Hospital

Preface

The National Cancer Center Hospital (NCCH) serves the highest level of standard of care with the missions of overall research and development for cancer, striving for novel diagnostic and treatment approaches, palliative care, and patient support.

Followed by the major reorganization in 2012 consisting of 13 common departments and 30 clinical departments, the Orphan Cancer Center was newly set up in collaboration with the National Cancer Center East Hospital (NCCHE) this year. Patients with orphan cancer have been taken care of the appropriate clinical department, however, it is more beneficial, not only in terms of efficient service for patients but also the overall approach to treatment and research to establish a cross-sectional organization consisting of several clinical departments in both the NCCH and NCCHE, Research Institute, and Exploratory Oncology Research & Clinical Trial Center. In addition, it works very closely with the Center for Information Service, which provides information related to orphan cancer.

The construction of the new Medical Examination Building was completed in December. The Department of Radiation Oncology is located in this building and plans to start boron-neutron capture therapy (BNCT) as the first hospital-based BNCT center in the world. On the first basement level, screening is planned to start in May 2014 in the medical examination unit of the Research Center for Cancer Prevention and Screening. Some medical equipment has been moved for use in the examination from the NCCH, so that we expect more effective work and better overall service in the Tsukiji campus. There are chief offices of each clinical department on the second and third floor, and on the fourth and fifth levels, we have placed the Endoscopy Center, which is the largest and well known in Japan. The Center for Information Service and the research units of the Research Center for Cancer Prevention and Screening are placed on the sixth, seventh and eighth levels. We plan to renovate the endoscopy rooms as an ambulant treatment center in the hospital building and to prepare offices for head physicians and attending staff members.

In January, the electronic health record system was renewed, and renamed as MISSION.

In March, we integrated several departments and sections supporting patients, such as the Departments of Palliative Care and Psycho-oncology, Patient Counseling Center and Appearance Supportive Center into the Patient Supportive Care Center (tentative). This center will start full-scale operation in the fiscal year 2014.

At the end of the fiscal year 2013, as a part of the personnel system, the position of the chief in each of twenty-five clinical departments was filled through open recruitment.

We have almost completed the reformation of the NCCH into a regenerated National Cancer Center this year with major changes in the organization and personnel affairs.

Yasuaki Arai, M.D.
Director, National Cancer Center Hospital

Organization

President:
Tomomitsu Hotta

Director:
Yasuaki Arai

Deputy Director:
Clinical Management
Hisao Asamura
Education
Tomoo Kosuge
Research
Yasuhiro Shimada
Safety Management
Hirokazu Chuuman

Office of Safety Management
Chief: Hirokazu Chuuman

Office of Infection Control and Prevention
Chief: Minoru Esaki

Clinical Departments — Departments
Chiefs

Common Departments

Outpatient Treatment Center
Chief: Kenji Tamura

Endoscopy Center
Chief: Yutaka Saito

Consultation, Counseling and Support Service Center
Chief: Masashi Kato

Appearance Support Center
Chief: Keiko Nozawa

Rare Cancer Center
Chief: Akira Kawai

Radiation
Chief Technologist: Tomohiko Aso
Chief Technologist: Yoshihisa Abe

Clinical Laboratories
Chief Technologist: Satoshi Nakajima

Surgical Center
Chief: Hitoshi Katai

Physician Referral Service Office
Chief: Hidehito Horinouchi

Clinical Trial Coordination (& Support) Office
Chief: Noboru Yamamoto

Nutrition Management Office
Chief: Mayumi Miyauchi

Health Information Management Office
Chief: Hiroshi Nishimoto

Department of Pharmacy
Chief: Yoshikazu Hayashi

Department of Nursing
Chief: Kazuko Nasu

Clinical Departments

Director:
Yasuaki Arai

Deputy Director:
Clinical Management
Hisao Asamura
Education
Tomoo Kosuge
Research
Yasuhiro Shimada
Safety Management
Hirokazu Chuuman

- Department of Neurosurgery and Neuro-Oncology
  Chief: Soichiro Shibui
  Deputy Chief: Yoshitaka Narita
- Department of Ophthalmic Oncology
  Chief: Shigenobu Suzuki
- Department of Head and Neck Oncology
  Chief: Seiichi Yoshimoto
- Department of Plastic and Reconstructive Surgery
  Chief: Shimpei Miyamoto
- Department of Breast Surgery
  Chief: Takayuki Kinoshita
- Department of Breast and Medical Oncology
  Chief: Kenji Tamura
- Department of Thoracic Surgery
  Chief: Hisao Asamura
- Department of Thoracic Oncology
  Chief: Tomohide Tamura
- Department of Esophageal Surgery
  Chief: Yuji Tachimori
- Department of Gastric Surgery
  Chief: Hitoshi Katai
- Department of Colorectal Surgery
  Chief: Yukihide Kanemitsu
- Department of Gastrointestinal Medical Oncology
  Chief: Yasuhiro Shimada
- Department of Endoscopy
  Chief: Yutaka Saito
- Department of Hepatobiliary and Pancreatic Surgery
  Chief: Kazuaki Shimada
- Department of Hepatobiliary and Pancreatic Oncology
  Chief: Takuji Okusaka
- Department of Urology
  Chief: Hiroyuki Fujimoto
- Department of Gynecology
  Chief: Takahiro Kasamatsu
- Department of Musculoskeletal Oncology and Rehabilitation
  Chief: Hirokazu Chuman
- Department of Dermatologic Oncology
  Chief: Naoya Yamazaki
- Department of Hematology
  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: Vacant
- Departments of General Internal Medicine, Dentistry, Oncologic Emergency
  Chief: Ken Ohashi
- Department of Anesthesia and Intensive Care
  Chief: Tetsufumi Sato
- Department of Palliative Care
  Chief: Motohiro Matoba
- Department of Psycho-Oncology
  Chief: Ken Shimizu
- Department of Diagnostic Radiology
  Chief: Yasuaki Arai
  Deputy Chief: Masahiko Kusumoto
- Department of Radiation Oncology
  Chief: Jun Itami
- Departments of Pathology and Clinical Laboratories
  Chief: Atsushi Ochiai

Activities of the Departments

Department of Neurosurgery and Neuro-Oncology

Soichiro Shibui, Yoshitaka Narita, Yasuji Miyakita, Makoto Ohno, Hideyuki Arita

Introduction

Patients with primary and metastatic brain tumors are treated by four neurosurgeons and one senior resident in the Department of Neurosurgery and Neuro-Oncology. Three hundred thirty-four patients were admitted and 106 craniotomies for tumor removal were carried out in 2013 including 39 gliomas, 40 metastatic brain tumors, 7 primary CNS lymphomas, and 12 meningiomas (Table 1). Fifteen ventriculo-peritoneal shunts and 1 neuroendoscopic surgical procedure were also carried out for patients with hydrocephalus. Every craniotomy was performed with the aid of a surgical navigation system (Stealth station). The site of the craniotomy and the extent of tumor removal were visualized on the CRT of this system 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. Twelve awake surgeries were also performed, particularly for removal of gliomas near the speech center. We started work with our intraoperative MRI system in February 2012 and this system was used for most craniotomies. Patients with malignant brain tumors are 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 is held with doctors of the Department of Radiation Oncology on the diagnosis and treatment of patients with brain tumors. Usually 20 patients are hospitalized and two or three of them undergo surgical treatment every week. The Stealth navigation system is used for surgical planning during every craniotomy. 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. (Table 2). 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 Brain Tumor Registry of Japan (BTRJ) since 1969. More than 100,000 patients have been registered and followed up. The Department of Neurosurgery and Neuro-Oncology, 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 Cancer Genomics, the National Cancer Center Research Institute. Tumor samples of malignant gliomas were collected and were analyzed with a DNA microarray. FISH analysis using 1p/19q/EGFR/PTEN probes, the determination of the methylation status of O^6-methylguanine-DNA methyltransferase (MGMT) and the mutation of IDH1/2 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 entitled "A randomized controlled phase II/III study of chemoradiotherapy using ACNU versus procarbazine and ACNU for astrocytoma grade 3 and 4" was conducted. The overall survival of both arms was longer than that of a Temozolomide (TMZ) study conducted by EORTC, however, adverse events such as granulocytopenia and thrombocytopenia were observed more frequently. The enrollment of patients for another randomized study entitled "A multicenter randomized phase II trial of Interferon-beta and Temozolomide combination chemoradiotherapy for newly diagnosed glioblastomas (JCOG 0911)" was finished in January 2012 and the result will be published soon. A clinical trial for metastatic brain tumors is also still ongoing: "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)". The efficacy of the gamma knife will be compared to that of whole brain irradiation. A new clinical trial for primary CNS lymphoma and grade III gliomas will start in 2014. 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.

Table 1. Number of surgeries by year, 2011-2013

	2013	2012	2011
Glioma	43	47	35
Metastatic brain tumor	41	33	39
Meningioma	12	7	5
Primary CNS lymphoma	7	4	6
Other brain tumor	8	5	7
Others	27	36	31
Total	140	132	123

Table 2. Type of procedure

Craniotomy	106
V-P shunt	15
Placement of Ommaya's reservoir	4
Others	15

Table 3. Survival rates

Diagnosis	MST (mo)	5-yr survival (%)
Diffuse astrocytoma	76.0	55.6
Oligoastrocytoma	n.v.	94.1
Anaplastic oligoastrocytoma	82.4	66.1
Anaplastic astrocytoma	30.6	35.6
Glioblastoma	13.6	10.0

MST, median survival time; n.v., not verified

List of papers published in 2013
Journal

1. Shibui S, Narita Y, Mizusawa J, Beppu T, Ogasawara K, Sawamura Y, Kobayashi H, Nishikawa R, Mishima K, Muragaki Y, Maruyama T, Kuratsu J, Nakamura H, Kochi M, Minamida Y, Yamaki T, Kumabe T, Tominaga T, Kayama T, Sakurada K, Nagane M, Kobayashi K, Nakamura H, Ito T, Yazaki T, Sasaki H, Tanaka K, Takahashi H, Asai A, Todo T, Wakabayashi T, Takahashi J, Takano S, Fujimaki T, Sumi M, Miyakita Y, Nakazato Y, Sato A, Fukuda H, Nomura K. Randomized trial of chemoradiotherapy and adjuvant chemotherapy with nimustine (ACNU) versus nimustine plus procarbazine for newly diagnosed anaplastic astrocytoma and glioblastoma (JCOG0305). Cancer Chemother Pharmacol, 71:511-521, 2013
2. Arita H, Narita Y, Ohno M, Miyakita Y, Okita Y, Ide T, Shibui S. Management of glioblastoma in an NF1 patient with moyamoya syndrome: a case report. Childs Nerv Syst, 29:341-345, 2013
3. Arita H, Narita Y, Fukushima S, Tateishi K, Matsushita Y, Yoshida A, Miyakita Y, Ohno M, Collins VP, Kawahara N, Shibui S, Ichimura K. Upregulating mutations in the TERT promoter commonly occur in adult malignant gliomas and are strongly associated with total 1p19q loss. Acta Neuropathol, 126:267-276, 2013
4. Okita Y, Narita Y, Suzuki T, Arita H, Yonemori K, Kinoshita T, Fujiwara Y, Tsuda H, Komoike Y, Nakagawa H, Tamaki Y, Tomita Y, Shibui S, Maruno M. Extended trastuzumab therapy improves the survival of HER2-positive breast cancer patients following surgery and radiotherapy for brain metastases. Mol Clin Oncol, 1:995-1001, 2013
5. Ohno M, Narita Y, Miyakita Y, Matsushita Y, Yoshida A, Fukushima S, Ichimura K, Shibui S. Secondary glioblastomas with IDH1/2 mutations have longer glioma history from preceding lower-grade gliomas. Brain Tumor Pathol, 30:224-232, 2013
6. Nomura M, Narita Y, Miyakita Y, Ohno M, Fukushima S, Maruyama T, Muragaki Y, Shibui S. Clinical presentation of anaplastic large-cell lymphoma in the central nervous system. Mol Clin Oncol, 1:655-660, 2013
7. Momota H, Narita Y, Miyakita Y, Shibui S. Secondary hematological malignancies associated with temozolomide in patients with glioma. Neuro Oncol, 15:1445-1450, 2013
8. Fukushima S, Narita Y, Miyakita Y, Ohno M, Takizawa T, Takusagawa Y, Mori M, Ichimura K, Tsuda H, Shibui S. A case of more than 20 years survival with glioblastoma, and development of cavernous angioma as a delayed complication of radiotherapy. Neuropathology, 33:576-581, 2013
9. Sato A, Okada M, Shibuya K, Watanabe E, Seino S, Suzuki K, Narita Y, Shibui S, Kayama T, Kitanaka C. Resveratrol promotes proteasome-dependent degradation of Nanog via p53 activation and induces differentiation of glioma stem cells. Stem Cell Res, 11:601-610, 2013
10. Arita H, Narita Y, Takami H, Fukushima S, Matsushita Y, Yoshida A, Miyakita Y, Ohno M, Shibui S, Ichimura K. TERT promoter mutations rather than methylation are the main mechanism for TERT upregulation in adult gliomas. Acta Neuropathol, 126:939-941, 2013

Department of Ophthalmic Oncology

Shigenobu Suzuki, Yukiko Aihara

Introduction

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

Routine activities

Our outpatient service is open for three 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) Retinoblastomas

Unless the patient's family has anxiety about preserving the affected eye, if the eye has already suffered from complications 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 procedures, 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 in the Western literature 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. A 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, rhabdomyosarcomas are a malignant tumor that require systemic chemotherapy and radiation after biopsy. The most common orbital tumors in adults include cavernous hemangiomas, lacrimal gland tumors, lymphomas, metastatic tumors, and orbital inflammatory diseases. Patients with a biopsy-confirmed orbital lymphoma are referred to the Department of Hematology, and Hematopoietic Stem Cell Transplantation. Total resection with 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 carcinomas, sebaceous carcinomas, and squamous cell carcinomas. 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 retinoblastomas via selective ophthalmic artery infusion using a balloon catheter. This procedure was first introduced in our hospital in 1987, and has been modified and performed after 2009 in more than 20 countries. We are planning a clinical trial on selective ophthalmic

artery injection therapy for an initial treatment method.

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% of eyes were rescued using this strategy.

The National Registry of Retinoblastomas 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 provides epidemiological data.

A clinical study on the development of retinoblastoma patients with visual disturbance, and maternal psychological burden, is now ongoing. The result will be helpful to establish the social and psychological approach to retinoblastoma patients and their families.

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

Ocular adverse events by anti-cancer drugs used for systemic disease have recently been 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 associated with kinase inhibitor drugs, stenosis or occlusion of lacrimal drainage systems are common events associated with S-1, and cystoid macular edema (CME) with some other drugs. The mechanisms of these events have not yet been clarified, but most are classified as grade 1-2, and are reversible or self-limited. We examine and follow these adverse events, with or without additional treatment, to support clinical studies, to contribute to establishing protocols, and to disseminate knowledge of these events to general ophthalmologists.

Table 1. Number of patients

Retinoblastoma	54
Choroidal melanoma	27
Other intraocular tumors	27
Eyelid tumor	21
Conjunctival tumor	11
Orbital tumor	16
Ocular adnexal lymphoma	14
Other	24
Total	194

Table 2. Type of procedure

Retinoblastoma	
Selective ophthalmic arterial injection	122
Laser and/or vitreous injection	138
Ruthenium brachytherapy	11
Enucleation	18
Examination under general anesthesia	6
Choroidal melanoma	
Ruthenium brachytherapy	6
Enucleation	2
Resection of ciliary body tumor	2
Resection of eyelid tumor	13
Resection of conjunctival tumor	8
Resection of orbital tumor	5
Others	17
Total	349

List of papers published in 2013
Journal

1. Inaba K, Ito Y, Suzuki S, Sekii S, Takahashi K, Kuroda Y, Murakami N, Morota M, Mayahara H, Sumi M, Uno T, Itami J. Results of radical radiotherapy for squamous cell carcinoma of the eyelid. J Radiat Res, 54:1131-1137, 2013
2. Honda K, Yamamoto N, Nokihara H, Tamura Y, Asahina H, Yamada Y, Suzuki S, Yamazaki N, Ogita Y, Tamura T. Phase I and pharmacokinetic/pharmacodynamic study of RO5126766, a first-in-class dual Raf/MEK inhibitor, in Japanese patients with advanced solid tumors. Cancer Chemother Pharmacol, 72:577-584, 2013

Department of Head and Neck Oncology

Seiichi Yoshimoto, Fumihiko Matsumoto, Tsutomu Nomura, Daisuke Maki, Sadahiro Kishishita

Introduction

The treatment strategy for head and neck cancer is to improve the survival rates while preserving 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 procedures based on the clinic-pathological findings and our large database of the patients with head and neck cancer.

Our Department has developed and performed the original surgical procedures 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 the National Cancer Center Hospital (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 2013, 303 patients with head and neck tumors underwent surgery under local or general anesthesia; 95 and 208, respectively, including 46 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. Table 3 shows the rate of postoperative complications.

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 a multi-institutional study of intra-arterial chemo-radiotherapy for maxillary cancer.

Clinical trials

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

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

Tongue	40
Oral Cavity (without tongue)	35
Nasal and paranasal cavity	22
Nasopharynx	3
Oropharynx	26
Hypopharynx	63
Cervical esophagus	10
Larynx	15
Salivary Gland	11
Thyroid	20
Parathyroid	1
Neck	52
Others	5
Total	303

Table 2. Type of procedure

Skull base (+reconstruction)	1(1)
Maxillectomy (+reconstruction)	21(2)
Glossectomy (+reconstruction)	33(6)
Resection of Oral Cavity (+reconstruction)	33(11)
Nasopharyngectomy	3
Oropharyngectomy (+reconstruction)	16(4)
Endoscopic resection of hypopharynx	35
Partial pharyngectomy (+reconstruction)	11(7)
Total laryngopharyngectomy (+recon.)	10(10)
Partial laryngectomy	3
Total laryngectomy (+reconstruction)	5(2)
Thyroidectomy	20
Parathyroidectomy	1
Parotidectomy	10
Neck dissection (+reconstruction)	24(1)
Resection of parapharyngeal tumor	3
Voice prosthesis	7
Lymphadenectomy	49
Others (+reconstruction)	18(2)
Total	303(46)

Table 3. Operative morbidity and mortality

Major surgical complications	7 cases	(3.4%)
Postoperative death within 30 days	0 case	
Postoperative hospital death	0 case	

List of papers published in 2013
Journal

1. Ohtomo R, Mori T, Shibata S, Tsuta K, Maeshima AM, Akazawa C, Watabe Y, Honda K, Yamada T, Yoshimoto S, Asai M, Okano H, Kanai Y, Tsuda H. SOX10 is a novel marker of acinus and intercalated duct differentiation in salivary gland tumors: a clue to the histogenesis for tumor diagnosis. Mod Pathol, 26:1041-1050, 2013
2. Yamazaki H, Mori T, Yazawa M, Maeshima AM, Matsumoto F, Yoshimoto S, Ota Y, Kaneko A, Tsuda H, Kanai Y. Stem cell self-renewal factors Bmi1 and HMGA2 in head and neck squamous cell carcinoma: clues for diagnosis. Lab Invest, 93:1331-1338, 2013

Department of Plastic and Reconstructive Surgery

Shimpei Miyamoto, Shuji Kayano, Masanobu Sakisaka, Masaki Arikawa

Introduction

The Plastic and Reconstructive Surgery Division 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 a pedicled flap, local flap, skin graft, and so on, 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 functional and morphological reconstruction.

Routine activities

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

Research activities

Plastic and reconstructive surgery has focused on the following four aspects in the surgical treatment of cancer, for the purpose of contributing to the improvement of the quality of life of patients.

1. Obtaining good functional recovery
2. Reduction of postoperative complications
3. Achieving less donor site morbidity
4. Treatment of postoperative complications after cancer ablation.

With the objective of addressing these four aspects, establishing a standard of reconstructive surgery and developing new techniques of reconstructive surgery are the most important aims of our studies.

A multi-institutional analysis of postoperative function after total pharyngolaryngectomy is now going on. This study is supported by a Grant-in-Aid for Cancer Research from the Ministry of Health Labour and Welfare of Japan. The aim of the study is to clarify the relationship between operative procedures and postoperative swallowing functions.

Other developments in reconstructive procedures in cooperation with other Divisions such as Orthopedic Surgery, Breast Surgery, and so on, are proceeding, as shown in Table 1.

Table 1. Cooperative efforts with other divisions

Head and Neck	48
Orthopedic Surgery	67
Breast Surgery	81
HB&P Surgery	4
Esophageal Surgery	2
Dermatology	2
Others	5

Table 2. Operative Procedures

Free flap	106
Other microsurgery	12
Pedicled flap	36
Others	138

List of papers published in 2013
Journal

1. Miyamoto S, Kayano S, Umezawa H, Fujiki M, Sakuraba M. Vastus lateralis muscle flaps for monitoring buried anterolateral thigh flaps. J Craniofac Surg, 24:1739-1740, 2013
2. Miyamoto S, Kayano S, Umezawa H, Fujiki M, Sakuraba M. Flow-through fibula flap using soleus branch as distal runoff: a case report. Microsurgery, 33:60-62, 2013
3. Miyamoto S, Nakao J, Kamizono K, Nakantani F, Sakuraba M. Free descending genicular artery perforator flap harvested with the free-style approach: a case report. J Plast Reconstr Aesthet Surg. 66:1604-1606, 2013
4. Miyamoto S, Sakuraba M, Nagamatsu S, Kamizono K, Fujiki M, Hayashi R. Combined use of free jejunum and pectoralis major muscle flap with skin graft for reconstruction after salvage total pharyngolaryngectomy. Microsurgery, 33:119-124, 2013
5. Umezawa H, Sakuraba M, Miyamoto S, Nagamatsu S, Kayano S, Taji M. Analysis of immediate vascular reconstruction for lower-limb salvage in patients with lower-limb bone and soft-tissue sarcoma. J Plast Reconstr Aesthet Surg, 66:608-616, 2013

Department of Breast Surgery

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

Introduction

The Breast Surgery Division deals with the treatment of breast cancer, as well as the diagnosis of breast diseases and assessment of lymph nodes in the axillary and clavicular regions which are suspected of harboring metastases. Although breast-conserving therapy (BCT) has accounted for 51.8% of the cases, BCT was not indicated in more than 40% of the cases even when the cancer was at an early stage. In 2010, immediate breast reconstruction became one of the choices for these patients in whom breast preservation was impossible, and a total of 65 immediate breast reconstructions were performed in 2013, comprising more than 12% of all the cases. The number of cases of immediate breast reconstruction has gradually increased year by year to match the increased needs of patients. Sentinel lymph node (SLN) biopsies (SLNB) were performed in 74.2% of the cases. Following SLNB, the axillary lymph node dissection (ALND) could be avoided when the SLNB was negative. In conjunction with the one-step nucleic acid amplification (OSNA) assay, more positive nodes including micrometastases have been detected, compared to traditional diagnosis by frozen section alone and 20.6% of the cases after SLNB needed additional ALN dissection.

Routine activities

The Division is staffed by four staff surgeons, one chief resident, and three or four rotating residents. From 7:20 every morning, all the staff and the residents perform patient rounds together. A journal club and research conference are scheduled on every Tuesday morning after rounds. A weekly conference is held on Wednesdays 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 the 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.

BCT usually consists of local excision of the tumor followed by postoperative irradiation of the remaining breast, and is usually indicated for a tumor smaller than 3 cm. Patients with multi-focal lesions or extensive micro-calcifications detected with mammography are not eligible for BCT. Neo-adjuvant chemotherapy (NAC) and neo-adjuvant endocrine therapy (NAET) for operable advanced breast cancer are performed to avoid a mastectomy and to test the tumor sensitivity to therapeutic agents. Patients receive adjuvant chemo-endocrine therapy depending upon their prognostic and predictive factors, which include the number of lymph nodes involved, the histological grade of the tumor and secondary prognostic markers (HER2/neu, ER, PgR, and so on). Widely accepted factors that predict a response to a specific therapy are estrogen and progesterone receptors for hormone therapy and HER2 for trastuzumab. Since hormone-receptor positive patients tend to receive less chemotherapy nowadays, NAC has been decreasing and only 7.0% of all patients received neoadjuvant therapy in 2013.

Research activities

Sentinel node biopsy after Neo-adjuvant chemotherapy

As indications for NAC become more widespread, the question arises if SLNB is appropriate for axillary staging in patients after NAC. The accuracy and feasibility of SLNB after NAC have been evaluated (Kinoshita et al.).

MR guided-surgery and Real-time Virtual Sonography

A feasibility study to establish the standard surgery for breast tumors using diagnostic images during surgery in an MRX operating room is ongoing (Hojo et al.). A study to evaluate the utility of the impact of supine MRI on surgical decision making was conducted. Supine MRI had more accuracy in the measurement of invasive ductal carcinoma compared to prone MRI, suggesting the usefulness

of supine MRI before breast conserving surgery (Kinoshita et al.). A feasibility study using Real-time Virtual Sonography (RVS) is also being planned for breast conserving surgery. RVS can synchronize the US images and the MRI or CT images using a position tracking system with a magnetic sensor. It is thought to be useful for making an accurate excision line when US cannot detect suspicious daughter lesions or intraductal spread revealed with MRI or CT.

Radiofrequency Ablation (RFA)

With the widespread application of screening mammography and novel imaging techniques such as MRI, the mean size of the breast tumors detected has continued to decrease.

RFA, which is thought to be a less invasive surgical maneuver, has been introduced in the field of breast cancer therapy. We previously validated the safety and efficacy of RFA of small breast cancers (less than 1.0 cm) using saline-cooled electrodes (Phase I/II study; Kinoshita et al.). Our secondary goals are to determine the size, configuration and pathological features of acute RFA treatment of breast cancers, and clinical studies have been conducted to evaluate the oncologic safety of RFA in terms of local recurrence.

Sentinel lymph node biopsy with One-Step Nucleic acid Amplification (OSNA)

The OSNA assay that quantitatively measures CK19 mRNA detects sentinel lymph node metastases even at the molecular level. To evaluate the clinical significance of intraoperative SLN metastases detected by OSNA, we compare the OSNA results with that from conventional histological diagnosis. Furthermore, we examine the possibility of omitting axillary lymph node dissection in limited subsets of patients by using both methods.

Clinical trials

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

   A trial of image-guided radiofrequency ablation (non-surgical therapy) has been accomplished for early-stage breast carcinomas of less than 1.0 cm in diameter. After the trial period of some years, the indication has just been expanded up to 1.5 cm in diameter and this technique is certified as an advanced medical treatment by the Ministry of Health, Labour and Welfare.

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 started, 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 in order to slow or halt hair loss during chemotherapy.

5) Sentinel lymph node (SLN) biopsy

   A multi-center feasibility study to test the SLN identification rate using a radioisotope (RI) vs indocyanine green (ICG) has been ongoing since 2011.

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

   This multi-center randomized trial started in 2012 and compares invasive disease-free survival in patients with or without TS-1 administration together with adjuvant endocrine therapy.

7) Registration Data-base System of breast cancer patients who underwent lymph node metastasis diagnosis with the OSNA® method (LynoLog Data-base)

   The aim of this study is to accumulate the administrative data of cases with OSNA method in a common database, LynoLog, and to construct various new treatment guidelines based on the data.

Table 1. Number of patients

		2012	2013
Primary breast cancer		494	555
	cStage 0	76	99
	I	199	215
	II	194	203
	III	17	33
	IV	8	5
	unknown	2	0
Other malignant breast disease		3	4
Total		497	559

16 case were bilateral breast cancer.

Table 2. Type of procedure

	2010		2011		2012		2013	
Total number of operations	482		576		581		613	
Total numbers of primary breast cancer	482		525		494		555	
Mastectomy (%)	213	(44)	250	(48)	234	(45)	263	(47)
Breast-conserving surgery (%)	269	(56)	269	(51)	275	(53)	283	(51)
Radiofrequency ablation (%)			6	(1)	6	(1)	9	(2)
Axillary lymph node dissection (ALND) (%)	136	(28)	205	(42)	188	(38)	93	(18)
Sentinel lymph node biopsy (SLNB) (%)	316	(66)	402	(81)	409	(83)	347	(66)
ALND after SLNB (%)			113	(23)	103	(21)	83	(16)
Immediate breast reconstruction (%)	13	(3)	74	(14)	62	(13)	65	(12)
Neoadjuvant therapy	72	(15)	57	(11)	45	(8)	38	(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

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Journal

1. Jimbo K, Kinoshita T, Suzuki J, Asaga S, Hojo T, Yoshida M, Tsuda H. Sentinel and nonsentinel lymph node assessment using a combination of one-step nucleic acid amplification and conventional histological examination. Breast, 22:1194-1199, 2013
2. Tamura K, Kurihara H, Yonemori K, Tsuda H, Suzuki J, Kono Y, Honda N, Kodaira M, Yamamoto H, Yunokawa M, Shimizu C, Hasegawa K, Kanayama Y, Nozaki S, Kinoshita T, Wada Y, Tazawa S, Takahashi K, Watanabe Y, Fujiwara Y. 64Cu-DOTA-trastuzumab PET imaging in patients with HER2-positive breast cancer. J Nucl Med, 54:1869-1875, 2013
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6. Sugie T, Sawada T, Tagaya N, Kinoshita T, Yamagami K, Suwa H, Ikeda T, Yoshimura K, Niimi M, Shimizu A, Toi M. Comparison of the indocyanine green fluorescence and blue dye methods in detection of sentinel lymph nodes in early-stage breast cancer. Ann Surg Oncol, 20:2213-2218, 2013
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Department of Breast and Medical Oncology

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

Introduction

The Breast and Medical Oncology Division is engaged in the clinical management of and research into adult malignancies including breast cancer, gynecologic cancer, soft-tissue sarcoma, tumors of unknown primary sites and other rare types of solid tumors. We envision becoming a premier 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 pursue the development of new effective cancer treatment through clinical and translational research, and to nurture specialists in breast and medical oncology. An evidence-based, research-oriented and multi-disciplinary approach is the core value of our practice.

Clinical activities

1. Setup

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

2. Performance

There were a total of 782 first visits of new patients in 2013 (Table 1). Approximately two thirds of the new patients were referred from other division of NCCH. About half of the new patients are breast cancer patients, but it is noteworthy that there were 111 and 87 patients with primary unknown cancers and adult sarcomas, respectively. The number of outpatient chemotherapy procedures delivered by our division was 7777, which accounts for 30% of the total number and ranks first among the number of treatments delivered at the Outpatient Treatment Center.

We have approximately 26 (range 22-35) inpatients daily. Terminally-ill patients are transferred to palliative care units or in-home care clinics outside the National Cancer Center Hospital (NCCH), and 29 patients from our Division died in NCCH in 2013. An autopsy was undertaken in five patients.

3. Conference

The Briefing Conference is held every morning to discuss the evidenced-based care for individual patients. The research conference is held on Thursdays, and the Journal Club on Fridays. Multidisciplinary Case Conferences with diagnostic radiologists, surgeons, and pathologists are held once a week for breast and gynecologic cancer patients. We also participate in the Exploratory Oncology Research and Clinical Trial Center Conference on Monday as an active member.

A monthly Breast Cancer Conference is held with the participation of multidisciplinary specialists to discuss recent topics in breast oncology and to update institutional treatment guidelines. The treatment guidelines for breast cancer, both primary and metastatic, were updated in January, 2013.

4. Coordination of care

Three board-certified Breast Cancer Specialist Nurses help the smooth running of the Department through providing seamless and comprehensive care to breast cancer patients. Group-assigned pharmacists support patients in the ward and in the clinic. We encourage patients who receive chemotherapy to participate in the "Cosmetic Program" which is run by the Appearance Care Center.

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 the Tokyo Breast Consortium network (http://breastcons.com/).

Research activities

Our research interests extend across a wide range of topics related to treatment and clinical program development. Many of our studies are secured by public and consignment research grants. In 2013, we conducted ten research programs as the primary investigator and also participated in an additional nine programs as the co-investigator in research programs secured by competitive research funds.

In 2013, we actively enrolled patients in phase I studies as well as national and international studies

(Table 2). Of note we launched a pharmacokinetic and dose-finding study on eriburin/oraparib in anthracycline- and taxane-pretreated triple negative breast cancer as our fourth investigator-initiated clinical trial. A new molecular imaging study has been launched in cooperation with the Research Institute.

We value cancer survivorship as our research theme in order to develop a patient-centered comprehensive care program. In 2013 we took leadership in developing a guideline for young breast cancer patients who wish to preserve their fertility after treatment in cooperation with gynecologist and reproductive specialists. The study is planned to be published this year (2014).

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 presentations at local and national conferences. We vigorously support basic, clinical, or translational studies conducted by postgraduate students.

Future prospects

We continue in proposing a near-future model of the clinical management of adult solid tumors. Based in particular on our rich clinical experience in rare adult tumors, we aim to build a comprehensive program which includes a tumor registry, translational research, clinical trials and patient care. We would also like to improve the efficiency and efficacy of drug development by coordinating basic and translational studies in early-phase clinical trials.

List of papers published in 2013
Journal

1. Shimma S, Takashima Y, Hashimoto J, Yonemori K, Tamura K, Hamada A. Alternative two-step matrix application method for imaging mass spectrometry to avoid tissue shrinkage and improve ionization efficiency. J Mass Spectrom, 48:1285-1290, 2013
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6. Asano J, Hirakawa A, Hamada C, Yonemori K, Hirata T, Shimizu C, Tamura K, Fujiwara Y. Use of Cox's Cure Model to Establish Clinical Determinants of Long-Term Disease-Free Survival in Neoadjuvant-Chemotherapy-Treated Breast Cancer Patients without Pathologic Complete Response. Int J Breast Cancer, 2013:354579, 2013
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11. Nozawa K, Shimizu C, Kakimoto M, Mizota Y, Yamamoto S, Takahashi Y, Ito A, Izumi H, Fujiwara Y. Quantitative assessment of appearance changes and related distress in cancer patients. Psychooncology, 22:2140-2147, 2013
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Table 1. Demographics of Patients at their first Visit to the Clinic of the Breast and Medical Oncology Division (Jan - Dec, 2013)

No of 1st Visits	n	%	
Total	782		
Breast	372	47.5	
GYN	131	16.8	
Cancer of primary unknown origin	111	14.1	
Sarcoma	87	11.1	
Others	81	10.3	
Purpose of consultation			
2nd opinion	34	4.3	
Treatment at NCCH	67	8.5	
Referrals from other hospitals	219	28.0	
Referrals from other divisions in NCCH	503	64.3	(100)
Breast surgery	320		(63.6)
GYN	82		(16.3)
Urology	21		(4.2)
Orthopedics	16		(3.1)
Others	64		(12.7)
Others	1	0.1	

Table 2. Active Clinical Trials (Jan. 2013-Dec. 2013)

Disease	Clinical setting	Phase	Protocol	Regimen	status
Breast	Adjuvant	III	BEATRICE	CTx vs CTx + bevacizumab	Active, not recruiting
		III	ALTTO	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	CTx+HCN/placebo vs CTx/HCN/ pertuzumab	Active
		III	POTENT	HTx+S1 vs HTx alone	Active
	Metastatic	III	JCOG1017	Surgery vs no surgery for primary Stage IV BC	Active
		III	MARIANNE	RO5304020+/- RO4368451 vs HCN/ PTX	Active
		III	NK105	NK105 vs paclitaxel	Active
		III	PALOMA-2	Letrozole +/- PD0332991	Active
		III	ELTOP (WJOG)	lapa/capecitabine vs HCN/capecitabine	Active
		II	CAPTURE	Paclitaxel/bevacizumab vs maintenance endocrine therapy	Active
		II	TARGET	Tamoxifen vs high-dose tamoxifen	Active
		II	lapaHER	lapatinib/HCN	Active
		II	CBDCA/S1 for TNBC	CBDCA/S1	Active
		I/II	CAPIRI	capecitabine/CPT-11	Active
		I/II	S1/docetaxel	S1/docetaxel	Active
		I/II	Lapatinib/eriburin	Lapatinib/eriburin	Active
		I/II	EO	Eriburin/AZD2281	Active
		PK	Eriburin PK	eriburin	Active
Ovary	Adjuvant	III	AZD2281	Chemotherapy+/-AZD2281	
	Advanced	III	JCOG0602	primary surgery vs NAC	Active
		III	JGOG3017	TC vs. CDDP/CPT-11	Active
		III	GOG213	TC +/- bavacizumab	Active
		III	GOG218 (RDT)	TC +/- bevacizumab	Active
		III	AMG386	PTX+/-AMG386	Active, not recruiting
		III	AZD2281	Chemo +/- AZD2281	Active
		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	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 tumors		I	AZD1208	AZD1208	Active
		I	AZD5363	AZD5363	Active
		I	PD0332991	PD0332991	Active
Soft tissue sarcomas		II	ET-743	ET-743	Active
CIPN SNPs		translational	Paclitaxel induced peripheral neuropathy	Paclitaxel	Active
Molecular Imaging		0	Molecular imaging JST/MEXT-	nano-dose, radio-labeled trastuzumab	Active

Department of Thoracic Surgery

Hisao Asamura, Shun-ichi Watanabe, Hiroyuki Sakurai, Kazuo Nakagawa, Tsugumasa Kamata, Kyohei Masai, Yukio Watanabe

Introduction

The Thoracic Surgery Division 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 division, 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 division has four attending surgeons. Three subteams with attending surgeons and residents perform all of the inpatient care, operations, examinations, and outpatient care. In 2013, we performed a total of 669 operations; for lung cancer in 451 patients, metastatic tumors in 96, mediastinal tumors in 29, and others in 93.

The treatment strategy for patients with lung cancer is based on the tumor histology (non-small cell vs. small cell), the extent of the disease (clinical stage), and the 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 of the tumor. VATS resection of mediastinal tumors is indicated exclusively for small thymomas.

As for meetings, there are two division meetings. One is for the preoperative evaluation and postoperative inpatient review on Fridays and the other is for the journal club on Wednesdays. 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 Thursdays.

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 was closed in 2013.

Lymph node dissection for lung cancer has been a major issue in lung cancer treatment, and has been extensively studied in our division. We continue to improve the surgical dissection technique 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 division. 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 adenocarcinomas. 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 adenocarcinomas had been planned in the Japan Clinical Oncology Group (JCOG)- Lung Cancer Study Group, and two 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 the JCOG 0804 trial has been already closed. Eighty-nine cases have been registered for the JCOG 0802 from our division.

As for postoperative adjuvant therapy, a phase III clinical trial to compare the effectiveness of UFT with that of TS-1 for stage IA of 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 in 2013

Primary lung cancer	451
Metastatic lung tumor	96
Mediastinal tumor	29
Pleural disease	27
Chest wall tumor	8
Benign lung nodule	28
Others	30
Total	669

Table 2. Type of procedure in 2013

Lung resection	578
Lobectomy	349
Pneumonectomy	18
Segmentectomy	78
Wedge resection	133
Tracheal resection	0
Surgery for mediastinal tumors	30
Surgery for pleural tumors	19
Surgery for chest wall tumors	6
Others	36
Total	669

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

Pathological stage (TNM-7)	No. of pts	5-yr survival (%)
IA	1902	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
Total	3,551	

Operation period: 2003.1-2011.12

List of papers published in 2013
Journal

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Department of Thoracic Oncology

Tomohide Tamura, Noboru Yamamoto, Hiroshi Nokihara, Yutaka Fujiwara, Hidehito Horinouchi, Shintaro Kanda, Shinji Nakamichi, Satoru Kitazono, Hidenori Mizugaki, Kuniko Sunami, Shigehiro Yagishita, Yuichiro Koga, Takahiro Tsuji

Introduction

Lung cancer is the leading cause of cancer death in Japan and worldwide. The majority of lung cancer patients are diagnosed at an advanced stage, and the prognosis of these patients is poor. The standard treatments for non-small cell lung cancer (NSCLC) are chemoradiotherapy for locally advanced disease and platinum doublet chemotherapy for metastatic disease. Recently, several driver gene alterations such as EGFR mutation and ALK, Ros 1, or RET fusion gene, have been identified in NSCLC. Inhibitors for these molecules show excellent response against tumors with these driver gene alterations. Optimal treatment selection based on tumor molecular analysis and biomarker analysis is a major research issue in this field. The standard treatments for small cell lung cancer (SCLC) are chemoradiotherapy with etoposide plus cisplatin (EP) and accelerated hyperfractionated thoracic radiotherapy (AH-TRT) for limited disease and irinotecan plus cisplatin (IP) for extensive disease.

The Department of Thoracic Oncology provides the most effective treatment available for each patient and also works on the establishment of new effective treatments against lung cancer and other thoracic malignancies.

Routine activities

The Department of Thoracic Oncology includes 6 staff physicians. A total of 5 chief residents, 9 residents and 4 short-term residents joined the Department during 2013. The staff physicians attend outpatient services for thoracic diseases, and the division has 55-60 beds in the hospital. Inpatient care is carried out by five teams. Each team consists of one staff physician and one or two chief residents and residents. Case conferences are scheduled every Monday afternoon and Thursday evening. Protocol conference and a journal club are scheduled every Monday morning and Thursday morning, respectively. The chest conference, a tumor board, is held on Thursday afternoons to discuss cases with thoracic surgeons, pathologists, radiologists and radiation oncologists.

A total of 299 new patients were admitted in 2013 (328 and 305 patients in 2012 and 2011, respectively). The diagnoses for these patients and initial treatments for 270 lung cancer patients are listed in Tables 1 and 2, respectively. The survival outcomes of lung cancer patients treated in the Department are shown in Table 3.

Research activities

The Research activities of the Department can be classified into four categories: (1) phase I/II studies to develop new effective chemotherapy regimens including new drugs; (2) multi-institutional phase III studies such as Japan Clinical Oncology Group (JCOG) studies to establish new standard treatments against thoracic malignancies; (3) translational research using clinical samples for the development of biomarkers and innovative treatment strategies; and (4) pharmacokinetic and pharmacodynamic (PK/PD) studies to investigate optimal drug exposure and interpatient variability.

Clinical trials

The Department carried out more than 40 clinical trials in 2013. Some studies were based on the JCOG Lung Cancer Study Group research program, and some were carried out under contract with pharmaceutical companies or as an in-house protocol. In the JCOG 0509 study, amrubicin pus cisplatin failed to show non-inferiority to the standard IP for extensive-stage SCLC (J Clin Oncol, in press). In the JCOG0202 study, IP was not superior to EP after chemoradiotherapy with 1 cycle of EP and AH-TRT in limited-stage SCLC (Lancet Oncol). Alectinib, a new ALK inhibitor, showed an excellent response rate and progression-free survival with minimum toxicity for ALK-fusion positive NSCLC in a phase I/II study (Lancet Oncol). The translational study to investigate circulating endotherial cells (CEC) as a biomarker for response to anti-angiogenic agents, and PK/PD studies of erlotinib and crizotinib are ongoing.

Table 1. Number of New Inpatients in 2013

Non-small cell lung cancer	234
Adenocarcinoma	180
Squamous cell carcinoma	38
Others	16
Small cell lung cancer	36
Mesothelioma	3
Thymic cancer	8
Thymoma	1
Others	17
Total	299

Table 2. Initial Treatments for New Inpatients with Lung Cancer in 2013

Chemotherapy	167
Chemoradiotherapy	40
Adjuvant chemotherapy following surgery	40
Preoperative chemoradiotherapy	1
Thoracic radiotherapy	1
Supportive care alone (including palliative radiotherapy)	21
Total	270

Table 3. Survival Outcomes

Non-small cell lung cancer			
Unresectable stage III	204 patients treated with concurrent chemoradiotherapy in 1994-2005	Median	24.0 mo
		1-Year	75.5 %
		3-Year	34.7 %
		5-Year	22.8 %
Stage IV	480 patients treated with initial chemotherapy in 2000-2006	Median	13.2 mo
		1-Year	52.7 %
		3-Year	14.8 %
		5-Year	4.8 %
Small cell lung cancer			
limited disease	50 patients treated with concurrent chemoradiotherapy in 2001-2004	Median	28.8 mo
		2-Year	60.0 %
		5-Year	31.7 %
Extensive disease	108 patients treated with initial chemotherapy in 2001-2004	Median	12.1 mo
		2-Year	15.7 %
		3-Year	5.6 %

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Journal

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Department of Esophageal Surgery

Yuji Tachimori, Hiroyasu Igaki, Nobukazu Hokamura, Takayoshi Kishino, Hidetsugu Nakazato

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. 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. In Japan, squamous cell carcinomas still constitute the largest proportion of esophageal tumors, and the proportion of adenocarcinomas was 7% in our hospital in 2013.

Routine activities

The Department of Esophageal Surgery consists of three staff surgeons, one chief resident and 2-3 rotating senior residents. A multidisciplinary conference 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. Ninety one patients underwent esophagectomy including 2 patients with cervical esophageal cancer and 12 with adenocarcinoma in the esophagogastric junction, and also including four with carcinosarcoma and two with malignant melanoma. Of the 91 patients who underwent esophagectomy, a curative resection was completed for 90%. No hospital death occurred due to an operative complication. Preoperative chemotherapy was recommended for 48 patients and preoperative chemoradiotherapy was recommended for 11 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 54 patients as our standard procedure. Video-assisted thoracic surgery was introduced for esophagectomy as minimally invasive surgery in 23 patients.

In a paradigm shift toward organ-sparing procedures, the number of patients who receive definitive chemoradiotherapy as their primary treatment for resectable tumor, especially squamous cell carcinoma, is increasing. Of 33 patients with stage I squamous cell carcinoma, only 5 patients underwent esophagectomy. Persistent or recurrent loco-regional disease is not infrequent after chemoradiotherapy. Ten patients underwent salvage esophagectomy after the failure of definitive chemoradiotherapy in 2013. 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. Establishing a cell line of squamous cell carcinoma floating in the thoracic duct is being carried out. 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

The results of a multi-institutional randomized controlled trial (JCOG9907) confirmed preoperative chemotherapy with cisplatin and 5FU before esophagectomy as standard therapy for resectable Stage II-III esophageal cancer. A new 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) started on December, 2012 and is ongoing. A Phase II trial for definitive chemoradiotherapy with or without salvage esophagectomy (JCOG0909) is continuing 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. For a Stage I lesion, a multi-institutional randomized controlled comparison between surgery and definitive chemoradiotherapy (JCOG0502) has finished registration.

Table 1. Number of patients who underwent surgery

Cervical esophageal squamous cell carcinoma	2
Thoracic esophageal squamous cell carcinoma	85
Adenocarcinoma	12
Carcinosarcoma	4
Malignant melanoma	2
GIST	1
Gastric tube cancer	1
Total	106

Table 2. Type of surgical procedure

Esophagectomy with reconstruction	58
Salvage esophagectomy with reconstruction	8
Video-assisted esophagectomy with reconstruction	21
Video-assisted salvage esophagectomy with reconstruction	2
Esophagectomy without reconstruction	2
Staged reconstruction	5
Enucleation of esophageal submucosal tumor	1
Gastric tube resection with reconstruction	1
Salvage lymph node dissection	8
Exploration	1
Total	108

Table 3. Table 3 Survival after esophagectomy (2004-2008)

pStage (UICC TNM 6th)	Number	5-year survival (%)
pStage I	114	91.0
pStage IIA	76	64.5
pStage IIB	103	62.6
pStage III	193	34.7
pStage IVA	27	37.0
pStage IVB	84	26.6

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2. Wang S, Tachimori Y, Hokamura N, Igaki H, Kishino T, Kushima R. Diagnosis and surgical outcomes for primary malignant melanoma of the esophagus: a single-center experience. Ann Thorac Surg, 96:1002-1006, 2013
3. Hara H, Tahara M, Daiko H, Kato K, Igaki H, Kadowaki S, Tanaka Y, Hamamoto Y, Matsushita H, Nagase M, Hosoya Y. Phase II feasibility study of preoperative chemotherapy with docetaxel, cisplatin, and fluorouracil for esophageal squamous cell carcinoma. Cancer Sci, 104:1455–1460, 2013
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Department of Gastric Surgery

Hitoshi Katai, Takeo Fukagawa, Shinji Morita, Masaki Ohashi, Hiroshi Katayama, Masahiro Maeda, Nao Yoshizawa

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 Gastrointestinal Medical Oncology Division, so that specialists from both divisions 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 tumors.

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 to be an important function. In 2013, more than 20 surgeons from various countries visited this Department for 2 weeks to 6 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 Division 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. JCOG0705 is a trial to evaluate the significance of reduction surgery. 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 is a study to prove the non-inferiority of laparoscopic gastrectomy over its open counterpart for patients with clinical stage IA and IB gastric cancer. 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. A phase II study to check feasibility of Oxaliplatin, and S-1 neoadjuvant chemotherapy for stage III disease has been carried out.

Table 1. Number of Patients

Adenocarcinoma	443
GIST	12
Others	20
Total	475

Table 2. Operative morbidity and mortality after gastrectomy

	Number of patients	%
Major complications	41	12.0
Minor complications	96	28.0
Postoperative hospital deaths	0	0
Total	342	

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	167
Total gastrectomy	71
Completion gastrectomy	11
Pylorus-preserving gastrectomy	46
Proximal gastrectomy	18
Wedge resection	15
Pancreaticoduodenectomy	1
Laparoscopic distal gastrectomy	14
Laparoscopic pylorus preserving gastrectomy	14
Other (bypass, exploration, etc.)	118
Total	475

Table 4. Survival Rates

Stage	No. of patients	5-yr survival
IA	1766	94.2%
IB	545	91.4%
II	468	78.6%
IIIA	345	60.3%
IIIB	191	45.1%
IV	703	14.5%
Total	4018	73.4%

Stage: Japanese classification (13th ed.)
Period: 1995-2004

List of papers published in 2013
Journal

1. Kawabata H, Oda I, Suzuki H, Nonaka S, Yoshinaga S, Katai H, Taniguchi H, Kushima R, Saito Y. Bone metastasis from early gastric cancer following non-curative endoscopic submucosal dissection. World J Gastroenterol, 19:5016-5020, 2013
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Department of Colorectal Surgery

Yukihide Kanemitsu, Dai Shida, Shunsuke Tsukamoto, Taihei Oshiro, Ryouhei Sakamoto

Introduction

The Colorectal Surgery Division deals with colorectal cancer and allied malignancies in the colon and rectum. Liver metastasis from colorectal cancer is treated in cooperation with the Hepatobiliary and Pancreatic Surgery Division. Lung metastasis from colorectal cancer is also treated in cooperation with the Thoracic Surgery Division. 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 Gastrointestinal Oncology Division, Endoscopy Division, Radiology Division and Pathology Division every week, and decide treatment strategy with a multi-disciplinary team (MDT) before treatment is started.

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 8B and 15A, B. An MDT meeting is held for cancer patients as a form of institutionalized 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 division. Thus, we operate upon 450 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 (JCOG1007, iPACS) is ongoing. Patients with resectable liver metastasis are treated in cooperation with the Hepatobiliary and Pancreatic Surgery Division 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. Twelve clinical trials are underway, and the details are described in "Clinical Trials". 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. In 2013, we published papers, and the results of our research in 2013 are summarized as follows.

Clinical trials

Our division 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 division is participating in nine phase III JCOG studies.

1. JCOG0205: A randomized study that compares adjuvant oral UFT + LV to intravenous 5-FU +l-LV for pathological stage III colorectal cancer. One thousand, one hundred and ten eligible patients were enrolled and recruitment is complete. Follow-up is on-going.
2. 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.
3. JCOG0404: A randomized study that compares laparoscopic to open colectomy for clinical stage II or stage III colon cancer located at the cecum, ascending colon, sigmoid colon or rectosigmoid cancer. One thousand and fifty-seven eligible patients were enrolled and recruitment is complete. Follow-up is on-going.
4. 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.
5. JCOG0903: A phase I/II trial of chemoradiotherapy concurrent with S-1 plus mitomycin C in patients with clinical stage II/III squamous cell carcinoma of the anal canal is on-going.
6. JCOG0910: A randomized study that compares adjuvant Capecitabine to TS-1 for pathological stage III colorectal cancer. One thousand five hundred and five patients have been enrolled and recruitment is complete. Follow-up is on-going.
7. 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.
8. JCOG1007: A randomized controlled trial comparing resection of primary tumor plus chemotherapy with chemotherapy alone in incurable Stage IV colorectal cancer is ongoing.
9. 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.
10. 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	108	122
High anterior resection	12	8
Low anterior resection	60	38
Abdominoperineal resection	18	1
Hartmann's operation	5	
Intersphincteric resection	10	3
Total extirpation of large intestine	1	1
Total pelvic exenteration	2	
Total pelvic exenteration with sacrectomy	0	
Bypass	5	
Colostomy or ileostomy	52	
Local excision	1	
Other	55	

List of papers published in 2013
Journal

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Department of Gastrointestinal Medical Oncology

Yasuhiro Shimada, Yasuhide Yamada, Tetsuya Hamaguchi, Ken Kato, Satoru Iwasa, Yoshitaka Honma, Atsuo Takashima, Natsuko Okita, Hirokazu Shoji

Introduction

The Gastrointestinal Medical Oncology Division is focused on the development of new drugs and standard chemotherapy regimens combined with or without surgery and radiation for advanced colorectal, gastric and esophageal cancer, gastrointestinal stromal tumors and other gastrointestinal (GI) malignancies. Over recent years, a new generation of therapeutic agents has been developed. The highlights include the development of a molecular-targeted antibody directed against vascular endothelial growth factor (bevacizumab [BV]), and the finding that it causes changes in the microenvironment of the tumor by inhibiting angiogenesis. Another two molecular target-based drugs are the anti-epidermal growth factor receptor antibodies, cetuximab and panitumumab, which were approved in 2008 and 2010 for metastatic colorectal cancer. A multi-kinase inhibitor, regorafenib, was approved for colorectal cancer in 2013. For gastric cancer, an anti-HER2 monoclonal antibody, named trastuzumab, was also approved in 2011. In the near future we expect to identify other novel agents for the treatment of metastatic GI cancers that inhibit intracellular signal transduction or cellular interactions. However, many unusual adverse effects and a marked increase in medical cost have led to extensive discussion on more accurate targeting of the population using biomarkers. Although the response rates of these molecular-targeted drugs up to now have not been high (about 10 to 20%) when used broadly in 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, *K-ras* mutation in tumor tissue is one of negative predictive factors for the response to cetuximab. Accordingly, the identification of molecular markers that can be used to monitor tumor shrinkage or assist prognosis will be critical for the identification of possible new targets and for tailored treatments based on patient genotype or marker expression.

Routine activities

The staff of the GI Medical Oncology Division consists of 8 medical oncologists, 1 senior resident, and 3 or 4 residents. We hold a daily case conference together at 8 am before the morning rounds. Inter-group meetings with each surgical division (the Colorectal, Gastric, and Esophageal Surgery Divisions) and the Radiation Oncology Division are held weekly to decide upon treatment strategies for each individual case or to discuss future treatment strategies for the disease. Palliative care that considers the physical and psychological aspects of each case is another important issue discussed in staff meetings. The Palliative Care team and psycho-oncologists advise us on how to minimize patient discomfort and anxiety throughout end-of-life care. In 2013, we treated 2,210 hospitalized patients (635 of whom were newly diagnosed). Of these patients, 162 were entered in protocol studies.

Research activities

An endoscopic biopsy before chemotherapy provides an excellent opportunity for the use of microarray analysis to study biomarkers related to therapy-induced tumor response rates, overall survival, or time to recurrence. Biopsy specimens and blood samples were taken from patients before chemotherapy. Correlations between gene expression profiles and survival time or tumor shrinkage have been evaluated, and follow-up data in survival or recurrence are still being collected. Gene expression profiling of cancer tissues with microarray and real-time RT-PCR techniques would be useful for predicting outcomes in GI cancer. These studies are being performed in collaboration with the Center for Medical Genomics, National Cancer Center Research Institute, and other institutions.

We also measured the gene mutations of possible predictive biomarkers in 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 with a RT-PCR assay. Some of these results on the correlation between gene mutation profile and cancer outcomes

led to the clinical development of novel molecular targeted drugs, for example an anti-FGF antibody or FGF kinase inhibitor for gastric cancer. We also collected the serum of esophageal cancer patients who received neoadjuvant chemotherapy or chemoradiotherapy, and subjected it to a proteomics analysis. We detected some biomarkers which can predict the efficacy of the neoadjuvant treatment of esophageal cancer patients. We are going to confirm and validate these markers in a large phase III trial, JCOG1109.

Clinical trials

We carried out several clinical trials in collaboration with the Surgery and Radiation Oncology Divisions in our hospital and other institutes. These clinical trials are summarized in the Table. Major trials are conducted in collaboration with JCOG (Japan Clinical Oncology Group)

1. Colorectal Cancer

We investigated establishing combination chemotherapy regimens based on the oral fluoropyrimidine, S-1 (S-1/oxaliplatin/BV [SOXB], S-1/irinotecan/BV [SIRB]), for metastatic disease. Combination treatment with oral fluoropyrimidines is an important candidate to improve patient QOL, medical cost and medical staff burden. From the result of a randomized phase III trial to compare SOXB with FOLFOX plus BV at first-line chemotherapy for metastatic colorectal cancer (SOFT), non-inferiority of SOXB to FOLFOX plus BV has been demonstrated (Yamada Y et al. Lancet Oncol. 2013). We are also investigating whether SIRB is non-inferior to XELOX plus BV at first-line chemotherapy for metastatic colorectal cancer in a multicenter phase III trial (TRICOLORE).

For second-line chemotherapy, we are investigating the additive effect and feasibility of Aflibercept, a human recombinant fusion protein with antiangiogenic effects that functions as a decoy receptor to bind VGEF-A and B and placental growth factor, combined with FOLFIRI (5-FU/l-LV/Irinotecan) for colorectal cancer patients who failed to respond to first line treatment with FOLFOX or XELOX plus BV.

An adjuvant trial, JCOG0910, comparing S-1 with one of the standard regimens, capecitabine alone, started in March 2010 and finished patient recruitment (more than 1500 patients had been accrued from JCOG hospitals) in August 2013 on schedule. The phase III part of JCOG0603, a randomized study of adjuvant chemotherapy with mFOLFOX6 after complete resection of liver metastasis from colorectal cancer, is ongoing. The phase II part of JCOG0903, a phase I/II trial of chemoradiation with S-1/MMC for anal canal squamous cell carcinoma, continues to enroll patients.

2. Gastric cancer

A phase III study comparing three regimens (5-FU vs CPT-11/CDDP vs S-1) (JCOG9912) was already published in 2009. This was a pivotal study that established a new standard care protocol for advanced gastric cancer and cited the "New Japanese guidelines for diagnosis and treatment of carcinoma of the stomach", 2010 edition. A new pivotal phase III trial comparing S-1/CDDP (CS) to S-1/CDDP/Docetaxel (DCS) was started from April, 2012, and is progressing as expected. A phase I/II study of 5-FU/l-LV/paclitaxel (FLTAX) combination therapy as first-line therapy against this population has finished. A phase II/III study, comparing FLTAX with 5FU alone for patients who are inappropriate for CDDP usage due to severe peritoneal dissemination, started from April 2013. From the result of a randomized phase III trial to compare SOX with CS as first-line chemotherapy for metastatic gastric cancer (G-SOX), the non-inferiority of SOX to CS has been shown on PFS in the ASCO-GI meeting 2013.

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 additive effect of Nimotuzumab, an anti-epidermal growth factor receptor antibody, combined with irinotecan in second-line chemotherapy (ENRICH) has started as targeted on patients with high expression of EGFR. We also started a phase III trial which evaluates the additive effect of Olaparib, an inhibitor of poly ADP ribose polymerase (PARP), combined with paclitaxel in second-line treatment for the population against ENRICH trial.

For HER2 positive gastric cancer, we evaluated the second-line activity of trastuzumab with weekly paclitaxel in a multicenter phase II trial, and the feasibility and efficacy were shown in the 2013 ASCO meeting. We started a phase III trial which is evaluating the additive effect of Pertuzumab with capecitabine and cisplatin plus trastuzumab in the first-line treatment of metastatic HER2 positive gastric cancer. In second-line treatment of HER2 positive gastric cancer, a phase II/III trial comparing TDM-1 (ado-trastuzumab emtansine) with paclitaxel also started.

3. Esophageal Cancer

The results of our phase III study of preoperative versus postoperative 5-FU/CDDP (FP) (JCOG9907) were reported in 2007. Preoperative

FP was proven to be significantly superior to postoperative FP with regard to overall survival. Based on the results of this trial, the standard care for stage II/III esophageal cancer has been changed to preoperative FP followed by surgery. The large pivotal trial JCOG1109 which compared standard preoperative FP to DCF regimen (FP+Docetaxel) or FP +radiation regimen started from December 2012, and is progressing on schedule. A phase II study (JCOG0909) on the FP/RT (50.4 Gy) regimen plus salvage surgery with endoscopic resection in stage IB, II or III esophageal cancer is ongoing. A phase I/II study (JCOG0807) of a triplet regimen (5-FU+CDDP+Docetaxel) has finished the final analysis and has shown the feasibility of bi-weekly DCF regimen and a better tumor response compared with historical data at the 2013 ASCO meeting. A phase III trial comparing biweekly DCF with the standard FP regimen for metastatic esophageal cancer is under preparation in JCOG. Nimotuzumab is one of the anti-EGFR antibodies, which has shown activity for head and neck, gastric, and lung cancer. A phase I study of 5-FU+CDDP+Radiation with Nimotuzumab has finished and showed feasibility for stage IB/II/III/IVA esophageal cancer patients. A phase II study of BKM120, a PIK3CA inhibitor, in salvage line treatment is ongoing.

4. Other

An international phase III trial, RADIANT-4, which compared RAD001 to best supportive care in neuroendocrine tumor (NET) patients, has finished. For metastatic neuroendocrine carcinoma (NEC) in the GI-tract and hepato-billiary-pancreatic field, a phase III trial comparing irinotecan plus CDDP with etoposide plus CDDP as first-line treatment is under preparation in JCOG. We are participating in a phase II trial on neoadjuvant imatinib treatment for large gastric GIST, proceeding in Asian countries. Several phase I studies have been conducted as in the Table.

Table 1. Number of Patients Treated

	Total no. of hospitalized pts.	No. of newly diagnosed pts.	No. of pts. enrolled protocol
1) Esophageal cancer	770	188	
BKM120 (phase II)			7
Stage IB/II/III CRT+Salvage JCOG0909 (phase II)			8
Stage IB/II/III neoadjuvant CF vs DCF vs CF-RT JCOG1109 (phase III, NExT study)			24
2) Gastric cancer	767	191	
Bevacizumab/capecitabine/cisplatin (AVAGAST)			1
CS vs DCS JCOG1013 (phase III)			37
FL vs FLTAX JCOG1108 (phase II/III)			1
wPTX±Olaparib (phase III)			4
CPT-11±DE766 (phase III)			9
XP+Tmab±Pertuzumab (phase III)			1
T-DM1 vs wPTX (phase II/III)			6
3) Colorectal cancer	540	208	
Adjuvant Capecitabine vs S-1 JCOG0910 (phase III)			23
OCV*C02 (vaccine, phase I)			5
FOLFIRI+aflibercept (phase II)			3
Observation vs adjuvant FOLFOX for colorectal cancer after hepatic metastatectomy JCOG0603 (phase II/III)			3
Stage II/III S-1/MMC for anal canal cancer JCOG0903 (phase I/II)			3
FOLFIRI±IMC-1121B (ramucirumab/placebo) (phase III)			3
CapeOX+bevacizumab vs TS-1/irinotecan+bevacizumab (TRICOLORE, phase III)			19
mFOLFOX7 or CAPOX+Bevacizumab vs 5-Fluorouracil/Leucovorin or Capecitabine+Bevacizumab JCOG1018 (phase III)			12
4) Others	133	48	
NC6004 (phase I)			1
MSB0010718C (PDL-1, phase I)			2
LEE001 (phase I)			6
AMN107 vs imatinib (GIST, phase III			1
RAD001 vs BSC (NET, phase III)			3
BYL719 (phase I)			3
Total	2210	635	185

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Journal

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Department of Endoscopy, Gastrointestinal Endoscopy Divison

Yutaka Saito, Takahisa Matsuda, Ichiro Oda, Yasuo Kakugawa, Takeshi Nakajima, Shigetaka Yoshinaga, Yosuke Otake, Haruhisa Suzuki, Satoru Nonaka, Taku Sakamoto, Seichiro Abe and Minori Matsumoto, Shinji Sasada, Takaaki Tsuchida, Takehiro Izumo

Introduction

Our Endoscopy Division moved to a 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 has been increased to 16 and two endoscopy engineers are working with us.

The Gastrointestinal Endoscopy Division has 12 staff physicians in the National Cancer Center Hospital (NCCH) and in the Screening Technology and Development Division, four chief residents, 11 residents, three trainees and several rotating residents.

The Bronchoscopy Division has three staff and resident doctors and the total number of bronchoscopies and therapeutic procedures has 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 11,314, 3,367, 477, 85, 45, 140 and 29 screening and/or diagnostic procedures were performed in 2013 with gastroscopy, colonoscopy, EUS, EUS-fine needle aspiration (EUS-FNA), endoscopic retrograde cholangiopancreatography (ERCP), capsule endoscopy and double balloon endoscopies, respectively.

Due to the increasing number of patients with superficial gastrointestinal neoplasms, the number of therapeutic endoscopy procedures is also increasing in this field. In 2013, 2,146 endoscopic resections were carried out (pharynx 34, esophagus 189, stomach 375 and colon 1,582). Among these, ESD, which was developed for large en-bloc resections with a low-risk of local recurrence, was performed for 92 superficial esophageal cancers, 375early gastric cancers and 184 superficial colorectal neoplasms. For colorectal ESDs and some esophageal ESDs, the newly developed B-knife and IT-knife nano were used together with CO_2 insufflation. These procedures and devices were originally developed by our colleagues.

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. Endoscopy Center

Year	2007	2008	2009	2010	2011	2012	2013
Upper GI Endoscopy	10,910	10,909	10,174	10,644	10,810	11,193	11,314
Colonoscopy	3,569	3,161	2,670	2,756	2,924	3,232	3,367
EUS	373	375	402	395	372	393	477
EUS-FNA				48	59	69	85
Therapeutic Endoscopy	1,854	1,848	1,849	1,756	1,984		
Gastric EMR/ESD	24/410	19/397	36/375	23/334	23/343	361	375
Esophageal EMR/ESD	89/25	94/25	95/43	102/45	132/61	115/66	97/92
Colorectal EMR/ESD	1,212/97	1,216/97	1,177/123	1,132/120	1,210/125	1,402/133	1,398/184

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 a 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 multicenter 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.

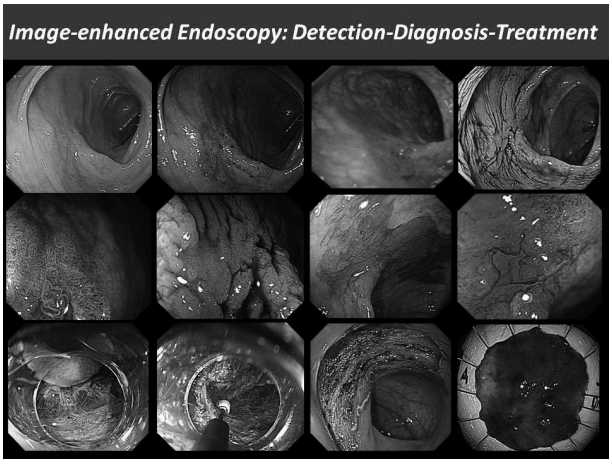

Figure 1. Endoscopic diagnosis using image-enhanced endoscopy (high-resolution endoscopy, narrow-band imaging and autofluorescence imaging) and endoscopic submucosal dissection (ESD) procedure for treating early colon cancer

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 chemoradiotherapy 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 using a high-resolution colonoscope with the removal of all detected neoplasia including flat and depressed lesions.. Finally, about 4,000 patients were enrolled in this study. This multicenter RCT has been 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 the 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 chemoradiotherapy for high-risk rectal submucosal cancer after endoscopic resections.

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Journal

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Department of Endoscopy, Respiratory Endoscopy Division

Shinji Sasada, Takaaki Tsuchida, Takehiro Izumo

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 on CT imaging, which can lead to earlier surgical treatment and less-invasive treatments including bronchoscopic procedures. This is facilitated by a multi-purpose bronchoscopy system consisting of a flat-panel fluoroscope in combination 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 is held. Furthermore, we attend 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 five 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 (9 cases), photodynamic therapy and endobronchial electrocautery ablation (11 cases). Medical thoracoscopy under local anesthesia in the operation suite was performed in 20 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

Our efforts have been focused on new diagnostic and therapeutic strategies including bronchoscopy, which involve CT-screening for lung cancer and lead to cure of, and less-invasive treatments for lung cancer. To achieve a more accurate endoscopic diagnosis for solitary peripheral lung nodules, we are using three-dimensional computed tomography (3D-CT) navigation, an ultrasound-guided approach and onsite cytology. With 3D-CT navigation and/or the ultrasound-guided approach and onsite cytology, the accuracy and sensitivity of transbronchial biopsy could be improved.

We also tried to improve the accuracy of GGO (ground grass opacity) imaging which had been impossible to visualize using routine chest radiography or X-ray fluoroscopy. Chest tomosynthesis (the SONIALVISION safire radiography/fluoroscopy system, Shimadzu, Japan) is a term coined from "tomography" and "synthesis" and is a device that permits reconstruction of the coronal section image at a desired depth in a single session of photography. It is used mainly in the field of orthopedics currently, but there has been a report recently that it is excellent in visualizing chest nodules. Tomosynthesis was able to confirm the site of the lesion at a desired depth of the coronal section using chest tomosynthesis image mapping before bronchoscopic examination, and the lesion was diagnosed as an adenocarcinoma with a transbronchial biopsy.

Clinical trials

We have started a clinical trial on detection of biomarker profiling using small specimens obtained with bronchoscopy or thoracoscopy in patients with lung cancer. We are additionally planning a prospective study for evaluation of the use of the IT knife for medical thoracoscopy.

Table 1. Type of procedure

Diagnostic bronchoscopy under X-ray fluoroscopy	554
Diagnostic bronchoscopy without X-ray fluoroscopy	211
Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA)	175
Medical thoracoscopy	20
Airway stent placement	9
Photodynamic therapy (PDT), Electrocautery ablation	11
Bronchial occlusion (EWS)	6
Total	986

List of papers published in 2013
Journal

1. Izumo T, Sasada S, Chavez C, Nagai Y, Kitagawa M, Torii J, Iwase T, Aso T, Nakamura Y, Mizumori Y, Deng C, Xu W, Tsuchida T, Moriyama N. The value of chest tomosynthesis in locating a ground glass nodule (GGN) during endobronchial ultrasonography with a guide sheath: a case report. J Thorac Dis, 5:E75-77, 2013
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Department of Hepatobiliary and Pancreatic Surgery

Kazuaki Shimada, Tomoo Kosuge, Minoru Esaki, Satoshi Nara, Yoji Kishi, Shutaro Hori, Yasuhito Iwao

Introduction

The Hepatobiliary and Pancreatic (HBP) Surgery Division 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 Diagnostic Radiology Division, HBP Oncology Division and Pathology Division.

Routine Activities

The HBP Surgery Division consists of five staff surgeons and we perform around 300 surgeries each year, along with one chief resident and three or four residents. Occasionally, trainees from both Japan and overseas join our group.

Operation and perioperative care

Five to seven major operations for hepatobiliary and pancreatic malignancies are performed every week. One staff surgeon and one resident are in charge of each patient, and conduct the operation and provide postoperative care. The chief resident attends all the operations, supervises the four 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 the "Cherry Conference," surgeons and radiologists discuss imaging studies of selected patients. 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, the situation regarding the progress of academic studies, including clinical research and paper writing, is evaluated.

Surgical strategies for HBP malignancies

Hepatocellular carcinoma (HCC): Surgical treatment for HCC is always determined based on the balance between the 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. 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 adjuvant chemotherapy has become the standard strategy for this potentially incurable disease. Resection of borderline malignancies, such as pancreatic cystic neoplasms and 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 the extent of the cancer, 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 extrahepatic bile duct resection is considered as the first-line procedure for hilar cholangiocarcinoma.

Research Activities and Clinical trials

Dr. Kosuge et al. reported on 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 the "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 devices 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 an energy-based device 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' recruitment and registration have finished and data are being analyzed. Dr. Nara et al. are now proceeding with a study to evaluate the feasibility of laparoscopic hepatectomy in this hospital. These studies are supported by Grants-in-Aid for scientific research from the Ministry of Health, Labour and Welfare of Japan.

Table 1. Number of patients

	n
Invasive pancreatic cancer	81
Other pancreatic neoplasms	36
Hepatocellular carcinoma	32
Hepatic metastases	69
Intrahepatic cholangiocarcinoma	4
Bile duct cancer	23
Gallbladder cancer	10
Ampullary cancer	8
Duodenal cancer	3
Others	46
Total	312

Table 2. Type of procedures

	n
Hepatectomy without biliary resection	105
Hepatectomy with biliary resection	16
Left hemihepatectomy and pancreaticoduodenectomy (HPD)	2
Classical Whipple (CW)	25
Pylorus-preserving pancreaticoduodenectomy (PPPD)	45
Distal pancreatectomy	35
Appleby operation	1
Medial pancreatectomy	4
Total pancreatectomy	6
Extended cholecystectomy	10
Other resections	33
No resection	30
Total	312

Table 3. Survival rates

Invasive ductal carcinoma (2001-2010)

Stages	n	3-year survival rate (%)	5-year survival rate (%)
I	12	57	57
II	7	67	50
III	88	54	42
IVa	254	40	27
IVb	126	25	15
Total	487	40	28

Hepatocellular carcinoma (2001-2010)

Stages	n	3-year survival rate (%)	5-year survival rate (%)
I	37	86	71
II	156	88	80
III	216	72	59
IV	77	58	41
Total	486	76	64

List of papers published in 2013
Journal

1. Otsuka T, Morizane C, Nara S, Ueno H, Kondo S, Shimada K, Kosuge T, Ikeda M, Hiraoka N, Okusaka T. Gemcitabine in patients with intraductal papillary mucinous neoplasm with an associated invasive carcinoma of the pancreas. Pancreas, 42:889-892, 2013
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Department of Hepatobiliary and Pancreatic Oncology

Takuji Okusaka, Hideki Ueno, Chigusa Morizane, Shunsuke Kondo, Yasunari Sakamoto, Hideyuki Hayashi, Satoshi Shiba

Introduction

The Hepatobiliary and Pancreatic Oncology Division 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 Division consists of five staff oncologists and three to four residents. In 1990, the Division 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 division are made by all staff oncologists and residents every morning and evening.

Research activities

A phase III study was designed to investigate the noninferiority of S-1 alone and superiority of gemcitabine plus S-1 compared with gemcitabine alone with respect to overall survival (Ueno et.al). The participants were chemotherapy-naive patients with locally advanced or metastatic pancreatic cancer. In the total of 834 enrolled patients, the median overall survival was 8.8 months in the gemcitabine group, 9.7 months in the S-1 group, and 10.1 months in the gemcitabine plus S-1 group. The noninferiority of S-1 to gemcitabine was demonstrated (hazard ratio, 0.96; 97.5% CI, 0.78 to 1.18; $P < .001$ for noninferiority), whereas the superiority of gemcitabine plus S-1 was not (hazard ratio, 0.88; 97.5% CI, 0.71 to 1.08; $P = .15$). All treatments were generally well tolerated, although hematologic and GI toxicities were more severe in the gemcitabine plus S-1 group than in the gemcitabine group. Monotherapy with S-1 demonstrated noninferiority to gemcitabine in overall survival with good tolerability and presents a convenient oral alternative for locally advanced and metastatic pancreatic cancer.

A randomized phase II trial was designed to evaluate the safety and efficacy of two regimens: gemcitabine plus S-1 (GS) and S-1 (Morizane et al). The regimen with a higher 1-year survival would be selected for a subsequent phase III trial. For the GS (n = 51) and S-1 (n = 50) arms, the 1-year survival was 52.9% (95% confidence interval, 38.5-65.5) and 40.0% (95% confidence interval, 26.5-53.1), and the median survival times were 12.5 and 9.0 months, respectively. Grade 3/4 hematological toxicities were more frequent in the GS arm than in the S-1 arm. In conclusion, GS was considered to be more promising and was selected as the test regimen for a subsequent phase III trial comparing GS with gemcitabine plus cisplatin combination therapy.

Using pancreatic carcinoma cell lines and gene transfectant, we measured the long pentraxin (PTX3) level in culture solution and carried out a cellular migration assay *in vitro* (Kondo et al). Elevated PTX3 production was observed in several cell lines, and a direct relationship between migratory activity and the PTX3 level was identified *in vitro*. A high PTX3 level (117 days) was significantly less than that of patients with a low PTX3 level (357 days,

P<0.001). A multivariate analysis of the pancreatic carcinoma revealed a strong correlation between pentraxin family member expression and prognosis of pancreatic carcinoma. Pentraxin family members, especially PTX3, may be used as promising biomarkers in the prognosis of pancreatic carcinoma patients.

Clinical trials

Thirty-two clinical trials are ongoing, including seven phase III trials, such as adjuvant chemotherapy versus placebo in HCC patients who had undergone hepatic resection or local ablation therapy, and chemotherapy with a new regimen versus standard chemotherapy in biliary cancer patients. Two studies are collaboration trials with the Department of Diagnostic Radiology, and one with the Department of Radiation Oncology. Three trials are being conducted to evaluate cancer immunotherapy. Our studies are supported by the National Cancer Center Research and Development Fund (Grant No. 23-A-22, No. 23-B-5), Health and Labour Sciences Research Grants (Grant No. H23-ganrinsho-ippan-006, No. H25-sanjigan-shitei-006, No. H25-kanen-ippan-014) from the Ministry of Health, Labour, and Welfare of Japan.

Table 1. Number of patients

	No. of pts.
Pancreatic cancer	
Invasive ductal	126
Neuroendocrine	6
Others	12
Biliary tract cancer	
Extrahepatic bile duct	7
Gallbladder	10
Papilla of Vater	2
Liver cancer	
Hepatocellular	208
Intrahepatic cholangiocarcinoma	6

Table 2. Type of procedure

	No. of pts.
Pancreatic cancer	
Systemic chemotherapy	128
Chemoradiotherapy	14
Biliary tract cancer and Intrahepatic cholangiocarcinoma	
Systemic chemotherapy	25
Hepatocellular carcinoma	
Ethanol injection	11
Radiofrequency ablation	46
Transcatheter arterial (chemo)embolization	111
Intra-arterial chemotherapy	18
Systemic chemotherapy	32
Radiotherapy	9

Table 3. Survival rates

Diagnosis	No. of pts.	MST (mo)	Survival (%)
Pancreatic cancer			
Advanced	392	10.2	1-yr: 42.3
Biliary tract cancer and Intrahepatic cholangiocarcinoma			
Advanced	184	11.6	1-yr: 47.3
Hepatocellular carcinoma			
Radiofrequency ablation	63	87.7	5-yr: 65.5
Transcatheter arterial embolization	263	40.4	3-yr: 55.4
Systemic chemotherapy	46	8.5	1-yr: 40.9

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Department of Urology

Hiroyuki Fujimoto, Hiroyuki Nakanishi, Motokiyo Komiyama, Takashi Kawahara, Tomohiko Hara

Introduction

In the Urology Division, 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 five staff physicians and two residents. 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. A clinicopathological conference is scheduled on alternating Wednesdays.

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 an M-VAC regimen. N+, systemic chemotherapy, radiation; sometimes urinary diversion alone. M+, chemotherapy with a 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 1st 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. In local advanced disease, a phase III study to evaluate the survival benefit of continuous endocrine therapy after 3D conformal radiotherapy is still underway. For hormone-refractory prostate cancer, a study on a new hormonal regime with TAK700 has completed enrollment.
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: TAK700 for hormone-refractory prostate cancer
5. A phase II study: IKT1 for chemo-refractory prostate cancer

Table 1. Patient statistics: Major treatment

	2008	2009	2010	2011	2012	2013
Radical/partial nephrectomy	28	43	35	30	46	39
Nephroureterectomy	11	16	15	12	17	8
Total cystectomy	22	26	31	24	25	24
TURBT	161	163	130	140	130	117
M-VAC	31	42	62	50	62	45
GC	-	50	71	84	83	70
Radical prostatectomy	105	111	98	111	87 (RALP 2)	84 (RALP32)
Prostatic biopsy	186	247	168	175	151	128
High orchiectomy	7	6	12	8	6	6
Retroperitoneal lymphadenectomy	10	7	8	13	6	5
Chemotherapy for testicular cancer	10	9	14	30	35	7
Retroperitoneal tumor resection	9	9	15	10	18	13

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Department of Gynecology

Takahiro Kasamatsu, Tomoyasu Kato, Mitsuya Ishikawa, Shun-ichi Ikeda, Satoshi Okada

Introduction

The Gynecologic Oncology Division 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 three 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 five gynecologic oncologists. In addition, our division includes 2 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 high-grade dysplasia, carcinoma in situ, or Ia1 cervical cancer. Patients with stages Ia2 to IIIa 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. 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. In our practice, positive peritoneal cytology is not a poor prognostic factor for patients with a well-differentiated tumor confined to the uterus, whereas 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 several courses of chemotherapy, an interval debulking surgery (IDS) is usually performed for these patients. Surgery alone can offer the chance of cure for patients with recurrence, but only when the disease is completely resectable. The type of surgical procedure, patient number, and survival rates are shown in Tables 1, 2, and 3.

Research activities

A phase III study of dose dense TC chemotherapy (JCOG PC1311) for patients with advanced or recurrent cervical cancer is now being projected. 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 is also being planned. A multicenter retrospective study on rare tumors of . gynecologic malignancy is in progress.

Clinical trials

A phase III study to compare treatment starting with neoadjuvant chemotherapy and primary cytoreductive surgery followed by postsurgical chemotherapy (JCOG 0602) for advanced ovarian cancer is ongoing as planned. A nonrandomized confirmatory trial of modified radical hysterectomy for patients with FIGO stage Ib1 (< 2 cm) uterine cervical cancer (JCOG1101) has been started. A phase I/II study on Heavy Ion Radiotherapy with concurrent chemotherapy for locally advanced cervical adenocarcinoma using the Heavy Ion Medical Accelerator is ongoing in Chiba (HIMAC, National Institute of Radiological Sciences).

Table 2. Type of procedure

Radical hysterectomy	27
Simple hysterectomy	165
±Salpingo-oophorectomy	
± Lymphadenectomy	
± Omentectomy	
± Lymphadenectomy	
Conization	10
Vulvectomy	1
Others	17
Total	220

Table 1. Number of patients

	Stage	2007	2008	2009	2010	2011	2012
Cervical cancer	IA	6	8	7	5	4	7
	IB	29	32	33	40	33	23
	II	18	13	13	5	4	15
	III	18	12	7	13	12	10
	IV	2	4	8	2	5	10
	Total	73	69	68	65	58	65
Endometrial cancer	I	40	42	42	41	39	49
	II	7	5	6	4	8	5
	III	14	20	15	9	22	10
	IV	3	1	9	4	2	2
	Total	64	68	72	58	71	66
Ovarian cancer	I	15	15	13	16	9	13
	II	9	3	4	3	4	3
	III	8	11	18	13	11	17
	IV	7	2	5	3	2	1
	NAC[a]	8	9	5	8	9	13
	Total	47	40	45	43	39	47

[a] Neo adjuvant chemotherapy

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Department of Musculoskeletal Oncology and Rehabilitation

Hirokazu Chuuman, Akira Kawai, Fumihiko Nakatani, Yoshikazu Tanzawa, Eisuke Kobayashi, Koichi Ogura, Daisuke Kubota, Nokitaka Setsu, Tomohiro Fujiwara

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 Chuman, 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 consults are held every weekday. A consistent number of about 34 patients are hospitalized to undergo an operation, chemotherapy or radiation therapy. Five or six major operations are routinely performed every week. In 2013, 272 operations were performed under general anesthesia, including palliative operations for pathological fractures or spinal cord compression from metastatic bone and soft tissue tumors. Sarcomas in the trunk, including the thoracic wall, retroperitoneal space and head and neck lesions, were excised in cooperation with thoracic, general or head-neck surgeons, respectively. A total of 54 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 Research Institute of the NCC 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 sarcomas of soft tissues.. 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 sarcomas and osteosarcomas with the aim of developing novel molecular targeted therapies

Clinical trials

We have been conducting clinical trials of image-guided surgery to improve the accuracy of operation procedures using multi-modality imaging systems including open MRI, self-mobile CT and the angio-system C-arm in the surgical room (MR/CT operation suite). Using this system, we are trying to establish an optimum minimally invasive surgerical approach but with adequate safe surgical margins to eliminate local recurrences.

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 3 clinical trial of multidrug adjuvant chemotherapy for osteosarcomas (JCOG 0905) ongoing since 2010.
2. A multi-institutional phase 3 study of trabectedin for advanced soft tissue sarcoma active since 2012.
3. A multi-institutional phase 2 study of Eribulin (an inhibitor of microtubule dynamics) for advanced soft tissue sarcoma which started in 2011.
4. A multi-institutional phase 3 clinical trial of multidrug adjuvant chemotherapy for high grade soft part sarcoma (JCOG 1309) has started in February 2014.

Table 1. New patients (2013)

1	Soft tissue sarcomas	101
2	Bone sarcomas	32
3	Benign bone and soft tissue tumors	74
4	Spine or bone metastasis	11
Total		217

Table 2. Type of procedure

1	Soft tissue sarcomas	105
2	Bone sarcomas	29
3	Benign bone and soft tissue tumors	99
4	Spine or bone metastasis	31
	Plastic surgery combined	54
	Reconstruction with prosthesis	15
	Spine surgery	3
Total		290

List of papers published in 2013
Journal

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Department of Dermatologic Oncology

Naoya Yamazaki, Arata Tsutsumida, Akira Takahashi, Kenjiro Namikawa, Wataru Omata, Kohei Oashi, Kohei Nojima

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 1800 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 191, which was approximately twice - the number 3 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 four staff dermatologic oncologists and three residents. We are also engaged in routine outpatient activities on Wednesdays and Thursdays in the National Cancer Center East.

In 2013, a total of 327 patients were examined for the first time in the Dermatology Department for a malignant skin tumor. The numbers of patients with malignant melanoma (191) and extramammary Paget's disease (16) were particularly large, and were approximately 4 times and 2 times, respectively, the numbers 15 years ago. There were also 10 cases of the rare cancer, angiosarcoma.

About 20 patients are hospitalized to undergo surgery, chemotherapy, or radiation therapy. In 2013, 254 operations were performed including 106 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 melanoma

The Department of Dermatologic Oncology has been part of the melanoma research group in Japan and its work is partly supported by Management Expenses Grants from the Government to the National Cancer Center.

In 2011 the JCOG Dermatologic Oncology Group was established to improve the standard treatment for Japanese skin cancer patients.

We have taken part in a Japanese multicenter joint study on sentinel lymph node (SLN) biopsies. At the Department of Dermatologic Oncology, SLN biopsies for malignant melanoma are performed with the injection of technetium tin colloid, blue dye plus the fluorescence method (combination of indocyanine green and the Photodynamic Eye System). The addition of a real-time fluorescent navigation system with indocyanine green as a new technique achieved a detection rate of 100%. Of all the patients in whom SLNs were identified and biopsied, about 35% had metastasis.

We planned a phase 2 clinical study of an original nivolumab administration method: 2 mg/m^3, every 3 weeks. Enrolment of the 35 patients was started all over Japan in December 2011 and was completed in 4 months. That was quite a surprise, because it was very quick. At the same time it was once again very clear that there are many melanoma patients, and not only was it clear that melanoma patients exist, but that both patients and physicians are troubled by the lack of drugs for treatment and have been hoping for the development of new drugs. The results of the phase 2 study of nivolumab showed a response rate of 22.9%. The most dangerous adverse effect, interstitial pneumonia, developed in only one patient.

Extramammary Paget's disease

When extramammary Paget's disease infiltrates the dermis, it becomes apocrine adenocarcinoma and gives rise to regional lymph node metastasis in a high

proportion of cases. Despite the poor prognosis for patients with lymph node metastasis, management of this disease without clinical evidence of involved nodes is controversial, and yet there is still not a TNM stage classification. We have reported that a favorable outcome is achieved with radical lymph node dissection only when there is a solitary regional lymph node metastasis. The 5-year extramammary Paget's disease specific survival rate for patients with a solitary regional lymph node metastasis was 100%, although that with more than three lymph nodes metastases was 0 %. Therefore, SLN biopsies for extramammary Paget's disease are important in the initial surgical treatment.

Clinical trials

This fiscal year we were supported in part by Management Expenses Grants from the Government to the National Cancer Center, and Health and Labour Science Research Grants from the Ministry of Health, Labour and Welfare.

(1) Sentinel lymph node detection in malignant melanoma patients using real-time fluorescence navigation with indocyanine green.
(2) Postoperative natural interferon beta therapy in stage II, III cutaneous malignant melanoma.
(3) A phase I dose-escalation, safety/tolerability and preliminary efficacy study of intratumoral administration of GEN0101 in patients with advanced melanoma.

The clinical trials (industry-sponsored registration trials) are summarized in Table 3.

(1) We have conducted seven kinds of industry-sponsored registration trials for malignant melanoma.
(2) We are carrying out some clinical trials in collaboration with the Investigational Drug Development and Hematology Divisions in our hospital.

Table 1. Number of New Patients

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

Table 2. Operative Procedures (total number)

Wide local excision	150
Local excision	74
Sentinel node biopsy	42
Lymph node biopsy	9
Lymph node dissection	25
(neck)	6
(axilla)	7
(inguinal)	4
(groin)	8
(popliteal)	0
(epitrochlear)	0
Skin graft	23
Local flap	6
Free flap	1
Amputation	8
others	2

Table 3. New Agent Studies in 2013

Agent	Eligible Cancer Type	Trial Phase
ONO-4538	Melanoma	II
ONO-4538	Solid Tumors	I
MAGE-A3	Melanoma	III
BCX1777	T/NK-Cell Lymphoma	I
E7777	Peripheral/Cutaneous T Cell Lymphoma	I/II
Lenalidomide	ATL, Peripheral T Cell Lymphoma	I
PDX	Peripheral T Cell Lymphoma	I/II
Romidepsin	Peripheral/Cutaneous T Cell Lymphoma	I/II
Vemurafenib	Melanoma	I/II
Ipilimumab	Melanoma	II
SCH54031	Melanoma	I
Dabrafenib	Solid Tumors	I
BYL719	Solid Tumors	I
RO4987655	Solid Tumors	I
WT4869	Solid Tumors	I
AZD8931	Gastric Cancer	II
PF-00299804	Lung Cancer	III
Lenalidomide	ATL	II
Dabrafenib/Trametinib	Melanoma	I/II
LGX818	Solid Tumors	I
MEK162	Melanoma	III

List of papers published in 2013
Journal

1. Namikawa K, Yamazaki N. A case of scalp angiosarcoma with lung metastases presenting as multiple thin-walled cysts. Jpn J Clin Oncol, 43:101, 2013
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Department of Hematology

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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 Department 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 four rotating residents are involved in these activities.

Research activities

In addition to immunophenotypic analyses, molecular diagnosis is routinely performed, using the 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, etc. 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 the A20 gene as a tumor suppressor gene in various B-cell malignancies (Nature 2009;459:712-6). The gene is involved in NFkappaB signaling and its status could be a biomarker for BCR inhibitors.

This year, we authored or coauthored 23 original articles related to hematological malignancies. We have constructed a tumor sample banking system, collecting the rest of samples taken as routine diagnostic procedures. The DNA and RNAs are extracted from the samples and reserved for future use.

Clinical trials

In 2013, we conducted 27 new-agent studies, including 8 international studies, and 7 cooperative group studies in Japan (Tables 2 and 3). The numbers are still increasing including the domestic studies. 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, Labour and Welfare (MHLW).

Various phase I and II trials are ongoing on T-cell malignancies. The agents include mogamulizumab, lenalidomide, romidepsin, forodesine, and denileukin diftitox. Some of the agents are being evaluated in global studies. For indolent ATL, we started to evaluate anti-viral agents of interferon-alfa and AZT, as a phase III study (JCOG 1111).

A phase I study of oligopeptide vaccine OCV-501 against WT1 protein in AML cells to keep patients in complete remission, was completed and moved on to a randomized phase II trial. The agent was developed in Japan, and this is the first study against hematological malignancies aiming at approval by the MHLW.

For treatment of B-cell malignancies, a phase III trial for newly diagnosed, diffuse large B-cell lymphoma (JCOG 0601) is ongoing. In this trial, a dose-intense schedule of rituximab is being

compared with that of a standard 3-weekly regimen. We completed a phase II study of a rituximab-incorporating dose-intensified chemotherapy for untreated mantle cell lymphoma (JCOG 0406), using high-dose chemotherapy with autologous stem cell transplantation. For symptomatic multiple myeloma patients ineligible for transplantation, we initiated 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
Acute myelocytic leukemia (AML)	9	10	6	10	8	13	12	7
Acute lymphocytic leukemia (ALL)	4	9	8	2	2	1	1	6
Chronic myelocytic leukemia (CML)	10	11	3	3	2	2	2	2
Myelodysplastic syndrome (MDS)	3	9	8	20	9	3	3	6
Hodgkin lymphoma (HL)	21	11	12	7	11	16	15	13
Non-Hodgkin lymphoma (NHL)	265	210	208	151	185	243	172	193
Adult T-cell leukemia-lymphoma (ATL)	6	4	5	5	3	6	6	4
Chronic lymphocytic leukemia (CLL)	4	5	6	4	2	1	4	1
Multiple myeloma (MM)	9	8	10	12	9	10	7	8
Waldenström macroglobulinemia (WM)	0	2	3	1	2	2	1	0
Total	331	279	269	215	233	297	223	240

Table 2. Clinical trials for new agents

Disease	Agents	Phase	Enrolment in 2013	Total
CML	Nilotinib	III	0	1
	Bosutinib	I/II	0	3
	Ponatinib	I	2	3
MDS	Panobinostat + Azacitidine	Ib	4	4
	Rigosertib	I	1	1
AML	WT1 vaccine	I	1	4
	WT1 (maintenance)	I	2	4
	Volasertib	I	5	6
ALL	Inotuzumab ozogamicin	I	1	1
MM	Carfilzomib	I	1	1
	Carfilzomib	I/II	5	8
	Anti-BAFF antibody	I	2	2
	Pomalidomide	I	2	2
ATL	Lenalidomide	II	0	1
PTCL	Forodesine	I/II	3	3
	Romidepsin	I/II	0	6
FL	Ofatumumab vs. Rituximab	III	6	31
	Ofatumumab + Bendamustine	III	2	4
	Obinutuzumab	III	4	16
MCL	R-B +/- Ibrutinib	III	1	1
DLBCL	Ofatumumab	III	2	3
	Inotuzumab ozogamicin	III	0	7
	Obinutuzumab	III	2	2
	Alisertib (MLN8237)	I	2	5
HL	SGN-35	III	2	2
B-NHL	Ibrutinib	I	4	7
AML, ML, MM	OPB-51602	I	1	2

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 97	III	(98-01)	15	79%	47% (5-yr)
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
Therapy-related leukemia	II	(96-99)	16	75%	40% (3-yr)
ALL/Lymphoblastic lymphoma					
JCOG 9004	II	(91-94)	14	83%	31% (7-yr)
JCOG 9402	II	(94-99)	10	81%	29% (5-yr)
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
Hodgkin lymphoma					
JCOG 9305	II	(93-97)	7	79%	89% (5-yr)
JCOG 9705	II	(98-00)	6	70%	81% (5-yr)
Aggressive NHL					
JCOG 9505	II(c)	(95-98)	2	56%	42% (4-yr)
JCOG 9506	II	(95-97)	6	50%	49% (5-yr)
JCOG 9508	II	(96-99)	19	80%	68% (5-yr)
JCOG 9809	III	(99-02)	55	62%	56% (8-yr)
JCOG 0601	III	(08-)	49	NA	NA
JCOG 0406	III	(08-)	5	NA	NA
JCOG 0908	III	(08-)	16	NA	NA
Indolent B-cell lymphoma					
JCOG 0203	II/III	(02-07)	52	77%	88% (6-yr)
Adult T-cell leukemia-lymphoma					
JCOG 9303	II	(94-97)	6	36%	31% (2-yr)
JCOG 9801	III	(98-03)	6	33%	19% (3-yr)
JCOG 1111	III	(13-)	1	NA	NA
Nasal NK/T-lymphoma					
JCOG 0211-DI	I/II	(03-07)	8	77%	78% (2-yr)
Multiple myeloma					
JCOG 9301	III	(93-98)	10	50% (d)	50% (4-yr)
JCOG 0112	III	(02-05)	9	46% (d)	63% (2-yr)
JCOG 0904	II	(09-)	7	NA	NA
JCOG 1105	III	(13-)	1	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

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Journal

1. Tamura S, Maruyama D, Miyagi Maeshima A, Taniguchi H, Kakugawa Y, Mori M, Azuma T, Kim SW, Watanabe T, Kobayashi Y, Tobinai K. Epstein-Barr virus-associated enteropathy as a complication of infectious mononucleosis mimicking peripheral T-cell lymphoma. Intern Med, 52:1971-1975, 2013
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Department of Hematopoietic Stem Cell Transplantation

Takahiro Fukuda, Takuya Yamashita, Sung-Won Kim, Saiko Kurosawa, Shigeo Fuji, Yoshiki Hayashi, Ayumu Ito, Yoshitaka Inoue, Reiko Ito

Introduction

At the National Cancer Center Hospital (NCCH), the Hematopoietic Stem Cell Transplantation (HSCT) Division specializes in patients who undergo allogeneic or autologous HSCT. Twenty-six 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

Five staff physicians (Drs. Yamashita, Kim, Kurosawa, Fuji, and Fukuda) and 4 chief residents (Drs. Hayashi, Ito A, Inoue and Ito R) participate in the transplant program. Children who have undergone HSCT are managed in collaboration with Dr. Ogawa, the medical staff of the Pediatric Oncology Division, and the transplant team. In 2013, a total of 110 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 2013 are shown in Tables 1 and 2, respectively. At the weekly conference on Monday afternoons, in collaboration with doctors of the Hematology Divisions, 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 2013, 416 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 (mini-transplant) for elderly patients. One clinical trial of gene therapy using the HSV-TK suicide gene for T-cell add-back following haploidentical HSCT is ongoing. A clinical trial of post-transplant consolidation with the WT1 vaccine is also ongoing.

We have been working on expansion of the indication of drugs used for the treatment of GVHD and infections. In the Division, 18 clinical trials are ongoing, and 5 trials have completed patient accrual. A nationwide large survey of quality of life (QOL) was conducted for 576 patients with acute leukemia who received chemotherapy or HSCT. In 2013, we have published 26 articles in peer-reviewed international journals and 6 manuscripts have been accepted for E-pub before print or are in press for publication.

Table 1. Number of each type of HSCT

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

Table 2. Number of patients who underwent HSCT between 2008 and 2013

Diagnosis	Allogeneic	Autologous
Acute myeloid leukemia	197	1
Myelodysplastic syndrome	39	0
Acute lymphocytic leukemia	73	0
Malignant lymphoma (including ATL)	173	67
Multiple myeloma	0	25
Solid tumors	2	25
Others	11	0
Total	495	118

List of papers published in 2013
Journal

1. Kurosawa S, Miyawaki S, Yamaguchi T, Kanamori H, Sakura T, Moriuchi Y, Sano F, Kobayashi T, Yasumoto A, Hatanaka K, Yanada M, Nawa Y, Takeuchi J, Nakamura Y, Fujisawa S, Shibayama H, Miura I, Fukuda T. Prognosis of patients with core binding factor acute myeloid leukemia after first relapse. Haematologica, 98:1525-1531, 2013
2. Kurosawa S, Yakushijin K, Yamaguchi T, Atsuta Y, Nagamura-Inoue T, Akiyama H, Taniguchi S, Miyamura K, Takahashi S, Eto T, Ogawa H, Kurokawa M, Tanaka J, Kawa K, Kato K, Suzuki R, Morishima Y, Sakamaki H, Fukuda T. Recent decrease in non-relapse mortality due to GVHD and infection after allogeneic hematopoietic cell transplantation in non-remission acute leukemia. Bone Marrow Transplant, 48:1198-1204, 2013
3. Kurosawa S, Yakushijin K, Yamaguchi T, Atsuta Y, Nagamura-Inoue T, Akiyama H, Taniguchi S, Miyamura K, Takahashi S, Eto T, Ogawa H, Kurokawa M, Tanaka J, Kawa K, Kato K, Suzuki R, Morishima Y, Sakamaki H, Fukuda T. Changes in incidence and causes of non-relapse mortality after allogeneic hematopoietic cell transplantation in patients with acute leukemia/myelodysplastic syndrome: an analysis of the Japan Transplant Outcome Registry. Bone Marrow Transplant, 48:529-536, 2013
4. Fuji S, Ueno N, Hiramoto N, Asakura Y, Yakushijin K, Kamiyama Y, Kurosawa S, Kim SW, Heike Y, Yamashita T, Fukuda T. Reduced-intensity conditioning regimen with low-dose ATG-F for unrelated bone marrow transplant is associated with lower non-relapse mortality than a regimen with low-dose TBI: a single-center retrospective analysis of 103 cases. Int J Hematol, 98:608-614, 2013
5. Kim SW, Yoon SS, Suzuki R, Matsuno Y, Yi HG, Yoshida T, Imamura M, Wake A, Miura K, Hino M, Ishikawa T, Kim JS, Maeda Y, Lee JJ, Kang HJ, Lee HS, Lee JH, Izutsu K, Fukuda T, Kim CW, Yoshino T, Ohshima K, Nakamura S, Nagafuji K, Suzumiya J, Harada M, Kim CS. Comparison of outcomes between autologous and allogeneic hematopoietic stem cell transplantation for peripheral T-cell lymphomas with central review of pathology. Leukemia, 27:1394-1397, 2013
6. Tada K, Kurosawa S, Hiramoto N, Okinaka K, Ueno N, Asakura Y, Kim SW, Yamashita T, Mori SI, Heike Y, Maeshima AM, Tanosaki R, Tobinai K, Fukuda T. Stenotrophomonas maltophilia infection in hematopoietic SCT recipients: high mortality due to pulmonary hemorrhage. Bone Marrow Transplant, 48:74-79, 2013
7. Yanada M, Kurosawa S, Yamaguchi T, Uchida N, Miyawaki S, Kanamori H, Usuki K, Kobayashi T, Watanabe M, Nagafuji K, Yano S, Nawa Y, Tomiyama J, Tashiro H, Nakamura Y, Fujisawa S, Kimura F, Emi N, Miura I, Fukuda T. Effect of related donor availability on outcome of AML in the context of related and unrelated hematopoietic cell transplantation. Bone Marrow Transplant, 48:390-395, 2013
8. Ogata M, Satou T, Kadota J, Saito N, Yoshida T, Okumura H, Ueki T, Nagafuji K, Kako S, Uoshima N, Tsudo M, Itamura H, Fukuda T. Human herpesvirus 6 (HHV-6) reactivation and HHV-6 encephalitis after allogeneic hematopoietic cell transplantation: a multicenter, prospective study. Clin Infect Dis, 57:671-681, 2013
9. Kato M, Matsumoto K, Suzuki R, Yabe H, Inoue M, Kigasawa H, Inagaki J, Koh K, Hashii Y, Tauchi H, Suminoe A, Kikuta A, Sakamaki H, Kawa K, Kato K, Fukuda T. Salvage allogeneic hematopoietic SCT for primary graft failure in children. Bone Marrow Transplant, 48:1173-1178, 2013
10. Nakasone H, Kurosawa S, Yakushijin K, Taniguchi S, Murata M, Ikegame K, Kobayashi T, Eto T, Miyamura K, Sakamaki H, Morishima Y, Nagamura T, Suzuki R, Fukuda T. Impact of hepatitis C virus infection on clinical outcome in recipients after allogeneic hematopoietic cell transplantation. Am J Hematol, 88:477-484, 2013
11. Nakasone H, Onizuka M, Suzuki N, Fujii N, Taniguchi S, Kakihana K, Ogawa H, Miyamura K, Eto T, Sakamaki H, Yabe H, Morishima Y, Kato K, Suzuki R, Fukuda T. Pre-transplant risk factors for cryptogenic organizing pneumonia/bronchiolitis obliterans organizing pneumonia after hematopoietic cell transplantation. Bone Marrow Transplant, 48:1317-1323, 2013
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13. Hirokawa M, Fukuda T, Ohashi K, Hidaka M, Ichinohe T, Iwato K, Kanamori H, Murata M, Sakura T, Imamura M, Adachi S, Suzuki R, Morishima Y, Sakamaki H. Efficacy and long-term outcome of treatment for pure red cell aplasia after allogeneic stem cell transplantation from major ABO-incompatible donors. Biol Blood Marrow Transplant, 19:1026-1032, 2013

14. Ogata M, Satou T, Inoue Y, Takano K, Ikebe T, Ando T, Ikewaki J, Kohno K, Nishida A, Saburi M, Miyazaki Y, Ohtsuka E, Saburi Y, Fukuda T, Kadota J. Foscarnet against human herpesvirus (HHV)-6 reactivation after allo-SCT: breakthrough HHV-6 encephalitis following antiviral prophylaxis. Bone Marrow Transplant, 48:257-264, 2013

15. Ishida T, Hishizawa M, Kato K, Tanosaki R, Fukuda T, Takatsuka Y, Eto T, Miyazaki Y, Hidaka M, Uike N, Miyamoto T, Tsudo M, Sakamaki H, Morishima Y, Suzuki R, Utsunomiya A. Impact of graft-versus-host disease on allogeneic hematopoietic cell transplantation for adult T cell leukemia-lymphoma focusing on preconditioning regimens: nationwide retrospective study. Biol Blood Marrow Transplant, 19:1731-1739, 2013

16. Murata M, Nakasone H, Kanda J, Nakane T, Furukawa T, Fukuda T, Mori T, Taniguchi S, Eto T, Ohashi K, Hino M, Inoue M, Ogawa H, Atsuta Y, Nagamura-Inoue T, Yabe H, Morishima Y, Sakamaki H, Suzuki R. Clinical factors predicting the response of acute graft-versus-host disease to corticosteroid therapy: an analysis from the GVHD Working Group of the Japan Society for Hematopoietic Cell Transplantation. Biol Blood Marrow Transplant, 19:1183-1189, 2013

17. Kanda Y, Oshima K, Kako S, Fukuda T, Uchida N, Miyamura K, Kondo Y, Nakao S, Nagafuji K, Miyamoto T, Kurokawa M, Okoshi Y, Chiba S, Ohashi Y, Takaue Y, Taniguchi S. In vivo T-cell depletion with alemtuzumab in allogeneic hematopoietic stem cell transplantation: Combined results of two studies on aplastic anemia and HLA-mismatched haploidentical transplantation. Am J Hematol, 88:294-300, 2013

18. Nishiwaki S, Miyamura K, Ohashi K, Kurokawa M, Taniguchi S, Fukuda T, Ikegame K, Takahashi S, Mori T, Imai K, Iida H, Hidaka M, Sakamaki H, Morishima Y, Kato K, Suzuki R, Tanaka J. Impact of a donor source on adult Philadelphia chromosome-negative acute lymphoblastic leukemia: a retrospective analysis from the Adult Acute Lymphoblastic Leukemia Working Group of the Japan Society for Hematopoietic Cell Transplantation. Ann Oncol, 24:1594-1602, 2013

19. Nakasone H, Kanda J, Yano S, Atsuta Y, Ago H, Fukuda T, Kakihana K, Adachi T, Yujiri T, Taniguchi S, Taguchi J, Morishima Y, Nagamura T, Sakamaki H, Mori T, Murata M. A case-control study of bronchiolitis obliterans syndrome following allogeneic hematopoietic stem cell transplantation. Transpl Int, 26:631-639, 2013

20. Kanda Y, Kanda J, Atsuta Y, Maeda Y, Ichinohe T, Ohashi K, Fukuda T, Miyamura K, Iida H, Mori T, Iwato K, Eto T, Kawa K, Morita S, Morishima Y. Impact of a single human leucocyte antigen (HLA) allele mismatch on the outcome of unrelated bone marrow transplantation over two time periods. A retrospective analysis of 3003 patients from the HLA Working Group of the Japan Society for Blood and Marrow Transplantation. Br J Haematol, 161:566-577, 2013

21. Kanamori H, Mizuta S, Kako S, Kato H, Nishiwaki S, Imai K, Shigematsu A, Nakamae H, Tanaka M, Ikegame K, Yujiri T, Fukuda T, Minagawa K, Eto T, Nagamura-Inoue T, Morishima Y, Suzuki R, Sakamaki H, Tanaka J. Reduced-intensity allogeneic stem cell transplantation for patients aged 50 years or older with B-cell ALL in remission: a retrospective study by the Adult ALL Working Group of the Japan Society for Hematopoietic Cell Transplantation. Bone Marrow Transplant, 48:1513-1518, 2013

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23. Espinoza JL, Takami A, Onizuka M, Morishima Y, Fukuda T, Kodera Y, Akiyama H, Miyamura K, Mori T, Nakao S. Recipient PTPN22 -1123 C/C genotype predicts acute graft-versus-host disease after HLA fully matched unrelated bone marrow transplantation for hematologic malignancies. Biol Blood Marrow Transplant, 19:240-246, 2013

24. Kanda J, Ichinohe T, Kato S, Uchida N, Terakura S, Fukuda T, Hidaka M, Ueda Y, Kondo T, Taniguchi S, Takahashi S, Nagamura-Inoue T, Tanaka J, Atsuta Y, Miyamura K, Kanda Y. Unrelated cord blood transplantation vs related transplantation with HLA 1-antigen mismatch in the graft-versus-host direction. Leukemia, 27:286-294, 2013

25. Imahashi N, Suzuki R, Fukuda T, Kakihana K, Kanamori H, Eto T, Mori T, Kobayashi N, Iwato K, Sakura T, Ikegame K, Kurokawa M, Kondo T, Iida H, Sakamaki H, Tanaka J, Kawa K, Morishima Y, Atsuta Y, Miyamura K. Allogeneic hematopoietic stem cell transplantation for intermediate cytogenetic risk AML in first CR. Bone Marrow Transplant, 48:56-62, 2013

Department of Blood Transfusion and Cellular Therapy

Ryuji Tanosaki

Introduction

The Department of Blood Transfusion and Cellular Therapy was formerly a division of the Department of Pathology and Clinical Laboratories. It just started in July 2012, to enable us to focus more on the management of patients with hematologic malignancies in collaboration with the Departments of Hematology-Oncology, Hematopoietic Stem Cell Transplantation, and Pediatrics. Our missions are not only to handle in-hospital transfusion services but also to provide support for the hematology and stem cell transplantation team in respect of blood transfusion and cellular therapy. In common with the Department of Pathology and 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 4 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 this Department and the Clinical Departments of Surgery and Internal Medicine, chief of the Department of Pharmacy, vice-chief of the Nursing Division, and a secretary. An administrative meeting is also held weekly, the attendees consisting of two chief doctors and three head doctors of this Department and the Department of Pathology and Clinical Laboratories, and the head and vice-head medical technologists. An all-staff meeting is held once a month.

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. Last year, the total units of red cell concentrates (RCC), platelet concentrates (PC) and fresh frozen plasma (FFP), which were consumed in our hospital, were 9545, 38835 and 4746, respectively. In 2013, the wastage of total blood products was 0.3%; RCC 1.2%, PC 0.03%, FFP 1.1%. Thanks to the Tokyo Red Cross and the convenient location of our hospital, blood products are available within 1 hour almost every time when they are needed in an emergency.

We employ the Type & Screen and computer cross-match system, but 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 very solid 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 electric medical record system is planned to be renewed in January 2014, the safety system for blood transfusion has also been strengthened.

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 a 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, all of which have been cryopreserved in liquid nitrogen. Each graft is registered and allotted its unique code number, which is recognized as its bar code. We believe that this bio-vigilant system is important for improving the practical aspects of cell therapy because the incidence of adverse reactions associated with graft infusion is significantly high.

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 and clinical trials

One of the Department's research projects is to develop a new enumeration technique for hematopoietic stem cells using an automated hematology analyzer, which started in 2006, in collaboration with a medical diagnostic company. 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. 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, Tokyo University.

List of papers published in 2013

Journal

1. Tamai Y, Hasegawa A, Takamori A, Sasada A, Tanosaki R, Choi I, Utsunomiya A, Maeda Y, Yamano Y, Eto T, Koh K-R, Nakamae H, Suehiro Y, Kato K, Takemoto S, Okamura J, Uike N, Kannagi M. Potential contribution of a novel Tax epitope-specific CD4+ T cells to graft-versus-Tax effect in adult T cell leukemia patients after allogeneic hematopoietic stem cell transplantation. J Immunol, 190:4382-4392, 2013
2. Ishida T, Hishizawa M, Kato K, Tanosaki R, Fukuda T, Takatsuka Y, Eto T, Miyazaki Y, Hidaka M, Uike N, Miyamoto T, Tsudo M, Sakamaki H, Morishima Y, Suzuki R, Utsunomiya A. Impact of graft-versus-host disease on allogeneic hematopoietic cell transplantation for adult T cell leukemia-lymphoma focusing on preconditioning regimens: nationwide retrospective study. Biol Blood Marrow Transplant, 19:1731-1739, 2013

Department of Pediatric Oncology

Chitose Ogawa, Hiroshi Kawamoto, Naoko Yasui, Chika Kohno, Ako Hosono, Yuko Araki, Hide Kaneda

Introduction

Pediatric oncology includes a wide variety of malignancies in children and adolescents such as acute leukemia and malignant lymphomas, as well as solid tumors including osteosarcomas, soft tissue sarcomas, neuroblastomas, Wilms' tumors and retinoblastomas. 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 four pediatric oncologists and two pediatric surgeons. 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 8 teachers work daily.

Routine activities

The pediatric outpatient clinic is open from Monday through Friday to manage new patients 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 stem cell transplantation (SCT), as indicated.

A Pediatric Conference is held every morning, mainly to decide on individual treatment plans. The pediatric staff 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.

We provide personnel training and education for the global standard skills of diagnosis/treatment for hematological malignancies and solid tumors, which we regard as an important role of this center.

Research activities

1. For newly diagnosed patients, we participate in several multicenter studies, including those by the Japan Ewing Sarcoma Study Group (JESS) and the Rhabdomyosarcoma Study Group (JRSG). 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 veno-occlusive disease which is one of the fatal complications in SCT, a phase I registration trial for the standard drug in EU and USA has been finished.
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

The two trials (3 and 6 below) are investigator-initiated 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 neuroblastomas.
(5) A phase Ib study of VPA and 13-cis-RA (isotretinoin) combination therapy for advanced and recurrent neuroblastomas.
(6) A feasibility trial of ch14.18 combined with IL-2 and various colony-stimulating factors for recurrent neuroblastomas.
(7) A phase I trial of immunotherapy using HLA-A2- and A24-restricted glypican-3 peptide vaccine for pediatric tumors.

Table 1. Number of patients

Acute lymphoblastic leukemia	3
Acute myeloid leukemia	1
Non-Hodgkin lymphoma	0
Hodgkin lymphoma	1
Other hematologic malignancies	0
Neuroblastoma	7
Retinoblastoma*	9
Osteosarcoma	10
Ewing sarcoma family	9
Rhabdomyosarcoma	7
Other soft tissue tumors	10
Germ cell tumor	2
Other solid tumors	3
Total	62

*; advanced case only

Table 2. Type of procedure

Tumor resection	
retroperitoneum	3
pelvic	1
abdominal wall(Lap)	1
ovary	3
Tumor biopsy(Lap)	2
Lung wedge resection(Lap assist)	4
Surgery for mediastinal tumor(Lap assist)	2
Surgery for pleural tumor(Lap assist)	1
Pylorus-preserving pancreaticoduodenectomy(PPPD)	1
Lymph node dissection	5
Lymph node biopsy	4
Central venous(CV) port / catheter	
placement	31
cutdown	1
remove	9
Total	68

List of papers published in 2013
Journal

1. Yasui N, Koh K, Kato M, Park MJ, Tomizawa D, Oshima K, Uchisaka N, Gocho Y, Arakawa A, Seki M, Oguma E, Kishimoto H, Watanabe S, Kikuchi A, Hanada R. Kasabach-Merritt phenomenon: a report of 11 cases from a single institution. J Pediatr Hematol Oncol, 35:554-558, 2013
2. Kato M, Yasui N, Seki M, Kishimoto H, Sato-Otsubo A, Hasegawa D, Kiyokawa N, Hanada R, Ogawa S, Manabe A, Takita J, Koh K. Aggressive transformation of juvenile myelomonocytic leukemia associated with duplication of oncogenic KRAS due to acquired uniparental disomy. J Pediatr, 162:1285-1288, 1288.e1, 2013

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 number of cancer patients who visit the National Cancer Center Hospital (NCCH) 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 have experience and expertise in their respective fields 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 NCCH cancer specialists. The 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 NCCH. Since April of 2011, we have expanded diabetes consultation service into NCCH-East (NCCH-E), improving the quality of diabetes care there.

Cardiology:

Cardiologists take charge of ECG, echocardiography, in-hospital consultation, and the 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 2000 a year. When an 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 500 diabetes consultations in 2013, 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 NCCH.

Infectious diseases:

Our main job is to provide infection-related medical care for cancer patients. We receive about 30 consultations monthly, such as surgical site infection, febrile neutropenia, catheter related infection, nosocomial pneumonia and so on. In addition we also monitor and manage infection control.

Nephrology:

To deal with the consultations from NCCH cancer specialists is the main work (332 consultations per year in 2013). The details of the consultations are as follows: assessment and treatment of acute kidney injury (AKI), management of chronic kidney disease (CKD) (including assessment of the optimal drug dose for CKD patients), treatment of electrolyte imbalance (hyponatremia, hypernatremia, hyperkalemia, hypokalemia, hypercalcemia, hypocalcemia, hypomagnesemia), assessment of polyuria (diabetes insipidus, salt wasting syndrome (SWS), diabetes mellitus and so on), assessment of edema, management of hypertension (including refractory hypertension, like renovascular hypertension), assessment and treatment of the nephrotic syndrome especially after hematopoietic stem cell transplantation, and so on. In case of the necessity for further evaluation of a patient, this is done in cooperation with the Department of Internal Medicine, Keio University Hospital.

An apparatus for hemodialysis was installed in October, 2012. Therefore, hemodialysis patients have been able to receive cancer treatment at NCCH.

Research activities

An article with the title "Complete remission of repeated recurrent membranous nephropathy after non-myeloablative allogeneic peripheral blood stem cell transplantation" was published in The Japanese Journal of Nephrology.

List of papers published in 2013

Journal

1. Kasuga M, Ueki K, Tajima N, Noda M, Ohashi K, Noto H, Goto A, Ogawa W, Sakai R, Tsugane S, Hamajima N, Nakagama H, Tajima K, Miyazono K, Imai K. Report of the Japan Diabetes Society/Japanese Cancer Association Joint Committee on Diabetes and Cancer. Cancer Sci, 104:965-976, 2013
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Department of Dentistry

Takao Ueno

Introduction

Oral complications are common in patients receiving chemotherapy or undergoing radiation therapy of the head and neck. To prevent and treat oral complications of cancer therapy, we check the oral condition of the patients, identify the patients at risk, start preventive measures before cancer therapy begins, and treat complications as soon as they appear. Continuing good oral hygiene during cancer treatment can reduce oral complications such as mouth sores, oral mucositis, and infections.

Routine activities

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, pharyngeal and esophageal surgery
4) Making prostheses for restoration of postoperative facial defects
5) Prevention and treatment of bisphosphonate-associated osteonecrosis
6) Cooperation enterprises with departments of medicine and dentistry in the Kanto area to seek optimum solutions to dental problems associated with the cancer patient)

Research activities

Research into the treatment of, and preventive steps against oral complications due to cancer treatment is performed with pan-specialty cooperation.

1) So that all cancer patients may receive dental support during cancer treatment, a coordinated approach has been started with the Japan Dental Association. Problems in the construction of a medical-dental coordinated system are under study.
2) Prospective study about the onset frequency of pneumonia after the operation of esophagus cancer
3) Prospective study of the taste disorder associated with stomach cancer adjuvant postoperative treatment

Table 1. Number of new patients

oral care before operation (head and neck, esophagus) and radiation therapy to the head and neck	158
Introduction to the cooperation dental clinic (oral health care before operation)	338
oral care and treatment of mucositis , oral infection during chemotherapy	312
dental check up and oral care before chemotherapy	165
dental check up and oral care before using bone modifying agents	142
Total	1023

Department of Genetic Counseling

Teruhiko Yoshida, Kokichi Sugano, Takeshi Nakajima

Introduction

Approximately 5% of all cancer cases are considered to have a highly penetrant monogenic mutation. Most of the causative genes for major hereditary cancer syndromes were identified in the 1990s, and genetic diagnosis has been introduced as the standard medical care for some tumors. However, cancer medical genetics still has a number of issues to be addressed (Figure 1).

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 research and clinical practice.

Routine activities

The National Cancer Center Hospital (NCCH) launched the Outpatient Genetic Counseling Clinic in 1998 as a part of collaboration with the Research Institute, and since then, total 1,124 clients from 744 families have visited the Clinic as of December 2013. Based on the present, past and detailed family histories, risks of the most likely hereditary cancer syndrome, if any, will be explained followed by the discussion about the prevention scheme for clients and relatives. If appropriate, genetic tests may be offered, too.

Regular conferences of the Genetic Counseling Clinic were held from June 1998 to December 2005. In December 10, 2013, hereditary cancer syndromes were selected as the theme of the 7th Research Conference, and the avid discussion by a large audience from various sectors of the NCC resulted in the new series of the Genetic Counseling Clinic conferences which resumed from February 2014.

Research activities

In general, sensitivity of the current standard genetic tests has remained approximately 70-80% even for the cases well-matched to the clinical criteria for hereditary cancer syndromes. To exploit the latest genome technology for the undiagnosed patients, a variant call pipeline based on the whole-exome sequencing by the next generation sequencer and genome-wide SNP array has been established in the Division of Genetics and Genome Core Facility of the NCC Research Institute, which have been in charge of the area of in-house genetic tests at the Genetic Counseling Clinic. However, the technology alone cannot solve the problem, and the importance of family study, ascertaining genome samples and clinical information from relatives with or without the disease, has been confirmed.

Clinical trials

The Genetic Counseling Clinic has participated in a prospective clinical study to optimize BRCA1/2 genetic tests and a clinical trial of PARP inhibitor for patients with ovarian cancer both directed by the Department of Breast and Medical Oncology.

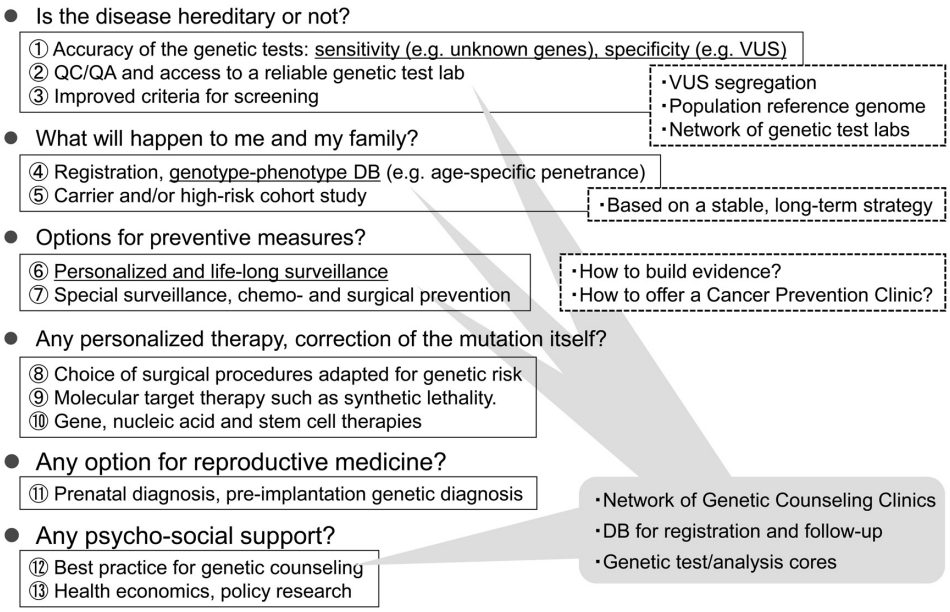

Figure 1. Major Questions by the Patients and Families with Hereditary Cancer Syndromes

Table 1. Number of patients by condition

	Proband	Relative	Total
Lynch syndrome (Hereditary Non-Polyposis Colon Cancer; HNPCC)	16	15	31
Familial Adenomatous Polyposis (FAP)	6	4	10
Retinoblastoma	10	2	12
Hereditary Breast and Ovarian Cancer Syndrome (HBOC)	56	8	64
MEN I (Multiple Endocrine Neoplasia Type I)	0	0	0
Other diseases	4	0	4
Counseling only	3	0	3
Total	95	29	124

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Department of Anesthesia and Intensive Care

Tetsufumi Sato, Yoko Kinoshita, Minako Arai, Takashi Matuzaki, Nobuko Yokokawa, Rie Suzuki, Yousuke Kawaguchi, Kazumasa Hiroi, Takuma Hiraiwa, Sayo Iwasaki, Miyabi Takemura, Takuya Ohata, Kihoko Ichikawa

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 (ICU) has 8 beds and provides care for all specialties including general medical and general surgical cases. There are over 400 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 13 staff anesthetists who are involved in critical care, education and research. Our Department provides perioperative care to the all patients required general anesthesia and spinal analgesia. Our operation theater performs approximately 4,000 surgical procedures per year, which include neurosurgical, orthopedic, plastic, ophthalmologic, gynecologic, urologic, and general surgery (Table 1). We also provide care to patients undergoing procedures in locations outside the main operating room such as sessions in the endoscopy suite. In addition, many patients are seen in the Anesthesia Consult Clinic, which runs every weekday. Many staff also have other clinical appointments including attendance 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 a closed system, supported by two certificated intensivists and trainee. There are 8 operational ICU beds and 484 patient admissions annually. The ICU is also responsible for resuscitation services within the hospital.

A weekly conference is held with all anesthesiologist and intensivists to keep up-to-date with the current world standard of acute care medicine. A weekly lecture is also held for the education of intensive care nurses. Occasionally, a mortality and morbidity conference is held with doctors of other department.

Clinical trials

One of our members is on the faculty of the clinical trial group in the Japanese Society of Intensive Care Medicine. To understand the incidence and risk factors of severe adverse event in post-operative patients, epidemiological analyses have been performed. To improve current care for perioperative patients, prospective studies are currently being conducted.

Table 1. Cases for anesthetic management

Thoracic surgery	643
Breast surgery	427
Colon surgery	458
Urologic surgery	257
Ophthalmologic surgery	319
Orthopedic surgery	264
Hepato-Biliary-Pancreatic surgery	281
Gynecologic surgery	197
Esophageal surgery	119
Head-neck surgery	168
Skin surgery	104
Other	351
Total	4193

Department of Palliative Care

Motohiro Matoba, Osamu Saito, Chio Shuto, Hironori Mawatari

Introduction

It was in June, 1999, when a palliative care team was established as a multi-disciplinary team, and the Department of Palliative Care and Psycho-Oncology was established in April, 2010, with the reorganization of the National Cancer Center Hospital NCCH). The team provides palliative care to attenuate the total pain of cancer patients and their families, comprising physical, psychological, social, and spiritual pain. About 300 patients yearly are referred to the Division mainly for pain management. As a multi-disciplinary team, we provide palliative care for total pain. . Other than physicians, various paramedical professionals such as psychiatrists, pharmacists, acupuncturists, psychologists, cosmetic specialists, child care specialists, hospital play specialists and social workers take part in the team. Under the auspices of our team, regular seminars and conferences are held to facilitate the partnership with other hospitals and organizations.

Routine activities

The main routines of the team are to manage the symptoms of terminal patients and to educate the residents to help them to acquire the knowledge and skills required of a palliative care physician. We are usually in charge of about 20 inpatients, and make a morning round and hold conferences twice a day. In the outpatient department, we treat approximately 20 patients per week. Besides conventional drug therapy, we perform various neuronal blockades, place emphasis on mental support for the patient and their families and sometimes refer the patients to the Division of Psycho-Oncology, the Department of Orthopedic Surgery, the Department of Pediatric Oncology and the Department of Diagnostic Radiology to attain better symptom management. For the purpose of equilibration of palliative medicine, bimonthly conferences are held, and consequently coordination with the community palliative care in the vicinity is strengthened.

Education for residents

With regard to their clinical education and training, all the residents of the NCCH are required to train with our team for 1 month, within which a one-week home hospice course is mandatory. In total, 21 residents trained with our team during 2013. The course is whole-person-care oriented. The home hospice course offers an opportunity to understand the role of various occupations other than doctors, such as visiting nurses and care managers.

Research activities

In particular, establishment of a pain management monitoring system and a program for improving opioid consumption have been started at Aomori Prefectural Central Hospital.

Also, construction of a supporting system has been completed for children and their families whose father/mother are suffering and dying from advanced cancer.

Table 1. Number of patients

sarcoma	30
Lung cancer	19
Gastric cancer	13
Breast cancer	10
Colon cancer	9
Rectal cancer	9
Renal cancer	9
Pancreatic cancer	8
Primary unknown cancer	7
Malignant melanoma	6
Prostate cancer	5
Uterine cancer	5
Esophageal cancer	5
Leukemia	5
Malignant lymphoma	4
Others	37
Total	181

Table 2. Type of procedure

Adjustment of non-opioid analgesics	54
Commencement of opioid analgesics	21
Adjustment of opioid analgesics	77
Opioid rotation	30
Adjustment of adjuvant analgesics	33
Nerve block	5
Management of side effect of analgesics	39
Others	15

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Journal

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Department of Psycho-Oncology

Ken Shimizu, Rika Nakahara, Yoshio Oshima, Masashi Kato, Tomomi Takahashi

Introduction

The Psycho-Oncology Division was reestablished in September 1995, together with establishment of the Psycho-Oncology Division, National Cancer Center Research Institute East (reorganized to the Psycho-Oncology Division, Research Center for Innovative Oncology, National Cancer Center Hospital East (NCCHE) in 2005). One of the most important clinical activities of the Psycho-Oncology Division is the management of cancer patients' behavioral and social problems as well as their psychological distress. Furthermore, this division's aim is to alleviate the distress of patients, the patients' families and our staff members. 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 Psychiatry Division consists of two full time staff psychiatrists and one part time psychiatrist, and one chief resident. One staff psychotherapist and two part-time psychotherapists are available four days a week. The division provides two major services; a clinic for outpatients (four 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 division has played an active role as a member of the palliative care team.

A range of psychiatric diagnoses is based on the DSM-IV criteria (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) shown in the Table. In 2013, a total of 778 patients were referred for psychiatric consultation. The mean age was 50.9 years old and 13.2% of the referrals were outpatients. Three-hundred and eighty seven (49.7%) of the total number of referred patients were males. The most common psychiatric diagnosis was delirium (26.3%), followed by adjustment disorders (19.6%), and major depression (9.1%), while 19.6% of the referrals had no psychiatric diagnosis. The three common mental disorders; adjustment disorder, major depression and delirium, were responsible for half of the psychological problems. The most common cancer referrals were patients with sarcomas (16.4%), followed by hematological cancer (11.4%), breast cancer (9.5%), lung cancer (8.7%), stomach cancer (6.5%), colorectal cancer (6.5%), and esophageal cancer (6.4%).

A clinical and research activities conference is held every Thursday evening with staff members from the Psycho-Oncology Division of the NCCHE, the psychiatry division of the Chugoku Cancer Center, plus members of the Kyushu Cancer Center, Saitama Cancer Center, Hokkaido Cancer Center, Chiba Cancer Center, Hiroshima University, Chiba Cancer Center, and Nagoya City University Graduate School of Medical Sciences. Difficult cases are discussed with the attendees. Ongoing and planned protocols are also discussed. Important relevant articles from international medical journals are reviewed together with the members of the Psycho-Oncology Division of the NCCHE every Tuesday evening. Additionally, the members of the Division have played active roles in the palliative care team. There is a joint meeting with other members of the team every Friday evening.

Research activities

Although implementation of routine screening for cancer patients' distress is desirable, it is hard to perform this function adequately in a busy clinical oncology practice. We are now developing Distress Screening tools which can be of practical use in the real world, the purpose of which is to facilitate treatment for patients with major depression and adjustment disorders. This year, we have validated the Screening tool.

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

Table 1. Patient demographics

Patients	Total number	778	
	Age	50.9 years	
	Male	387	49.7%
	Inpatients	674	86.6%

Table 2. Number of cancers by site

Cancer site	Sarcoma	128	16.4%
	Hematological	89	11.4%
	Breast	74	9.5%
	Lung	57	8.7%
	Stomach	51	6.5%
	colorectal	51	6.5%
	Esophageal	50	6.4%

Table 3. Breakdown of diagnoses

Diagnosis	Delirium	205	26.3%
	Adjustment Disorders	153	19.6%
	Major Depression	71	9.1%
	No Diagnosis.	153	19.6%

List of papers published in 2013
Journal

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Department of Diagnostic Radiology

Yasuaki Arai, Masahiko Kusumoto, Ryutaro Kakinuma, Yasunori Mizuguchi, Gen Iinuma, Takashi Terauchi, Miyuki Sone, Hiroaki Onaya, Hiroaki Kurihara, Nachiko Uchiyama, Hirokazu Watanabe, Minoru Machida, Seiko Kuroki, Mari Kikuchi, Tomoko Manabe, Mototaka Miyake, Hiroaki Ishii, Syunsuke Sugawara, Hirotaka Tomimatu, Shinichi Morita, 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. 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	39,980
2	MRI	8,061
3	IVR	4,148
4	RI	4,356
5	Ultrasound	13,610
6	Radiograph	79,877
7	Gastrointestinal study	1,856

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 CO2 gas insufflation systems have been established in 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.

We evaluated the usefulness of additional ADc value in predicting extracapsular extension of prostate cancer using 3.0 T MR imaging.

Regarding the pulmonary subsolid nodules, a prospective multicenter study to clarify natural history of subsolid nodules on Chest CT is ongoing.

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 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.

A multi tracer consisting of [18F]FDG, [18F] FBPA, anti-[18F]FACBC, [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, known as an evaluator for boron neutron capture therapy (BNCT), has been conducted in 22 cancer patients in this year. Anti-[18F]-FACBC PET/CT has been also carried out in prostate cancer patients as a phase II clinical trial. [11C]-choline and [11C]-methionine PET/CT examinations have been scheduled routinely two day 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 19 thyroid cancer patients with use of radioactive iodine (I-131) chloride and 1 neuroblastoma patient with I-131 MIBG.

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) and a phase II study evaluating the efficacy of arterial infusion chemotherapy and radiotherapy for unresectable maxillary carcinoma (JIVROSG-0808).

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Department of Radiation Oncology

Jun Itami, Minako Sumi, Yoshinori Ito, Madoka Morota, Naoya Murakami, Koichi Inaba, Kotaro Yoshio

Introduction

The role of the Department is to provide state of art radiation therapy to all the 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. In this year, a new building for the hospital-based boron neutron capture therapy (BNCT) system using an accelerator was constructed and finished in Dec. 2013. 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. Four linear accelerators, one X-ray simulator, one XCT-simulator, and 7 treatment planning computers are working together under on-line networks to provide state-of-art precision external beam radiation therapy. In 2010, the X-ray simulator was updated to the newest machine, the Accusim from Varian. 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 to improve local control. Stereotactic brain irradiation was originally invented in this Department under the name of stereotactic multiarc radiation therapy (SMART) and has been employed 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. Three of the 4 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. From Dec. 2011, gold markers have been implanted to improve geometric precision of radiation field reproducibility. In the new building, the CyberKnife STI and True Beam Linac have already been installed and they will be clinically used from April 2014.

Brachytherapy is also performed very intensively to obtain local control and many patients are referred to us from all over Japan. For brachytherapy the following modalities are being employed, an Ir-192 high dose rate (HDR) afterloading system including a 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 in 2013 as in the past. 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 a shortened fractionation regimen for various malignancies, especially for breast cancer and vocal cord cancer; 3) 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 an accelerator based BNCT system. These studies are financially supported by grants from the Ministry of Health, Labour and Welfare (MHLW), Japan.

Clinical Trials

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

Lung cancer: A 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 nonverified lung tumors.

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

Head and Neck cancers: Accelerated fractionation versus conventional fractionation radiation therapy for glottis cancer of T1-2N0M0, a phase III study (JCOG 0701).

Breast cancer: A phase II trial on accelerated partial breast irradiation in T1 breast cancer after partial mastectomy.

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

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

Development of an Adaptive Radiation Therapy System

Table 1. Number of Radiation Treatment Plans

Primary Sites	No. of All Treatment Plans					
	2008	2009	2010	2011	2012	2013
Head & neck	115	95	128	166	158	257
Brain	117	99	113	97	77	83
Lung	397	431	429	348	430	425
Breast	549	452	487	503	485	582
Esophagus	220	213	265	237	268	248
Stomach	34	29	25	15	35	37
Colorectal	86	78	66	119	113	100
Pancreas and hepatobiliary	38	48	69	68	64	69
Gynecological	255	331	274	328	418	327
Genitourinary	128	159	192	169	172	191
Bone & soft tissue	75	69	103	92	86	90
Skin	16	26	58	71	58	54
Pediatric	22	32	25	66	49	24
Hematological	137	220	159	157	202	165
Other	47	52	19	14	39	25
Total	2236	2334	2412	2450	2654	2677

*: No. of Cases

Table 2. Purpose of Radiation Therapy

	No. of All Treated Patients					
	2008	2009	2010	2011	2012	2013
No. of Treatment Plans	2236	2334	2412	2450	2654	2677
Curative Intent	1535	1500	1587	1662	1858	1819
Palliative Treatment	701	834	825	788	796	858
Curative/Palliative	2.19	1.80	1.92	2.11	2.33	2.12
New Patients	1181	1210	1277	1288	1271	1861

Table 3. Special Radiation Therapy

	No. of Treated Patients			
	2010	2011	2012	2013
IORT	0	1	0	0
TBI	41	52	51	58
SRT-Brain	3	2	6	5
SRT-Body	33	45	37	55
IMRT-Brain	7	11	12	26
IMRT-H&N	34	45	62	108
IMRT-Thorax	1	3	6	2
IMRT-Gyne	6	14	23	13
IMRT-Prostate	46	55	56	69
IMRT-Others	11	9	13	24
Intracavitary RT 192Ir-HDR	50	49	40	48
Intracavitary RT 192Ir-LDR	0	0	0	0
Interstitial RT 192Ir-HDR	6	25	37	43
Interstitial RT 192Ir-LDR	0	0	1	0
Interstitial RT 198Au-LDR	6	4	7	7
Interstitial RT 125I-LDR	26	16	28	22
Interstitial RT 106Ru-LDR	10	13	17	20
Non-Sealed Radionuclide Therapy 89Sr	5	12	4	3
Non-Sealed Radionuclide Therapy 131I	14	21	24	16
Non-Sealed Radionuclide Therapy MIBG				1

IORT; intraoperative radiotherapy
TBI; total body irradiation

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Journal

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Department of Pathology and Clinical Laboratories, Pathology Division

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Introduction

In the Pathology Division the practice and education of, and research into diagnostic and anatomic pathology are carried out. Diagnostic pathology practice comprises all issues regarding 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 consists of the autopsy and post-mortem systemic gross and microscopic examination of patients. Case conferences with each clinical division are held periodically. Residents and trainees are accepted for training of diagnostic pathology on a rotating basis. To provide more accurate and informative diagnoses in the future, the staff members conducted basic, clinical, or translational research by themselves or in collaboration with other divisions or institutions.

Routine activities

In 2013, a total of 14 board-certified pathologists, 8 residents and 11 medical technologists, including 11 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, and education of the residents. Seven pathologists working exclusively in the NCCH also shared management of the Department. Another 7 pathologists are concurrently on the staff of NCC Research Institute (NCCRI).

1. Surgical pathology

A total of 20,205 histological diagnoses were provided consisting of 16,371 biopsy specimens including 1,886 intraoperative frozen sections and 3,834 surgically resected specimens. The intraoperative frozen sections comprised primary tumors, regional lymph nodes, and surgical margins of specimens. The one-step nucleic acid amplification (OSNA) assay was performed for 436 patients to examine metastasis intraoperatively.

2. Cytopathology

Cytopathological diagnoses were provided for a total of 12,188 patients including 357 for intraoperative diagnosis. The specimens comprised smears, sputa, body fluids, urine, and needle aspirates submitted from various departments. Intraoperative cytological examination of body fluids was utilized for disease staging and treatment decisions in the fields of gastric surgery and gynecology.

3. Autopsy

Thirty autopsies were performed to examine the extent of tumor spread, the cause of death, therapeutic and adverse effects, and systemic pathological conditions. Immediately after each autopsy examination, a table discussion on gross findings was held among the physicians and the pathologists. These cases were further discussed in monthly autopsy conference after completion of histological examinations.

4. Outpatient clinic for pathology consultation (second opinion)

To 210 patients, we provided histopathological/cytopathological diagnosis as second opinion.

Research activities

1. Gastrointestinal pathology

Clinicopathological characteristics of adenocarcinoma at the esophago-gastric junction, and the GNAS and KRAS status of gastrointestinal neoplasia were studied in collaboration with clinical departments and research institute.

2. Hematopathology

Clinicopathological prognostic indicators of follicular lymphoma and transformed follicular lymphoma were studied. Long follow-up data of patients with B-cell lymphoma with a CD20-negative phenotypic change after rituximab-containing therapy were reported.

3. Pulmonary and mediastinal pathology

The clinical significance of *IGF-1R* gene copy number alterations, *ROS1* rearrangement, and IASLC

classification were studied in lung adenocarcinoma. Pitfalls of immunohistochemistry for ALK as well as squamous cell carcinoma and adenocarcinoma markers were studied.

4. Bone and soft tissue pathology

Anaplastic lymphoma kinase status was comprehensively assessed in >100 rhabdomyosarcomas using sensitive immunohistochemistry, FISH, and sequencing. A new fusion variant of PPFIBP1-ALK was discovered in an inflammatory myofibroblastic tumor.

5. Breast and gynecological pathology

The benefit of combination method for sentinel and nonsentinel lymph node assessment using one-step nucleic acid amplification and conventional histological examination was shown. The risk factors of early stage endometrial carcinoma were also assessed

Table 1. Numbers of Histopathological Specimens Diagnosed in the Pathology Section in 2013

Field	Number of specimens Total
Gastrointestinal tracts	8376
Breast	2501
Respiratory organs	2103
Hematology	1441
Gynecology	1241
Urology	830
Hepatobiliary and Pancreas	664
Head and Neck	657
Dermatology	564
Orthopedics	516
Others	947
Research Center for Cancer Prediction and Screening	365
Total	20205

Table 2. Numbers of Cytopathological Specimens Diagnosed in the Pathology Section in 2013

Field	Number of specimens Total
Gynecology	3949
Urology	2973
Respiratory organs	1876
Gastrointestinal tracts	778
Breast	458
Hepatobiliary and Pancreas	445
Hematology	290
Head and Neck	208
Radiation Oncology	178
Others	213
Research Center for Cancer Prediction and Screening	820
Total	12188

Table 3. Numbers of Autopsies Performed in the Pathology Section in 2013

Deaprtment/Division	Number
Hematology and Hematopoietic Stem Cell Transplantation	10
Gastrointestinal Oncology	6
Breast and Medical Oncology	5
Thoracic Oncology	3
Orthopedics	3
Neurosurgery	1
Thoracic Surgery	1
Esophageal Surgery	1
Total	34

List of papers published in 2013
Journal

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Department of Pathology and Clinical Laboratories, Clinical Laboratory Division

Atsushi Ochiai, Koh Furuta

Introduction

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 strict internal and external quality control. After a nearly one-year preparation, the laboratories in this Department 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

Fifty full-time and 9 part-time medical technologists, 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 National Cancer Center Hospital (NCCH); and in the sections of phlebotomy and physiological examination in the Research Center for Cancer Prevention and Screening (RCCPS). The sections of 1) to 5) are supervised by Dr. Koh Furuta. The pathology section staff are supervised by the doctors in the Pathology Division, and the transfusion and phlebotomy staff are supervised by a doctor of the Department of Transfusion Therapy. In addition, the physiological examination staff are directly supervised by Dr. Yasunori Mizuguchi Department of Diagnostic Radiology, and Dr, Masaaki Syoji and Dr. Takeshi Iwasa, the General Internal Medicine Division* The bacteriology staff are members of the Infection Control Team (ICT) and participate in the activities of infection management in collaboration with the staff physicians.

An administrative meeting is held weekly, attending members of which consist of two chief doctors and three head doctors of this Department and the Department of Transfusion Therapy, and the head and vice-head medical technologists. The quality control meeting is regularly held twice a month, and an all-staff meeting is held once a month. The division also participates in several domestic and international programs for inter-laboratory standardization and external quality control including the College of American Pathologists (CAP) Survey. The actual number of laboratory tests performed in this Division in 2013 is shown in Table 1.

Table 1. Number of laboratory tests examined in the Clinical Laboratories Division (2013)

Section	Number
General laboratory medicine	506,790
Hematology	1,308,723
Biochemistry	2,928,640
Endocrinology, immunology, and tumor markers	372,534
Bacteriology	54,125
Physiology	87,188
Genetic diagnostics	739
Total	5,258,739

Research activities

An in-hospital bio-bank, which was established in 2002, has been maintained for use by various researchers, and more than 700,000 post clinical test blood samples have been cryo-preserved at -20 °C as of the end of 2013.

Three sections, general laboratory medicine and hematology, biochemistry, and endocrinology, immunology and tumor markers, participated in the external quality control program endorsed by the Japanese Society of Laboratory Medicine. In this particular program, the precise degradation processes of routine clinical specimens were investigated with other eight domestic university hospitals.

Using the Metafer system (an automated image analysis-assisted fluorescence in situ hybridization [FISH] system), the technique to evaluate the FISH imaging ofHER2 gene amplification was established. Furthermore, using the Metafer system, we tried to establish a method to evaluate FISH images of ALK-rearranged, ROS-rearranged, and RET-rearranged lung cancers.

The molecular pathology laboratory has been set up, FISH of epidermal growth factor receptor (tHoFR) in stomach cancer was performed, and

data are under acquisition. Many case reports with important ultrasound findings were presented in scientific meetings by the staff of the physiology section.

Under the education committee in the IS015189 scheme, a monthly seminar by the staff was started from this year for the purpose of promoting research activity in the Division.

List of papers published in 2013
Journal

1. Yoshida A, Shibata T, Wakai S, Ushiku T, Tsuta K, Fukayama M, Makimoto A, Furuta K, Tsuda H. Anaplastic lymphoma kinase status in rhabdomyosarcomas. Mod Pathol, 26:772-781, 2013
2. Yoshida A, Kohno T, Tsuta K, Wakai S, Arai Y, Shimada Y, Asamura H, Furuta K, Shibata T, Tsuda H. *ROS1*-rearranged lung cancer: a clinicopathologic and molecular study of 15 surgical cases. Am J Surg Pathol, 37:554-562, 2013
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9. Morita S, Yoshida A, Goto A, Ota S, Tsuta K, Yokozawa K, Asamura H, Nakajima J, Takai D, Mori M, Oka T, Tamaru J, Itoyama S, Furuta K, Fukayama M, Tsuda H. High-grade lung adenocarcinoma with fetal lung-like morphology: clinicopathologic, immunohistochemical, and molecular analyses of 17 cases. Am J Surg Pathol, 37:924-932, 2013
10. Makuuchi Y, Honda K, Osaka Y, Kato K, Kojima T, Daiko H, Igaki H, Ito Y, Hoshino S, Tachibana S, Watanabe T, Furuta K, Sekine S, Umaki T, Watabe Y, Miura N, Ono M, Tsuchida A, Yamada T. Soluble interleukin-6 receptor is a serum biomarker for the response of esophageal carcinoma to neoadjuvant chemoradiotherapy. Cancer Sci, 104:1045-1051, 2013
11. Hiramoto N, Kobayashi Y, Nomoto J, Maruyama D, Watanabe T, Tochigi N, Furuta K, Takeda K, Chuman H, Yagyu S, Hosoi H, Tobinai K. Ewing sarcoma arising after treatment of diffuse large B-cell lymphoma. Jpn J Clin Oncol, 43:417-421, 2013
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Office of Infection Control and Prevention

Minoru Esaki, Keiji Okinaka, Yasuko Ishida, Michi Shouji, Keiichi Koido, Yoshiko Nakayama

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, Infection control microbiological technologist, Board certified pharmacist in infection control, Office clerk, and Director. The team works very closely with staff from all areas of the hospital to prevent and control infection. The annual goals of our team for 2013 were

- to announce the 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 "ICT web"
- to collaborate with regional hospitals to keep cancer patient safe from healthcare-associated infections.
- to deliver 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

Our team provides

- Advice about the prevention and management of outbreaks, and delivering education programs to all staff including lectures by staff of 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 providing advice about building and refurbishment projects in the hospital from the infection control aspect.

Outpatient Treatment Center

Kenji Tamura

Introduction

The Outpatient Treatment Center deals with all kinds of malignant neoplasm. Our mission is to provide safe, smooth and high quality of standard chemotherapy regimens in the outpatient setting. Several groups collaborate to ensure the best chemotherapeutic approach, consisting of medical oncologists, nurses, pharmacists, medical social workers and clinical research coordinators. Our visions are 1) To provide findings based on evidenced based medicine, 2) To provide safe and efficient treatments, and 3) To maintain the quality of life of the patients.

Routine activities

From January to December 2013, The Outpatient Treatment Center supported at total of 22,162 patients who received anticancer drugs by intravenous administration (Table 1) and a total of 3678 patients whose drugs were administered by intramuscular or subcutaneous injection (Table 2, for example, endocrine therapy or interferon), making a grand total of 25,840 patients. The breakdown by cancer type was as follows: gastrointestinal (23%), breast (20%), gynecologic (15%), hepatobiliary and pancreatic (14%), hematology (10%), thoracic (10%) and other malignancies (6%). General infusions, general intramuscular or subcutaneous injections, blood transfusions, bone marrow punctures, lumbar punctures, intraperitoneal or chest drainage and blood gas analyses were conducted in the center.

Conference

A case conference is held biweekly on Monday with the participation of multidisciplinary specialists, including medical oncologists, nurses, and pharmacists. The monthly stuff meeting is held on the 2nd Tuesday of every month with the participation of physicians and nurses who are the main members in the center. The steering committee is held on the 3rd Thursday of every month.

Research Activities

- Efficacy of frozen gloves in the treatment of nail toxicities with docetaxel.
- Efficacy of frozen caps in the prevention of chemotherapy-mediated alopecia.
- Allergic reaction to oxaliplatin in outpatients.
- Telephone hot line for emergency for outpatients who are undergoing chemotherapy.

Education

We provide educational opportunities for multidisciplinary specialists, including medical oncologists, nurses, and pharmacists. We also provide an educational program for medical oncologists, nurses, pharmacists and medical social workers in designated hospital for cancer treatment in each prefecture.

Future Prospects

We continue to propose a near-future model of the clinical trials in outpatient style. We aim at shortening the waiting time, achieving smooth administration of novel molecular targeted drugs for outpatients, and to put into practice multidisciplinary care for cancer patients who received chemotherapy in the Outpatient Treatment Center.

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

	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Total
Department	701	632	670	700	711	584	702	656	591	624	582	624	7777
Breast and Medical Oncology	458	430	423	384	458	389	453	459	423	504	439	444	5264
Hepatobiliary and Pancreatic Oncology	295	266	249	261	272	218	295	287	249	277	259	250	3178
Hematology	224	205	176	178	230	181	245	192	200	225	180	191	2427
Thoracic Oncology	202	185	191	210	195	179	182	148	166	163	157	173	2151
Others	87	90	95	97	101	110	174	133	122	129	115	112	1365
Total	1967	1808	1804	1830	1967	1661	2051	1875	1751	1922	1732	1794	22162

Table 2. Cumulative total number of patients who were treated except for intravenous administrations of anticancer drugs

	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Total
Intramuscular or subcutaneous injection as anti-cancer drug	317	309	307	318	286	278	315	271	300	337	299	341	3678
General infusions-short	27	17	27	20	46	32	47	47	29	33	31	39	395
General infusions-long	2	4	0	2	0	0	1	1	3	0	5	1	19
General intramuscular or subcutaneous injections	195	167	212	234	223	192	223	203	231	217	208	195	2500
Blood transfusions	37	33	39	42	34	30	28	49	60	70	61	71	554
Bone marrow puncture	32	42	41	46	51	54	45	45	43	42	46	51	538
Lumbar puncture	3	1	3	3	4	2	1	0	1	1	1	0	20
Intraperitoneal drainage	3	2	0	1	0	2	1	2	0	2	4	0	17
Chest drainage	2	3	2	2	2	3	1	9	1	0	3	0	28
Blood gas analyses	35	30	28	42	26	32	26	34	28	27	27	21	356
Orientation	158	144	133	145	164	122	162	140	131	152	157	167	1775
Other treatments	38	28	37	32	38	21	23	22	19	30	38	40	366
Total	849	780	829	887	874	768	873	823	846	911	880	926	10246

Consultation, Counseling and Support Service Center

Masashi Kato, Yukiko Higuchi, Kayoko Miyata, Natsuko Moroi, Rieko Shimizu, Naoko Goto, Yasuko Arimoto, Mayumi Miura, Yuko Ogo, 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 cope 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 group for families of brain tumor patients
- CLIMB (Children's Lives Include Moments of Bravery) Support Program

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.

Table 1. The number of cases (April 2012 - March 2013)

1	Total	8,580
2	New cases	4,940
	New cases from NCCH	1,972
	New cases from other hospitals	2,968

Appearance Support Center

Keiko Nozawa, Naoya Yamazaki, Chikako Shimizu, Shu-ji Kayano, Shoko Toma, Kazuko Aoki

Introduction

The Appearance Support Centre is a new department of the National Cancer Center Hospital (NCCH), established on April 1, 2013. The outpatient consultation space is located on the first floor of the hospital, and it began operating from July 1st. We aim to support patients to be able to 'live in society' and to 'live as a human being', through clinical, research and educational practices regarding issues around the patients' physical appearance. In the current year, our goal is to establish the foundation of an organization and activities to fulfill our duty.

Routine activities

Our team consists of two Clinical Psychologists (1 full-time and 1 part-time) specialized in cosmetic knowledge, and they consult with both in- and outpatients as well as their families for questions and concerns regarding the patients' physical appearance. Examples of issues dealt with are the side effects of chemotherapy and radiotherapy on skin, nails and hair loss, scarring and post-surgery epitheses, and coping with mastectomies. 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 Monday-Thursday from 12-1 pm, providing a space in which patients can try on different products and consult staff. Despite limited hours for security reasons, we have had 445 users from July to December 2013. Additionally, we also run a patient support program titled *Cosmetic Information* every Tuesday and Thursday from 1 pm. Its main aim is the provision of information to patients through group sessions. We have conducted 51 sessions in which 229 patients participated.

For individual consultations for new patients, within six months there were a total of 287 consultations by 106 in- and outpatients. Main concerns were coping strategies with hair loss and specific symptoms of the skin and nails. Reasons for consultation 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, especially on account of the lack of evidence and increased risks of information regarding physical appearance that is currently available. Current research projects are: the multi-faceted examination of the efficacy of support programs for patients regarding physical appearance, research for establishment of guidelines for cancer patients' appearance support, and investigation and development of the appearance-care educational training system. Additionally, the study of patients' needs and the development and trials of products as possible solutions are carried out continuously through daily clinical practice.

Education

In order to foster medical staff that can practice appearance-care, a basic educational workshop was conducted for medical staff from designated regional cancer centers and hospitals. Additionally in order to enable implementation of the same program at the Kyushu Cancer Center and Shikoku Cancer Center, we conducted a special educational workshop as well.

We are contributing to the fostering of medical staff that possess understanding of physical appearance support by not only conducting workshops for nurses and pharmacists but also by allowing intern visits, holding hospital study sessions, and accepting internships as "Orange Casts" (Young patient volunteers) as well as from surviving student cancer patients.

Future prospects

We anticipate the emergence of new issues regarding physical appearance as the variety in treatment drugs increases, survival rates increase, cosmetic surgeries develop, and innovations continue in cosmetic products. Although responding to the

needs of all patients is difficult as fulltime workers are scarce, we hope to expand human resources and develop this emerging field based on research. Additionally in clinical practice, we aspire to conduct more workshops in order to improve cooperative networks within and outside the hospital.

List of papers published in 2013

Journal

1. Nozawa K, Shimizu C, Kakimoto M, Mizota Y, Yamamoto S, Takahashi Y, Ito A, Izumi H, Fujiwara Y. Quantitative assessment of appearance changes and related distress in cancer patients. Psychooncology, 22:2140-2147, 2013

Rare Cancer Center

Akira Kawai, Hirokazu Chuman, Eisuke Kobayashi, Motokiyo Komiyama, Satoshi Okada, Makoto Kodaira, Mayu Yunokawa, Shunsuke Kondo, Chitose Ogawa, Miyuki Sone, Minako Sumi, Akihiko Yoshida, Takuro Sakurai, Yoshitaka Narita, Naoya Yamazaki, Shigenobu Suzuki, Tadashi Kondo, Naohiro Higashi, Makiko Murase, Yoko Kato, Umio Yamaguchi, Naoto Gotohda, Toshihiko Doi, Yoichi Naito, Ako Hosono, Tetsuo Akimoto, Junya Ueno

The Rare Cancer Center was established in December 2013 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 no generally agreed definition of rare cancers. Rare diseases are often defined as those with a prevalence of < 50/100,000. In the US, the Orphan Drug Act defined rare diseases as those affecting < 200,000 persons. According to the definition of the project Surveillance 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 cancers is combined, it corresponds to up to 15% of all new cancer diagnoses.

Information (epidemiologic, medical, and social) 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.

The Rare Cancer Center plays a central role in the treating and managing of rare cancers in the 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 Hospitals.

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

Top enable the Center to play its role, a total of 27 doctors, nurses and researchers dealing with rare cancers have joined as members of the Center. They originate from the Departments of Musculoskeletal Oncology and Rehabilitation, Neurosurgery and Neuro-Oncology, Ophthalmic Oncology, Urology, Gynecology, Dermatologic Oncology, Gastric Surgery, Breast and Medical Oncology, Pediatric Oncology, Diagnostic Radiology, Radiation Oncology, Phase I Unit, Pathology, Nursing, Research Institute and the Center for Cancer Control and Information Services.

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. In addition to the daily clinical activities, the Center members supported "A workshop on the measures against rare cancers in Japan" which was held by the Center for Cancer Control and Information Services on February 16th 2014.

The Rare Cancer Center provides consultation to the patients and relatives with rare cancers on the telephone (Rare Cancer Hotline). The Center is now planning to provide comprehensive, scientifically based, up-to-date unbiased information about rare cancers to all patients, families and health professionals fighting against rare cancers via our website.

Surgical Center

Hitoshi Katai

Introduction

The Surgical Center deals with all kinds of malignant neoplasms. 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 2013, the Surgical Center supported more than 4,835 surgical cases and more than 4,193 general anesthesia surgical cases, a 2.9% increase in the number of cases and a 2.3% increase in the general anesthesia cases over 2012. 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.

The Da Vinci robotic surgical system has been introduced to provide less invasive surgery for the patients.

The Surgical Center staff work as part of a multidisciplinary team active in planning the best utilization of the 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.

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	1768
General and epidural	202	193	188	210	207	199	205	200	206	226	193	199	2428
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	4835

Table 2. Number of general anesthesia cases

	Jan.	Feb.	March	Apr.	May	June	July	Aug.	Sep.	Oct.	Nov.	Dec.	Total
Neurosurgery	12	10	11	11	11	11	13	8	9	11	11	7	125
Opthalmology	24	30	32	26	26	31	27	22	21	26	26	26	319
Head & Neck Surgery	12	13	15	16	12	13	16	14	13	16	16	11	168
Breast Surgery	42	42	41	37	43	28	34	32	30	32	32	29	427
Thoracic Surgery	49	52	45	55	55	54	56	55	50	60	60	57	643
Esophageal Surgery	9	9	13	12	5	10	8	11	10	10	10	8	119
Gastric Surgery	38	39	36	45	36	50	40	35	40	38	38	37	480
Colorectal Surgery	35	38	40	39	36	38	37	36	48	34	34	33	458
Hepatobiliary & Pancreatic Surgery	19	19	27	22	28	23	29	25	21	22	22	23	281
Gynecology	15	18	17	20	17	15	11	19	17	14	14	16	197
Urology	20	21	16	20	24	23	24	24	17	23	23	18	257
Dermatology	9	8	7	8	11	10	9	9	7	7	7	7	104
Orthopedic Surgery	21	21	14	18	21	23	23	23	20	23	23	23	264
Others	20	18	16	25	24	32	41	41	29	32	32	40	351
Total	325	338	330	354	349	361	354	354	332	348	348	335	4193

Physician Referral Service Office

Hidehito Horinouchi, Makiko Murase, Rieko Shimizu, Yukiko Higuchi, Hisako Tanaka, Keiko Tsutsumi, Kayoko Yamada, Hiroe Ishii

Introduction

The Physician Referral Service Office was established as an independent section directly under the Director of National Cancer Center Hospital (NCCH) and started its service in April 2013. The mission of this office is to provide appropriate access to best cancer practice for more patients and their physicians.

To help cancer patients with various needs to visit the NCCH, the Physician Referral Service Office consists of a physician, a nurse, a medical social worker and three clerks. This office also deals with inquiries for patients' medical records from their physician. Another important activity is to record and analyze the information concerning patients' referrals to the NCCH.

Routine activities

1. Physician referral service

Under strong collaboration with the reservation center, this office supports patients and their physicians to select the most appropriate doctor promptly.

2. Inquiries for patients' medical records

We receive and deal with inquiries regarding medical records from physicians who see patients from our hospital.

3. Relationship with affiliated hospitals and clinics

We send reminders to patients' physicians on the occasion of the patients' first visit to our hospital. To maintain the relationship, we hold regular meetings and invite physicians from affiliated hospitals and clinics.

4. Recording and analysis of clinical information

The information regarding all patients and their physicians is appropriately recorded in order to analyze the data and apply them for planning the subsequent strategies for a better service.

5. Cooperation with intramural departments and staff

To provide best practice, we make the utmost efforts to collaborate with intramural departments, sections and staff.

Table 1. Routine activities of Physician Referral Service Office

	Referral reply letters	Medical record inquiries	FAX	Reservation support
April	-	2	-	-
May	-	21	-	3
June	340	16	2	8
July	773	17	7	14
August	695	18	11	11
September	725	11	6	9
October	809	54	15	14
November	722	46	7	20
December	695	52	30	17
Total	4759	237	78	96

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 (the Clinical Research Coordinating Division and Administrating Division). The staff members, nurses, pharmacists and laboratory technologists, participate in this division 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 many of the industry-sponsored registration trials as well as the physician-initiated registration directed clinical trials. A total of 22 CRCs (clinical research coordinators) are supporting these trials. The number of the industry-sponsored registration trials is increasing year by year, and we supported 232 registration-directed clinical trials including 10 physician-initiated registration directed clinical trials in 2013 (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 2013

Phase	Ongoing	New (since 2013)	Total
I	41	25	66
I/II	16	5	21
II	27	18	45
II/III	2	1	3
III	51	23	74
POS	13	1	14
Medical device	2	2	4
In vitro diagnostics	0	1	1
IITs	8	5	13
Total	160	81	241

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

Nutrition Management Office

Mayumi Miyauchi, Tomoko Suzuki, Masahiro Sunaga, Hiroko Takashima, Noriko Aoki, Yasuko Muramatsu

Introduction

In 2013, we increased the number of staff exclusively engaged in the Nutrition Support Team and those almost exclusively engaged in the NST, resulting in enhancement of the NST activities.

The Metabolism and Clinical Nutritional Society released the results of an investigative study into the "Improvement of taste disorder through development of supportive care".

We started "An investigative commission regarding meal functional disorders in cancer medical treatment" in December.

We are creating an assessment sheet to enable nutritional management tailored for patients who have ingestion-retarding side effects. Through coordinating nutritional management with other appropriate hospitals, we believe that the completion of such assessment sheets and translating the results into dietary changes can help to improve the rate of improvement brought about by the medical treatment, and in the training of newly-starting dietitians.

Six years ago, the NST started working on a nutritional assessment of cancer patients, and measured resting metabolic changes in body constituents in the course of treatment, such as esophageal surgery and hepatobiliary-pancreatic surgery. This study has continued to accumulate data, and the results were released at The Clinical Nutrition meeting.

Routine activities

Dietary meals totaled 427,859 in 2013, and we gave nutrition-related dietary advice to 1,285 persons. There have been 951 requests for consultation to the NST, 79 per month on average, and this aspect of the Office has shown strong growth by 18% annually (Table 1).

Following release of our leaflet, "A hint when troubled at the time of food", We obtained the cooperation of the Foundation for Promotion of Cancer Research, and we have created "Hints for an appropriate diet before medical cancer treatment". These leaflets have been widely supplied to cancer treatment institutions all over the country and to many related organizations, with good utilization being seen by both medical staff and patients.

In the field of human resource development, we have a strong commitment to education and training and we conducted 10 University courses for registered dietitians within the University. By strengthening our cooperation with universities, our aim is to enhance research activities in the future through the development of human resources.

Research activities

1) The Nutritional Management Workshop for cancer patients has reached its the 32nd anniversary, and "Nutrition past, present and future" was delivered as the President's lecture in Kanazawa.
2) In cooperation with nutritionists of the Nutritional Management of Cancer Course we held lectures to help target the general public regarding a cancer-preventative diet (Ishikawa, Tokyo).
3) Research projects
   1. Survey of dysgeusia
   2. Studies on nutrition in the surgical treatment of esophageal cancer
   3. Perioperative nutritional assessment after pancreaticoduodenectomy

Future Prospects

The central goal of the Nutrition Management Office continues to be promotion of nutritional management for cancer patients to help them, and their families, across the country. Studies continue to lead to a practical research project that will seek to enhance the outcomes for cancer patients and their families.

Table 1. Number of NST consultations in 2013

Clinical Departments	Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sept	Oct	Nov	Dec	Total
Esophageal Surgery	2	4	5	1	1	4	5	3	2	5	4	3	39
Head and Neck Surgery	5	6	4	2	5	1	7	7	4	8	5	5	59
Gastrointestinal Medical Oncology	10	15	9	13	18	12	20	15	14	17	9	11	163
Hematopoietic Stem Cell Transplantation	13	12	14	8	12	10	6	21	7	14	9	12	138
Thoracic Oncology	7	3	11	7	4	4	2	3	3	3	3	2	52
Thoracic Surgery		2		1	1		1	2	2	2			11
Hepatobiliary and Pancreatic Oncology	4	4	3	2	1	1	2	2		2	2	1	24
Hepatobiliary and Pancreatic Surgery	10	7	7	7	11	8	10	9	8	5	6	6	94
Breast Oncology and Mecal Oncology	2	4	8	4	10	7	6	7	4	5	5	4	66
Gynecology	4	2	1	1	2	1		2	2	2	3	1	21
Neurosurgery and Neuro-Oncology	1	1			1		1	1	1	2			8
Gastric Surgery	4	4	1	5	2	5	5	1	2	31	27	28	115
Colorectal Surgery		1	2	2	1	2	2	1	1			1	13
Urology	3	3	4	6	3	3	5	2	2	3	4	3	41
Pediatric Oncology		2		2	1					1			6
Orthopedic Surgery		1	2	2	1	4	2		1	1	1	2	17
Dermatologic Oncology	1		2	2	2		2		3			1	13
Hematology	2	1	1	5	6	4	2	2	2	2	4	2	33
Radiation Oncology			1	2		3	2	5	2	4	4	3	26
Diagnostic Radiology		3	4		1								8
Breast Surgery													0
Gastrointestinal endoscopy								1		1			
Respiratory Endoscopy									1	1			2
Total	68	75	79	72	83	69	80	84	61	109	86	85	951
												mean	67

Health Information Management Office

Hiroshi Nishimoto, Mieko Furumoto, Tomoko Takehara, Marika Noduki, Yukiko Sekimizu, Hisayo Nishizawa, Mari Samejima

Introduction

The Health Information Management Office was established in April, 2011. We are taking over several duties from the Cancer Information Services and Surveillance Division. One of them was the Audit of Discharge Summary, and another was the National Cancer Center Hospital (NCCH) Cancer Registry which is executed as a hospital-based cancer registry. Some statistical duties for the NCCH and Prognostic Investigation were taken over by the Medical Affairs Office, but since the main initiatives of the NCCH are activities against cancer, we will expand our role as the major statistics office of the NCCH.

Routine Activities

Auditing Discharge Summary (Quantitative inspection)

Data on discharge summaries should be entered by the attending physician. We inspected and checked about 12,000 summaries and, where required, gave some advice regarding correct input.

NCCH Cancer Registry (Hospital-based Cancer Registry)

The Office has managed the NCCH Cancer Registry since 2004, handling more than 6,000 records a year. We have provided our data to the Japanese Institutional Cancer Database that is handled by the Center for Cancer Control and Information Services of the NCC.

Table 1. National Cancer Center Hospital Cancer Registry

Year of Diagnosis	Numbers of New Cancer Cases		
	Total	Male	Female
2009	6,721	3,895	2,826
2010	6,636	3,926	2,710
2011	6,471	3,721	2,750
2012	6,486	3,662	2,824

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 in keeping with the National Cancer Center Hospital's (NCCH) 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 electronic 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.

Education and Training

The NCCH offers a three-year postgraduate pharmacist residency 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. Moreover, residents provide pharmaceutical care to ambulatory care patients and participate in an oncology-focused Drug Information Program. This clinical acumen coupled with didactic training in the basic science of oncology will prepare the resident to investigate therapeutic questions related to the care of cancer patients. In the third year, residents participate in specialized pharmaco-clinical practice and research activities, which may be tailored to the resident's goals. There are also 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 1. Number of Prescriptions in 2013

1) Oral and topical preparations	
Prepared in the hospital pharmacy	148,728
Inpatients	134,884
Outpatients	13,844
Taken to outside pharmacies	75,813
(% of prescription filled outside)	84.6
2) Injections	
Inpatients	279,808
Outpatients	39,509

Table2. Amounts of Drugs Consumed in 2013

	(including sales tax)	(%)
Total	4,819,668	100.0
Internal medicines	618,303	12.8
External	8,395	0.2
Injection	3,315,578	68.8
Narcotics	141,831	2.9
Blood	411,608	8.5
X-ray imaging	227,332	4.7
RI	47,896	1.0
Others	48,724	1.0

Unit:1000 yen

Table 3. Aseptic Preparation of Injectable Drugs in 2013

Anticancer Drugs	52,598
Others	33,521

Table 4. House Preparations in 2013

Sterilized	65
Non-sterilized	104

Table 5. Investigational Drugs

Newly registered	75
Ongoing study	148
Total	223

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

1) Continuous Nursing for Cancer Survivorship

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 of Nursing 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 11 units, comprising an 8-hour day shift and a 16-hour night shift. Inpatient unit nurses work together more 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 6 patient education programs and consultation services, 3 outpatient clinics by nurses, and 2 support programs 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.

2) Educational Activities

(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 a favorable work-related stress-free environment.

(2) Development of knowledge and skills for cancer nursing

To develop the skills associated with 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 large-group training and 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; Pressure ulcer care; Dysphagia nursing; Radiotherapy and IVR nursing; and Support for discharge and home care coordination nursing. A total of 202 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, 9 certified nurse specialists and 31 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, 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 members.

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

Research activities

We presented 20 studies on nursing at some annual conferences in 2013. 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 through getting support from physicians and statisticians. We expect our nurses from the National Cancer Center Hospital to create and develop cancer nursing to even higher levels of proficiency and expertise.

List of papers published in 2013

Journal

1. Kubota K, Inoue A, Shimizu Y, Kagata S, Yong R, Hirama Y, Shiga M, Kawazoe T. Health-Related Problems after the Great East Japan Earthquake: An Evaluation Based on the Annual Health Examination. Journal of Nursing & Care, 2:134, 2013