Yoshida A, Kobayashi E, Kawai A, Ozaki T, Ochiya T. Clinical relevance and therapeutic significance of microRNA-133a expression profiles and functions in malignant osteosarcoma-initiating cells. Stem Cells, 32:959-973, 2014
11. Kubota D, Yoshida A, Kawai A, Kondo T. Proteomics identified overexpression of SET oncogene product and possible therapeutic utility of protein phosphatase 2A in alveolar soft part sarcoma. J Proteome Res, 13:2250-2261, 2014
12. Setsu N, Yoshida A, Takahashi F, Chuman H, Kushima R. Histological analysis suggests an invasion-independent metastatic mechanism in alveolar soft part sarcoma. Hum Pathol, 45:137-142, 2014
13. Totoki Y, Yoshida A, Hosoda F, Nakamura H, Hama N, Ogura K, Yoshida A, Fujiwara T, Arai Y, Toguchida J, Tsuda H, Miyano S, Kawai A, Shibata T. Unique mutation portraits and frequent COL2A1 gene alteration in chondrosarcoma. Genome Res, 24:1411-1420, 2014
14. Ueda T, Kakunaga S, Ando M, Yonemori K, Sugiura H, Yamada K, Kawai A. Phase I and pharmacokinetic study of trabectedin, a DNA minor groove binder, administered as a 24-h continuous infusion in Japanese patients with soft tissue sarcoma. Invest New Drugs, 32:691-699, 2014
15. Blay J-Y, Sleijfer S, Schoffski P, Kawai A, Brodowicz T, Demetri GD, Maki RG. International expert opinion on patient-tailored management of soft tissue sarcomas. Eur J Cancer, 50:679-689, 2014
16. Ogura K, Miyamoto S, Sakuraba M, Chuman H, Fujiwara T, Kawai A. Immediate softtissue reconstruction using a rectus abdominis myocutaneous flap following wide resection of malignant bone tumours of the pelvis. Bone Joint J, 96-B:270-273, 2014
17. Nishida Y, Kobayashi E, Kubota D, Setsu N, Ogura K, Tanzawa Y, Nakatani F, Kato Y, Chuman H, Kawai A. Chronic expanding hematoma with a significantly high fluorodeoxyglucose uptake on ^{18}F-fluorodeoxyglucose positron emission tomography, mimicking a malignant soft tissue tumor: a case report. J Med Case Rep, 8:349, 2014
18. Fujiwara T, Takahashi RU, Kosaka N, Nezu Y, Kawai A, Ozaki T, Ochiya T. RPN2 Gene Confers Osteosarcoma Cell Malignant Phenotypes and Determines Clinical Prognosis. Mol Ther Nucleic Acids, 3:e189, 2014
19. Hayashi K, Iwata S, Ogose A, Kawai A, Ueda T, Otsuka T, Tsuchiya H. Factors that influence functional outcome after total or subtotal scapulectomy: Japanese Musculoskeletal Oncology Group (JMOG) study. PLoS One, 9:e100119, 2014
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23. Kobayashi E, Satow R, Ono M, Masuda M, Honda K, Sakuma T, Kawai A, Morioka H, Toyama Y, Yamada T. MicroRNA expression and functional profiles of osteosarcoma. Oncology, 86:94-103, 2014
24. Odagiri H, Kadomatsu T, Endo M, Masuda T, Morioka MS, Fukuhara S, Miyamoto T, Kobayashi E, Miyata K, Aoi J, Horiguchi H, Nishimura N, Terada K, Yakushiji T, Manabe I, Mochizuki N, Mizuta H, Oike Y. The secreted protein ANGPTL2 promotes metastasis of osteosarcoma cells through integrin $\alpha^5\beta^1$, p38 MAPK, and matrix metalloproteinases. Sci Signal, 7:ra7, 2014

Surgical Center

Hitoshi Katai

Introduction

The Surgical Center deals with all kinds of malignant neoplasm. Our mission is to provide safe surgical care to the patients (Safe Surgery Saves Lives). Several groups collaborate to ensure the best surgical care, consisting of anesthesiologists, surgeons from 15 surgical oncology groups, nurses, and medical-technical staff with support staff from Radiology and the Laboratory.

Routine activities

During 2014, the Surgical Center supported 4,708 surgical cases and 4,208 general anesthesia surgical cases, a 0.3% increase in the general anesthesia cases over 2013. Sentinel node navigation surgery in breast cancer, autonomic nerve preservation proximal gastrectomy with jejunal interposition in early gastric cancer, hepatectomy and pancreatectomy in patients with hepato-biliary and pancreas diseases, and placement of an artificial urinary sphincter for bladder incontinence after prostate cancer treatment are unique treatments in our institution, and occasionally performed in the Surgical Center. Over the years, minimally invasive procedures have increased remarkably. Endobronchial brachytherapy under general anesthesia in lung cancer and endoscopic resection under general anesthesia in GI cancer are also unique treatments and are carried out in the Surgical Center.

Da Vinci robotic surgical system has been introduced to provide less invasive surgery to the patients for not only prostate cancer but also rectal cancer.

Post-anesthesia care unit has been a part of the Surgical Center during this year.

The multidisciplinary meeting has started in 2014. The multidisciplinary team includes medical doctors, nurses, and ME meets to plan the best surgical pathway during operation.

The Surgical Center staff works as part of a multidisciplinary team active in planning the best utilization of operating rooms. Scheduling, equipment usage, and staffing in the 16 operating suites were evaluated to establish an optimal work flow, streamline room turnover, and improve start times.

Medical device nurse, who is engaged in equipment usage, has been assigned.

Education and Training

All surgical oncology groups have their own training programs for their fellows with the support of the Surgical Center staff. Our center also provides virtual reality simulators to allow fellows to develop the skills used in laparoscopic and thoracoscopic surgery. About 50 foreign doctors have visited our surgical center.

Table 1. Total number of operations

	Jan.	Feb.	March	Apr.	May	June	July	Aug.	Sep.	Oct.	Nov.	Dec.	Total
Anesthesia													
General	123	145	142	147	142	162	165	154	126	171	155	136	1,768
General and epidural	202	193	188	210	207	199	205	200	206	226	193	199	2,428
Epidural and lumbar	0	0	0	1	0	0	0	0	0	0	0	1	2
Epidural and lumbar	0	0	0	0	0	0	1	0	0	0	0	0	1
Lumbar	1	3	9	12	6	3	7	4	0	1	9	5	60
Local	32	44	43	48	55	31	45	34	39	43	37	41	492
Others	8	8	7	5	7	7	10	7	6	7	8	4	84
Total	366	393	389	423	417	402	433	399	377	448	402	386	4,835

Table 2. Number of general anesthesia cases

	Jan.	Feb.	March	Apr.	May	June	July	Aug.	Sep.	Oct.	Nov.	Dec.	Total
Neurosurgery	6	7	12	13	10	12	9	13	9	12	9	11	123
Opthalmology	23	24	25	20	25	28	25	24	25	29	22	29	299
Head & Neck Surgery	9	16	20	18	19	20	24	20	20	21	23	24	234
Breast Surgery	39	37	36	43	40	45	41	40	38	45	37	46	487
Thoracic Surgery	46	49	51	51	46	57	56	59	52	63	55	65	650
Esophageal Surgery	8	10	11	10	12	13	14	12	9	12	14	9	134
Gastric Surgery	36	42	34	39	32	33	38	34	37	36	41	36	438
Colorectal Surgery	34	37	44	39	38	52	45	43	42	44	34	45	497
Hepatobiliary & Pancreatic Surgery	22	19	23	25	19	26	28	29	24	30	19	29	293
Gynecology	17	18	16	13	18	19	23	19	17	21	16	20	217
Urology	20	22	23	23	25	23	26	23	23	33	26	18	285
Dermatology	8	4	8	11	9	11	13	10	8	9	7	11	109
Orthopedic Surgery	16	25	23	26	14	22	24	19	23	29	21	25	267
Plastic and Reconstructive surgery	9	10	10	4	3	4	3	7	5	8	8	12	83
Endoscopy	2	0	2	0	3	2	0	0	3	1	1	1	15
Radiation oncology	2	3	2	2	2	8	5	4	4	2	2	5	41
Transplantation	1	2	1	1	2	4	1	3	3	3	3	3	27
Pediatric Surgery	1	1	1	1	0	0	0	1	2	0	1	1	9
Total	299	326	342	339	317	379	375	360	344	398	339	390	4,208

Physician Referral Service Office

Hidehito Horinouchi, Makiko Murase, Maya Ozawa, Yukiko Higuchi, Hisako Tanaka, Keiko Tsutsumi, Kayoko Yamada

Introduction

The Physician Referral Service Office was established as an independent section directly under the director of hospital. The mission of the Office is to provide appropriate access to the best cancer practice for more patients and their physicians. To help cancer patients with various needs to visit the National Cancer Center Hospital, the Physician Referral Service Office consists of a physician, a nurse, a medical social worker and 3 clerks. The Office also correspond inquiries for patients' medical records from their physician. Other important activity is to record and analyze the information concerning patients' referral to the National Cancer Center Hospital.

Routine activities

1. Physician referral service

Under strong collaboration with the reservation center, the Office support patients and their physicians to select proper doctor promptly.

2. Inquiry for patients' medical record

We receive and correspond inquiries of medical records from physicians who see patients of our hospital.

3. Relationship with affiliated hospitals and clinics

We send reminder to patients' physician at the timing of patients' first visit to our hospital. To maintain relationship, we hold regular meetings and invite physicians from affiliated hospitals and clinics.

4. Record and analysis of clinical information

The information of all patients and their physicians is appropriately recorded in order to analyze and apply for next strategies for a better service.

5. Corporation with intramural departments and staff members

To provide best practice, we make great effort to collaborate with intramural departments, sections and staff members.

Table 1. Total number of operations

	"Referral reply letters"	"Medical record inquiries"	"FAX Service"	"Reservation support"
January	662	65	23	21
February	634	42	30	17
March	700	81	36	26
April	692	70	41	15
May	593	60	39	16
June	717	83	26	21
July	826	72	29	24
August	766	75	40	20
September	847	89	36	30
October	903	101	49	23
November	772	98	47	23
December	772	87	37	23
Total	8,884	923	433	259

Clinical Trial Coordination (& Support) Office

Noboru Yamamoto

Introduction

The Clinical Trial Coordination (& Support) Office aims to promote clinical trials on unapproved drugs and medical devices, with the goal of allowing patients to receive the benefits arising from life science research as quickly as possible. The task of the Clinical Trial Coordination (& Support) Office is to facilitate smooth implementation of industry-sponsored registration trials ("*Chiken*"), physician-initiated registration directed clinical trials ("*Ishishudou-chiken*") and other clinical research studies (investigator-initiated trials). This Office consists of 2 Divisions (Clinical Research Coordinating Division and Administrating Division). The staff members, nurses, pharmacists and laboratory technologists, participate in these Divisions independently from outpatient divisions, wards, the nursing division and pharmacy, thus breaking through the conventional framework of profession based organizations.

Routine activities

The Clinical Trial Coordination (& Support) Office supports a lot of the industry-sponsored registration trials as well as the physician-initiated registration directed clinical trials. A total of 27 CRCs (clinical research coordinators) are supporting these trials. The number of the industry-sponsored registration trials is increasing year by year, and we supported 269 registration-directed clinical trials including 17 physician-initiated registration directed clinical trials in 2014 (Table 1). The number of the supported clinical trials is increasing as previously described, and the supporting area covered by the CRCs will be expanded to include not only registration trials but also other investigator-initiated clinical trials. Therefore, the expansion of CRC staff members is highly anticipated. In view of the plan for the National Cancer Center Hospital (NCCH), all members of this Office will work together to contribute to reinforcing the clinical research capabilities of the NCCH and to making this Office a valuable unit for all members of our hospital.

Table 1. Supported Trials in Clinical Trial Coordination (& Support) Office in 2014

Phase	Ongoing	New (since 2013)	Total
I	55	28	83
I/II	17	3	20
II	32	20	52
II/III	1	0	1
III	65	22	87
POS	5	1	6
Medical device	2	1	3
In-vitro diagnostics	0	0	0
IITs	12	5	17
Total	189	80	269

POS: post marketing study
IITs: physician-initiated registration directed clinical trials

Nutrition Management Office

Mayumi Miyauchi, Tomoko Suzuki, Hiroko Abe, Hiroko Takashima, Yasuko Muramatsu, Noriko Aoki, Moe Nishio, Maki Miura, Satoru Suzuki, Masato Fujii, Yasushi Ogaki, Nobuyuki Hirose, Masahiro Kikuchi, Kenichi Koshikawa, Takeshi Fujioka

Introduction

We aim to provide a highest quality food service for patients who are suffering from cancer, and therefore we have made efforts to prepare many kinds of meals appropriate for individual patients with allergic diseases. In addition, we strive to use seasonal menus, and meals for special occasions, as well as choice of special meals as an alternative to regular meals for pediatrics patients.

In the "taste-disorder restitution as an exploitation of a supportive treatment" research projects, in order to perform nutrition management which corresponds to the patient suffering from side effects and create an assessment sheet, Japan Society of Metabolism and Clinical Nutrition released this result.

Even a rookie dietitian, is able to offer adequate nutritional management in accordance with various status of the patients by using this sheet.

Routine activities

The therapeutic diet, which is provided as part of nutritional therapy, was 429,912 meals. We also provided 1,379 dietary consultations. Nutrition Support Team (NST) accepted 931 patients; the average number of consultations was 78 cases per month.

In the Grant-in-Aid for carcinoma set up by Foundation for Promotion of Cancer Research, the survey on understanding of complementary and alternative medicine in cancer care by a hospital dietitian was conducted and the result was reported in the Cancer Patients Nutritional Management Study Group, the Japan Society of Metabolism and Clinical Nutrition, and the Carcinoma Patient Nutrition Management Society. We participated in the symposium voluntary as a lecturer and provided cancer survivorship support. The Research Department providing meal support to cancer patients was subjected to enlighten a regional movement.

In the field of education, we actively accept university students for training. We also put effort into cultivating human resources for registered dietitians.

Research activities

1) The Nutritional Management Workshop for cancer patient has reached its 33rd anniversary, and “Nutrition past, present and future” was delivered as the president’s lecture in Yokohama.
2) Through the meal courses and cancer nutritional management courses being carried out at universities where cancer prevention is taught, cooperation with universities has been enhanced.
3) Research enterprise
   1. The factual survey of a taste disorder
   2. Studies on nutrition in surgical treatment of esophageal cancer.
   3. Prospective nutritional assessment after pancreaticoduodenectomy.

Department of Pharmacy

Yoshikazu Hayashi

Introduction

The Pharmacy stores and dispenses drugs, prepares injections (including aseptic mixtures), collects and disseminates drug information and provides patients with guidance regarding the proper use of drugs. Its services have improved toward the hospital's goal of envisaging the highest quality of medical care, practice and research. A state-of-the-art computerized system and other pharmacy-related equipment ensure quality control and inventory management, promote the proper use of drugs, and enhance the efficiency and quality of our services.

Routine activities

As part of the fundamental function of the hospital, the Pharmacy prepares and dispenses oral and topical medicines and injections for individual patients. All outpatients and inpatients are provided with aseptic mixtures of injectable chemotherapy agents prepared in the Pharmacy. As the importance of providing drug information for patients has been widely acknowledged, clinical pharmacists visit inpatients and give advice on taking medicine, focusing especially on pain control with opioids, and participate in the palliative-care support team, while the Pharmacy provides outpatients with guidance in the proper use of opioids and anti-cancer agents. The Pharmacy also places pharmacists in every hospital ward to provide the medication reconciliation service for inpatients, with a view to enhance the quality of chemotherapy as well as to ease the burden of doctors and nurses.

Pharmacists collect, compile, and maintain a database of drug information and distribute pertinent information to the medical staff. Drug information is disseminated quickly throughout the hospital by paper distribution and/or on the in-hospital computer network. Pharmacists individualize dosage regimens for specified drugs such as tacrolimus, aminoglycosides, and vancomycin based on both measured blood concentrations and pharmacokinetic analysis to maximize their efficacy and minimize adverse events.

A physician places an order through the hospital's computerized electric medical record system. The prescription order is then redirected to the medicine-package-printing system which provides drug information. The medicine-package information, instructions and explanations, which are easy to understand by patients, for the proper use of drugs, such as those regarding efficacy and effectiveness, precautions, and guidance concerning symptoms at the early stage of adverse reactions, are automatically printed out for patients when a prescription is ordered.

The injection-order is directly linked to an automatic "picking system" device, and this linkage ensures that injections are made properly and efficiently. This injection-ordering system contains an additional function, a regimen-ordering system for anti-cancer drugs which makes it possible to check the dose as well as the interval of chemotherapy. The Pharmacy has a robot which prepares injection preparations without human assistance.

Research activities

Since an important mission of the Pharmacy is to contribute to the development of new drugs, inventory control and handling of new investigative drugs are performed in accordance with Good Clinical Practice regulations. Research on the safety management of chemotherapy is conducted including handling of chemotherapeutic drugs, reduction of incidents regarding drugs, and improvement of pain control for patients

who need palliative care through the use of guidance materials. A couple of studies on the pharmacokinetics and pharmacodynamics of cancer-related drugs have been performed and some of the results have been reported in international conferences and journals.

Information Services

The mission of the Pharmacy Information Services is to provide an evidence-based foundation for safe and effective drug therapy for cancer patients. The internal online pharmacy journal is published monthly. Current safety information, newly adopted drugs, questions-and-answers, and topic of approvals are available for medical staff on the in-hospital computer network. The Pharmacy also provides a variety of information on the internet to the general public and medical experts outside the hospital.

Table 1. Number of Prescriptions in 2014

1) Oral and topical preparations	
Prepared in the hospital pharmacy	142,675
Inpatients	132,559
Outpatients	10,116
Taken to outside pharmacies	74,744
(% of prescription filled outside)	88.1
2) Injections	
Inpatients	352,391
Outpatients	39,575

Table 2. Amounts of Drugs Consumed in 2014

	(including sales tax)	(%)
Total	5,247,217	100.0
Internal medicines	408,944	7.8
External	47,385	0.9
Injection	3,823,835	72.9
Narcotics	124,007	2.4
Blood	494,016	9.4
X-ray imaging	218,276	4.2
RI	74,605	1.4
Others	56,149	1.0

Unit:1,000 yen

Education and Training

The National Cancer Center Hospital offers a three-year postgraduate pharmacy residency training in clinical oncology. In the first year, the program attaches the most importance to technical aspects of cancer care. In the second year, through required rotations in a variety of focused hematology/oncology services, the resident will refine his/her clinical problem-solving skills in cancer management and patient education, as well as provide pharmaceutical care to ambulatory care patients and participate in an oncology-focused drug information program. In the third year, residents participate in specialized pharmaco-clinical practice and research activities, which may be tailored to the resident's goals. The hospital also provides a two-year chief residency program in which post-residency trainees may develop their clinical research capabilities to a higher level. Moreover, there are opportunities for educational activities, such as a training course for visiting expert pharmacists and post-graduate students of pharmacy, and participation in a multi-institutional TV conference.

Table 3. Aseptic Preparation of Injectable Drugs in 2014

Anticancer Drugs	58,632
Others	34,352

Table 4. House Preparations in 2014

Sterilized	67
Non-sterilized	119

Table 5. Investigational Drugs

Newly registered	71
Ongoing study	152
Total	223

List of papers published in 2014

Journal

1. Terazawa T, Nishitani H, Kato K, Hashimoto H, Akiyoshi K, Iwasa S, Nakajima TE, Hamaguchi T, Yamada Y, Shimada Y. The feasibility of a short bevacizumab infusion in patients with metastatic colorectal cancer. Anticancer Res, 34:1053-1056, 2014

2. Kiba T, Ito T, Nakashima T, Okikawa Y, Kido M, Kimura A, Kameda K, Miyamae F, Tanaka S, Atsumi M, Sumitani Y, Shitakubo Y, Niimi H. Bortezomib and dexamethasone for multiple myeloma: higher AST and LDH levels associated with a worse prognosis on overall survival. BMC Cancer, 14:462, 2014

Department of Nursing

Kazuko Nasu

Introduction

The Department of Nursing bears responsibility for team healthcare at the National Cancer Center Hospital (NCCH), the core institution for national cancer treatment and control in Japan. The responsibility of the Department of Nursing is to develop and improve the quality of cancer nursing as well as to contribute to the appropriate management of the hospital. The Department is also expected to foster nursing staff to achieve the best cancer nursing.

Routine activities

Based on the philosophy of the Department of Nursing, which is to create and provide the best cancer nursing geared to the needs of patients, the Department is working to provide safe and reliable nursing in response to advances in medicine with consciousness and responsibility as a nurse in the NCCH.

We adopted the two-shift nursing system in 13 units, comprising an 8-hour day shift and a 16-hour night shift. Inpatient unit nurses work together more as closely than nurses in an outpatient clinic. Moreover, we have strengthened the support for the patient discharge process so that patients can return earlier to their own home or area.

We are accepting and meeting the challenge to provide many patient education programs produced by Certified Nurse Specialists and Certified Nurses. We have 5 patient education programs and consultation services, 3 outpatient clinics by nurses, and a support program for patients and their families. Many patients and families have participated in the educational program for their self-care and survivorship in their daily life.

Research activities

We presented 20 studies on nursing at some annual conferences in 2014. We organized the Nursing Research Committee, the members of which must have a master's degree or a doctor's degree. They must also have sufficient experience regarding nursing research activities. They support nurses to challenge nursing research based on their clinical questions. We are making effort to improve the quality of nursing research with through getting support from some physicians and statisticians. We expect our nurses from the NCCH to create and develop cancer nursing to even higher levels of proficiency and expertise.

Education

1. Assist and support new nurses

We have worked to reduce the gap between the technical skill level of new nurses and the clinical nursing required for actual cancer care by carrying out practical nursing training. During the first month, we provided training courses on basic nursing skills for new nurses. New nurses learn about clinical nursing practices by shadowing a senior nurse for the first one month. We ensure that new nurses can work in an adverse a favorable work-related stress-free environment.

2. Development of knowledge and skills for cancer nursing

To develop the skills associated with of cancer nursing, the Department of Nursing is enhancing a system that can bring out individual expertise and an educational system to improve the careers of nurses. In particular, the interaction between a large-group training and a small-group training was increased to implement the knowledge and techniques acquired from years of continuing education, which resulted in improved patient care.

We have 11 specialized nurse training courses: Cancer chemotherapy nursing I and II; Clinical trial nursing; Palliative care nursing I and II; Lymphedema care; Wound and skin care; Dysphagia nursing; Radiotherapy and IVR nursing; Support for discharge and home care coordination nursing and nursing research. A total of 215 nurses have participated, all of whom have over 4 years' nursing experiences. Many nurses want to participate in the courses. Through evaluation of the result of these courses this year, issues in the future are to improve the educational content for nurses to enable career development.

3. Certified Nurse Specialists and Certified Nurses

Currently, 10 certified nurse specialists and 34 certified nurses are working at the NCCH. They represent the role model for cancer nursing practice in both the inpatient and outpatient settings. The number of consultations is increasing, which proves that the use of Certified Nurse Specialists and Certified Nurses is being accepted by the nurses in this hospital.

As members of teams where different professionals work together in special areas, such as infection control, palliative care, nutritional support, and care of decubitus ulcers, and respiratory support, these Certified Nurses contribute to effective cooperation. The identification of problems and discussions from the point of view of multidisciplinary teams serve as a good model for other nurses and provide an important educational role in the clinical setting.

Certified Nurse Specialists contribute to the education and coordination for ethical issues in the clinical setting. They support and empower not only patients and families, but also nursing staff.

Certified Nurse Specialists and Certified Nurses also engage in educational activities both within and outside the hospital, and contribute to the development of educational program by giving lectures and practice training for the curricula of Certified Nurse Specialists or Certified Nurses.

List of papers published in 2014

Journal

1. Hiramatsu T, Sugiyama M, Kuwabara S, Tachimori Y, Nishioka M. Effectiveness of an outpatient preoperative care bundle in preventing postoperative pneumonia among esophageal cancer patients. Am J Infect Control, 42:385-388, 2014