Hospital East

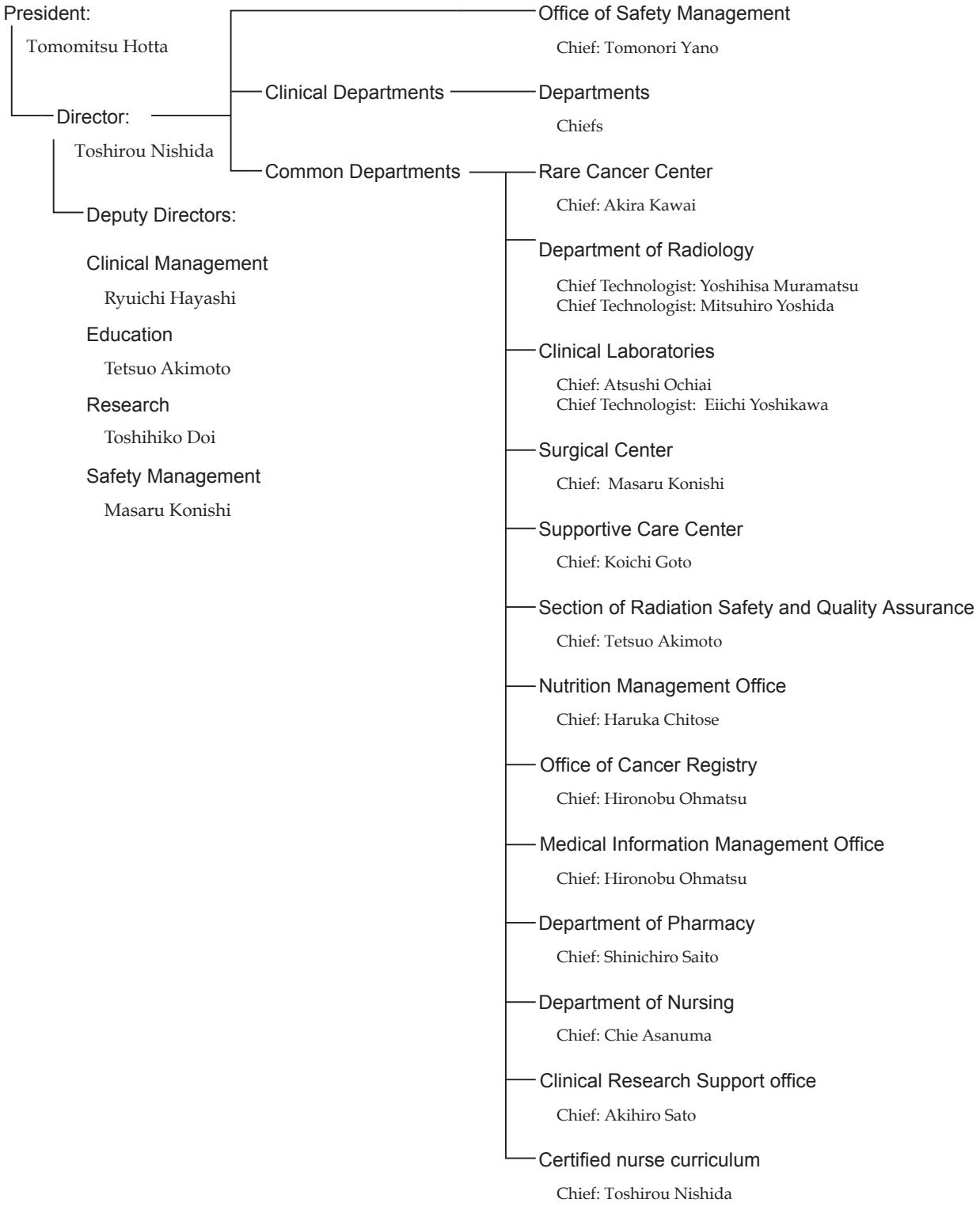
Preface

In 2015, the number of new cancer patients in the Hospital East increased constantly: the number of average patients in hospital stays was 388.9/day, with an occupied bed rate of 98.6%, and the number of outpatients was 1,071.2/day, respectively, which was the highest number in our hospital history. We opened a new outpatient ward in 2014, and expanded the Ambulance Treatment Center in response to the growing number of patients. In addition, the Center for Developing Next-generation Endoscopic-surgical Treatment (NEXT) will be completed in spring 2017, with plans for further expansion of the operating and endoscopy rooms. From a treatment perspective, our staff breaks down departmental barriers and works together laterally (under informed consent) to carry out the best treatment for patients. In addition, we provide patient support from multi-occupational teams consisting of physicians, nurses, pharmacists, nutritionists, social workers, certified social insurance labor consultants, and others. These teams give patients physical, emotional, and social aid through surgery and multiple hospital visits. As the Supportive Care Center, we have integrated multi-occupational teams since 2014, and have built a system by which we can provide patients with seamless support from the time of their first visit. We have also established a medical treatment concierge to treat patients from within Japan as well as from overseas. We have achieved top-level results in Japan in all the fields including the surgical field which performed high-difficulty minimally invasive surgery by specialists with a wealth of experience; the internal medicine field conducted the latest treatments with anticancer agents by experts in drug therapy; in radiation therapy, we implemented intensity-modulated radiation therapy (IMRT) under high-quality control in addition to taking the advantage of Japan's first proton radiation therapy facility; and the endoscopic field boasted skilled techniques and performed historic contributions to the development of endoscopic equipment.

From a research perspective, our hospital was selected as the "Core Hospital for Clinical Research" designated by the Ministry of Health, Labour, and Welfare in 2015. Together with the EPOC and Tsukiji campus, our hospital has realized numerous global achievements as a central hub for the development of cancer-related pharmaceutical products and medical devices in Japan. These facilities have realized top-class global achievements for promising new treatment drugs, from domestic and international FIH (first-in-human) studies to clinical development studies before approval, and have realized the best achievements in Japan for an investigator-initiated trial of an unapproved drug. In 2015, we launched a nationwide consortium for genomic cancer screening (SCRUM-Japan), in cooperation with more than 200 Japanese facilities and 15 pharmaceutical companies. Our institutes are the driving force behind construction of a system for precision medicine in cancer treatment in Japan, wherein the optimal treatment drug is selected according to the results of genetic analysis. In addition, current advances employ the latest equipment, even in remarkable immunotherapies; and research aimed at improved treatment outcomes and optimization for patients is progressing. In device development, our hospital was selected in recognition of activities to promote the practical use of innovative pharmaceutical products, medical devices, and regenerative therapy products (endoscopic field) in 2012, and has produced several recognized or approved devices in this field. In 2015, the "C-square", an academia-industry consortium for surgical devices development was started with the support of Chiba Prefecture Chamber of Commerce and Industry. Next year, the NEXT building, a high-level device developing center with a coordinating organization, will be launched.

Atsushi Ohtsu, M.D., Ph.D.
Director
National Cancer Center Hospital East

Organization



Clinical Departments

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Deputy Directors:

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Ryuichi Hayashi

Education
Tetsuo Akimoto

Research
Toshihiko Doi

Safety Management
Masaru Konishi

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  Chief: Ryuichi Hayashi
- Department of Head and Neck Medical Oncology
  Chief: Makoto Tahara
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  Chief: Atsushi Ochiai
- Department of Experimental Therapeutics
  Chief: Toshihiko Doi

Activities of the Departments

Department of Head and Neck Surgery

Ryuichi Hayashi, Masakazu Miyazaki, Takeshi Shinozaki, Toshifumi Tomioka, Takashi Maruo, Takashi Mukaigawa, Kazuki Hashimoto

Introduction

Surgical treatment of head and neck cancer must meet two contradictory requirements: (1) the resection volume must be sufficiently large to remove all cancer cells, and (2) the resection volume should be sufficiently small to preserve important functions such as swallowing, speech, vision, and cosmetic appearance. The Department of Head and Neck Surgery resolves these conflicting requirements mainly by two distinct approaches: (1) conservative surgery and (2) extensive resection with microsurgical reconstruction. We have been developing various larynx-preserving operations following the establishment of the National Cancer Center. These procedures include a partial laryngectomy which is indicated for T1/T2 recurrent glottis carcinoma after radiotherapy. Another example of conservative surgery is partial hypopharyngectomy with preservation of the larynx for hypopharyngeal carcinoma. Recently, trans-oral resection, such as ER or ELPS, for pharyngo-laryngeal cancer using an endoscope has been increasing after detection of superficial head and neck cancer. On the other hand, extensive resection with microsurgical reconstruction is designed to minimize loss of function following ablative surgery by employing the microsurgical transfer of various flaps.

Routine activities

The current treatment policy for head and neck cancer is multimodal therapy. To effectively implement available therapeutic modalities, four staff surgeons at the Department work closely with plastic surgeons, radiotherapists, medical oncologists, pathologists, dentists, psycho-oncologists, nurses, and other hospital staff. To facilitate regular communication among the members of this large team, several weekly conferences are conducted. The number of new cases who were treated in the hospital was 543 and the number of operations was 531. A total of 68 cases underwent ESD or ELPS and 97 cases underwent free flap reconstruction.

Research activities

1) Cystadenocarcinoma of the salivary glands with potential lymph node metastasis.

Cystadenocarcinoma is classified as a low-grade histological subtype of salivary gland tumors. Although the tumor has the potential to produce lymph node metastases, it is generally an indolent tumor with a good prognosis as compared with high-grade subtypes. Long-term follow-up paying close attention to lymph node metastases is necessary for cystadenocarcinoma.

2) Nine cases of carcinoma with neuroendocrine features in the head and neck: clinicopathological characteristics and clinical outcomes

As neuroendocrine carcinomas in the head and neck region are extremely rare, their clinicopathological characteristics remain largely unknown. Moreover, the 2005 World Health Organization classification criteria for head and neck carcinomas with neuroendocrine features have numerous limitations. Therefore, the clinicopathological features and patient outcomes of these tumors must be clarified. Carcinomas with neuroendocrine features were found to have an aggressive clinical course, which corresponded with the Ki-67 index and mitotic count. Owing to the difficulty in appropriately diagnosing head and neck carcinomas with neuroendocrine features using the current classification system, a new classification system should be developed for use in these cases.

Clinical trials

1) Multicenter study to establish the indication of neck dissection for head and neck squamous cell carcinoma. A prospective observation study is being conducted and over 300 cases have been enrolled to this study from nine hospitals. Neck dissection at Level IIb and V areas influence the rate of postoperative accessory nerve palsy but the necessity of dissection of these areas is still controversial because of the low prevalence rate of lymph node metastasis. A randomized clinical trial will be run after evaluating the results of this study.
2) Evaluation of swallowing function related to the treatment for head and neck cancer

This prospective observation study is conducted to evaluate the swallowing function after treatment for oropharyngeal cancer. This study is related to standardizing the assessment of the swallowing function.

Education

Two senior residents and two residents were recruited to our department in 2015. One head and neck surgeon from Hong Kong visited our department for training. Our Department was assigned as one of the observation centers of the International Federation of Head and Neck Oncologic Societies (IFHNOS) fellowship program from 2014.

Future prospects

Trans-oral resection by using an endoscope has become a standard surgical procedure for superficial pharyngeal cancer. We are going to get authorization for insurance about endoscopic resection and are planning to develop new surgical equipment for these operations.

Table 1. Number of new patients

Oral cavity	125
Pharynx	158
Larynx	73
Sino-nasal cavity	33
Thyroid gland	85
Major salivary glands	34
Others	35
Total	543

Table 2. Number of surgery patients

Oral cavity	149
Pharynx	165
Larynx	45
Sino-nasal cavity	10
Thyroid gland	66
Major salivary glands	25
Others	71
Total	531

List of papers published in 2015

Journal

1. Hamamoto T, Fujii S, Miyazaki M, Shinozaki T, Tomioka T, Hayashi R. Nine cases of carcinoma with neuroendocrine features in the head and neck: clinicopathological characteristics and clinical outcomes. Jpn J Clin Oncol, 45:328-335, 2015

Department of Head and Neck Medical Oncology

Makoto Tahara, Susumu Okano, Tomoko Yamazaki, Tomohiro Enokida, Tetsuro Wakasugi

Introduction

The Department of Head and Neck Medical Oncology is engaged in the clinical management of patients with head and neck cancer (HNC), and research into anticancer drugs for the treatment of HNC.

Our missions are to: 1) provide the best evidence-based treatment; 2) promote the importance of supportive care in the treatment of patients with HNC; 3) facilitate the timely approval of new drugs by active participation in global clinical trials to eliminate the drug lag; 4) develop cutting-edge treatments; and 5) train experts in head and neck medical oncology.

Routine activities

Our department consists of three physicians, one senior resident and one resident. We manage the treatment of HNC patients who receive anticancer drugs. An estimated 60% of HNC patients require a multidisciplinary approach, including surgery, radiotherapy, and chemotherapy. Furthermore, HNC patients are at risk of injury and impairment of vital organs both from the cancer itself and from the series of treatments provided to cure it. In treating patients, we therefore, carefully assess both the curability of the condition and possible subsequent complications, such as swallowing dysfunction and cosmetic changes. Given the increasing complexity of the management of HNC, the recommended treatment for patients who are referred to our institution is decided at weekly tumor board meetings attended by a multidisciplinary team.

A total of 276 patients were referred to our department from January 2015 to December 2015 (Table 1). The outpatient service of our department is available from Monday to Friday. We carefully follow patients during and after treatment and provide palliative chemotherapy as an outpatient service.

Research activities

Our research activity has focused on two areas: the development of new treatments in clinical trials for HNC and biomarker analysis in HNC.

1) Development of new treatments

Based on the results of our previously reported feasibility study (Kiyota N, Tahara M, et. al, The Japanese Journal of Clinical Oncology 2012), a multicenter phase II/III trial of postoperative concurrent chemoradiotherapy with weekly CDDP compared with postoperative concurrent chemoradiotherapy with 3-weekly CDDP for high risk squamous cell carcinoma of the head and neck (SCCHN) (The Japan Clinical Oncology Group (JCOG) 1008) is now ongoing. In phase II, the safety of both treatment arms has been confirmed.

After the approval of cetuximab for HNC in Japan, the following multicenter clinical trials that we planned as the primary investigator are ongoing: 1) CSPOR-HN01: The phase II study of docetaxel, cisplatin and cetuximab (TPE) followed by cetuximab with concurrent radiotherapy in patients with local advanced SCCHN, 2) CSPOR-HN02: Phase II trial of a combination with paclitaxel, carboplatin and cetuximab (PCE) as a first line treatment in patients with recurrent and/or metastatic SCCHN. Patient enrollments of both trials have been completed and the results will be open soon.

2) Biomarker analysis

An analysis of gene expression profiles in tongue squamous cell carcinoma (TSCC) is being carried out to determine the biomarker that can predict treatment outcomes. We then identified 27 genes with the most predictive value for recurrence, five genes highly expressed in the low-risk

group and 22 highly expressed in the high-risk group. Clustering into high- and low-risk groups based on this 27-gene expression in a validation study also showed a significant association with recurrence. Clinicopathological and biomarker analyses of early stage (T1/2) TSCC are also ongoing.

A prospective study to compare the miRNA expression patterns in head and neck cancer patients revealed that an extreme change of expression was observed in 6 miRNAs before and after completion of surgery and 20 miRNAs between healthy volunteers and head and neck cancer patients. These results suggest that these miRNAs will be good candidates for biomarkers to predict either incidence or recurrence for HNC.

Clinical trials

A feasibility study of a combination with docetaxel, cisplatin and 5-FU (TPF) as an induction chemotherapy (IC) for locally advanced SCCHN has been completed. A total of 48 patients were accrued. 41 patients (85.4%) received the full course of IC and 33 patients (82.5%) received the planned cardiac resynchronization therapy (CRT). To evaluate the feasibility of a combination with paclitaxel, carboplatin and cetuximab (PCE) as IC, a feasibility study for unresectable locally advanced SCCHN is now ongoing.

To facilitate the timely approval of new drugs and eliminate the drug lag, we have also participated in the global phase trials including immune-checkpoint inhibitors.

Education

We educate not only medical staff in our institute but also outside of our institute by conducting the following education program: 1) Seminar of Japan society of supportive care for patients with HNC and 2) Preceptorship in HNC. A number of Asian physicians participated in preceptorship in HNC this year. Furthermore, our department is accepting trainees all the time.

Future prospects

We hope that ongoing or planned clinical trials will change the standard of care for HNC and our biomarker analysis will lead to the development of new treatment strategies. Our education program will increase the number of medical oncologists who take charge of treatment for HNC, leading to improving patient's quality of life.

Table 1. Number of patients according to sites

Primary site	No. of patients (N=276)
Nasal cavity	33
Nasopharynx	17
Oropharynx	44
Hypopharynx	55
Oral cavity	57
Larynx	16
Salivary	14
Thyroid	28
Other	12

Table 2. Number of patients according to procedure

Type of procedure	No. of patients (N=263)
Induction chemotherapy followed by CRT	45
CRT	34
Palliative chemotherapy	47
Study drug	12
Others	136

List of papers published in 2015

Journal

1. Tahara M, Kiyota N, Mizusawa J, Nakamura K, Hayashi R, Akimoto T, Hasegawa Y, Iwae S, Monden N, Matsuura K, Fujii H, Onozawa Y, Homma A, Kubota A, Fukuda H, Fujii M. Phase II trial of chemoradiotherapy with S-1 plus cisplatin for unresectable locally advanced head and neck cancer (JCOG0706). Cancer Sci, 106:726-733, 2015

2. Zenda S, Ishi S, Akimoto T, Arahira S, Motegi A, Tahara M, Hayashi R, Asanuma C. DeCoP, a Dermatitis Control Program using a moderately absorbent surgical pad for head and neck cancer patients receiving radiotherapy: a retrospective analysis. Jpn J Clin Oncol, 45:433-438, 2015

3. Zenda S, Kawashima M, Arahira S, Kohno R, Nishio T, Tahara M, Hayashi R, Akimoto T. Late toxicity of proton beam therapy for patients with the nasal cavity, para-nasal sinuses, or involving the skull base malignancy: importance of long-term follow-up. Int J Clin Oncol, 20:447-454, 2015

4. Schlumberger M, Tahara M, Wirth LJ, Robinson B, Brose MS, Elisei R, Habra MA, Newbold K, Shah MH, Hoff AO, Gianoukakis AG, Kiyota N, Taylor MH, Kim SB, Krzyzanowska MK, Dutcus CE, de las Heras B, Zhu J, Sherman SI. Lenvatinib versus placebo in radioiodine-refractory thyroid cancer. N Engl J Med, 372:621-630, 2015

5. Kiyota N, Tahara M, Fujii M. Adjuvant treatment for post-operative head and neck squamous cell carcinoma. Jpn J Clin Oncol, 45:2-6, 2015

6. Machiels JP, Haddad RI, Fayette J, Licitra LF, Tahara M, Vermorken JB, Clement PM, Gauler T, Cupissol D, Grau JJ, Guigay J, Caponigro F, de Castro G, de Souza Viana L, Keilholz U, Del Campo JM, Cong XJ, Ehrnrooth E, Cohen EE, LUX-H&N 1 investigators. Afatinib versus methotrexate as second-line treatment in patients with recurrent or metastatic squamous-cell carcinoma of the head and neck progressing on or after platinum-based therapy (LUX-Head & Neck 1): an open-label, randomised phase 3 trial. Lancet Oncol, 16:583-594, 2015

7. Schlumberger M, Tahara M, Wirth LJ. Lenvatinib in radioiodine-refractory thyroid cancer. N Engl J Med, 372:1868, 2015

8. Kiyota N, Schlumberger M, Muro K, Ando Y, Takahashi S, Kawai Y, Wirth L, Robinson B, Sherman S, Suzuki T, Fujino K, Gupta A, Hayato S, Tahara M. Subgroup analysis of Japanese patients in a phase 3 study of lenvatinib in radioiodine-refractory differentiated thyroid cancer. Cancer Sci, 106:1714-1721, 2015

9. Tahara M, Fuse N, Mizusawa J, Sato A, Nihei K, Kanato K, Kato K, Yamazaki K, Muro K, Takaishi H, Boku N, Ohtsu A. Phase I/II trial of chemoradiotherapy with concurrent S-1 and cisplatin for clinical stage II/III esophageal carcinoma (JCOG 0604). Cancer Sci, 106:1414-1420, 2015

Book

1. Tahara M. Systemic chemotherapy. In: Kirita T, Omura K (eds), Oral Cancer - Diagnosis and Therapy, Japan, Springer Japan, pp 307-318, 2015

Department of Plastic and Reconstructive Surgery

Minoru Sakuraba, Takuya Higashino, Azusa Oshima, Yaso Saito, Shuchi Azuma, Satsuki Tachibana

Introduction

The Department of Plastic and Reconstructive Surgery has mainly focused on surgical reconstruction following cancer ablation. In our institution, reconstructive procedures using free flap transfer with microvascular anastomosis are the most important operations (Figure 1). In addition, several methods such as tissue transfer with pedicled flaps, local flaps and skin grafts are used for reconstructive surgery. The objectives of reconstructive surgery are not only morphological reconstruction, but also the restoration of postoperative functions after ablative surgery. The quality of life (QOL) of the patients can be improved with functional and morphological reconstruction.

Routine activities

Five plastic surgeons cover reconstructive operations both in the National Cancer Center Hospital (NCCH) East in Kashiwa and the NCCH in Tokyo, and train the residents in the two hospitals. These reconstructive surgeries are performed in cooperation with the surgeons of other departments of the hospital, such as the Department of Head and Neck Surgery, Breast Surgery, Orthopedic Surgery, Esophageal Surgery, and Colorectal Surgery and Urology (Table 1). In the NCCH East, Head and Neck reconstruction is the most frequently performed operation accounting for about 60% of reconstructive surgery. In the Head and Neck region, a free jejunal transfer and anterolateral thigh flap transfer are the most frequently used procedures (Table 2). A weekly conference is held with doctors of the Department of Head and Neck surgery, Radiation Oncology and Head and Neck Oncology. Breast reconstruction using autologous tissue transfer was employed in 2005, since then, patients' needs for breast reconstruction is increasing. Also, lymphatico-venular anastomosis as a surgical treatment for lymphedema of the extremities was introduced in 2013.

Research activities and Clinical trials

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 QOL 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 for reconstructive surgery and developing new techniques of reconstructive surgery are the most important aims of our studies. Multi-institutional analysis of postoperative complication and swallowing function after total pharyngo-laryngo-esophagectomy and reconstruction with a free jejenal graft was performed continuously. This study was supported by a Grant-in-Aid for Cancer Research. The aim of the study is to clarify the relationship between surgical procedures and postoperative complication and function.

Another multi-institutional analysis of postoperative complication after microsurgical head and neck reconstruction was carried out to clarify the risk factor of postoperative vascular thrombosis. Data registration was closed and the data is now under evaluation.

In 2015, we also started to take an active part in a new multi-institutional analysis of risk factors for functional outcome after tongue reconstruction.

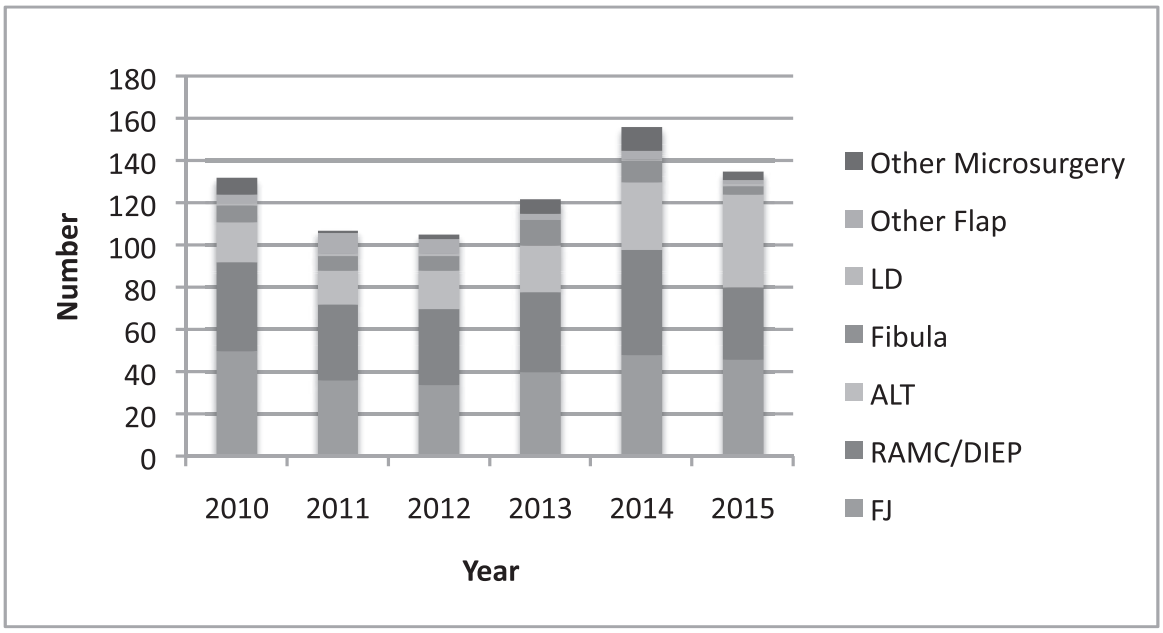

Figure 1. Number of Microsurgeries

Table 1. Number of patients

Cooperation with other divisions	
NCCH East	No. of patients
Head and neck surgery	130
Musculoskeletal oncology	7
Esophageal surgery	5
Breast surgery	66
Dermatologic oncology	—
Urology	0
Hepatobiliary and pancreatic surgery	2
Ophthalmic oncology	—
Colorectal surgery	4
Gastric surgery	1
Thoracic surgery	2
Gynecology	—
Plastic and reconstructive surgery	9
Others	2
Total	228

Table 2. Type of procedures

Operative procedures	
NCCH East	No. of flaps
Microvascular free flap	131
Jejunum	46
RAMC / DIEP	25 / 9
Anterolateral thigh	44
Fibula bone	4
Latissimus dorsi	1
Radial forearm	1
Other flaps	1
Other Microsurgery	4
Supe charge	0
Nerve graft	0
Limb salvage	0
Hepatic artery	1
Lymphatico-Venular anast	2
Others	1
Subtotal	135
Pedicled flaps	33
PMMC	9
Latissimus dorsi	5
RAMC	2
Other flaps	17
Breast reconstruction	43
Tissue expander	19
Silicone breast implant	11
(Autologous tissue	13)
Other procedures	32
Total	230

Department of Breast Surgery

Kimiyasu Yoneyama, Takashi Hojo, Chisako Yamauchi

Introduction

We treat patients with operable malignant mammary glands. Diagnosis of breast disease, surgical treatment and follow-up for breast cancer patients are mainly our professional practice. The Department consists of three staff surgeons and one resident, and is committed to providing the latest, most comprehensive breast treatments for our patients. The multidisciplinary approach to the diagnosis and treatment of cancer are carried out through cooperation between related specialists: surgeons, radiologists, plastic surgeons, pathologists, medical oncologists, specialized nurses, and technicians.

The Department mainly focuses on "minimally invasive surgery" and performs a thorough investigation for an oncologically safe approach, less morbidity and good cosmesis. For example, although sentinel lymph node (SLN) biopsy has already been established as the standard care for clinical node negative patients, omitting axillary lymph node dissection (ALND) for positive SLNs with micro- or macrometastasis has started in clinical practice as an expanded indication. On the other hand, preoperative systemic therapy provides the opportunity for a curative operation or breast-conserving surgery to avoid mastectomy. Moreover, we can provide breast reconstructive surgery in collaboration with the Plastic Surgery Division. These procedures will contribute to a better quality of life for patients with breast cancer.

Routine activities

For the regular activities of the Department, a daily morning routine round is scheduled for inpatients by all staff and residents. Moreover, our weekly preoperative diagnostic imaging conference on breast cancer is conducted on Monday evenings to discuss the surgical treatment planning for each patient. A clinical conference to decide on courses of treatment by multidisciplinary breast care team members is held twice a month. A monthly pathological conference on breast cancer is also conducted on the last Friday of each month. At those conferences, individual cases are presented to a team of highly trained cancer specialists, including radiologists, breast surgeons, pathologists, radiation oncologists, and medical oncologists. Indeed, our multidisciplinary team approach to breast cancer treatment sets the quality of care we provide for our patients well apart from the norm.

Changes in the annual number of patients with breast cancer who underwent surgery are shown in Table 1. A total of 313 patients with primary breast cancer and 46 patients with recurrence or other breast disease were operated on. 14 immediate breast reconstruction surgeries were included. Of the patients with primary breast cancer, 71 (23%) underwent primary systemic therapy. The types and number of operative procedures performed in 2015 are shown in Table 2. The rate of breast-conserving surgeries (including two radiofrequency ablation alone cases) was 60% (187/313). Sentinel node biopsy was performed in 255 patients, and 238 patients were spared from ALND.

Research activities

1) Evaluation of the potential role of Ki67 as a biomarker for breast cancer patients.

The Ki67 index is a marker for cell proliferation. A retrospective search of a prospectively maintained clinical breast cancer database was performed. It was concluded that the pre-therapy Ki67 index was a useful predictor for the therapeutic response to neoadjuvant chemotherapy and Ki67 post-therapy was shown to predict outcomes for patients with residual invasive disease.

2) Long-term results of patients treated with sentinel node biopsy (SNB) omitting ALND.

In an observational study, there was not a significant difference in the overall survival and relapse-free survival between SLN negative patients without ALND and those with ALND. We concluded that SLN biopsy without ALND is validated as a safe and effective method for regional node treatment of SLN negative breast cancer patients. We are planning to omit ALND even in SLN positive patients.

3) In vivo cancer detection with a newly designed fluorescent probe.

γ -glutamyl hydroxymethyl rhodamine green (gGlu-HMRG) is a small-molecule aminopeptidase probe which was enzymatically cleaved, revealing a bright fluorescent region of cancer cells which overexpress the enzyme γ -glutamyltranspeptidase (GGT). Visualized tiny cancerous nodules may allow us to delineate the border of tumors and confirm that there are no residual tumors.

Clinical trials

1) Radiofrequency ablation (RFA) using a Cool-tip electrode system (RAFAELO study).

A phase II study on RFA without resection was performed for T=<1.5 cm, N0 breast cancer patients with no extensive intraductal components using a Cool-tip electrode system. This study is certified as an advanced medical treatment by the Ministry of Health, Labour and Welfare.

2) Effectiveness of primary tumor resection for metastatic breast cancer (The Japan Clinical Oncology Group (JCOG) 1017).

In this multicenter clinical trial, the primary tumor resection plus systemic therapy arm is compared to the systemic therapy alone arm in metastatic breast cancer.

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

This is a multi-center randomized phase III trial which started in 2012. This clinical trial is to confirm the superiority of an intensive follow-up to standard follow-up in terms of overall survival in high-risk breast cancer patients.

4) Postoperative therapy with endocrine and TS-1 (POTENT study).

This multi-center randomized trial started in 2012 and is a randomized, controlled study to determine whether S-1 combined with standard postoperative endocrine therapy more effectively inhibits recurrence than standard postoperative endocrine therapy alone in patients with estrogen receptor (ER)-positive, HER2-negative primary breast cancer.

5) Observational study of axilla treatment for breast cancer patients with SLN positive.

This multi-center study is designed to evaluate the outcome of no ALND in sentinel node-positive breast cancer using the propensity score. Patients with 1 to 3 positive micrometastasis or macrometastasis in sentinel lymph nodes are eligible. The primary endpoint is the recurrence rate of regional lymph nodes in patients treated with SNB. Patients treated with SNB followed by ALND are also registered simultaneously to compare the prognosis.

Education

Our education targets are to raise knowledge about breast disease and to operative technical improvement.

Future prospects

We want to solve the appropriate postoperative follow-up that was a longtime problem in breast cancer medical care by clinical trial. And aim at operative development with more minimally invasive surgery.

Table 1. Number of primary breast cancer patients operated on during 2006-2015

Clinical stage	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Stage 0	34	27	23	38	39	43	28	25	29	17
Stage I	79	94	84	86	80	86	91	112	88	131
Stage II	103	87	87	122	137	112	128	138	123	136
Stage III	34	25	33	42	32	43	49	29	39	26
Stage IV	1	4	0	3	1	1	4	2	3	3
Total	251	237	227	291	289	285	300	306	282	313

Table 2. Type of operative procedures performed in 2015 for primary breast cancer

Type of operation	N
BT + SNB	76
BT + SNB→ALND	13
BT + ALND	37
BT alone	0
BP + SNB	149
BP + SNB→ALND	4
BP + ALND	13
BP alone	8
RFA + SNB	13
Total	313

Total mastectomy with immediate breast reconstruction was performed in 30 patients.
BP: partial mastectomy, BT: total mastectomy, SNB: sentinel node biopsy, ALND: axillary lymph node dissection, RFA: radio frequency ablation

List of papers published in 2015

Journal

1. Hojo T, Masuda N, Mizutani T, Shibata T, Kinoshita T, Tamura K, Hara F, Fujisawa T, Inoue K, Saji S, Nakamura K, Fukuda H, Iwata H. Intensive vs. Standard Post-Operative Surveillance in High-Risk Breast Cancer Patients (INSPIRE): Japan Clinical Oncology Group Study JCOG1204. Jpn J Clin Oncol, 45:983-986, 2015
2. Komoike Y, Inokuchi M, Itoh T, Kitamura K, Kutomi G, Sakai T, Jinno H, Wada N, Ohsumi S, Mukai H, Japanese Breast Cancer Society. Japan Breast Cancer Society clinical practice guideline for surgical treatment of breast cancer. Breast Cancer, 22:37-48, 2015

Department of Breast and Medical Oncology

Tetsuo Akimoto, Hirofumi Mukai, Nobuaki Matsubara, Yoichi Naito, Masaoki Sasaki, Ako Hosono, Mai Onomura, Yoko Yamada, Hiroaki Izumi, Tetsuya Urasaki, Yujiro Ueda, Takaaki Yokoyama

Introduction

Patients with different types of cancer, including those with breast and genitourinary tract cancers, are treated with standard chemotherapy and/or managed in clinical trials in daily medical practice at the Department of Breast/Medical Oncology. Gynecological malignancies and soft tissue sarcomas are also treated with chemotherapy. Another major target of the Department is cancer of unknown primary origin. The clinical and research activities of the Department primarily focus on the following fields: Standard chemotherapeutic treatment in medical practice, disease-oriented clinical trials, developmental therapeutics of new anticancer agents sponsored by pharmaceutical companies and development of combination chemotherapy involving newly developed drugs or new combinations of currently available drugs.

Routine activities

The major and specific target disease of the Department comprised breast cancer. Eligible patients were invited to participate in large phase II/III studies. The Department also treated cancers of the genitourinary tract, cancer of unknown primary origin, soft tissue sarcomas and gynecological cancers including uterine and ovarian cancers. For patients with diseases treated with established standard chemotherapeutic regimens, standard chemotherapy was administered in routine medical practice. Patients in whom standard chemotherapy had failed and those with cancers for which standard chemotherapy was unavailable were invited to participate in clinical studies on experimental drugs and regimens. In 2015, 624 patients with different types of cancer visited the Department for consultation. Approximately 400 patients per month received routine chemotherapy as an outpatient service by the Department. The overall inpatient care system of the held on every morning. A weekly educational meeting is conducted on Thursday morning. Moreover, a biweekly joint conference is held on Wednesday evenings and on Monday evenings with breast surgeons and with urologists, respectively. Morning journal clubs also meet on Mondays and Fridays at the Department in collaboration with the Division of hematology.

Research activities

Phase I studies of the following anticancer agents were conducted: K912 (epirubicin-incorporating micellar nanoparticle formulation) for patients with solid tumors for which standard chemotherapy was unavailable, and NK105 (paclitaxel-incorporating micellar nanoparticle formulation) for patients with advanced or metastatic cancer. Phase I/II studies of new anticancer agents for specific disease targets are conducted in collaboration with pharmaceutical companies.

In addition, many phase III studies are being conducted as follows: Randomized, optimal dose finding, Phase II Study of triweekly Abraxane in patients with metastatic breast cancer; Evaluation of Oral Care to Prevent Oral Mucositis in Estrogen Receptor Positive Metastatic Breast Cancer Patients Treated with Everolimus. (Oral Care-BC): Randomized Controlled Phase III Trial; A randomized controlled trial comparing primary tumor resection plus systemic therapy with systemic therapy alone in metastatic breast cancer; Intensive vs. standard post-operative surveillance in high risk breast cancer patients; Adjuvant Chemotherapy Trial of S-1 for breast cancer with ER-positive and HER2-negative; a randomized double-blind placebo-controlled trial of neratinib (an erbB1/2/4

inhibitor) after trastuzumab in women with early-stage HER-2 overexpressed/amplified breast cancer; a randomized multicenter, double-blind, placebo-controlled comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with operable HER2-positive primary breast cancer (APHINITY: Adjuvant Pertuzumab and Herceptin IN Initial Therapy); a randomized phase III study on NK105 versus paclitaxel in patients with recurrent or metastatic breast cancer; and a randomized phase III study on lapatinib, trastuzumab, and both lapatinib and trastuzumab, combined with aromatase inhibitor in patients with HER-2 overexpressed breast cancer who received neo-/adjuvant therapy with trastuzumab and endocrine therapy.

Table 1. Number of new patients

Breast cancer	278
Genitourinary cancers	191
Gynecological cancers	30
Cancer of unknown primary	58
Others	67
Total	624

List of papers published in 2015

Journal

1. Hayashi N, Niikura N, Masuda N, Takashima S, Nakamura R, Watanabe K, Kanbayashi C, Ishida M, Hozumi Y, Tsuneizumi M, Kondo N, Naito Y, Honda Y, Matsui A, Fujisawa T, Oshitanai R, Yasojima H, Yamauchi H, Saji S, Iwata H. Prognostic factors of HER2-positive breast cancer patients who develop brain metastasis: a multicenter retrospective analysis. Breast Cancer Res Treat, 149:277-284, 2015

2. Mukai H, Saeki T, Shimada K, Naito Y, Matsubara N, Nakanishi T, Obaishi H, Namiki M, Sasaki Y. Phase 1 combination study of eribulin mesylate with trastuzumab for advanced or recurrent human epidermal growth factor receptor 2 positive breast cancer. Invest New Drugs, 33:119-127, 2015

3. Taira N, Arai M, Ikeda M, Iwasaki M, Okamura H, Takamatsu K, Yamamoto S, Ohsumi S, Mukai H, Japanese Breast Cancer Society. The Japanese Breast Cancer Society clinical practice guideline for epidemiology and prevention of breast cancer. Breast Cancer, 22:16-27, 2015

4. Mukai H, Masuda N, Ishiguro H, Mitsuma A, Shibata T, Yamamura J, Toi M, Watabe A, Sarashina A, Uttenreuther-Fischer M, Ando Y. Phase I trial of afatinib plus vinorelbine in Japanese patients with advanced solid tumors, including breast cancer. Cancer Chemother Pharmacol, 76:739-750, 2015

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7. Mukai H, Aihara T, Yamamoto Y, Takahashi M, Toyama T, Sagara Y, Yamaguchi H, Akabane H, Tsurutani J, Hara F, Fujisawa T, Yamamoto N, Ohsumi S, Japanese Breast Cancer Society. The Japanese Breast Cancer Society Clinical Practice Guideline for systemic treatment of breast cancer. Breast Cancer, 22:5-15, 2015

8. Tozaki M, Isomoto I, Kojima Y, Kubota K, Kuroki Y, Ohnuki K, Ohsumi S, Mukai H, Japanese Breast Cancer Society. The Japanese Breast Cancer Society Clinical Practice Guideline for screening and imaging diagnosis of breast cancer. Breast Cancer, 22:28-36, 2015

9. Mukai H, Noguchi S, Akiyama F, Inaji H, Iwase H, Horiguchi J, Kurebayashi J, Hirata K, Toi M, Kurosumi M, Kohno N, Nishimura R, Nakamura S, Imoto S, Iwase T, Endo T, Saeki T, Ogawa Y, Ito Y, Tokuda Y, Ikeda T. 2013 clinical practice guidelines (The Japanese Breast Cancer Society): history, policy and mission. Breast Cancer, 22:1-4, 2015

10. Horii R, Honma N, Ogiya A, Kozuka Y, Fukuda T, Yoshida M, Ohsumi S, Mukai H, Japanese Breast Cancer Society. The Japanese Breast Cancer Society Clinical Practice Guideline for pathological diagnosis of breast cancer. Breast Cancer, 22:59-65, 2015

11. Sekiguchi K, Ogawa Y, Sanuki N, Arahira S, Ogo E, Yoshimura M, Yamauchi C, Oguchi M, Ohsumi S, Mukai H, Japanese Breast Cancer Society. The Japanese Breast Cancer Society clinical practice guideline for radiotherapy of breast cancer. Breast Cancer, 22:49-58, 2015

12. Ueda Y, Matsubara N, Takizawa I, Nishiyama T, Tabata K, Satoh T, Kamiya N, Suzuki H, Kawahara T, Uemura H. A multicenter retrospective analysis of sequential treatment of abiraterone acetate followed by docetaxel in Japanese patients with metastatic castration-resistant prostate cancer. Jpn J Clin Oncol, 45:774-779, 2015

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14. Iwata H, Fujii H, Masuda N, Mukai H, Nishimura Y, Katsura K, Ellis CE, Gagnon RC, Nakamura S. Efficacy, safety, pharmacokinetics and biomarker findings in patients with HER2-positive advanced or metastatic breast cancer treated with lapatinib in combination with capecitabine: results from 51 Japanese patients treated in a clinical study. Breast Cancer, 22:192-200, 2015

15. Yamaguchi T, Mukai H, Yamashita S, Fujii S, Ushijima T. Comprehensive DNA methylation and extensive mutation analyses of HER2-positive breast cancer. Oncology, 88:377-384, 2015

Department of Thoracic Surgery

Masahiro Tsuboi, Junji Yoshida, Tomoyuki Hishida, Keiju Aokage, Masahito Naito, Tomohiro Miyoshi

Introduction

The Department of Thoracic Oncology has three missions: surgical treatment, surgical resident training, and clinical research. Thoracic surgeries involve the treatment of thoracic neoplasms, primary and metastatic lung tumors, as well as mediastinal, pleural, and chest wall tumors. The Department specializes in the surgical treatment of pulmonary carcinomas. Routine surgical treatment modalities for carcinomas include limited resection (wedge or segmental resection) and simple resection (lobectomy or pneumonectomy) with or without systematic lymph node dissection. Thoracoscopic assistance is almost always used. Non-routine surgical procedures involve complex approaches such as broncho-/angio-plasty, combined resection with adjacent structures, and perioperative adjuvant treatment.

Since its establishment in 1992, the Department has been one of the most active leaders in the field of lung cancer in Japan. Moreover, it has been an active participant in international and national scientific venues. This year, in addition to 13 scientific papers published in English, the Department made 31 presentations: 4 international, 23 national, and 4 regional.

Routine Activities

The Department is presently composed of four consultant surgeons and five or six residents.

The Department has adopted a team approach in patient treatment and resident training. Potential surgical intervention candidate cases are presented every Tuesday evening at a multidisciplinary team conference of thoracic surgeons, oncology physicians, radiologists and residents. Each case is thoroughly and vigorously reviewed and discussed. To improve the English fluency of staff members and residents in preparation for international presentations, and to better involve visiting physicians from other countries, treatment modality discussions are conducted in English. Moreover, selected patients' records are radiologically and cytopathologically reviewed every Friday morning. These reviews aim to improve the interpretation of radiologic indications to pathology findings, accurately evaluate surgical indications, and upgrade knowledge on rare histologies. The Department believes that these activities improve the knowledge base, treatment indications, and surgical treatment.

For non-small cell histology, primary pulmonary carcinomas in clinical stages I/II and IIIA without bulky or multistation-involved mediastinal nodes, and primary pulmonary small cell carcinomas in clinical stage I, surgical resection is indicated for the cure. Optimum treatment modalities are being sought via clinical trials with the aim of improving the poor prognosis of patients with bulky or clinically and histologically proven multistation mediastinal lymph node metastases, with disease invading the neighboring vital structures, or with small cell cancers in clinical stage II and later.

Resection of metastatic lung tumor is attempted based on modified Thomfold's criteria after consultation with the patient. The majority of these cases are metastases from colorectal carcinomas, while most of the mediastinal tumors are thymic epithelial tumors.

The surgical procedures of the Department have generally remained similar for the past decade, but we have employed port-access thoracoscopic surgery more often for the last several years. Approximately 20% of the surgeries are completed via a 3-port access, and 70% of the surgeries are video-thoracoscopically assisted. To date, the average postoperative hospital stays of patients in the Department have improved and became shorter; three days being the shortest with a median

of seven days for cases of primary lung cancer. These shorter hospital stays are achieved with a slightly better complication rate than the normal rate. This year, 30-day operative mortality occurred in 2 patients undergoing surgery for primary lung cancer.

Research Activities

Research in the area of combined treatments, especially immunotherapy, has now advanced to clinical trials. It is a goal of researchers in the Department to acquire a basic understanding of the cellular and molecular mechanisms leading to the development and progression of lung cancer and apply these findings to further the development of immunotherapy-based prevention and treatment strategies

Clinical Trials

1) Surgical margin lavage cytology examination in limited resection for primary and metastatic lung cancer patients [observational].
2) Primary investigator and a member of an organized trial of TS-1 vs. UFT adjuvant chemotherapy for completely resected pathologic stage I (> 2 cm) non-small cell lung cancer [JCOG0707, phase III, patient accrual completed].
3) Primary investigator and a member of an organized trial of sublobar resection for peripheral GGO dominant cT1aN0M0 lung adenocarcinomas [JCOG0804, phase II, patient accrual completed].
4) Study coordinator and a member of an organized trial of segmental resection vs. lobectomy for peripheral T1aN0M0 non-small cell lung cancers [JCOG0802, phase III, patient accrual completed].
5) Study coordinator and a member of an organized trial of sublobar resection for peripheral GGO dominant cT1bN0M0 lung adenocarcinomas [JCOG1211, phase III, patient accrual completed]
6) Primary investigator and a member of an organized trial of Cisplatin/Pemetrexed vs. Cisplatin/Vinorelbine adjuvant chemotherapy for completely resected pathologic stage II-IIIA non-small cell lung cancer [JIPANG, phase III, patient accrual ongoing].
7) A member of an organized trial of Human Atrial Natriuretic Peptide during perioperative period for completed resectable non-small cell lung cancer [JANP, randomized phase II, patient accrual ongoing].
8) A member of an organized trial of postoperative maintenance adjuvant immunotherapy with S-588410 for completed resected stage II-IIIA non-small cell lung cancer [S-588410, phase II, patient accrual ongoing]

Education

Our educational program is to educate residents by expanding their knowledge and technical skills in the treatment of lung cancer, other thoracic malignancies and benign tumors, such as hamartoma and mediastinal cystic lesions. In addition, we seek to instill in the trainee a desire for continued introspection and self-education, open communication between all health care providers, while maintaining a respectful and professional demeanor.

Future prospects

Treatment advances in thoracic cancers including lung, mesothelioma, thymic malignancies and lung metastases have been slow to develop, even though these cancers are among the most common clinical problems. This clinical and laboratory research is vital to making progress.

Table 1. Number of patients

Lung cancer	411
Metastatic lung tumor	70
Mediastinal tumor	17
Others	65
Total	563

Table 2. Type of procedure-primary lung cancer

Pneumonectomy	15
Lobectomy	321
Segmentectomy	23
Wedge resection	35
(Combined resection)	(24)
Others	17
Total	411

Table 3. Overall survival

Diagnosis (primary lung cancer)	No. of pts	MST (mo)	5-yr survival (%)
Pathologic stage			
IA	1,334	NR	87.1
IB	540	127.0	71.7
IIA	315	73.5	56.4
IIB	226	47.8	46.1
IIIA	449	42.7	40.6

Data source from surgical records between 2002 and 2012;
Pathological stages according to the TNM Classification 7th edition;
NR: not reached.

List of papers published in 2015

Journal

1. Suzuki K, Watanabe S, Mizusawa J, Moriya Y, Yoshino I, Tsuboi M, Mizutani T, Nakamura K, Tada H, Asamura H, Japan Lung Cancer Surgical Study Group (JCOG LCSSG). Predictors of non-neoplastic lesions in lung tumours showing ground-glass opacity on thin-section computed tomography based on a multi-institutional prospective study†. Interact Cardiovasc Thorac Surg, 21:218-223, 2015

2. Sugiyama E, Umemura S, Nomura S, Kirita K, Matsumoto S, Yoh K, Niho S, Ohmatsu H, Tsuboi M, Ohe Y, Goto K. Impact of single nucleotide polymorphisms on severe hepatotoxicity induced by EGFR tyrosine kinase inhibitors in patients with non-small cell lung cancer harboring EGFR mutations. Lung Cancer, 90:307-313, 2015

3. Omori T, Tajiri M, Baba T, Ogura T, Iwasawa T, Okudela K, Takemura T, Oba MS, Maehara T, Nakayama H, Tsuboi M, Masuda M. Pulmonary Resection for Lung Cancer in Patients With Idiopathic Interstitial Pneumonia. Ann Thorac Surg, 100:954-960, 2015

4. Haruki T, Aokage K, Miyoshi T, Hishida T, Ishii G, Yoshida J, Tsuboi M, Nakamura H, Nagai K. Mediastinal nodal involvement in patients with clinical stage I non-small-cell lung cancer: possibility of rational lymph node dissection. J Thorac Oncol, 10:930-936, 2015

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7. Hamanaka R, Yokose T, Sakuma Y, Tsuboi M, Ito H, Nakayama H, Yamada K, Masuda R, Iwazaki M. Prognostic impact of vascular invasion and standardization of its evaluation in stage I non-small cell lung cancer. Diagn Pathol, 10:17, 2015

8. Hishida T, Tsuboi M, Shukuya T, Takamochi K, Sakurai H, Yoh K, Ohashi Y, Kunitoh H. Multicenter observational cohort study of post-operative treatment for completely resected non-small-cell lung cancer of pathological stage I (T1 >2 cm and T2 in TNM classification version 6). Jpn J Clin Oncol, 45:499-501, 2015

9. Noma D, Morohoshi T, Adachi H, Natsume I, Ookouchi M, Tsuura Y, Tsuboi M, Masuda M. A resected case of combined small cell lung carcinoma with carcinosarcoma. Pathol Int, 65:332-334, 2015

10. Udagawa H, Ishii G, Morise M, Umemura S, Matsumoto S, Yoh K, Niho S, Ohmatsu H, Tsuboi M, Goto K, Ochiai A, Ohe Y. Comparison of the expression levels of molecular markers among the peripheral area and central area of primary tumor and metastatic lymph node tumor in patients with squamous cell carcinoma of the lung. J Cancer Res Clin Oncol, 141:1417-1425, 2015

11. Adachi H, Tsuboi M, Nishii T, Yamamoto T, Nagashima T, Ando K, Ishikawa Y, Woo T, Watanabe K, Kumakiri Y, Maehara T, Morohoshi T, Nakayama H, Masuda M. Influence of visceral pleural invasion on survival in completely resected non-small-cell lung cancer. Eur J Cardiothorac Surg, 48:691-7; discussion 697, 2015

12. Koriyama H, Ishii G, Yoh K, Neri S, Morise M, Umemura S, Matsumoto S, Niho S, Ohmatsu H, Tsuboi M, Goto K, Ochiai A. Presence of podoplanin-positive cancer-associated fibroblasts in surgically resected primary lung adenocarcinoma predicts a shorter progression-free survival period in patients with recurrences who received platinum-based chemotherapy. J Cancer Res Clin Oncol, 141:1163-1170, 2015

13. Samejima J, Tajiri M, Ogura T, Baba T, Omori T, Tsuboi M, Masuda M. Thoracoscopic lung biopsy in 285 patients with diffuse pulmonary disease. Asian Cardiovasc Thorac Ann, 23:191-197, 2015

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17. Suzuki S, Ishii G, Matsuwaki R, Neri S, Hashimoto H, Yamauchi C, Aokage K, Hishida T, Yoshida J, Kohno M, Nagai K, Ochiai A. Ezrin-expressing lung adenocarcinoma cells and podoplanin-positive fibroblasts form a malignant microenvironment. J Cancer Res Clin Oncol, 141:475-484, 2015

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20. Tsubokawa N, Mimae T, Aokage K, Hattori A, Suzuki K, Nagai K, Tsuboi M, Okada M. Surgical outcomes of non-small-cell lung carcinoma in patients previously treated for gastric cancer. Eur J Cardiothorac Surg, 47:648-652, 2015

Department of Thoracic Oncology

Koichi Goto, Hironobu Ohmatsu, Seiji Niho, Kiyotaka Yoh, Shigeki Umemura, Shingo Matsumoto, Keisuke Kirita, Eri Sugiyama, Yoshitaka Zenke

Introduction

The Department of Thoracic Oncology provides care for patients with primary lung cancer, mediastinal tumors, and pleural tumors. The Department aims to provide the highest quality treatment and establish new effective treatments against lung cancer and other thoracic malignancies through innovative clinical and translational research. To provide assistance to our patients through multidisciplinary care, the staff members of the Department work closely with thoracic surgeons, radiation oncologists, pharmacists, clinical research coordinators, and psychiatrists who have expertise in these areas. Moreover, residents and trainees from other institutions have joined the Thoracic Oncology Program.

Routine activities

Our Outpatient Clinic, managed by the staff members and senior residents, is open from Monday to Friday for the examination of all new referred patients and the evaluation of returning patients. Returning patients also receive oral chemotherapy and/or intravenous chemotherapy in the Ambulatory Care Center. Bronchoscopy and EBUS for diagnosis is performed on Monday, Tuesday, and Thursday afternoon. Fluoroscopic-CT guided needle lung biopsies are carried out on Tuesday afternoon. For patient management, we use approximately 70 beds in 8F, 6A, 5A and 5B wards.

Case conferences on thoracic surgery and medical oncology are scheduled on Tuesday evenings and Wednesday evenings, respectively. The staff members and residents of the Department participate in a journal club on Monday and Wednesday mornings. At monthly meetings with physicians in private practice, the staff members and residents are teaching methods for reading chest X-ray and CT scan films.

Research activities

Our research activities are focused on four areas: 1) development of new and effective diagnosis and treatment modalities; 2) detection, diagnosis, and treatment of peripheral-type minute lung cancers that are not visible in plain chest X-rays; 3) collaborative studies with the Research Center for Innovative Oncology in the following areas: detection of driver mutation for small cell lung cancer; development of a new diagnostic method of rare driver gene alterations for lung cancer; correlation between gene abnormalities and clinical characteristics; correlation between sensitivity of EGFR-TKI and CAF (cancer-associated fibroblasts); and 4) translational research from bench to bed-side or from bed-side to bench for the development of innovative treatment strategies.

Especially, hole genome analysis of small cell cancer to detect new driver mutations and establishment of multiplex diagnosis methods for rare gene alteration of lung cancer such as ALK, RET and ROS1 fusion gene and BRAF mutation are under investigation as a collaboration with the Research Center for Innovative Oncology.

Clinical trials

The Department of Thoracic Oncology is currently conducting and participating in multi-institutional phase III studies to establish new standard treatments against lung cancer such as the Japan Clinical Oncology Group (JCOG) trials, West Japan Oncology Group (WJOG), Thoracic Oncology Research Group (TORG) and global trials conducted by pharmaceutical companies.

Recently, the usefulness of TS-1 and

pemetrexed combined with thoracic radiotherapy has been reported for locally advanced NSCLC. Therefore, a randomized phase II study of cisplatin plus TS-1 vs. cisplatin plus pemetrexed combined with thoracic radiotherapy for stage III non-squamous NSCLC is now ongoing.

Alectinib is a newly developing selective ALK inhibitor and very effective for ALK fusion positive NSCLC, although 4-5% of NSCLC are positive for ALK fusion protein. A phase I/II study of alectinib demonstrated durable response and higher than 90% response rate without severe toxicity. A phase III study of alectinib comparing with crizotinib for ALK positive lung cancer was conducted and the patient enrollment was completed. The study of AZD9291, 3rd generation EGFR-TKI, was conducted and a good response for T790M-resistant mutation positive lung cancer was observed with minimal toxicities.

In addition, many recent clinical trials indicated that PD-1/PD-L1 immune checkpoint inhibitors showed remarkable clinical response against advanced NSCLC including squamous cell lung cancer. Nivolumab, one of the PD-1 antibodies, was approved in December 2015, in Japan.

LC-SCRUM-Japan (Lung Cancer Genomic Screening Project for Individualized Medicine in Japan), a nationwide genomic screening project of lung cancer with rare driver oncogenes, such as ALK, RET and ROS1 fusion, and BRAF mutation was started in February 2013. As of December 2015, 2,301 patients were enrolled and 51 (3%) RET and 86 (4%) ROS1 fusion positive patients were detected. Many lung cancers with oncogenic alterations detected in LC-SCRUM-Japan had been entered into clinical trials of molecular targeting agents. In addition, from February 2015, to further develop genomic screening and to establish precision medicine in Japan, LC-SCRUM-Japan and genomic screening network for gastrointestinal cancer (GI-SCREEN), developed the collaborative genomic screening organization between academia and 14 pharmaceutical companies, named SCRUM-Japan.

Table 1. Number of patients in 2015

Lung Cancer		446
	Small cell lung cancer	68
	Adenocarcinoma	256
	Squamous cell carcinoma	74
	Large cell carcinoma	1
	NSCLC NOS	30
	Others	17
Thymic cancer		2
Thymoma		1
Malignant pleural mesothelioma		3
Other pleural tumor		5

Table 2. Initial treatment for lung cancer in 2015

Chemotherapy	274
Chemoradiotherapy	72
Surgery followed by chemotherapy	37
Radiotherapy	18
Palliative care	32
Others	13

List of papers published in 2015

Journal

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8. Udagawa H, Ishii G, Morise M, Umemura S, Matsumoto S, Yoh K, Niho S, Ohmatsu H, Tsuboi M, Goto K, Ochiai A, Ohe Y. Comparison of the expression levels of molecular markers among the peripheral area and central area of primary tumor and metastatic lymph node tumor in patients with squamous cell carcinoma of the lung. J Cancer Res Clin Oncol, 141:1417-1425, 2015

9. Koriyama H, Ishii G, Yoh K, Neri S, Morise M, Umemura S, Matsumoto S, Niho S, Ohmatsu H, Tsuboi M, Goto K, Ochiai A. Presence of podoplanin-positive cancer-associated fibroblasts in surgically resected primary lung adenocarcinoma predicts a shorter progression-free survival period in patients with recurrences who received platinum-based chemotherapy. J Cancer Res Clin Oncol, 141:1163-1170, 2015

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Department of Esophageal Surgery

Hiroyuki Daiko, Takeo Fujita

Introduction

The Esophageal Surgery Division deals with neoplasms arising from the esophagus. The surgical management of esophageal cancer has been the main clinical as well as research activity of this Division. In particular, the Division is striving to establish minimally invasive surgery that consists of neoadjuvant treatment followed by minimally invasive esophagectomy. The Division is conducting a study to define the role of surgery in the multimodal approach to the treatment of esophageal cancer, and is aiming for thoracolaparoscopic esophagectomy, which consists of thoracoscopic esophagectomy and laparoscopic reconstruction, to become a standard surgical procedure.

Routine activities

The Esophageal Surgery Division consists of two staff surgeons and four residents. An Esophageal Conference is held every Tuesday evening to discuss the diagnosis, staging, and treatment strategy for each patient and is attended by surgeons, medical oncologists, endoscopists, radiologists, radiation oncologists, and head and neck surgeons. Approximately four patients are operated upon every week. In 2014, 153 patients underwent esophagectomies. Transthoracic esophagectomies with extended lymph node dissection were performed on 39 non-treated cases. Thoracoscopic esophagectomies in the prone position with radical lymph node dissection were undertaken in 114 cases. A two-stage surgical procedure divided into resection and reconstruction for patients more than 80 years old or patients with multiple complications was undertaken in 12 cases. Postoperatively, within 30 days, 1 patient died due to complications after a salvage operation.

Clinical activities

Currently, the Division is examining the role of thoracolaparoscopic esophagectomy as a minimally invasive esophagectomy that consists of thoracoscopic esophagectomy and laparoscopic reconstruction. For patients without radical chemoradiotherapy, thoracoscopic esophagectomy in the prone position with radical lymph node dissection and laparoscopic reconstruction after esophagectomy for patients without a history of laparotomy are being attempted to become a standard surgical procedure for esophageal cancer.

For treating patients aged over 80 years or at high risk, a two-stage surgical procedure divided into resection and reconstruction is being attempted.

A randomized controlled phase III study comparing Cisplatin and 5-fluorouracil versus Cisplatin and 5-fluorouracil plus Docetaxel versus Cisplatin and 5-fluorouracil concurrent radiation as a neoadjuvant treatment for locally advanced esophageal cancer is ongoing.

A randomized controlled phase III study of minimally invasive versus open esophagectomy for thoracic esophageal cancer (JCOG1409, MONET trial) is ongoing.

Since 2000, the Division has started to perform salvage surgery for patients in whom definitive chemoradiotherapy has failed. The operative procedures and postoperative management have been refined gradually. The Division is also studying the role and efficacy of salvage surgery in the multimodal treatment of esophageal cancer.

Table 1. Type of Procedure

One-stage operation	141
Two-stage operation	12
Total number of esophagectomies	153
Rt-Transthoracic Esophagectomy	39
Thoracoscopic Esophagectomy	114
Others	35
Total	188

List of papers published in 2015

Journal

1. Fujita T, Daiko H. Optimal duration of prophylactic antimicrobial administration and risk of postoperative infectious events in thoracic esophagectomy with three-field lymph node dissection: short-course versus prolonged antimicrobial administration. Esophagus, 12:38-43, 2015

2. Daiko H, Fujita T. Laparoscopic assisted versus open gastric pull-up following thoracoscopic esophagectomy: A cohort study. Int J Surg, 19:61-66, 2015

3. Nozaki I, Kato K, Igaki H, Ito Y, Daiko H, Yano M, Udagawa H, Mizusawa J, Katayama H, Nakamura K, Kitagawa Y. Evaluation of safety profile of thoracoscopic esophagectomy for T1bN0M0 cancer using data from JCOG0502: a prospective multicenter study. Surg Endosc, 29:3519-3526, 2015

Department of Gastric Surgery

Takahiro Kinoshita, Hidehito Shibasaki, Akio Kaito, Toshirou Nishida, Takuya Hamakawa

Introduction

Our Division consists of three staff surgeons, one senior resident and six junior resident surgeons. Our managing of tumors includes common gastric adenocarcinoma, adenocarcinoma of the esophagogastric junction (AEG: Siewert type 2/3), and gastric submucosal tumors (GIST, etc.). Annually, 260-300 patients are operated on either by means of open surgery or laparoscopic surgery. Laparoscopic gastrectomy with radical node dissection was introduced in 2010, and now our department is one of the leading institutions in Japan. In 2014, about 80% of gastrectomies were performed under laparoscopy, and also robot-assisted surgery has been done as an advanced medical service system (endorsed by the government). The basis of our surgery is radical extirpation of cancer lesions, but at the same time, organ functions and better quality of life (QOL) should be maintained. In addition, we strive to obtain better clinical outcomes for patients with diseases with dismal prognoses (type 4 gastric cancer or with progressive metastasis) by surgery combined with a modern chemotherapy regimen, including molecular-targeting drugs in cooperation with medical oncologists.

Routine activities

Usually 12-14 patients are hospitalized and five to seven patients undergo operations per week. A clinical conference of our Division is held once a week to decide our treatment strategy. Further, a conference with internal medicine is held every Monday evening with doctors of the Department of Diagnostic Radiology, Gastrointestinal Endoscopy, and Gastrointestinal Oncology, discussing the accurate diagnosis of the patients with gastric tumors to decide the optimal treatment method for each patient. Every Tuesday morning, a small conference is held with medical oncologists to discuss border-line cases. In principle, patients with low-risk superficial gastric cancer lesions (cT1a) are treated by endoscopic submucosal dissection (ESD) following the criteria of the guideline. Some are required to undergo subsequent completion laparoscopic surgery with nodal dissection based on pathological findings of specimens obtained by ESD. Laparoscopic surgery covers distal, proximal, pylorus-preserving, and total gastrectomy. D2 dissection can also be done under laparoscopy, and its applicability for advanced cancer is under investigation. When the tumor infiltrates to adjacent organs, sometimes extended operations are chosen. Recently, due to the progress of modern chemotherapy regimen, down-staging from cStageIV is sometimes seen. For such patients, we selectively perform conversion surgery to achieve favorable outcomes. For AEGs, the transhiatal approach can be safely employed under laparoscopy with a better surgical view.

Research activities

We aggressively publish our clinical research data in domestic or international congresses. In addition, we participate in multi-institutional clinical trials conducted by the Japan Clinical Oncology Group (JCOG) – Gastric Surgery Study Group or other organizations. Patients with gastric cancer are, if eligible for each study, invited to take part in one of the ongoing clinical trials.

Clinical trials

The list of clinical trials in which we participated in 2015 is as below.

1) JCOG 1104 A phase II trial to define the optimal period of adjuvant S-1 chemotherapy for pathological stage II gastric cancer patients who underwent D2 gastrectomy

2) JCOG 1401 Nonrandomized confirmatory study of laparoscopic total/proximal gastrectomy for clinical stage I gastric cancer
3) A prospective study to evaluate safety, feasibility and economy of robot-assisted radical gastrectomy using da Vinci Surgical System (DVSS) (advanced medical service)
4) JLSSG 0901 A phase III randomized trial comparing open and laparoscopic distal gastrectomy for clinical stage II/III gastric cancer
5) A prospective randomized phase II trial comparing circular and linear stapled esophagojejunostomy after laparoscopic total/proximal gastrectomy (cooperation with Osaka University)
6) A prospective cohort study to evaluate the proper extent of lymph node dissection for esophagogastric junction cancer

Education

Resident doctors are trained to be specialized surgical oncologists with sufficient techniques and knowledge. Nowadays, opportunities to perform laparoscopic and open surgery are simultaneously given to them. We also place importance on the education of surgeons of other institutions. In 2015, surgeons from domestic and foreign hospitals (from China, Korea, Philippine, Spain and Germany) visited our division to learn surgical techniques.

Future prospects

We will keep striving to obtain better survival outcomes for the patients with far advanced diseases; for multidisciplinary therapy (chemotherapy, molecular-target agents or immune check-point inhibitor), collaborating with medical oncologists is essential. Additionally, we will continue to develop less-invasive as well as high-quality surgical methods (laparoscopic or robotic surgery), to increase patients' QOL and realize complete cures. It is also our obligation to expand our knowledge and experience globally as one of the most main countries in terms of gastric cancer occurrence.

Table 1. Number of patients

Gastric cancer	256
Others (GIST, etc.)	25

Table 2. Type of procedure

Open gastrectomy	60
Distal Gastrectomy	25
Pylorus-preserving Gastrectomy	2
Proximal Gastrectomy	4
Total Gastrectomy	22
Pancreaticoduodenectomy	0
Partial Gastrectomy	2
Others (bypass, exploration, etc.)	5
Laparoscopic Surgery (robot-assisted surgery)	221 (7)
Distal Gastrectomy	116 (6)
Pylorus-preserving Gastrectomy	9
Proximal Gastrectomy	16
Total Gastrectomy	24 (1)
Partial Gastrectomy	8
Others (bypass, exploration, etc.)	48

List of papers published in 2015

Journal

1. Kinoshita T, Kinoshita T, Saiura A, Esaki M, Sakamoto H, Yamanaka T. Multicentre analysis of long-term outcome after surgical resection for gastric cancer liver metastases. Br J Surg, 102:102-107, 2015

2. Nishida T, Doi T, Naito Y. Tyrosine kinase inhibitors in the treatment of unresectable or metastatic gastrointestinal stromal tumors. Expert Opin Pharmacother, 15:1979-1989, 2015

3. Fujii S, Fujihara A, Natori K, Abe A, Kuboki Y, Higuchi Y, Aizawa M, Kuwata T, Kinoshita T, Yasui W, Ochiai A. TEM1 expression in cancer-associated fibroblasts is correlated with a poor prognosis in patients with gastric cancer. Cancer Med, 4:1667-1678, 2015

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5. Yanagimoto Y, Takahashi T, Muguruma K, Toyokawa T, Kusanagi H, Omori T, Masuzawa T, Tanaka K, Hirota S, Nishida T. Re-appraisal of risk classifications for primary gastrointestinal stromal tumors (GISTs) after complete resection: indications for adjuvant therapy. Gastric Cancer, 18:426-433, 2015

6. Hirota M, Nakajima K, Miyazaki Y, Takahashi T, Kurokawa Y, Yamasaki M, Miyata H, Takiguchi S, Nishida T, Mori M, Doki Y. Clinical outcomes of laparoscopic partial gastrectomy for gastric submucosal tumors. Asian J Endosc Surg, 8:24-28, 2015

7. Joensuu H, Rutkowski P, Nishida T, Steigen SE, Brabec P, Plank L, Nilsson B, Braconi C, Bordoni A, Magnusson MK, Sufliarsky J, Federico M, Jonasson JG, Hostein I, Bringuier PP, Emile JF. KIT and PDGFRA mutations and the risk of GI stromal tumor recurrence. J Clin Oncol, 33:634-642, 2015

8. Takiguchi S, Fujiwara Y, Yamasaki M, Miyata H, Nakajima K, Nishida T, Sekimoto M, Hori M, Nakamura H, Mori M, Doki Y. Laparoscopic intraoperative navigation surgery for gastric cancer using real-time rendered 3D CT images. Surg Today, 45:618-624, 2015

9. Akamaru Y, Takahashi T, Nishida T, Omori T, Nishikawa K, Mikata S, Yamamura N, Miyazaki S, Noro H, Takiguchi S, Mori M, Doki Y. Effects of daikenchuto, a Japanese herb, on intestinal motility after total gastrectomy: a prospective randomized trial. J Gastrointest Surg, 19:467-472, 2015

10. Nishida T, Matsushima T, Tsujimoto M, Takahashi T, Kawasaki Y, Nakayama S, Omori T, Yamamura M, Cho H, Hirota S, Ueshima S, Ishihara H. Cyclin-Dependent Kinase Activity Correlates with the Prognosis of Patients Who Have Gastrointestinal Stromal Tumors. Ann Surg Oncol, 22:3565-3573, 2015

11. Komatsu Y, Doi T, Sawaki A, Kanda T, Yamada Y, Kuss I, Demetri GD, Nishida T. Regorafenib for advanced gastrointestinal stromal tumors following imatinib and sunitinib treatment: a subgroup analysis evaluating Japanese patients in the phase III GRID trial. Int J Clin Oncol, 20:905-912, 2015

12. Nishida T. The role of endoscopy in the diagnosis of gastric gastrointestinal stromal tumors. Ann Surg Oncol, 22:2810-2811, 2015

13. Maki RG, Blay JY, Demetri GD, Fletcher JA, Joensuu H, Martín-Broto J, Nishida T, Reichardt P, Schöffski P, Trent JC. Key Issues in the Clinical Management of Gastrointestinal Stromal Tumors: An Expert Discussion. Oncologist, 20:823-830, 2015

14. Joensuu H, Martin-Broto J, Nishida T, Reichardt P, Schöffski P, Maki RG. Follow-up strategies for patients with gastrointestinal stromal tumour treated with or without adjuvant imatinib after surgery. Eur J Cancer, 51:1611-1617, 2015

15. Isosaka M, Niinuma T, Nojima M, Kai M, Yamamoto E, Maruyama R, Nobuoka T, Nishida T, Kanda T, Taguchi T, Hasegawa T, Tokino T, Hirata K, Suzuki H, Shinomura Y. A Screen for Epigenetically Silenced microRNA Genes in Gastrointestinal Stromal Tumors. PLoS One, 10:e0133754, 2015

16. Barrios CH, Blackstein ME, Blay JY, Casali PG, Chacon M, Gu J, Kang YK, Nishida T, Purkayastha D, Woodman RC, Reichardt P. The GOLD ReGISTry: a Global, Prospective, Observational Registry Collecting Longitudinal Data on Patients with Advanced and Localised Gastrointestinal Stromal Tumours. Eur J Cancer, 51:2423-2433, 2015

17. Natatsuka R, Takahashi T, Serada S, Fujimoto M, Ookawara T, Nishida T, Hara H, Nishigaki T, Harada E, Murakami T, Miyazaki Y, Makino T, Kurokawa Y, Yamasaki M, Miyata H, Nakajima K, Takiguchi S, Kishimoto T, Mori M, Doki Y, Naka T. Gene therapy with SOCS1 for gastric cancer induces G2/M arrest and has an antitumour effect on peritoneal carcinomatosis. Br J Cancer, 113:433-442, 2015

18. Komatsu Y, Ohki E, Ueno N, Yoshida A, Toyoshima Y, Ueda E, Houzawa H, Togo K, Nishida T. Safety, efficacy and prognostic analyses of sunitinib in the post-marketing surveillance study of Japanese patients with gastrointestinal stromal tumor. Jpn J Clin Oncol, 45:1016-1022, 2015

Department of Colorectal Surgery

Masaaki Ito, Akihiro Kobayashi, Yuji Nishizawa, Takeshi Sasaki, Norio Saito, Kenichi Koshi, Yuichiro Tsukada, Koji Ikeda, Naoki Sakuyama

Introduction

The Colorectal and Pelvic Surgery Division was established 17 years ago. Its main purpose is to bring together the Divisions that are composed of colorectal surgeons and urologists. Cooperation between these Divisions contributes not only to the establishment of effective operative techniques but also to an oncological consensus including consensus on the quality of life (QOL) and the various functions of patients with pelvic malignancies. New surgical procedures, such as nerve-sparing surgery, sphincter-saving surgery, bladder-sparing surgery, pouch surgery and minimally invasive surgery are being developed to prevent postoperative dysfunctions. These new approaches will contribute to better curability and QOL among patients with pelvic malignancies

Routine activities

The Department of Colorectal Surgery comprises 6 consultants (four colorectal surgeons and two urologists) and 11 residents. The outpatient clinic is open five days a week. More than 360 new patients with colorectal carcinomas and more than 150 new patients with other pelvic malignancies visited this Department during the last year. Treatment plans are discussed at a weekly conference on GI malignancies and at another weekly conference on pelvic malignancies. Many treatment modalities, such as local excision with or without adjuvant chemo- or radiotherapy and other minimally invasive forms of surgery using laparoscopy, have been introduced for the treatment of patients in the early stages of cancer. Laparoscopy-assisted operations (Lap-Ops) with wider lymphadenectomy of up to more than D2 are also increasingly being performed in patients with advanced colorectal carcinomas. Abdominoperineal resection (APR) has, in the past, been the standard surgery in patients with very low rectal cancer; however, partial anal sphincter preserving surgery such as intersphincteric resection (ISR) and direct CAA have been performed in more than 500 patients with very low rectal tumors and has resulted in cure, preservation of anal function, and better QOL.

Research activities

1) A prospective randomized trial for extending the indications for Lap-Op (JCOG0404 CRC Surg-LAP vs. Open). A total of 77 patients have been registered in this Department. This study has been completed.
2) Intersphincteric resection with or without neoadjuvant mFOLFOX6 study (NAIR Study)- A prospective multi-center trial -A Phase II/III randomized multicenter trial of intersphincteric resection (ISR) with or without preoperative chemotherapy for very low-lying rectal cancer. APR has been the standard surgery for very low rectal cancer located within five cm of the anal verge. However, a permanent colostomy causes severe impairment of QOL. This study was designed to evaluate the feasibility and the oncological and functional outcomes of ISR for treatment of very low rectal cancer. Curability with ISR was verified histologically, and acceptable oncological and functional outcomes were obtained in many patients. However, patients need to be informed preoperatively regarding the potential functional adverse effects after ISR. This study is in progress, and 50 patients have been registered.
3) Bladder-sparing surgery for locally advanced rectal cancer involving the prostate. Total pelvic exenteration (TPE) is the standard procedure in such patients. This study aims to evaluate

the feasibility of bladder-sparing surgery as an alternative to TPE. This procedure has been performed in 39 patients with primary or recurrent tumors and permits conservative surgery in selected patients with advanced rectal cancer involving the prostate without compromising local control. The QOL of these patients appears to be better. Evaluation on usefulness and safety of cysto-urethral anastomosis with additional ileal flap in patients with rectal cancer involving the prostate (Ileal flap study) is also in progress.

4) A prospective randomized trial for the feasibility and effect of lateral node dissection in low rectal cancer – (Total) Mesorectal Excision (ME) vs. Lateral Node Dissection with preservation of autonomic nerves (D3 with nerve-sparing) [JCOG0212 CRC Surg.]. In this study, 76 patients have been registered.
5) Local excision with postoperative chemoradiotherapy for T1・T2 rectal cancer. This study aims to evaluate preoperatively the feasibility and the oncologic outcome of local therapy for T1 and a part of T2 rectal cancer without lymph node metastases. In this study, 82 patients have been registered.
6) A prospective cohort study of Reduced Port Surgery for colorectal cancer. Registration of this study is closed.
7) Study on Robotic surgery for rectal cancer. This study is currently in progress.

Clinical trials

Other clinical trials are also in progress as follows:

- A Phase I/II trial of chemoradiotherapy concurrent with S-1 plus MMC in patients with clinical stage II/III squamous cell carcinoma of the anal canal (JCOG0903)
- A randomized study of conventional technique vs. no-touch isolation technique (JCOG1006)
- A randomized controlled trial comparing resection of primary tumor plus chemotherapy with chemotherapy alone in incurable Stage IV colorectal cancer (JCOG1007)
- 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 (JCOG1018)
- A randomized controlled trial comparing laparoscopic surgery with open surgery in palliative resection of primary tumor in incurable Stage IV colorectal cancer (JCOG1107)
- A Prospective Phase II Trial of Laparoscopic Surgery for Ultra-low Rectal Cancers within Five Centimeters from the Anus or Three Centimeters from the Dentate Line. Under the Japanese Society for Cancer of the Colon and Rectum (JSCCR)
- A prospective study of urinary and sexual dysfunction after surgery for rectal cancer
- A Phase II study of neoadjuvant mFOLFOX6 (+ cetuximab) in patients with resectable pelvic recurrences after rectal cancer surgery
- T-REX Study; the International Prospective Observational Cohort Study for Optimal Bowel Resection Extent and Central Radicality for Colon Cancer (JSCCR)
- Development of LAP-instruments for colorectal surgery

Education

- Guiding university students in their studies
- Guiding colorectal surgeons for obtaining medical specialist

Future prospects

Establishment of less-invasive surgery for curing and function-preserving in cancer patients with colorectal malignances.

Table 1. Number of priniary colorectal patients (2015.1-2015.12)

Primary colorectal canter			Other cases
Colon	Rectum	Sub-total	
170	226	396	179

Table 2. Type of procedure

Operative Procedures (2015.1-2015.12)

Colon N=170 Laparoscopic (LAP): 146 Open: 24		
Sigmoidectomy	62	(LAP: 60)
	54	(LAP: 52)
Ileocecal resection	21	(LAP: 17)
Limited colectomy	14	(LAP: 10)
Hartmann procedure	1	
Low anterior resection	1	(LAP: 1)
Left (hemi) colectomy	5	(LAP: 4)
Stoma	7	
Others	5	(LAP: 2)

Rectum N=226 Laparoscopic (LAP): 188	Robot: 7	Open: 31	
Low anterior resection	99	(LAP: 87)	(Robot: 6)
Intersphincteric resection (ISR)	56	(LAP: 53)	
High anterior resection	24	(LAP: 23)	(Robot: 1)
Abdominoperineal resection (APR)	22	(LAP: 20)	
Hartmann procedure	4	(LAP: 3)	
Local excision	2		
Total pelvic exenteration	1		
Stoma	12		
Others	6	(LAP: 2)	

Table 3. Survival rates

Stage	Colon			Rectum		
	No. of pts	5-yr survival (%)		No. of pts	5-yr survival (%)	
		Overall	Cancer specific		Overall	Cancer specific
Stage 0	10	100	100	14	100	100
Stage Ⅰ	210	95.2	100	171	93.6	97.6
Stage Ⅱ	286	90.3	84.8	215	84.5	89.4
Stage Ⅲa	194	82.1	86.5	179	79.3	82.0
Stage Ⅲb	63	71.9	74.5	123	60.5	64.1
Stage Ⅳ	167	22.0	23.2	102	23.8	24.0

OP: 2000.1.1-2007.12

List of papers published in 2015

Journal

1. Shiomi A, Ito M, Maeda K, Kinugasa Y, Ota M, Yamaue H, Shiozawa M, Horie H, Kuriu Y, Saito N. Effects of a diverting stoma on symptomatic anastomotic leakage after low anterior resection for rectal cancer: a propensity score matching analysis of 1,014 consecutive patients. J Am Coll Surg, 220:186-194, 2015

2. Kawai T, Shin M, Nishizawa Y, Horise Y, Nishikawa A, Nakamura T. Mobile locally operated detachable end-effector manipulator for endoscopic surgery. Int J Comput Assist Radiol Surg, 10:161-169, 2015

3. Ohue M, Hamaguchi T, Ito Y, Sakai D, Noura S, Kinugasa Y, Fujita S, Shimada Y, Saito N, Moriya Y. A phase I trial of preoperative S-1 in combination with oxaliplatin and pelvic radiation for lower rectal cancer with T4 and lateral pelvic lymph node metastasis. Int J Clin Oncol, 20:338-344, 2015

4. Kobayashi S, Ito M, Yamamoto S, Kinugasa Y, Kotake M, Saida Y, Kobatake T, Yamanaka T, Saito N, Moriya Y. Randomized clinical trial of skin closure by subcuticular suture or skin stapling after elective colorectal cancer surgery. Br J Surg, 102:495-500, 2015

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6. Yokota M, Kobayashi A, Nomura S, Nishizawa Y, Ito M, Nagai K, Saito N. Patterns and treatment of recurrence following pulmonary resection for colorectal metastases. World J Surg, 39:1758-1766, 2015

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Department of Gastrointestinal Oncology

Takayuki Yoshino, Atsushi Ohtsu, Toshihiko Doi, Takashi Kojima, Kouhei Shitara, Hideaki Bando, Yasutoshi Kuboki, Nozomu Fuse, Ken Hatogai, Sawako Miyoshi, Shota Fukuoka

Introduction

In 2015, approximately 650 gastrointestinal (GI) cancer patients were treated by staff oncologists and skilled residents in the Department of GI Oncology, which focuses on optimal chemotherapy W/ or W/O radiation for the treatment of GI cancers.

Routine activities

The Inter-Divisional tumor board conferences with the Surgical/Radiation Oncology Divisions are held regularly to review the current treatment for each patient and to discuss further treatment strategies. Basically, routine chemotherapy is done on an outpatient basis, and there are approximately 1,900 selected patients who need hospitalization for the purpose of planned therapy with chemotherapy or palliation. Our activities for each type of GI cancer in 2015 are shown in Table 1 (Number), Table 2 (Treatment), and Table 3 (Efficacy). There are ongoing clinical trials that consist of 45 Phase I trials including globally first-in-class (FIC), first-in-human (FIH), investigational new drugs (INDs) and 30 Phase II/III clinical trials to approve the INDs.

Research activities

Phase I

Our Department has focused more on early-stage clinical development of INDs. The number of patients enrolled for Phase I trials has been increasing recently. Importantly, the number of FIH trials and trials around the same time as Western countries is increasing. Several results of phase I trials, such as the oral pan-AKT inhibitor (MK-2206), LY2603618, a CHK1 inhibitor, in combination with gemcitabine, TAS-114, a dUTPase inhibitor in combination with S-1, and VEGF receptor/MET-targeted kinase inhibitor (TAS-115), were published or presented at international meetings.

Esophageal Cancer (EC)

A prognostic or predictive biomarker study in patients who underwent surgery or received chemoradiotherapy for clinical stage I esophageal squamous cell carcinoma (JCOG0502-AI) was completed. The results of the phase I/II trial of chemoradiotherapy with concurrent S-1 and cisplatin for clinical stage II/III esophageal carcinoma (JCOG 0604) was published. And the sub-analysis of the JCOG9907 study for the accuracy of preoperative diagnosis of lymph node metastasis and prognostic Factors in Patients Receiving Neoadjuvant 5-Fluorouracil plus Cisplatin for Advanced Esophageal Cancer were published.

Gastric Cancer (GC)

The results of a global randomized phase III trial comparing 2nd-line chemotherapy with ado-trastuzumab emtansine (T-DM1), an antibody-drug conjugate (ADC) for HER2 and taxanes agents for advanced GC were presented in ASCO-GI 2016. The phase II study of adjuvant chemotherapy of S-1 plus oxaliplatin for patients with stage III gastric cancer after D2 gastrectomy was published. Several sponsored-initiated trials to evaluate molecular targeting agents as well as immune checkpoint inhibitors are currently ongoing. An investigator-initiated trial of the phase 1 trial of sulfasalazine (SSZ), which targets cancer stem-like cell fraction, plus cisplatin for CD44v gastric cancer which refractory to cisplatin finished its enrollment. Results of comprehensive molecular profiling of advanced GC using next generation sequencing and immunohistochemistry were also published, which identified several possible candidate genes that could be targets for precision medicine. Since September 2015, we have initiated an immune monitoring study to evaluate several

immunological properties such as classification of lymphocyte or expression of immune checkpoint in tumor infiltrating lymphocyte and peripheral blood mononuclear cell (PBMC) before and after treatment, which will hopefully lead to personalized therapy in the field of immune therapy.

Colorectal Cancer (CRC)

We have established the SCRUM-Japan GI-SCREEN 2013-01-CRC (UMIN000016343), which is the nationwide cancer genome screening project by using the Oncomine Cancer Research Panel. We also started GI-SCREEN CRC-MSI, which is the multi-center project for screening the microsatellite instability (MSI) status of Japanese CRC patients. Based on the screening system of GI-SCREEN 2013-01-CRC, we are currently planning the investigator-initiated clinical trials for patients with BRAF non-V600E mutations, HER2 amplifications, and high tumor-infiltrating lymphocytes (TILs). The clinical evaluation study of cell-free DNA-based RAS gene testing by using BEAMing technology will soon be started.

Clinical trials

Esophageal Cancer (EC)

The phase III study comparing preoperative CDDP+5-FU (CF) versus docetaxel+CF versus CF-radiation followed by esophagectomy with D2-3 lymphadenectomy for locally advanced esophageal squamous cell cancer (JCOG1109) and the phase III study comparing docetaxel, CDDP and 5-FU with CDDP and 5-FU in patients with metastatic or recurrent esophageal cancer (JCOG1314) is ongoing. A multicenter phase I study of HSP105-derived peptide vaccine for patients with advanced esophageal cancer/colorectal cancer and phase II trial of BKM120 in patients with advanced esophagus cancer is ongoing. As in the single institutional clinical study, the phase II trial of definitive chemoprotontherapy in patients with clinical stage I/II/III esophageal carcinoma is ongoing.

Gastric Cancer (GC)

The results of the GATSBY trial, which compared 2nd-line T-DM1 and taxanes agents for HER2 positive gastric cancer, was presented in ASCO-GI 2016, which could not meet its primary endpoint. The enrollment for a multicenter global trial (JACOB) of pertuzumab was completed. Multicenter global phase III trials of molecular targeting agents (ENRICH, BRIGHTER) are ongoing. Several phase 2 or 3 trials to evaluate the efficacy of an anti-PD1 antibody are also ongoing (KEYNOTE-59, 61 and 62). Several phase I or II studies of newer agents including c-MET tyrosine kinase inhibitor of MET high GC, FGFR-inhibitor for FGFR high GC as well as combination therapy of immune checkpoint inhibitors are ongoing. Several investigator-initiated trials of a multicenter phase III trial comparing DCS to cisplatin plus S-1 (JCOG 1013), a multicenter phase II trial comparing 12 months of S-1 to 6 months of S-1 as an adjuvant chemotherapy (JCOG 1104) are ongoing. After confirmation of the mode of action of SSZ as a cancer stem cell inhibitor, a phase 1 trial of SSZ in combination with cisplatin for cisplatin refractory GC patients was also conducted.

Colorectal Cancer (CRC)

The results of a global randomized phase III trial comparing TAS-102 to best supportive care (RECOURSE) were published in the New England Journal of Medicine. We have completed the phase 1b/2 trial of the novel combination of TAS-102 plus bevacizumab as an investigator-initiated trial (IIT). The patients' registration of an international phase III trial, which investigates the survival benefits of the oral multi-target kinase inhibitor nintedanib with placebo in a salvage setting (LUME-COLON 1), were finished. We are participating in two different international phase 1b/2 trials that target patients with BRAF V600E mutated CRC, of which results were reported in the ESMO World Congress on Gastrointestinal Cancer 2015. We are now recruiting the phase 1b/2 trial of the novel combination of TAS-102 plus nintedanib as an IIT. The phase II and III clinical trials of the immune checkpoint inhibitor pembrolizumab, for patients with deficiency in mismatch repair (KEYNOTE-164, KEYNOTE-177), are ongoing. We have conducted two randomized, multicenter, phase III studies called ACHIEVE and ACHIEVE-2 trials, together with other collaborative

groups in the US, UK/Australia, Italy, Greece and France.

Education

Our residents learn the latest evidence-based medicine and apply this knowledge pragmatically to enhance care for patients with GI cancers, and eventually obtain qualifications as comprehensive GI oncologists through daily practice and direct training from our staff. Accordingly, our staff actively provide a wealth of valuable opportunities to polish their skills regarding various chemotherapies, especially in collaboration with the Department of Experimental Therapeutics as well as diagnostic and therapeutic endoscopies in collaboration with the Department of Digestive Endoscopy. We regularly held tumor-related board meetings and frequently have numerous face-to-face meetings with experts in different specialties. We instruct them how to conduct valuable clinical trials, how to have the chance to attend international academic conferences, and the best way to present academic meetings and work on many high-impact articles in scholarly journals. To date, our department has helped many residents to become 'true' skilled GI oncologists who play major roles at leading cancer centers across the country.

Future prospects

We continue to provide the best treatment for cancer patients, the best education for residents, and aim to perform the following activities:

1) To provide the latest, cutting-edge medicine to cancer patients and to foster the next generation of skilled GI oncologists.
2) To achieve medical innovation in Japan, we aim to play leading roles in the clinical developments of INDs by contributing to various types of clinical trials including FIC, FIH early trials, IITs with proof-of-concept, and international clinical trials.
3) To enhance our research activities, we will establish research networks with cutting-edge researchers in Japan as well as globally.

Table 1. Number of new patients

Esophageal	328
Gastric	240
Colorectal	335
Other type of tumors	58
Total	961

Table 2. Treatment

Esophageal Cancer	Chemotherapy (include CRT*)	185
Gastric Cancer	Chemotherapy	175
Colorectal Cancer	Chemotherapy	317

List of papers published in 2015

Journal

1. Fujii S, Fujihara A, Natori K, Abe A, Kuboki Y, Higuchi Y, Aizawa M, Kuwata T, Kinoshita T, Yasui W, Ochiai A. TEM1 expression in cancer-associated fibroblasts is correlated with a poor prognosis in patients with gastric cancer. Cancer Med, 4:1667-1678, 2015

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3. Bando H, Takebe N. Recent innovations in the USA National Cancer Institute-sponsored investigator initiated Phase I and II anticancer drug development. Jpn J Clin Oncol, 45:1001-1006, 2015

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12. Kotaka M, Yoshino T, Oba K, Shinozaki K, Touyama T, Manaka D, Matsui T, Ishigure K, Hasegawa J, Inoue K, Goto K, Sakamoto J, Saji S, Ohtsu A, Watanabe T. Initial safety report on the tolerability of modified FOLFOX6 as adjuvant therapy in patients with curatively resected stage II or III colon cancer (JFMC41-1001-C2: JOIN trial). Cancer Chemother Pharmacol, 76:75-84, 2015

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20. Takebe N, Miele L, Harris PJ, Jeong W, Bando H, Kahn M, Yang SX, Ivy SP. Targeting Notch, Hedgehog, and Wnt pathways in cancer stem cells: clinical update. Nat Rev Clin Oncol, 12:445-464, 2015

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Department of Endoscopy

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Introduction

The Department of Endoscopy covers the fields of the gastrointestinal (GI) tract and head and neck regions. In 2015, approximately 12,000 examinations and treatments were performed. This is the highest number to date. A narrow band imaging (NBI) system and/or Blue LASER imaging (BLI) system has been included for routine examination in six endoscopy rooms since September 2009. The BLI system was introduced in 2013. Furthermore, endoscopic treatments such as endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), percutaneous endoscopic gastrostomy (PEG), endoscopic balloon dilation (EBD), radial incision and cutting (RIC), and photodynamic therapy (PDT) have been performed.

In addition, research studies have been conducted in various fields: endoscopic diagnosis and treatment, or prevention for cancer patients in the GI tract and head and neck. Many of the research projects are conducted as prospective clinical studies either in a single institution or in collaboration with other institutions. The present research activities mainly focus on the development of new instruments for endoscopic diagnosis and new endoscopic treatment modalities. In addition, molecular biology research is also performed using blood and tissue samples of patients in order to examine strategies to enable the early detection, prevention, or prediction of prognosis for treatment. These projects are conducted in collaboration with not only commercial companies but also the faculties of Technology and Science in certain universities.

Routine activities

Routine endoscopic examinations including magnifying NBI and endoscopic ultrasound are presently used for head and neck, esophageal, gastric, and colorectal cancers, and the NBI or BLI systems have become essential in detecting very early cancers and precursor lesions in these areas. With the NBI or BLI systems, a differential diagnosis between neoplasia and non-neoplasia can be performed without the need for any dye solution. Double-balloon enteroscopy and capsule endoscopy are mainly performed for examinations of the small intestine. Follow-up examinations after endoscopic treatment and chemotherapy are also performed in many cases, in addition to routine examinations.

With the recent progress in instruments and techniques, the number of endoscopic treatments has been increasing. EMR is indicated routinely for early GI tract cancers, and ESD is basically used not only for gastric cancers but also for esophageal or colorectal cancers. For the colon and rectum, colonoscopic day surgeries such as polypectomy and EMR are currently performed in one-third of all examinations. Furthermore, EMR and PDT are sometimes indicated as salvage treatments for local residual/recurrent tumors after chemoradiotherapy for esophageal cancer. PEG and EBD are valuable supporting techniques during the treatment of patients with head and neck, and esophageal cancers.

Research activities

Furthermore, molecular biological analysis of cancers of the esophagus, head and neck, stomach, and colorectum is under way. Importantly, analysis of the genetic polymorphism in the genes coding for alcohol dehydrogenase (ADH 1B) and aldehyde dehydrogenase (ALDH 2) regarding alcohol metabolism is performed as a useful novel strategic approach in the prevention of upper aerodigestive tract cancers. In addition, the relationships between the production of acetaldehyde and oral microflora after consumption of alcohol are being investigated

in our study group.

In contrast, developing research into novel endoscopy systems is being performed. Hypoxia imaging is detected for neoplastic lesions of the head and neck and alimentary tracts, with blue visualized images. The first in-human clinical trial of hypoxia imaging was finished, and we are preparing pharmaceutical approval. Another project is a new bioimaging system using near-infrared light with a wavelength of over 1,000 nm. This system is capable of penetrating through the gastrointestinal wall and obtaining images utilizing various spectrums. Furthermore, molecular imaging endoscopy with some agents such as small molecules, peptides, antibodies and nanoparticles has been developed in collaborate with some universities. With a low-temperature atmospheric pressure plasma system, endoscopic hemostasis and inactivation of bacteria are being investigated. A novel diagnosis system using photosensitizing agents, such as hypericin and 5ALA, has been constructed. Moreover, a new clinical trial of a biodegradable (BD) stent has been performed for patients with benign esophageal stricture after curative treatment, such as ESD, surgery, and chemoradiotherapy.

Clinical trials

A wide range of many prospective clinical trials is ongoing into the endoscopic treatment of cancers of the esophagus, stomach, and colorectum, as follows: clinical trial of hypoxia imaging for neoplasia of the alimentary tract in a single unit; a phase II clinical trial for BD stent implantation for benign esophageal stricture; a clinical trial for photodynamic diagnosis using 5ALA; multicenter clinical trials of a follow-up study after EMR of m1-3 esophageal cancers; a phase I/II study of PDT using Laserphyrin in residual/recurrent cases followed by chemoradiation for esophageal cancers; a multicenter clinical study for enrollment of early gastric cancer following endoscopic treatment for an enrollment system using the Web; a multicenter clinical trial of ESD for undifferentiated gastric cancer (JCOG1009); a randomized controlled phase II/III study comparing EBD combined with steroid versus RIC combined with steroid for refractory anastomotic stricture after esophagectomy (JCOG1207); a multicenter clinical study of a learning curve trial using NBI; a multicenter clinical study regarding residual/recurrent rates and observation periods of endoscopic piecemeal mucosal resection (EPMR) for colorectal neoplastic lesions; and the Japan Polyp Study (JPS) for determination of observation periods after endoscopic treatment for colorectal polyps.

Education

The aim is cultivation of human resources in specializing in endoscopic diagnosis and treatment for alimentary tract cancer. Staff supervise individual residents. The importance of positiveness is highlighted in periodic case conferences and joint conferences among internal medicine, surgery and radiology staff. Staff supervise academic congress presentations and writing manuscripts after deciding upon individual themes, and detailed discussion is undertaken in the department conference. For residents interested in development research, opportunities to study are supported after graduation.

Future prospects

Existing endoscopic diagnosis for neoplasia of the alimentary tract is performed on the basis of the morphological features of the tumor. Molecular imaging endoscopy is a novel system to visualize cancer using a specific laser source under phosphor combined with cancer-specific agents. We can obtain new imaging, since the function or metabolic state in cancer cells is visualized. In additional modalities, there are hypoxia imaging endoscopy, photodynamic diagnosis and endomicroscopy. These modalities, especially including near infrared light, are anticipated to be next generation endoscopy, and we will undertake innovative development to produce new endoscopy.

Table 1. Number of patients

Number of patients Examined in 2011-2015

Section	2011	2012	2013	2014	2015
Upper gastrointestinal endoscopy	6,350	6,647	6,846	6,825	7,309
Endoscopic ultrasonography	70	54	43	47	43
Endoscopic mucosal resection (esophagus)	181	168	220	196	196
Endoscopic mucosal resection (stomach)	205	215	203	218	185
Endoscopic balloon dilation	644	711	824	654	657
Percutaneous endoscopic gastrostomy	215	171	196	236	191
Photodynamic therapy (esophagus)	48	39	32	35	23
Colonoscopy	1,550	2,302	2,368	2,417	2,308
Polypectomy/EMR	800	912	832	903	906
Narrow Band Imaging (head and neck)	95	106	80	41	48
Endoscopic mucosal resection (head and neck)	41	46	52	49	105

EMR, Endoscopic mucosal resection including ESD.

Table 2. Endoscopic procedures in 2015

		2011	2012	2013	2014	2015
Esophagus	EMR	100	89	65	60	59
	ESD	45	79	155	136	137
Stomach	EMR	9	3	0	1	9
	ESD	202	212	203	217	172
Colon and rectum	EMR*	744	834	725	913	906
	ESD	17	78	98	92	107
Head and neck	EMR	6	7	1	0	3
	ESD	35	33	51	49	102

EMR , endoscopic mucosal resection; ESD, endoscopic submucosal dissection; *, including polypectomy

List of papers published in 2015

Journal

1. Osera S, Ikematsu H, Odagaki T, Oono Y, Yano T, Kobayashi A, Ito M, Saito N, Kaneko K. Efficacy and safety of endoscopic radial incision and cutting for benign severe anastomotic stricture after surgery for lower rectal cancer (with video). Gastrointest Endosc, 81:770-773, 2015

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Book

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Department of Hepatobiliary and Pancreatic Surgery

Masaru Konishi, Shinichiro Takahashi, Naoto Gotohda, Yuichiro Kato, Kazuhiko Kitaguchi, Yasunori Nishida, Yusuke Nakayama

Introduction

The recent development of various diagnostic techniques has led to the detection of an increasing number of early-stage and borderline malignancies, and for such patients, a limited resection preserving organ function is indicated. However, some diseases, such as invasive ductal pancreatic cancer, advanced gallbladder cancer, and hilar cholangiocarcinoma, remain a difficult challenge for surgeons and are still associated with dismal long-term prognoses. Recently, chemotherapy for hepatobiliary and pancreatic malignancies has been developed. In line with this development, several studies on adjuvant hemotherapy for malignancies with dismal prognoses have been conducted.

With the refinements in laparoscopic instruments and advances in surgical experience, laparoscopic surgery is a safe alternative for selected patients with hepatobiliary pancreatic neoplasms, and has fulfilled its indications. In our division, laparoscopic hepatectomies have been performed since 2002, and laparoscopic distal pancreatectomies since 2011.

Routine activities

Our group is composed of four attending surgeons, three chief residents, and four residents. The outpatient clinic is open five days a week. Staff meetings are held three times a week during which treatment strategies from medical and surgical points of view are discussed. A case conference on imaging diagnosis is conducted every Tuesday in cooperation with radiologists and medical oncologists, and a pathology conference is held every month with pathologists. In 2015, 253 patients with hepatobiliary and pancreatic diseases underwent surgical treatment including 51 laparoscopic hepatectomies and nine laparoscopic distal pancreatectomies.

Research activities

Sarcopenia is a newly identified marker of frailty. We assess whether preoperative sarcopenia has an impact on clinically relevant postoperative pancreatic fistula (POPF) formation. A total of 266 consecutive patients who underwent a pancreaticoduodenectomy (PD) between from 2010 and 2014 were enrolled in this retrospective study. Skeletal muscle mass was measured using preoperative computed tomography images. This study concluded that preoperative sarcopenia was identified as a strong and independent risk factor for clinically relevant POPF formation after PD.

Clinical trials

- JASPAC04 is a randomized phase II study on neoadjuvant chemotherapy using combination therapy with gemcitabine and S-1 vs. S-1 and concurrent radiotherapy in patients with resected pancreatic cancer. Recruitment started in 2014.
- JASPAC05 is a phase II study on neoadjuvant S-1 and concurrent radiotherapy for patients with borderline resectable pancreatic cancer. Recruitment started in 2012.
- JCOG1202 (ASCOT) is a phase III study to compare S-1 with surgery alone as adjuvant chemotherapy for patients with curatively resected biliary tract cancer including Intrahepatic cholangiocarcinoma, extrahepatic bile duct cancer, gallbladder cancer and ampullary cancer. Recruitment started in 2013.
- JCOG0605 is a randomized phase III trial to compare FOLFOX with surgery alone as adjuvant chemotherapy for patients with curatively resected liver metastasis from

colorectal cancer. Recruitment is on-going.

Education

'Board certified expert surgeons' is a high level of skill in the field of hepato-biliary-pancreatic surgery. To be qualified as a board certified surgeon, surgeons are required to perform a prescribed number of operations under the guidance of a board certified instructor. The residents of our department are training to get their certifications by the end of the chief resident course.

Table 1. Number of patients

Invasive pancreatic cancer	49
Other pancreatic neoplasms	25
Hepatocellular carcinoma	44
Hepatic metastases	55
Intrahepatic cholangiocarcinoma	8
Perihilar cholangiocarcinoma	11
Distal bile duct cancer	11
Ampullary cancer	8
Gallbladder cancer	4

Table 2. Type of procedure

Hepatectomy and pancreaticoduodenectomy	1
Pancreaticoduodenectomy	65
Distal pancreatectomy	17
Total pancreatectomy	6
Laparoscopic distal pancreatectomy	9
Hapatectomy with biliary reconstruction	13
Hapatectomy without biliary reconstruction	54
Laparoscopic hepatectomy	50
Others	38
Total	253

Table 3. Survival rates

Diagnosis	No. of pts	5-yr survival (%)
Invasive pancreatic cancer	364	24.6
Hepatocellular carcinoma	350	48.5
Hepatic metastases	575	51.7
Intrahepatic cholangiocarcinoma	60	39.0
Perihilar cholangiocarcinoma	121	42.0
Distal bile duct cancer	97	45.6
Ampullary cancer	68	52.1
Gallbladder cancer	82	47.1

List of papers published in 2015

Journal

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Department of Hepatobiliary and Pancreatic Oncology

Masafumi Ikeda, Shuichi Mitsunaga, Izumi Ohno, Yusuke Hashimoto, Hideaki Takahashi, Kazuo Watanabe, Kumiko Umemoto

Introduction

The Department of Hepatobiliary and Pancreatic Oncology is responsible for the treatment and management of patients with hepatic, biliary, and pancreatic cancers. Our goal is to provide high-quality cancer treatment with adequate palliative care, and to develop novel and effective treatments through well-designed clinical trials and research.

Routine activities

Our Department is composed of five staff oncologists and two residents, with an average of 45 beds in the hospital. We conduct clinical rounds for admitted patients every morning and evening. Most new patients with unresectable hepatobiliary and pancreatic tumors are hospitalized for the diagnosis and treatment of tumors. The treatment strategies on individual patients are discussed in weekly tumor board conferences attended by medical oncologists, surgeons, radiologists, radiation oncologists, and pharmacists. Furthermore, we are also responsible for external or endoscopic abdominal ultrasonographic examinations, endoscopic or percutaneous ultrasound-guided biopsies of abdominal masses, local ablative therapy for liver tumors, endoscopic or percutaneous biliary drainage and stenting for obstructive jaundice.

Research activities

1) Hepatocellular carcinoma (HCC)

Sorafenib is the only available standard of care for advanced HCC. We conducted a randomized phase II trial of sorafenib plus hepatic arterial infusion chemotherapy with cisplatin vs. sorafenib alone in patients with advanced HCC, and the combination therapy yielded favorable overall survival as compared to sorafenib alone. A further phase III trial is planned to confirm these results.

2) Pancreatic cancer (PC)

Gemcitabine (Gem) plus nab-paclitaxel was approved for the treatment of advanced PC in December 2014, following the approval of FOLFIRINOX in December 2014. Gem plus nab-paclitaxel has been reported to be comparable on efficacy to and more feasible on adverse events than FOLFIRINOX. In our hospital, Gem plus nab-paclitaxel has been adapted as a first line treatment of advanced PC, and it has been elucidated to have a favorable efficacy and manageable toxicities in daily practice. It should be clarified which is the better treatment in advanced PC patients: Gem plus nab-paclitaxel or FOLFIRINOX by large-scale phase III trial.

The diagnostic value of serum microRNAs on a highly sensitive microarray was found in PC and biliary tract cancer (BTC). A combination strategy of the microRNA markers has been reported to be effective in diagnosis of resectable PC. In addition, the cachexia-related factors that deteriorate during chemotherapy for PC and are associated with poor overall survival have been identified to evaluate the efficacy of the anti-cachexic treatment and to develop the newly arriving anti-cachexic treatment.

Clinical trials

Thirty-six clinical trials (sponsored: 21 trials, investigator-initiated: 15 trials) are ongoing, and eight clinical trials (sponsored: six trials, investigator-initiated: five trials) are being planned for the upcoming year. Recently, immune checkpoint inhibitors are noticed in all cancer treatment, and sponsored trials of these agents or combination therapies with these agents are increasing in this field.

1) HCC

A randomized phase II trial comparing

sorafenib vs. observation in combination with transcatheter arterial chemoembolization (TACE) is ongoing. Some sponsored trials of sorafenib plus resminostat, sorafenib plus LY2157299, sorafenib plus BBI503 are ongoing as first line chemotherapy. As the second line setting, the enrollment of some clinical trials of nivolumab, regorafenib, ONO-7268MX1, ONO-7268MX2, and so forth, have been finished, but some clinical trials of tivantinib, ramucirumab, other immune checkpoint inhibitors, and so forth, are ongoing.

2) BTC

A randomized phase III trial comparing adjuvant S-1 with observation in patients with resected BTC (The Japan Clinical Oncology Group (JCOG) 1202) is ongoing. As first line chemotherapy, a randomized phase III trial comparing Gem plus S-1 with Gem plus cisplatin (JCOG1113) is ongoing, and Gem cisplatin plus nivolumab is planned. As advanced BTCs refractory to Gem, some sponsored trials of resminostat plus S-1, immune checkpoint inhibitors or these combinations are under way.

3) PC

A multicenter phase II trial of neoadjuvant S-1 and concurrent radiotherapy for borderline resectable PC (JASPAC05) is ongoing. A phase II trial of Gem plus Z-360 vs. Gem+Placebo, a phase I trial of Gem plus LY2157299 in chemo-naïve PC patients, a phase III trial of mixed agents of S-1 plus leucovorin (TAS-118) vs. S-1 in Gem refractory PC patients, and a phase II trial of GBS-01 in refractory PC patients to Gem-based and fluoropyrimidine-based regimen have been finished on the enrollments. Some sponsored trials of immune check point inhibitors are planned as second line chemotherapy for advanced PC.

Education

For our residents, one-to-one training is provided on the daily practice of management of inpatients and outpatients. In addition, the residents can learn the indication, administration and management of the adverse events of all cancer treatments from local treatments to systemic chemotherapy for hepatic, biliary, and pancreatic cancer patients and the accompanied procedures to make diagnosis and drainage for obstructive jaundice. In addition, the residents can make a presentation of their research in domestic and overseas' meetings and present a paper in English under the instruction of staff physicians.

Future prospects

The prognosis of patients with hepatic, biliary, and pancreatic cancers remains bleak, and standard treatments for theses cancer is limited. In Japan, the incidences of these cancer, especially HCC and BTC, are higher than those in Western countries. Therefore, we must conduct a lot of novel and promising clinical trials and research that take the lead worldwide. And it is necessary to develop biomarker research accompanying cancer treatment in cooperation with our cancer research center and pharmaceutical companies to identify the more effective and less toxic patient subgroups.

Table 1. Number of patients

Hepatocellular carcinoma	103
Biliary tract cancer	
Intrahepatic cholangiocarcinoma	32
Extrahepatic cholangiocarcinoma	30
Gallbladder cancer	27
Papilla of vater carcinoma	5
Pancreatic cancer	
Locally advanced disease	67
Metastatic disease	161
Other	27
Total	452

Table 2. Type of procedure

Hepatocellular carcinoma	
Radiofrequency ablation	81
Transarterial chemoembolization	190
Intra-arterial chemotherapy	56
Systemic chemotherapy	49
Proton beam radiotherapy	28
Biliary tract cancer	
Systemic chemotherapy	96
Radiotherapy	3
Pancreatic cancer	
Systemic chemotherapy	286
Chemoradiotherapy	3
Total	792

List of papers published in 2015

Journal

1. Miura T, Mitsunaga S, Ikeda M, Shimizu S, Ohno I, Takahashi H, Furuse J, Inagaki M, Higashi S, Kato H, Terao K, Ochiai A. Characterization of patients with advanced pancreatic cancer and high serum interleukin-6 levels. Pancreas, 44:756-763, 2015

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10. Yamaue H, Tsunoda T, Tani M, Miyazawa M, Yamao K, Mizuno N, Okusaka T, Ueno H, Boku N, Fukutomi A, Ishii H, Ohkawa S, Furukawa M, Maguchi H, Ikeda M, Togashi Y, Nishio K, Ohashi Y. Randomized phase II/III clinical trial of elpamotide for patients with advanced pancreatic cancer: PEGASUS-PC Study. Cancer Sci, 106:883-890, 2015

11. Okusaka T, Aramaki T, Inaba Y, Nakamura S, Morimoto M, Moriguchi M, Sato T, Ikawa Y, Ikeda M, Furuse J. Phase I study of tivantinib in Japanese patients with advanced hepatocellular carcinoma: Distinctive pharmacokinetic profiles from other solid tumors. Cancer Sci, 106:611-617, 2015

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Department of Urology

Yasuyuki Sakai, Yoshinobu Komai

Introduction

The Department of Urology has existed as part of the Department of Pelvic Surgery at the National Cancer Center Hospital East from 2003. This Department mainly treats diseases of the pelvic organs, including urogenital cancer, with the aim of preserving the sexual and/or voiding functions under minimally invasive surgery.

Routine activities

Outpatient activities: The outpatient clinic is open two days a week as a Urology Department. Flexible cystoscopy, abdominal ultrasonography, retrograde pyelography and some prostate biopsies are performed in the outpatient clinic. Superficial bladder cancer (G3, cis, or recurrent tumor) after TUR-Bt is treated by instillation of BCG into the bladder. Advanced urogenital cancers including metastatic prostate cancer are referred to the medical oncology division for chemotherapy or hormonal therapy. Extrinsic obstructions of the upper urinary tract that directly result from invasion of an adjacent malignancy or peritoneal metastasis are also treated. In most cases, internal stenting is better tolerated than percutaneous nephrostomy. 54 patients newly received ureteral stents and 18 underwent nephrostomy for obstructive uropathy in 2015. Inpatient activities: A daily conference is held with doctors of the Department of Pelvic Surgery on diagnosis and treatment of the patients with colorectal and urological cancer. We performedabout 28 combination surgeries with colorectal surgeons. In the department of urology, 103 general anaesthesia surgeries, 81 spinal anesthesia surgeries and 42 prostate biopsies were performed this year. Other: We have a conference on urogenital cancers every other week among medical oncologists, radiation oncologists, and pathologists. Neoadjuvant chemotherapy for muscle invasive bladder cancer, combination therapy of hormone and radiation for prostate cancer, treatment strategies for metastatic renal cell carcinoma and testicular cancer, and so on, are determined in the meeting.

Research activities

To facilitate laparoscopic off-clamp partial nephrectomy, we presented the "patient-specific 3D kidney image and 3D printed kidney model" at the 28th congress of the Japanese Society of Endourology, and this presentation was accepted as part of the content of the Audio-Visual Journal of the Japanese Urological Association. And at the 31st annual congress of the European Association of Urology, we presented a time-lapse movie as a novel informed consent tool. It was commended for the Best Poster Award. Total pelvic exenteration (TPE) is the standard procedure for locally advanced rectal cancer involving the prostate and seminal vesicles. We evaluated the feasibility of bladder-sparing surgery as an alternative to TPE. We performed concomitant prostatectomy and cysto-urethral anastomosis.

Clinical trials

1) A retrospective study of perioperative results in partial nephrectomy for renal cell carcinoma
2) An estimate of the prevalence of Lynch syndrome in upper urinary tract urothelial cancer
3) Development and validation of a nomogram to predict recurrences of upper urinary tract urothelial cancer in Japanese patients
4) A retrospective study of the utility and safety of Imidafenacin for overactive bladder, which occurs after urinary tract stenting for urinary obstruction by a progressive malignant tumor
5) A phase II clinical study of robotic-assisted

radical prostatectomy by the da Vinci S/Si Surgical System

6) A phase III study: BCG instillation for high-grade T1 bladder cancer (JCOG1019)

Education

We accepted one voluntary resident of urology in 2015 and educated the resident on urological surgery.

Future prospects

New laparoscopic transurethral surgical devices for bladder cancer are being developed in cooperation with another institution. Also, we aim for the safe introduction of laparoscopic total cystectomy and the safe adaptation expansion of robot-assisted laparoscopic surgery.

Table 1. Number of patients

	No.
Renal cell carcinoma	38
Upper urinary tract urothelial carcinoma	7
Bladder cancer	36
Prostate cancer	39
Testicular cancer	1

Table 2. Type of procedure

	No.
Radical nephrectomy (laparoscopic surgery/total)	19/25
Partial nephrectomy (laparoscopic surgery/total)	4/13
Nephroureterectomy (laparoscopic surgery/total)	6/7
Radical cystectomy (laparoscopic surgery/total)	1/14
TURBT	72
Radical prostatectomy (robotic-assisted laparoscopic surgery/total)	39/39

Department of Musculoskeletal Oncology and Rehabilitation

Fumihiko Nakatani

Introduction

The Department of Musculoskeletal Oncology and Rehabilitation of the National Cancer Center Hospital East (NCCHE) is a team consisting of a panel of orthopedic surgeons and rehabilitation professionals that started from 2012. We strive to provide expert interdisciplinary care for a variety of benign and malignant bone and soft tissue tumors and tumor-like conditions, and we also provide comprehensive rehabilitation services. Currently, we have a chief orthopedic surgeon and three rehabilitation staff engaging in the treatment of a variety of patients with the aid of other orthopedic staff from the NCCH.

Routine activities

Our outpatient service is open three days a week (Mondays, Wednesdays and Fridays) for patients with a variety of musculoskeletal tumors or cancer patients who need rehabilitation care. We also manage the patients with bone metastases or other orthopedic diseases as a result of consultation from other cancer specialists on a daily basis. To provide the prosthetic and orthotic care for our patients a special outpatient service is open every Friday. In cases of patients who need multidisciplinary approaches to their treatment, we offer appropriate referral to the NCCH for further treatment.

In 2015, we conducted 37 operations in total, consisting of 17 resections of soft tissue tumors, four osteosyntheses of pathological fractures from bone metastases, 13 operations for bone tumors and three operations for other tumors/reasons.

In September 2014, we opened a spacious rehabilitation unit with start-of-the-art equipment with the aim to reduce the common side effects of cancer treatment, including fatigue, weakness, poor endurance, pain, nausea, anxiety, depression and loss of confidence. As a result, we conducted rehabilitation for 1,127 patients in 2015 (Table 1).

Table 1. Characteristics and number of patients enrolled for rehabilitation.

Department	2012	2013	2014	2015
Hematology	39	24	11	68
Thoracic oncology	35	44	54	83
Thoracic surgery	29	13	30	119
Head and neck oncology	21	10	5	17
Gastrointestinal oncology	21	23	59	89
Esophageal surgery	19	34	60	200
Musculoskeletal oncology	17	52	23	42
Palliative medicine	15	18	2	66
Colorectal surgery	13	2	42	29
Hepatobiliary and pancreatic oncology	12	15	24	70
Breast and medical oncology	–	27	34	87
Head and neck surgery	–	13	97	134
Gastrointestinal surgery	–	–	–	32
Hepatobiliary and pancreatic surgery	–	–	–	48
Others	24	19	52	43
Total	146	245	493	1,127

Research activities

We have been focusing on regional cooperation with the local physiotherapists of Kashiwa City with the aim to provide cancer patients of the community with seamless rehabilitation care after invasive cancer operations. Until now, we have established the standard methods of physiotherapy and functional evaluations in common.

Clinical trials

We have been focusing on the standardization of multidisciplinary treatment for bone and soft tissue sarcomas through cooperation with the musculoskeletal oncology department of the NCCH. Two multi-institutional clinical trials are active as follows:

1) A multi-institutional phase III clinical trial of multidrug adjuvant chemotherapy for

osteosarcoma (JCOG 0905) has been ongoing since 2010.

2) A multi-institutional phase III clinical trial of adjuvant chemotherapy for high-grade soft part sarcoma (JCOG 1306) started in February 2014.

Education

We have undertaken several educational lectures for the medical staff to highlight the importance of rehabilitation for cancer treatment. We also provide some instructive lectures for the medical staff of the community.

Future prospects

Recent evolution of cancer treatment increases the demand for the orthopedic care and rehabilitation of cancer survivors. We must consistently focus on standardization for the methodology of rehabilitation for all cancer patients, which will be beneficial for the augmentation of quality of life for these patients.

List of papers published in 2015

Journal

1. Yamaga K, Kobayashi E, Kubota D, Setsu N, Tanaka Y, Minami Y, Tanzawa Y, Nakatani F, Kawai A, Chuman H. Pediatric myositis ossificans mimicking osteosarcoma. Pediatr Int, 57:996-999, 2015

2. Fujiwara T, Ogura K, Kobayashi E, Tanzawa Y, Nakatani F, Chuman H, Kawai A. Clinical Outcomes of Surgical Treatments for Primary Malignant Bone Tumors Arising in the Acetabulum. Sarcoma, 2015:430576, 2015

3. Fujiki M, Miyamoto S, Nakatani F, Kawai A, Sakuraba M. Rotationplasty with vascular reconstruction for prosthetic knee joint infection. Case Rep Orthop, 2015:241405, 2015

4. Miyamoto S, Fujiki M, Nakatani F, Sakisaka M, Sakuraba M. Free flow-through anterolateral thigh flap for complex knee defect including the popliteal artery. Microsurgery, 35:485-488, 2015

Department of Hematology

Kunihiro Tsukasaki, Sachiko Seo, Kensuke Narukawa, Rumiko Okamoto, Kota Ohashi

Introduction

The staff physicians and residents of the Department of Hematology carry out clinical and research activities related to multi-disciplinary treatment of patients with hematological malignancies that consist of more than 100 disease entities in the WHO classification (version 2008). Our Department focuses on early and late phases of clinical trials in collaboration with the Research Center for Innovative Oncology and the Japan Clinical Oncology Group (JCOG), respectively, especially on lymphoid malignancies.

Routine activities

The number of patients with newly diagnosed hematologic malignancies in our Department is increasing, and approximately 298 patients with newly diagnosed hematological malignancies including non-Hodgkin's lymphoma, Hodgkin's lymphoma, multiple myeloma, macroglobulinemia, acute leukemia, myelodysplastic syndrome and chronic leukemia were cared for this year (Table 1). The Department is currently providing routine chemotherapy as an outpatient service to an increasing number of relatively aged patients with hematological malignancies. All patients undergoing intensive chemotherapy and autologous peripheral blood hematopoietic stem cell transplantation (APBSCT) (Table 2) are managed in laminar airflow rooms in the designated ward on the eighth floor. Besides managing patients, the Department also provides consultation on hematological abnormalities detected in Clinical Laboratories. A morning case conference on the inpatient care of our Department is held from Mondays to Friday, and a weekly case conference on new patients visiting our clinic is held on Thursday evenings. On Wednesday evenings, a weekly joint conference on lymphoid malignancies with expert pathologists and an educational cytology conference on bone marrow specimens are held. A joint morning journal club of our Department and the Department of Breast and Medical Oncology is held on Mondays and Fridays.

Research activities

Ancillary studies associated with retrospective case series and clinical trials at this Department have been continuously conducted focusing on several kinds on hematological malignancies and their complications. Recently, a nationwide survey of human T-lymphotropic virus type I (HTLV-1) associated adult T-cell leukemia-lymphoma (ATL) is ongoing by us under a grant for Cancer Research from the Ministry of Health, Labour and Welfare to elucidate the pathophysiology including geographical findings as compared to the surveys in 1980 to 1990.

Clinical trials

Clinical trials on hematological malignancies performed by our Department comprise protocols prepared in-house and participation in the Japan Clinical Oncology Group-Lymphoma Study Group (JCOG-LSG), the Japan Adult Leukemia Study Group (JALSG) and others. The Department participated in pharmaceutical company-sponsored and investigator-initiated new-agent trials including international ones for hematological malignancies. The following JCOG clinical trials are ongoing: a randomized phase III trial of rituximab administered weekly or tri-weekly with cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) in patients with newly diagnosed CD20+ diffuse large B cell lymphoma (DLBCL) (JCOG0601) in which a dose-intense schedule of rituximab is evaluated; a randomized phase II trial comparing biweekly

rituximab-CHOP or biweekly rituximab-CHOP/cyclophosphamide, cytarabine, dexamethasone, etoposide and rituximab (CHASER) followed by high dose melphalan, cyclophosphamide, etoposide and dexamethasone (LEED) with APBSCT in patients with newly diagnosed poor risk CD20+ DLBCL (JCOG0908); a randomized phase II study of two induction treatments of melphalan, prednisolone, plus bortezomib (MPB), JCOG-MPB versus modified PETHEMA-MPB, in elderly patients or non-elderly patients refusing transplants with untreated symptomatic myeloma (JCOG1105); and a single armed phase III study of mLSG15 chemotherapy followed by allo-HSCT, comparing the results with historical control in JCOG9801 of mLSG15 alone to evaluate the promising efficacy of allo-HSCT, possibly associated with a graft-versus-ATL effect, especially in view of a comparison with intensive chemotherapy (JCOG0907). A phase III study evaluating the efficacy of the combination of interferon-alpha (IFN) and zidovudine (AZT) as compared to watchful-waiting for indolent ATL (JCOG1111) is ongoing under a highly advanced medical technology assessment system because IFN and AZT are not covered for ATL by National Health Insurance in Japan. A single armed phase III study of interim-PET response adapted a switch-strategy from ABVD to ABVD/DE-BEACOP for advanced Hodgkin Lymphoma (JCOG1305).

Table 1. Number of patients

Non-Hodgkin's lymphoma	150
Hodgkin's lymphoma	8
Acute lymphoid leukemia	7
Chronic lymphoid leukemia	4
Acute myeloid leukemia	16
Chronic myeloid leukemia	5
Myeloproliferative neoplasm(excluding CML)	10
Multiple myeloma	22
Myelodysplastic syndrome	12
Others	64
Total	298

Table 2. Type of procedure

PBSCT for non-Hodgkin's lymphoma in relapse	5
PBSCT for myeloma in remission	5
Total	10

List of papers published in 2015

Journal

1. Katsuya H, Ishitsuka K, Utsunomiya A, Hanada S, Eto T, Moriuchi Y, Saburi Y, Miyahara M, Sueoka E, Uike N, Yoshida S, Yamashita K, Tsukasaki K, Suzushima H, Ohno Y, Matsuoka H, Jo T, Amano M, Hino R, Shimokawa M, Kawai K, Suzumiya J, Tamura K, ATL–Prognostic Index Project. Treatment and survival among 1594 patients with ATL. Blood, 126:2570-2577, 2015

2. Yoshida N, Tsuzuki S, Karube K, Takahara T, Suguro M, Miyoshi H, Nishikori M, Shimoyama M, Tsukasaki K, Ohshima K, Seto M. STX11 functions as a novel tumor suppressor gene in peripheral T-cell lymphomas. Cancer Sci, 106:1455-1462, 2015

3. Miura S, Akazawa Y, Kurashige T, Tukasaki K, Kondo H, Yokota K, Mine M, Miyazaki Y, Sekine I, Nakashima M. The Nagasaki Atomic Bomb Survivors' Tumor Tissue Bank. Lancet, 386:1738, 2015

4. Yoshida N, Imaizumi Y, Utsunomiya A, Miyoshi H, Arakawa F, Tsukasaki K, Ohshima K, Seto M. Mutation Analysis for TP53 in Chronic-Type Adult T-Cell Leukemia/Lymphoma. J Clin Exp Hematop, 55:13-16, 2015

5. Seo S, Boeckh M, Storer BE, Schubert MM, Rotta M, Sandmaier BM, Mielcarek M. The association between donor and recipient statin use and infections after allogeneic hematopoietic cell transplantation. Bone Marrow Transplant, 50:444-448, 2015

6. Erard V, Guthrie KA, Seo S, Smith J, Huang M, Chien J, Flowers ME, Corey L, Boeckh M. Reduced Mortality of Cytomegalovirus Pneumonia After Hematopoietic Cell Transplantation Due to Antiviral Therapy and Changes in Transplantation Practices. Clin Infect Dis, 61:31-39, 2015

7. Seo S, Renaud C, Kuypers JM, Chiu CY, Huang ML, Samayoa E, Xie H, Yu G, Fisher CE, Gooley TA, Miller S, Hackman RC, Myerson D, Sedlak RH, Kim YJ, Fukuda T, Fredricks DN, Madtes DK, Jerome KR, Boeckh M. Idiopathic pneumonia syndrome after hematopoietic cell transplantation: evidence of occult infectious etiologies. Blood, 125:3789-3797, 2015

8. Uy GL, Costa LJ, Hari PN, Zhang MJ, Huang JX, Anderson KC, Bredeson CN, Callander NS, Cornell RF, Perez MA, Dispenzieri A, Freytes CO, Gale RP, Garfall A, Gertz MA, Gibson J, Hamadani M, Lazarus HM, Kalaycio ME, Kamble RT, Kharfan-Dabaja MA, Krishnan AY, Kumar SK, Kyle RA, Landau HJ, Lee CH, Maiolino A, Marks DI, Mark TM, Munker R, Nishihori T, Olsson RF, Ramanathan M, Rodriguez TE, Saad AA, Savani BN, Schiller GJ, Schouten HC, Schriber JR, Scott E, Seo S, Sharma M, Ganguly S, Stadtmauer EA, Tay J, To LB, Vesole DH, Vogl DT, Wagner JL, Wirk B, Wood WA, D'Souza A. Contribution of chemotherapy mobilization to disease control in multiple myeloma treated with autologous hematopoietic cell transplantation. Bone Marrow Transplant, 50:1513-1518, 2015

Department of Dentistry

Tetsuhito Konishi , Toshiro Miyata, Tomoko Kaneda

Introduction

We aim to deal with the diverse intraoral complications associated with cancer treatment and to maintain and improve patients' quality of life (QOL) in the field of dentistry.

Cancer treatment is frequently associated with a variety of intraoral complications, such as mucositis, taste disorder, dry mouth, pain, and infection. In particular, in patients undergoing treatment for head and neck cancer (chemoradiotherapy, surgery) and hematopoietic stem cell transplantation, severe intraoral symptoms may occur, and strict infection control measures are needed.

When such measures are inadequate, composite complications may result in secondary complications such as eating disorders and undernutrition, and the oral cavity may serve as a source of systemic infections, which may lead to the need for deferring or discontinuing treatment, making continuation and completion of cancer treatment difficult.

To manage and prevent intraoral complications, we evaluate and stabilize the oral status before the initiation of cancer treatment. Proactive intervention by dentists or dental hygienists to educate the patients, their families, and the attending medical staff is extremely important.

Routine activities

We undertake efforts to prevent infection of wounds and aspiration pneumonia and to reduce other complications by oral hygiene management before and after surgery. To maintain postoperative functions of jaw defects, we are attempting to correct speech-language and eating functions by preparing appropriate artificial dentition and prostheses at an early stage, thereby improving the QOL of patients after treatment. For patients receiving chemotherapy and radiotherapy, we are supporting continuation and completion of treatment by taking measures to prevent infections arising from the dentistry realm and mucositis and by reducing pain. In regard to delayed complications, we are undertaking preventive and treatment activities for multiple dental caries, osteomyelitis of the jaw, and necrosis of the jaw bone. Patients treated over the long-term with zoledronic acid or denosumab may develop Medication-Related Osteonecrosis of the Jaw (MRONJ) as a result of contamination of the oral cavity and tooth extraction; thus, we are undertaking measures to prevent/treat this complication.

By participating in multidisciplinary conferences, we apply prevailing practices and information updates to future medical care support. In 2015, the numbers of new and revisiting patients were 1,006 and 8,375, respectively, and the total number of patients was 9,381. These numbers represent an approximately 1.8-fold increase as compared to those in the first year when dentists at the National Cancer Center Hospital East began to hold full-time positions. We believe that the importance of supportive care in cancer has been recognized.

Research activities

We are participating in a multicenter study being conducted to evaluate the effectiveness of proactive use of supportive care for preventing serious oral mucositis in patients with head and neck cancer undergoing chemoradiotherapy.

We are carrying out a study on multiple dental caries and radiation-induced osteomyelitis developing after radiotherapy for head and neck cancers. In addition, we are a part of the nutrition support team.

We cooperate with other facilities for the establishment of oral care programs for patients with head and neck cancers receiving chemoradiotherapy.

Department of Pediatric Oncology

Ako Hosono, Hiroshi Kawamoto, Naoko Yasui

Introduction

The Department of Pediatric Oncology was established in December 2011 to provide treatment for pediatric cancers including a wide variety of diseases such as hematologic malignancies comprising leukemia and lymphoma, embryonal tumors comprising neuroblastomas, nephroblastomas and hepatoblastomas, and mesenchymal tumors comprising Ewing sarcomas, rhabdomyosarcomas and osteosarcomas. Although they usually occur in children under the age of 15, they occasionally occur in adolescents and young adults (AYA). Most of the pediatric cancers are highly chemosensitive as well as radiosensitive. They are possibly curable in a certain situation where the intensity of multidisciplinary treatment and disease characteristics are balanced well. However, there are absolute refractory cases who need new treatments other than standard chemotherapy. Moreover, long-term survivors of pediatric cancers often suffer from complications secondary to chemotherapy and radiotherapy. The three major objectives of the Department of Pediatric Oncology in the NCCE are as follows: (1) To provide state-of-the-art treatment for AYA patients in collaboration with the Medical Oncology group. (2) To develop new treatments for pediatric cancer by sharing agents and knowledge with the Clinical Development Center. And (3) to provide less toxic proton-beam radiation therapy as one of the three proton centers for children in Japan. All three activities are currently on-going and several projects have already started (refer to "Research activities and clinical trials").

Routine activities

The pediatric outpatients service is open for three days a week, Monday, Wednesday and Friday, to treat newly diagnosed patients, patients who received chemotherapy in the outpatient setting and to provide follow-up treatment to patients who have completed an intensive treatment course. Also, the care of children receiving palliative treatment is carried out with the Palliative Care and Psycho-Oncology Group. Daily rounds and a conference are held every morning. We also attend conferences with the Medical Oncology, Orthopedic Surgery, Thoracic Surgery and Urology Department s at any time.

Research activities and clinical trials

As written above, several projects that are expected to achieve our objectives are ongoing. Proton-beam radiation therapy is currently provided as an Investigational Medical Care (Sensin-iryo). However, the medical costs related to the treatment with this system could possibly financially overburden patients and their families. To pursue the possibility of getting this technique approved under the Japanese Health Insurance system, we plan a clinical trial to gather data on safety for pediatric patients. Other projects include treatment development using relatively new off-label drugs as well as experimental agents such as peptide vaccines. One of the objectives of the following trials is gathering data on, and assessing the safety and efficacy data of, such off-label drugs and eventually getting them approved by the Ministry of Health, Labour and Welfare.

One clinical trial described below are currently active.

A phase I trial of immunotherapy using HLA-A2 and A24-restricted glypican-3 peptide vaccine for pediatric tumors.

Table 1. Number of patients

Benign bone tumors	8
Soft tissue sarcoma	2
Rhabdomyosarcoma	1
Ewing sarcoma	1
Leiomyosarcoma	2
Synovial sarcoma	1
Hepatoblastoma	2

Department of Anesthesiology and Intensive Care Unit

Hiroyuki Yamamoto, Aiko Ohshita, Katsuya Kobayashi, Kazuaki Hiraga, Kei Torigoe

Introduction

The Department of Anesthesiology and Intensive Care Unit (ICU) consists of five staff members (four Japanese Society of Anesthesiologists Board Certified Anesthesiologists and a Japanese Society of Anesthesiologists (JSA) Qualified Anesthesiologist) and two or three rotating residents. Each year, we provide more than 2,600 anesthesia services in eight operating rooms and over 1,300 patients have been admitted to the ICU. A large number of operations in the head and neck surgery division and procedures involving a thoracotomy for lung and esophageal cancer are one of the features of this hospital. Accordingly, a special anesthesia induction method for difficult airways and use of the one-lung ventilation technique are often necessary for anesthesiologists. Currently, our ICU admits mainly postsurgical patients who have undergone major abdominal, thoracic and complex surgical procedures, as well as patients who have suffered from serious preoperative complications. Increasingly complex procedures are being performed on more seriously ill patients with coronary disease, chronic obstructive pulmonary disease (COPD), neurological disorders and so on. The ICU needs to play an increasingly important role in postsurgical care for such patients. The goals of the Department of Anesthesiology and Intensive Care Unit are to provide anesthetic and perioperative care to patients, with their safety being the highest priority.

Routine activities

Five staff members (three full-time and two visiting anesthesiologists), four rotating residents and 12 part-time anesthesiologists cover eight operating rooms. A preanesthesia case presentation is held every morning to examine the case of the day and discuss the anesthesia problem and strategy for patients with various complications. In 2015, we provided 2,834 anesthesia services (Table 1). The annual number of patients admitted to the ICU was 1,347 and more than 95% of them were postsurgical patients (Table 2).

Research activities

The relationship between intraoperative blood loss and dry-side fluid management during liver resection was studied. Fluid management was performed based on the value of stroke volume variation (SVV) obtained by the FloTrac system, which has a strong correlation with central venous pressure (CVP). This technique demonstrated decreased intraoperative blood loss during liver resection.

Education

The Department of Anesthesiology and Intensive Care Unit has no resident. For rotating residents, we provide opportunities of epidural anesthesia, one-lung ventilation technique for thoracotomy, and difficult airway management including fiberoptic intubation. A Journal club is also held once a week in addition to the everyday morning conference. We support residents who hope to obtain the qualification of anesthesiologist or JSA Qualified Anesthesiologist during rotation periods.

Future prospects

In 2017, a new surgical and endoscopic center will be built, which has 12 operating rooms. We expect a 20 to 25% of increase in anesthesia cases. To accomplish this, an increase of the staff is essential. Next year, two staff anesthesiologists will join our department and we are preparing to increase the number of operations with these additional members.

Table 1. Number of Anesthesia Cases

Type of Surgery	2011	2012	2013	2014	2015
Head and Neck	424	454	423	409	443
Thoracic	466	473	501	520	561
Esophageal	126	182	201	215	199
Hepatobiliary and Pancreatic	269	231	253	282	260
Gastric	286	308	268	292	289
Colorectal	426	453	479	550	561
Urology	78	107	114	111	107
Orthopedic	—	22	43	34	33
Breast	291	309	325	315	347
Plastic and Reconstructive	—	3	8	20	34
Others	—	—	—	2	—
Total	2,366	2,542	2,668	2,697	2,834

Table 2. Number of Patients Admitted to the ICU

	2011	2012	2013	2014	2015
Number of Patients	1,228	1,412	1,458	1,348	1,347

Department of Palliative Medicine

Hiroya Kinoshita, Yoshihisa Matsumoto, Tomofumi Miura, Keita Tagami, Hanako Iwamoto, Yuki Sumazaki

Introduction

The purpose of our Department is to improve the quality of life for cancer patients and their family caregivers by management of irritable symptom burdens and establishment of a regional palliative care system. Therefore, we provide three palliative care services: 1) an outpatient clinic, 2) a supportive care team and 3) a palliative care unit.

Routine activities

1) Outpatient clinic

Patients with or without anti-cancer therapy consult our outpatient clinic for management of their symptoms or for support to decide where and how to spend their lives. The concept of early palliative care has gradually spread and consultations for patients undergoing anti-cancer therapy have been increasing.

2) Supportive care team

This team consist of a physician, psycho-oncologist, nurse, dietician, physiotherapist and speech-language-hearing therapist. Our supportive care team perform a multidisciplinary approach for inpatients with various sufferings in the oncology floor.

3) Palliative care unit

Our palliative care unit is the Japanese version of an acute palliative care unit (APCU). The features of APCU are multidimensional assessment, rapid symptom control and intensive psychosocial care with a shorter length of stay and lower death rate than in traditional PCU. Medical social workers greatly contribute to a transition to palliative home care and transfer to other hospitals.

Research activities

The aim of the research in our division is to establish a regional palliative care system and to integrate early palliative care with oncology. The following research is conducted:

1. System construction of screening and intervention for symptoms in patients with advanced cancer.
2. Development of the integration of early palliative care in metastatic lung cancer.
3. Surveys for patients about opioids adherence and for bereaved family members about opioids administration.
4. Registration for Japanese multicenter cohort studies and international multicenter projects.

Education

The purpose is to promote understanding about palliative care in cancer patients and their families for residents. Residents can train in home palliative care on request. To disseminate knowledge about primary palliative care, we held several workshops for medical staff in the National Cancer Center Hospital East (NCCHE) and for regional palliative care staff.

Future prospects

Our Department will continue the above activities and develop new research to improve quality of life (QOL) for cancer patients and their family caregivers.

List of papers published in 2015

Journal

1. Baba M, Maeda I, Morita T, Inoue S, Ikenaga M, Matsumoto Y, Sekine R, Yamaguchi T, Hirohashi T, Tajima T, Tatara R, Watanabe H, Otani H, Takigawa C, Matsuda Y, Nagaoka H, Mori M, Tei Y, Hiramoto S, Suga A, Kinoshita H. Survival prediction for advanced cancer patients in the real world: A comparison of the Palliative Prognostic Score, Delirium-Palliative Prognostic Score, Palliative Prognostic Index and modified Prognosis in Palliative Care Study predictor model. Eur J Cancer, 51:1618-1629, 2015

2. Hamano J, Morita T, Inoue S, Ikenaga M, Matsumoto Y, Sekine R, Yamaguchi T, Hirohashi T, Tajima T, Tatara R, Watanabe H, Otani H, Takigawa C, Matsuda Y, Nagaoka H, Mori M, Yamamoto N, Shimizu M, Sasara T, Kinoshita H. Surprise Questions for Survival Prediction in Patients With Advanced Cancer: A Multicenter Prospective Cohort Study. Oncologist, 20:839-844, 2015

3. Hamano J, Morita T, Ozawa T, Shishido H, Kawahara M, Aoki S, Demizu A, Goshima M, Goto K, Gyoda Y, Hashimoto K, Otomo S, Sekimoto M, Shibata T, Sugimoto Y, Matsunaga M, Takeda Y, Nagayama J, Kinoshita H. Validation of the Simplified Palliative Prognostic Index Using a Single Item From the Communication Capacity Scale. J Pain Symptom Manage, 50:542-547.e4, 2015

4. Maeda I, Morita T, Kinoshita H. Reply to H. Nakayama et al. J Clin Oncol, 33:2228-2229, 2015

5. Kizawa Y, Morita T, Miyashita M, Shinjo T, Yamagishi A, Suzuki S, Kinoshita H, Shirahige Y, Yamaguchi T, Eguchi K. Improvements in Physicians' Knowledge, Difficulties, and Self-Reported Practice After a Regional Palliative Care Program. J Pain Symptom Manage, 50:232-240, 2015

6. Miura T, Matsumoto Y, Hama T, Amano K, Tei Y, Kikuchi A, Suga A, Hisanaga T, Ishihara T, Abe M, Kaneishi K, Kawagoe S, Kuriyama T, Maeda T, Mori I, Nakajima N, Nishi T, Sakurai H, Morita T, Kinoshita H. Glasgow prognostic score predicts prognosis for cancer patients in palliative settings: a subanalysis of the Japan-prognostic assessment tools validation (J-ProVal) study. Support Care Cancer, 23:3149-3156, 2015

7. Umezawa S, Fujimori M, Matsushima E, Kinoshita H, Uchitomi Y. Preferences of advanced cancer patients for communication on anticancer treatment cessation and the transition to palliative care. Cancer, 121:4240-4249, 2015

8. Miura T, Mitsunaga S, Ikeda M, Shimizu S, Ohno I, Takahashi H, Furuse J, Inagaki M, Higashi S, Kato H, Terao K, Ochiai A. Characterization of patients with advanced pancreatic cancer and high serum interleukin-6 levels. Pancreas, 44:756-763, 2015

9. Igarashi T, Abe K, Miura T, Tagami K, Motonaga S, Ichida Y, Hasuo H, Matsumoto Y, Saito S, Kinoshita H. Oxycodone frequently induced nausea and vomiting in oxycodone-naïve patients with hepatic dysfunction. J Palliat Med, 18:399, 2015

10. Kinoshita H, Maeda I, Morita T, Miyashita M, Yamagishi A, Shirahige Y, Takebayashi T, Yamaguchi T, Igarashi A, Eguchi K. Place of death and the differences in patient quality of death and dying and caregiver burden. J Clin Oncol, 33:357-363, 2015

Department of Psycho-Oncology Service

Asao Ogawa, Yoshio Iwata, Daisuke Fujisawa, Hiroyuki Nobata, Hiroko Tanaka, Junko Ueda, Rina Kakinuma, Tomoko Nishimura

Introduction

The Department of Psycho-Oncology Service, established in July 1996, aims to manage and alleviate emotional distress of cancer patients, their families and caring staff. The Department, adjunctive with the Psycho-oncology Division of the Research Center for Innovative Oncology, also aims to study the influence of psychosocial issues upon quality of life and survival of cancer patients. Management of elderly patients with cancer, who are frequently comorbid with cognitive impairment or dementia, is another focus of interest.

Routine activities

The Department of Psycho-Oncology Service is composed of two attending psychiatrists, three clinical psychologists, and two psychiatry residents. The clinical activities include psychiatric consultation, involving comprehensive assessment and addressing of psychiatric problems of cancer patients. The patients are either self-referred or referred by their oncologists in charge. The consultation data are shown in the Table. Psychiatric diagnosis is based on the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th edition) criteria. Consultation data also includes individuals who are family members of cancer patients.

A conference with the Supportive Care Team is held on Wednesdays, and a multicenter joint clinical teleconference involving six cancer center hospitals and three university hospitals is held on Thursdays. In 2014, the Supportive Care Center was developed. This center provides multi-professional attention to the individual's overall physical, psychosocial, and social needs, and cooperates with the Psycho-Oncology Division.

Table 1. Psychiatric consultation data (n=973; January-December, 2015)

Section		N (%)
Age	Mean ± SD (median, range) (yr)	64.4±12.8(67, 15 ～ 93)
Gender	(male/female)	637 (58.6%) / 450 (41.4%)
Inpatient / Outpatient		725(66.7%)/362(33.3%)
Cancer patient / Family member		1,051 (96.7%) / 36 (3.3%)
Cancer site	Head and Neck	193 (17.8%)
	Lung	154 (14.2%)
	Esophagus	119 (10.9%)
Stage	Ⅰ/Ⅱ/Ⅲ/Ⅳ/Recurrent	83(7.6%)/101 (9.3%)/128(11.8%)/416(38.3%)/ 180(16.6%)/
PS	0/1, 2/3, 4	348 (32.0%) /504 (46.4%)/235 (21.6%)
Psychiatric diagnosis	Delirium	270 (24.8%)
	Adjustment disorders	164 (15.1%)
	Major depression	62 (5.7%)
	Dementia	125 (11.5%)
	No diagnosis	180 (16.6%)

Supportive Care Team

Hiroya Kinoshita, Yoshihisa Matsumoto, Tomofumi Miura, Asao Ogawa, Yoshio Iwata, Naoko Kobayashi, Chiyuki Sasaki, Junya Ueno, Yoshie Iino, Kazuaki Hiraga, Daisuke Fujisawa, Hiroyuki Nobata, Keita Tagami, Yuki Sumazaki, Hanako Iwamoto, Lina Orikabe, Naoko Yoshino, Noriko Fujishiro, Junko Ueda, Rina Kakinuma, Tomoko Nishimura, Hideo Uesugi, Kumi Nakamura, Taichi Watanabe, Hatoe Sakamoto

Introduction

The Supportive Care Team (SCT), established in October 2005, primarily aims to improve care for cancer patients and families facing a life-threatening illness. The role of the SCT is to implement comprehensive cancer care by assessing unrelieved symptoms (physical and psychiatric) and unattended needs, as well as efficiently managing physical symptoms, providing psychological support, and coordinating services.

Routine activities

The SCT is an interdisciplinary team composed of palliative care physicians, psychiatrists, certified nurse specialists, certified nurses, clinical psychologists, pharmacy practitioners, registered dietitians and social workers. The SCT keeps regular contact with clinician-teams in charge, discusses patients' needs, and refers patients and families to the appropriate services. Interdisciplinary team conferences and SCT rounds are held on Wednesdays. The SCT consultation data are shown in the table.

Clinical trials

Please refer to the "Department of Psycho-Oncology Service, Research Center for Innovative Oncology" section and the "Department of Palliative Medcine" sections.

Table 1. Supportive Care Team consultation data (n=1,009; January-December, 2015)

		N (%)
Age	Mean ± SD (range) (yr)	63.8±13.2
Gender	(male/female)	629 (62%) / 380 (38%)
Service	Palliative care/ Psycho-oncology	284/ 725
Performance status	0/1/ 2/ 3/ 4	146 (14%) / 230 (23%) / 261 (26%) / 245 (24%) / 127 (13%)
Physical symptoms (moderate - severe)	Pain	516 (51%)
	Appetite loss	375 (37%)
	Fatigue	484 (48%)
	Respiratory distress	233 (23%)
Psychiatric diagnosis (primary diagnosis)	Delirium	235 (23%)
	Adjustment disorders	76 (8%)
	Dementia	93 (9%)
	Major depressive disorders	28 (3%)
Outcome	Discharge/ Hospital transfer	892 (89%) / 110 (11%)

List of papers published in 2015

Journal

Please refer to the "Psycho-Oncology Service" sections.

List of papers published in 2015

Journal

1. Mori M, Shimizu C, Ogawa A, Okusaka T, Yoshida S, Morita T. A National Survey to Systematically Identify Factors Associated With Oncologists' Attitudes Toward End-of-Life Discussions: What Determines Timing of End-of-Life Discussions? Oncologist, 20:1304-1311, 2015

2. Shimizu K, Nakaya N, Saito-Nakaya K, Akechi T, Ogawa A, Fujisawa D, Sone T, Yoshiuchi K, Goto K, Iwasaki M, Tsugane S, Uchitomi Y. Personality traits and coping styles explain anxiety in lung cancer patients to a greater extent than other factors. Jpn J Clin Oncol, 45:456-463, 2015

3. Umezawa S, Fujisawa D, Fujimori M, Ogawa A, Matsushima E, Miyashita M. Prevalence, associated factors and source of support concerning supportive care needs among Japanese cancer survivors. Psychooncology, 24:635-642, 2015

4. Yokomichi N, Morita T, Nitto A, Takahashi N, Miyamoto S, Nishie H, Matsuoka J, Sakurai H, Ishihara T, Mori M, Tarumi Y, Ogawa A. Validation of the Japanese Version of the Edmonton Symptom Assessment System-Revised. J Pain Symptom Manage, 50:718-723, 2015

Book

1. Ogawa A. Long-term cognitive function. In: Bruera E, Higginson IJ, von Gunten CF, Morita T (eds), Textbook of Palliative Medicine and Supportive Care, Second Edition, USA, CRC Press, pp 1269-1275, 2015

Department of Diagnostic Radiology

Masahiko Kusumoto, Ryoko Iwata, Yoshihiro Nakagami, Tatsushi Kobayashi, Kaoru Shimada, Kotaro Sekiya, Hirohumi Kuno

Introduction

The Department of Diagnostic Radiology is committed to improving health through excellence in image-oriented patient care and research. Our Department performs more than 96,000 inpatient and outpatient procedures annually. The department also conducts clinical scientific research as well as basic scientific studies, with the results translated directly into better patient care.

Routine activities

Our Department has four multi-slice computed tomography (CT) scanners including two area detector CT scanners and one Dual Source CT, two 3T magnetic resonance imaging (MRI) systems, one interventional radiology (IR) CT system, one Multi-axis c-arm CT system, two gamma cameras with the capacity for single photon emission CT (SPECT), two digital radiographic (DR) systems for fluoroscopy, two mammographies (MMG), and four computed radiographic (CR) systems. Our IR-CT systems use digital subtraction angiography with multi-detector computerized tomography (MDCT). One is equipped with a 320 multi-slice CT. A positron emission tomography (PET) scanner and baby cyclotron have been installed, and tumor imaging using 18F-FDG (fluorodeoxyglucose) has been performed. These all-digital image systems enhance the efficacy of routine examinations.

This department has seven consulting radiologists and 22 technologists. As part of our routine activities, every effort is made to produce an integrated report covering almost all examinations, such as MMG, contrast radiological procedures, CT, MRI, RI, PET, angiography and IR, mainly transarterial chemoembolization (TACE).

The number of cases examined in 2015 is shown in the Table below. Several conferences are routinely held at our department including pre- and postoperative conferences. Furthermore, our Department contributes to decide treatment strategy through the image presentation at the weekly tumor board conference (especially, Hepatobiliary-Pancreatic and Head-Neck regions).

Research activities

The research activities of the Department of Diagnostic Radiology focus on diagnostic imaging and IR. These activities consist of 1) Development of new CT/MRI technology and 2) Development of new Nuclear Medicine tracers. The department also conducts clinical scientific research as well as basic scientific studies, with the results translated directly into better patient care.

1) Development of new CT/MRI technology

In the study with dual energy CT, for the larynx, hypopharynx, thyroid cancers and lymph node metastasis, the possibility of a quantitative evaluation with iodine uptake value measuring and histogram generation using monochromatic imaging technique have been confirmed. The results of this preliminary study have suggested that the quantitative analysis of tumors may aid differential diagnosis and the lymph node metastasis detection.

In 320-row area-detector CT, it is found that the effect of SEMAR (single energy metal artifact reduction: the algorithm to reduce metal artifacts without increasing the X-ray dose) influenced by the location of metal materials at the scan. In addition, it has been confirmed that the location adjustment of the metal materials can increase the effect of SEMAR and CT image quality. Furthermore, in the other study with 320-row area-detector CT, using the area-detector CT features as a four dimensional CT, the relationship between the perfusion parameters of the pancreas and the frequency of the

post-operative complication have been investigated.

In the 3-Tesla MR study, the imaging quality of mandibular cross-sectional multiplanar reconstruction (CS-MPR) using 3D sequences has been improved by optimization of the 3D imaging process. This optimization provides more accurate evaluation of bone marrow invasion.

In another study using 3T-MRI, the vessels of the tongue have been visualized by bright-blood time with a 3D sequence. It is suggested that this bright-blood imaging technique will provide more sensitive lymph node metastasis detection because the tongue cancer invasion into the lingual vascular bundle is known as a predictor of lymph node metastasis.

2) Development of new Nuclear Medicine tracers

Small interfering RNAs (siRNAs) were discovered as a promising gene silencing tool in research and in the clinic, and we succeeded in radiolabeling siRNA last year. However, siRNA is unstable for RNase in the living body. Therefore, the transfection reagent is usually required when siRNA is given to the living body.

We compared the degree of resistance against RNaseA among unlabeled siRNA, naked radiolabeled siRNA and radiolabeled siRNA with the transfection reagent. For Radiolabeled siRNA with the transfection reagent, slightly less than 60% of the RNA remained at 60 minutes after adding RNaseA. On the other hand, for naked unlabeled siRNA, almost all siRNA was broken down at seven minutes after adding RNaseA. For naked radiolabeled siRNA only, slightly over 30% of the RNA remained at 60 minutes after adding RNaseA, although we did not use the transfection reagent.

The results suggest that our labeled siRNA is stable not only as a complex with transfection reagents but also as naked labeled siRNA and should be deliverable to the specific regions overexpressing the target gene.

Table 1. Number of Anesthesia Cases

	2011	2012	2013	2014	2015
Plain X-ray examination	35,032	39,128	38,722	42,672	43,652
Mammography (MMG)	2,434	2,380	2,354	2,310	2,368
Fluoroscopic Imaging	3,903	4,029	4,628	4,748	4,691
CT	21,967	24,101	28,963	30,088	34,867
MRI	5,708	5,619	5,657	5,675	5,875
RI (Scintiscan)	1,582	1,586	1,363	1,396	1,302
PET	2,239	2,284	2,208	2,332	2,481
Angiography	656	742	511	801	807
Total	73,521	79,869	84,406	90,022	96,043

List of papers published in 2015

Journal

1. Sugimoto M, Takahashi S, Kobayashi T, Kojima M, Gotohda N, Satake M, Ochiai A, Konishi M. Pancreatic perfusion data and post-pancreaticoduodenectomy outcomes. J Surg Res, 194:441-449, 2015

2. Murata S, Onozawa S, Mine T, Ueda T, Sugihara F, Yasui D, Kumita S, Satake M. Retrograde-outflow percutaneous isolated hepatic perfusion using cisplatin: A pilot study on pharmacokinetics and feasibility. Eur Radiol, 25:1631-1638, 2015

3. Kakinuma R, Muramatsu Y, Kusumoto M, Tsuchida T, Tsuta K, Maeshima AM, Asamura H, Moriyama N. Solitary pure ground-glass nodules 5 mm or smaller: frequency of growth. Radiology, 276:873-882, 2015

4. Watanabe Y, Kusumoto M, Yoshida A, Suzuki K, Asamura H, Tsuta K. Surgically resected solitary cavitary lung adenocarcinoma: association between clinical, pathologic, and radiologic findings and prognosis. Ann Thorac Surg, 99:968-974, 2015

5. Okada H, Kaneda T, Sekiya K, Kawashima Y, Suemitsu M, Hayakawa Y, Sakae T. Basic study of parametric X-ray radiation for clinical diagnosis using 125MeV linear particle accelerator. J Hard Tissue Biol, 24:299-302, 2015

6. Kaneda T, Sekiya K, Suemitsu M, Sakae T, Hayakawa Y, Kawashima Y, Hirahara N, Muraoka H, Ito K, Muramatsu T, Ishida M, Okada H. Preliminary clinical application study of parametric X-rays in diagnostic imaging. Int J Oral-Med Sci, 14:8-12, 2015

7. Sekiya K, Ishida M, Sekiya K, Suemitsu M, Hara Y, Kaneda T. A case of impacted tooth in the maxillary sinus: CT findings. Int J Oral-Med Sci, 13:128-130, 2015

Department of Radiation Oncology

Tetsuo Akimoto, Naoki Nakamura, Sadatomo Zenda, Masakatsu Onozawa, Satoko Arahira, Masamichi Toshima, Atsushi Motegi, Yasuhiro Hirano

Introduction

Radiotherapy (RT) plays an essential role in the management of cancer patients. It is used as (1) a curative treatment for many patients with loco-regional localized malignant disease, (2) integrated therapy combined with chemotherapy and/or surgery, and (3) palliative treatment for patients for whom curative treatment is not a treatment option. In radiotherapeutic approaches, the radiation dose to the loco-regional tumor must be as high as possible, while the dose to the surrounding normal tissues should be kept as low as possible in order to maintain the severity of radiation-related complications within an acceptable level.

The primary aim of the Department of Radiation Oncology is to develop high precision RT such as intensity modulated radiation therapy (IMRT), image-guided radiation therapy (IGRT), stereotactic body RT (SBRT) and proton beam therapy (PBT) and establish the definitive role of RT in cancer treatment. Another important goal is to establish standard treatments for various cancers and optimal irradiation techniques including total dose, fractionation and radiation fields.

Routine activities

At present, the staff of the Radiation Oncology Department consists of seven consultant physicians (radiation oncologists), 19 radiation technologists, four medical physicists, one nurse, and one clerk. We have more than 1,000 new cases for conventional RT and 300 or more new patients for proton beam therapy every year, and quality assurances of both conventional RT and PBT are performed by medical physicists and radiation technologists, and the conference on verification of treatment planning is held every morning in addition to a weekly work conference regarding research activities. RT and PBT are routinely based on three-dimensional radiation therapy planning and PBT using RT-dedicated multi-detector-row helical computed tomography (CT) scanning in order to confirm a precise radiation dose to the targeted tumors. Respiratory-gating has been applied especially in radiotherapeutic management for patients with lung, esophagus and liver cancers.

Selection of treatment approaches is determined through clinical conferences between radiation oncologists, surgical oncologists and medical oncologists. Many clinical trials involving RT as the sole or combined treatment modalities for various cancers are now in progress.

The section is responsible for conventional (photon-electron) RT that consists of 4 linear accelerators, a CT simulator, four treatment planning computer workstations, and other important devices. IMRT and IGRT have been routinely applied for head and neck cancer and prostate cancer. The section is also responsible for PBT that is composed of seven operating staff members and one technician for fabricating the compensator and aperture; they are sent from manufacturing companies and work in collaboration with the other staff members of the Department. PBT consists of two treatment rooms and both rooms are routinely used for rotational gantry treatment. The Department ensures quality assurance and regular maintenance of the PBT machines for precise dose delivery and safe treatment.

Research activities

In the Radiation Oncology Department, the following research activities are in progress:

1) Establishment of optimal combined approaches including RT and chemotherapy for locally advanced head and neck cancer, non-small cell

lung cancer and esophageal cancer, and so on.
2) Establishment of clinical usefulness of IMRT for head and neck cancer, localized prostate cancer and cervical esophageal cancer.
3) Hypofractionated IMRT for localized prostate cancer.
4) Hypofractionated PBT for localized prostate cancer.
5) Evaluation of feasibility of PBT combined with chemotherapy for inoperable locally advanced non-small cell lung cancer and locally advanced esophageal cancer.
6) Evaluation of long-term complications after PBT for pediatric malignancies.
7) The role of gene polymorphism in development of acute and late radiation-related complications.
8) Exploration of biomarkers for head and neck cancer.
9) Radiobiological investigation of cellular response to radiation and proton beam.

Clinical trials

The following in-house and multi-institutional clinical trials are in progress:

1) The Japan Clinical Oncology Group (JCOG) 0701: Accelerated fractionation vs. conventional fractionation radiation therapy for glottic cancer of T1-2N0M0 phase III study.
2) JCOG0701-A1: Evaluation of single-nucleotide polymorphisms (SNPs) in development of acute and late complications after accelerated fractionation and/or conventional fractionation radiation therapy for glottic cancer of T1-2N0M0.
3) JCOG1015: A phase II study of intensity modulated radiation therapy (IMRT) with chemotherapy for loco-regionally advanced nasopharyngeal cancer (NPC).
4) Phase II study of PBT for malignant melanoma of nasal cavity.
5) Phase II trial of concurrent chemoradiotherapy with 5-FU plus cisplatin for resectable squamous cell carcinoma of cervical esophagus.
6) The Japanese Radiation Oncology Study Group (JROSG) phase II trial of IMRT with concurrent chemoradiotherapy for resectable squamous cell carcinoma of cervical esophagus.
7) JCOG1208: A non-randomized confirmatory study of intensity modulated radiation therapy (IMRT) for T1-2N0-1M0 oropharyngeal cancer.
8) JCOG1008: Phase II/III trial of postoperative chemoradiotherapy comparing 3-weekly cisplatin with weekly cisplatin in high-risk patients with squamous cell carcinoma of head and neck
9) Dose escalation study of PBT combined with concurrent chemotherapy for locally advanced esophageal cancer.
10) JCOG1408: Phase III study of SBRT for stage I non-small cell lung cancer.

Education

We established education and training systems for residents and junior radiation oncologists through clinical conferences and lectures on radiation oncology, physics and radiation biology. In addition, a training course about quality assurance of radiation therapy has been regularly held for medical physicists and radiological technologists.

Future prospects

We are now aiming at the establishment of a system that can provide high-quality and safe high-precision radiation therapy. In addition, we would like to promote research and development of innovative technologies regarding radiation therapy, radiation biology and medical physics.

Table 1. Number of patients treated with radiation therapy during 2011-2015

	2011	2012	2013	2014	2015
New patients	1,489	1,575	1,877	1,847	1,830
IMRT	147	225	256	279	280

Table: The changes in the number of patients treated with RT

List of papers published in 2015

Journal

1. Tahara M, Kiyota N, Mizusawa J, Nakamura K, Hayashi R, Akimoto T, Hasegawa Y, Iwae S, Monden N, Matsuura K, Fujii H, Onozawa Y, Homma A, Kubota A, Fukuda H, Fujii M. Phase II trial of chemoradiotherapy with S-1 plus cisplatin for unresectable locally advanced head and neck cancer (JCOG0706). Cancer Sci, 106:726-733, 2015

2. Hotta K, Kohno R, Nagafuchi K, Yamaguchi H, Tansho R, Takada Y, Akimoto T. Evaluation of monitor unit calculation based on measurement and calculation with a simplified Monte Carlo method for passive beam delivery system in proton beam therapy. J Appl Clin Med Phys, 16:228-238, 2015

3. Mizowaki T, Aoki M, Nakamura K, Yorozu A, Kokubo M, Karasawa K, Kozuka T, Nakajima N, Sasai K, Akimoto T. Current status and outcomes of patients developing PSA recurrence after prostatectomy who were treated with salvage radiotherapy: a JROSG surveillance study. J Radiat Res, 56:750-756, 2015

4. Hashimoto Y, Akimoto T, Iizuka J, Tanabe K, Mitsuhashi N. Correlation between the changes in the EPIC QOL scores and the dose-volume histogram parameters in high-dose-rate brachytherapy combined with hypofractionated external beam radiation therapy for prostate cancer. Jpn J Clin Oncol, 45:81-87, 2015

5. Motegi A, Kawashima M, Arahira S, Zenda S, Toshima M, Onozawa M, Hayashi R, Akimoto T. Accelerated radiotherapy for T1 to T2 glottic cancer. Head Neck, 37:579-584, 2015

6. Zenda S, Ishi S, Akimoto T, Arahira S, Motegi A, Tahara M, Hayashi R, Asanuma C. DeCoP, a Dermatitis Control Program using a moderately absorbent surgical pad for head and neck cancer patients receiving radiotherapy: a retrospective analysis. Jpn J Clin Oncol, 45:433-438, 2015

7. Zenda S, Kawashima M, Arahira S, Kohno R, Nishio T, Tahara M, Hayashi R, Akimoto T. Late toxicity of proton beam therapy for patients with the nasal cavity, para-nasal sinuses, or involving the skull base malignancy: importance of long-term follow-up. Int J Clin Oncol, 20:447-454, 2015

Department of Pathology and Clinical Laboratories

Atsushi Ochiai, Takeshi Kuwata, Genichiro Ishii, Satoshi Fujii, Motohiro Kojima, Masato Sugano, Chisako Yamauchi, Eiichi Yoshikawa, Shigehisa Yoshida, Masahiro Inoue, Masahiro Karibe, Seiji Iwasaki, Miki Goto, Masaki Takeda, Satoru Sunohara, Hiromi Kimura, Yasuharu Hashimoto, Yukihiro Okano, Akiko Yamada, Mari Hisano, Mika Sasanuma, Aya Koike, Takuya Yamaguchi, Takuya Aiba, Keiko Nakai, Ayumi Setsuta, Mayumi Motohashi, Ayumi Nakanishi, Sayuri Shibayama, Izumi Suzuki, Yasuko Yoshihara, Kazumi Yamaguchi, Rie Taniguchi, Sudo Kumiko, Saki Nakamura, Kazuki Motohashi, Atsushi Watanabe, Eriko Iwamoto, Yasuteru Yamagishi, Kazumi Tamura, Asami Sekine, Nagisa Bouno, Rie Kuroiwa, Masayuki Ito, Michiko Iida, Yuki Soeda, Megumi Michikawa, Tomoko Seto, Emiko Yoshikawa, Yoshiko Ohtake, Miwa Yamada, Megumi Yamaguchi

Introduction

The Department of Pathology and Clinical Laboratories (DPCL) has two divisions: Pathology Division (PD) and Clinical Laboratory Division (CLD). Both divisions play a fundamental role in routine hospital service and support research activities at the National Cancer Center Hospital East (NCCHE).

DPCL received ISO15189:2007 accreditation in 2012, and successfully transited to the newest version (ISO15189:2012) in 2014, ensuring quality control and quality assurance of testing, including the one for clinical trials, performed in the departments. In 2015, two sections, Physiology and Supporting laboratory testing in clinical studies, received ISO15189:2012, ensuring the quality control and quality assurance of the testing, including the ones for clinical trials, performed in the departments with global standards.

Routine activities

Primarily, the routine activity at the PD is surgical pathology. The Number of samples examined in the department in 2015 is listed in Table 1.

The CLD consists of seven sections: i) general laboratory medicine, ii) hematology, iii) biochemistry/serology, iv) Physiology, v) Bacteriology, vi) Blood transfusion and vii) Supporting laboratory tests in clinical studies. The numbers of tests performed in each division are listed in Table 2 and 3. The total number of tests performed in the DPCL in 2015 increased to 7.5% compared with the previous year; including a 94.4% and a 12.9% increase in the Blood transfusion and Serology sections, respectively.

Research activities

All of the pathologists were involved in research activities at RCIO (Research Center for Innovative Oncology). All the technologists working in the department are also highly motivated to develop advanced diagnostic technologies and various results are presented in several meetings.

Clinical trials

Practically, the CLD participated in all of the clinical trials operated at the NCCHE by providing laboratory data. The section for supporting laboratory testing in clinical studies was transferred to the DPCL in June 2014. The section, coordinating with the pathology and physiology sections, reinforces quality control and quality assurance for clinical tests performed in clinical trials at the NCCHE.

Education

Clinicopathological conferences are held regularly with each clinical department/section. In the PD, conference-style training sessions are open weekly for the residents.

Future prospects

Pathological diagnosis and laboratory tests

play a fundamental role not only in routine hospital work but also in medical research. As an ISO15189-certified clinical laboratory, the DPCL will be continuously involved in investigating new diagnostic technologies, developing new drugs and conducting translational/clinical research in the NCCHE.

Table 1. Number of pathology and cytology samples examined in Pathology Division in 2015

Department	Biopsy	Surgical	Cytology	Autopsy
Digestive Endoscopy	4,951	0	4	0
Gastrointestinal Oncology	154	0	74	0
Breast Surgery	593	358	132	0
Head and Neck Surgery	621	391	388	0
Thoracic Surgery	433	531	530	1
Thoracic Oncology	784	3	907	1
Hematology and medical oncology	545	3	209	2
Hepatobiliary and Pancreatic Oncology	489	1	450	0
Urology	264	103	736	0
Upper Abdominal Surgery	186	473	226	1
Radiation Oncology	149	3	4	0
Lower Abdominal Surgery	83	398	19	0
Orthopedics	43	16	1	0
Esophageal Surgery	8	182	19	0
Head and Neck Oncology	34	1	11	0
Obstetrics and Gynecology	18	0	199	0
Dental division	10	0	0	0
Anesthesiology	3	0	2	0
Dermatology	16	0	0	0
Plastic Surgery	2	5	2	0
Palliative medicine	1	1	4	0
Others	24	1	7	0
Total	9,411	2,469	3,924	5

Table 2. Number of laboratory tests examined in Clinical Laboratory Division in 2014 and 2015

	2014	2015
General laboratory medicine	48,199	48,199
Hematology	302,752	302,752
Biochemistry	1,970,515	1,970,515
Serology	164,382	270,112
Blood transfusion	10,720	11,438
Bacteriology	26,870	29,917
Physiology	22,730	24,703
Total	2,383,461	2,846,826

Table 3. Number of cases and samples prepared in Clinical Laboratory Division for clinical trials in 2015

	Cases	Samples
General laboratory test	3,204	5,972
Electrocardiogram (ECG)	998	1,397
Pathology	864	4,273

List of papers published in 2015

Journal

1. Fujii S, Fujihara A, Natori K, Abe A, Kuboki Y, Higuchi Y, Aizawa M, Kuwata T, Kinoshita T, Yasui W, Ochiai A. TEM1 expression in cancer-associated fibroblasts is correlated with a poor prognosis in patients with gastric cancer. Cancer Med, 4:1667-1678, 2015

2. Shinohara S, Kuroda K, Shimokawa H, Kuwata T, Takenaka M, Chikaishi Y, Oka S, Hirai A, Imanishi N, Uramoto H, Tanaka F. Pleural dissemination of a mixed ground-glass opacity nodule treated as a nontuberculous mycobacterial infection for 6 years without growing remarkably. J Thorac Dis, 7:E370-E373, 2015

3. Ishikawa T, Takahashi J, Kasai M, Shiina T, Iijima Y, Takemura H, Mizoguchi H, Kuwata T. Support system for pathologists and researchers. J Pathol Inform, 6:34, 2015

4. Neri S, Ishii G, Hashimoto H, Kuwata T, Nagai K, Date H, Ochiai A. Podoplanin-expressing cancer-associated fibroblasts lead and enhance the local invasion of cancer cells in lung adenocarcinoma. Int J Cancer, 137:784-796, 2015

5. Nishida Y, Kuwata T, Nitta H, Dennis E, Aizawa M, Kinoshita T, Ohtsu A, Ochiai A. A novel gene-protein assay for evaluating HER2 status in gastric cancer: simultaneous analyses of HER2 protein overexpression and gene amplification reveal intratumoral heterogeneity. Gastric Cancer, 18:458-466, 2015

6. Nagatsuma AK, Aizawa M, Kuwata T, Doi T, Ohtsu A, Fujii H, Ochiai A. Expression profiles of HER2, EGFR, MET and FGFR2 in a large cohort of patients with gastric adenocarcinoma. Gastric Cancer, 18:227-238, 2015

7. Sasaki T, Fuse N, Kuwata T, Nomura S, Kaneko K, Doi T, Yoshino T, Asano H, Ochiai A, Komatsu Y, Sakamoto N, Ohtsu A. Serum HER2 levels and HER2 status in tumor cells in advanced gastric cancer patients. Jpn J Clin Oncol, 45:43-48, 2015

8. Nakamura K, Kuwata T, Shimoda T, Mizusawa J, Katayama H, Kushima R, Taniguchi H, Sano T, Sasako M, Fukuda H. Determination of the optimal cutoff percentage of residual tumors to define the pathological response rate for gastric cancer treated with preoperative therapy (JCOG1004-A). Gastric Cancer, 18:597-604, 2015

Department of Experimental Therapeutics

Toshihiko Doi, Kiyotaka Yoh, Yoichi Naito, Takahiro Kogawa, Hideaki Takahashi, Tomoko Yamazaki, Yasutoshi Kuboki

Introduction

The Exploratory Oncology Research & Clinical Trial Center (NCC-EPOC) Phase I Group has been organized to promote early drug development especially the first in human (FIH) trial in 2012. The phase I group consists of two sub-units (NCCE-Kashiwa and NCC-Tsukiji), which are organized by each hospital. The goal of both/each unit is to perform initial clinical evaluations of promising new anti-cancer compounds emerging from laboratories. Our phase I unit is the largest program in both Japan and Asia, and we contribute to the development of new cancer drugs through early phase trials.

In April 2013, the Department of Experimental Therapeutics was launched to strongly promote the EPOC missions as previously described. The members of the Department of Experimental Therapeutics consist of specialists in their oncology fields. Also, we have conducted/contributed to IIT using yet-to-be-approved new drug and academia seeds.

Routine activities

This Department plays an important role in new anti-cancer drug development in our center as well as in Japan. The top priority is to conduct the FIH trials, while we also perform the phase I trials for solid tumors (that is, all comers). Recently, we joined a global phase I trial to accelerate new drug development in Japan. Web- and tele-conferences are held with EU and US sites, and we are discussing patient enrollment as well as further developmental strategy. Routine web-conferences are also held between Kashiwa and Tsukiji campuses every Friday morning, and we are sharing information about adverse events, patient enrollments and are referring candidates to each other to accelerate enrollment. Several IIT-FIH using new class seeds are conducted by each unit and also yet-to-be-approved company agents

Research activities

The elucidation of the proof of concept is essential in new anti-cancer drug development especially in the early phase; we conduct several translational research projects in collaboration with the adjoining research institute. In the Kashiwa campus, comprehensive genomic analyses, which is known as the ABC-study, is ongoing to facilitate patient enrollment for new molecular targeted drugs under investigation. Also, a new immune-monitoring system for immune agents has been established in the hospital; the system is controlled by Professor Nishikawa.

Clinical trials

In 2015, 38 phase I trials were conducted. (Table 1).

Table 1. Phase 1 Trials in 2015

No	Target	FIH	Target	Enrollment in 2014	Status
1	CDK4/6		Solid tumors	0	Closed
2	PD-L1		Solid tumors	2	Ongoing
3	FGFR	○	Solid tumors	0	Closed
4	FGFR	○	Solid tumors	3	Ongoing
5	CSC		Solid tumors	8	Ongoing
6	immuno checkpoint		Solid tumors	15	Ongoing
7	AKT		Solid tumors	3	Ongoing
8	HSP90	○	Solid tumors	3	Ongoing
9	HER2	○	Solid tumors	3	Ongoing
10	Chk-1		Solid tumors	2	Ongoing
11	PI3K6mTOR		Solid tumors	0	Ongoing
12	PD1		Solid tumors	0	Closed
13	ADC	○	Solid tumors	0	2015.1 Enrollment start
14	c-Met		Solid tumors	11	Ongoing
15	5FU enhancer		Solid tumors	14	Closed
16	anti-cancer-stem cell		Solid tumors	0	Closed
17	PTK2		Solid tumors	0	Closed
18	FGFR		Solid tumors	3	Ongoing
19	EGFR		Solid tumors	6	Closed
20	*****		Solid tumors	1	Ongoing
21	TEM-1		Solid tumors	0	Closed
22	PI3K		Solid tumors	0	Ongoing
23	MEK		Solid tumors	0	Closed
24	c-Met		Solid tumors	3	Ongoing
25	c-Met		Solid tumors	4	Ongoing
26	****		Solid tumors	0	Closed
27	FGFR	○	Solid tumors	14	Ongoing
28	IGFIR		Solid tumors	16	Ongoing
29	****		Solid tumors	2	Closed
30	****		Solid tumors	2	Ongoing
31	PI3K	○	Solid tumors	2	Ongoing
32	AKT	○	Solid tumors	10	Ongoing
33	****		Solid tumors	2	Ongoing
34	****	○	Solid tumors	7	Ongoing
35	****		Solid tumors	1	Ongoing
36	mTOR		Solid tumors	6	Ongoing
37	****		Solid tumors	5	Ongoing
38	****		Solid tumors	1	Ongoing
			Total enrollment	149	

FIH: first in human trial

List of papers published in 2015

Journal

1. Watanabe N, Umemura S, Niho S, Kirita K, Matsumoto S, Yoh K, Ohmatsu H, Goto K. Docetaxel for platinum-refractory advanced thymic carcinoma. Jpn J Clin Oncol, 45:665-669, 2015

2. Fouad TM, Kogawa T, Liu DD, Shen Y, Masuda H, El-Zein R, Woodward WA, Chavez-MacGregor M, Alvarez RH, Arun B, Lucci A, Krishnamurthy S, Babiera G, Buchholz TA, Valero V, Ueno NT. Overall survival differences between patients with inflammatory and noninflammatory breast cancer presenting with distant metastasis at diagnosis. Breast Cancer Res Treat, 152:407-416, 2015

3. Fujii T, Le Du F, Xiao L, Kogawa T, Barcenas CH, Alvarez RH, Valero V, Shen Y, Ueno NT. Effectiveness of an Adjuvant Chemotherapy Regimen for Early-Stage Breast Cancer: A Systematic Review and Network Meta-analysis. JAMA Oncol, 1:1311-1318, 2015

4. Kai M, Kogawa T, Liu DD, Fouad TM, Kai K, Niikura N, Hsu L, Willey JS, Theriault RL, Valero V, Ueno NT. Clinical characteristics and outcome of bone-only metastasis in inflammatory and noninflammatory breast cancers. Clin Breast Cancer, 15:37-42, 2015

5. Hayashi N, Niikura N, Masuda N, Takashima S, Nakamura R, Watanabe K, Kanbayashi C, Ishida M, Hozumi Y, Tsuneizumi M, Kondo N, Naito Y, Honda Y, Matsui A, Fujisawa T, Oshitanai R, Yasojima H, Yamauchi H, Saji S, Iwata H. Prognostic factors of HER2-positive breast cancer patients who develop brain metastasis: a multicenter retrospective analysis. Breast Cancer Res Treat, 149:277-284, 2015

6. Mukai H, Saeki T, Shimada K, Naito Y, Matsubara N, Nakanishi T, Obaishi H, Namiki M, Sasaki Y. Phase 1 combination study of eribulin mesylate with trastuzumab for advanced or recurrent human epidermal growth factor receptor 2 positive breast cancer. Invest New Drugs, 33:119-127, 2015

7. Yoshida T, Yoh K, Niho S, Umemura S, Matsumoto S, Ohmatsu H, Ohe Y, Goto K. RECIST progression patterns during EGFR tyrosine kinase inhibitor treatment of advanced non-small cell lung cancer patients harboring an EGFR mutation. Lung Cancer, 90:477-483, 2015

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Office of Safety Management

Tomonori Yano, Keiji Okinaka, Masami Muto, Hisae Matsuhashi, Masahito Yonemura, Chika Hara

Introduction

The Office of Safety Management has been created as the department responsible for cross-organizational safety management in our hospital in order to practice best medical service and care for cancer patients.

Routine activities

This year, we organized the medical safety reporting system both in clinical practice and clinical trials to clarify the governance of the directors of our hospital as the top authority. And, we started the medical record survey of all in-hospital death cases, mortality and morbidity conferences, and prompt case study conferences in the hospital in order to correspond to the medical accident investigation system that started this October.

An infectious disease physician arrived at our hospital this year, and a support system for treatment of infectious diseases related to cancer itself or anti-cancer treatment was put in place. In addition, we also enhanced the infectious control abilities of staff at our hospital.

Research activities

The total number of cases reported was 2,832; from doctors: 296 cases (10%), from nurses: 2,169 cases (77%), from pharmacists: 209 cases (7%), from radiological technicians 70 cases (2%), from laboratory technicians: 22 cases (1%), from nutritionists: 20 cases (1%), from clerical staff: 15 cases (1%), and from others: 31 cases (1%).

Education

Medical safety

Training course of Team Strategies and Tools to Enhance Performance and Patient Safety (STEPPS), Training course of basic life support (BLS) and advanced cardiovascular life support (ACLS)

Infectious control

Countermeasures for tuberculosis, Countermeasures for flu

Future prospects

This year, we clarified the medical safety reporting system, and it resulted in an increase in the incident report number. We could improve the awareness of medical safety of all the staff. In addition, infectious disease physicians arrived at our hospital, making the office more efficient. Future goals, including for next year, are zero patient misidentifications, doubling of incident reporting from non-nursing staff, and prevention of infectious outbreaks, and we will continue to make every effort in order to achieve these goals.

Rare Cancer Center

(NCCH) Akira Kawai, Yoshitaka Narita, Shigenobu Suzuki, Seiichi Yoshimoto, Kan Yonemori, Mayu Yunokawa, Makoto Kodaira, Tatsunori Shimoi, Yasushi Goto, Yoshitaka Honma, Chigusa Morizane, Motokiyo Komiyama, Tomoyasu Kato, Hirokazu Chuuman, Yoshikazu Tanzawa, Eisuke Kobayashi, Makoto Endo, Naoya Yamazaki, Arata Tsutsumida, Akira Takahashi, Kenjiro Namikawa, Wataru Munakata, Chitose Ogawa, Ayumu Arakawa, Miyuki Sone, Shunsuke Sugawara, Hiroshi Igaki, Kana Takahashi, Akihiko Yoshida, Noboru Yamamoto, Shunsuke Kondo, Koichi Ichimura, Tadashi Kondo, Takahiro Higashi, Takuro Sakurai, Makiko Murase, Yoko Katoh, Natumi Takeuchi,
(NCCHE) Naoto Gotohda, Tetsuo Akimoto, Fumihiko Nakatani, Ako Hosono, Toshihiko Doi, Yoichi Naito, Junya Ueno

Introduction

The Rare Cancer Center was launched in December 2013 and officially opened in June 2014 as a multidisciplinary team to take measures against the innate problems associated with rare cancers. Based on discussions, rare cancers are defined as those with an incidence < 6/100,000/year. Although each rare cancer is rare in itself, when the number of each rare cancer is combined, it corresponds to up to 15% of all new cancer diagnoses. Information on rare cancers is scarce. Rare cancers are often inadequately diagnosed and treated in relation both to lack of knowledge and clinical expertise. Patients with rare cancers face great difficulty in having their diseases treated adequately.

Activities

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

To enable the Center to play its role, a total of 45 doctors, nurses and researchers dealing with rare cancers have joined as members of the Center. Each staff member of the Rare Cancer Center provides specialized, high-quality medical care to patients with rare cancers in cooperation with his/her Department staff.

The Rare Cancer Center provides consultation to the patients and relatives with rare cancers on the telephone (Rare Cancer Hotline). The number of telephone call was 3,006 cases in 2015. (Figure 1) The Center also provides comprehensive, scientifically based, up-to-date unbiased information about rare cancers to all patients, families and health professionals fighting against rare cancers via its website (Rare Cancer Center Homepage). The Rare Cancer Center organized the 1st International Cancer Research Symposium "Rare Cancers: Seeking Ideal Medical Care" on February 12 to 13, 2015. Also, staff of the Rare Cancer Center served as members of the committee on rare cancers (March to August 2015) set up by the Ministry of Health, Labour and Welfare.

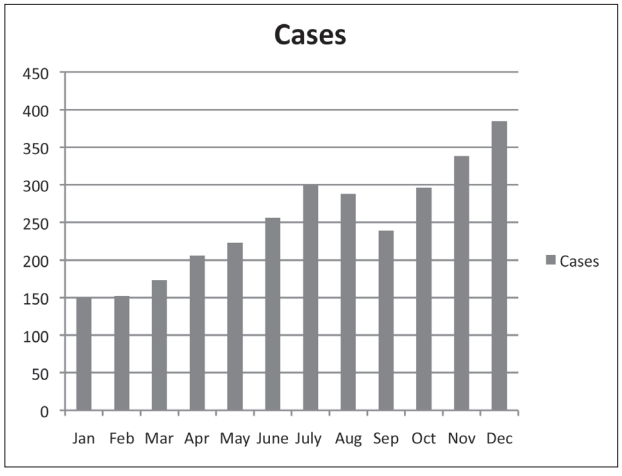

Figure 1. The Number of telephone calls to the Rare Cancer Hotline in 2015

List of papers published in 2015

Journal

1. Tahara M, Kiyota N, Mizusawa J, Nakamura K, Hayashi R, Akimoto T, Hasegawa Y, Iwae S, Monden N, Matsuura K, Fujii H, Onozawa Y, Homma A, Kubota A, Fukuda H, Fujii M. Phase II trial of chemoradiotherapy with S-1 plus cisplatin for unresectable locally advanced head and neck cancer (JCOG0706). Cancer Sci, 106:726-733, 2015

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Department of Radiology

Yoshihisa Muramatsu, Mitsuhiro Yoshida, Kazuyoshi Yamano, Kazutoshi Yokoyama, Koichi Nemoto, Takaki Ariji, Kuniji Naoi, Keisuke Takahashi, Naotaka Yamazawa, Satoe Kito, Hiroyuki Ohta, Hajime Ohyoshi, Kaoru Ikeno, Tsunemichi Akita, Keiichi Nomura, Hiroyuki Shitara, Daiki Kumagai, Fuminori Shimizu, Shogo Amano, Asami Tanaka, Ryuzo Uehara, Tatsuya Mogaki, Hiromi Baba, Shota Hosokawa, Kaori Yanagisawa, Syun Aoyagi, Yukihiro Matsukawa, Yuto Iwabuchi, Yuki Tanaka, Toshiyuki Shibuya, Kazuto Kano, Hikaru Sugahara, Hiroyuki Asai, Fumiya Tanaka, Toshiya Rachi, Daiki Kanke, Taku Tochinai, Yohei Takeda, Makoto Gohdo, Tomohiro Ohishi, Hiroshi Tsuruoka, Moeka Funakoshi, Hikari Inagawa, Hirokazu Kobayashi

Routine activities and research activities

Subsequent to the previous year, the number of radiographic examinations and radiation therapies in 2015 increased, as shown in Table 1.

Due to the increase in the number of clinical trials, the number of computed tomography (CT) examinations significantly increased. By reinforcing the medical cooperation service, the number of online reserved PET-CT examinations and Low-dose lung cancer CT screenings for working people has increased.

In the photon radiation therapy section, stereotactic irradiation targeting the liver was launched. By using a linear gold marker, CT image acquisition under respiratory gating and respiratory-gated irradiation was possible. In the proton therapy section, line scanning irradiation, which provides dose administration localized to a small area, has been launched.

Triennial inspections and checks under the "Law concerning Prevention of Radiation Hazards due to Radioisotopes, etc." were completed without any problems being highlighted.

Research findings

In collaboration with manufacturers (CH26088), to study dose simulation in CT examinations, the simulation environment was constructed at a level approximately 10% that of the actual measurement.

By participating in the Ishigaki section (Grants-in-Aid for Scientific Research: No.25713028), software that manages the exposure dose of radiological examinations is under development. For intensity-modulated radiation therapy (IMRT), as a verification of the dose accuracy of the plan, a treatment planning system based on independent software and a 3D radiation counter were proposed.

These achievements were presented at the study group and in papers of both domestic and overseas scientific societies.

Education

Radiological technologists whose experience was less than three years were given the opportunity to rotate between the radiation diagnostics department and the radiation therapy department, which helped them study a variety of radiation technologies.

All staff are actively involved in efforts to raise awareness such as highlighting the fact that radiation technology is a work in progress; this was reported through multipoint conferencing. As for medical safety education and associated activities, a movie, which prepares for shock caused by contrast medium, was filmed, a magnetic field experience program was carried out with new employees as targets and use of an assessment sheet for radiation therapy patients was started. Also, two radiological technologists obtained overseas training grants, and visited London in the UK and Texas in the United States. Three radiological technologists studied on a master's course and one studied on a graduate school doctoral course in 2015. One of them received a master's degree. In addition to that, we also accepted and educated 12 trainees from three universities in radiological technology.

Future prospects

On the basis of medical safety, we plan to provide more efficient, high-accuracy radiation inspection and radiation treatment. Because international clinical trials are increasing, verifying the quality management of medical equipment in accordance with international approaches is necessary. Introducing the information and communication technology (ICT) as the recording evaluation and storage means in accordance with legal provisions, we will facilitate the conversion to electronic media from paper media.

Table 1. Transition of Number of Radiological Examination and Radiation Therapy by Year.

Number of Cases	2011	2012	2013	2014	2015
Plain X-ray examination	35,032	39,128	38,722	42,672	43,652
Mammography (MMG)	2,434	2,380	2,354	2,310	2,368
"Fluoroscopic Imaging (GI-series, etc.)	3,903	4,029	4,628	4,748	4,691
CT	21,967	24,101	28,963	31,995	34,867
MRI	5,708	5,619	5,657	5,675	5,875
RI (Scintiscan)	1,582	1,586	1,363	1,396	1,302
PET	2,239	2,284	2,208	2,332	2,481
Angiography	656	742	511	801	807
Radiation therapy	16,798	19,254	32,453	29,510	30,633
Proton therapy	4,941	5,910	11,460	9,513	9,047
Total	95,260	105,033	128,319	130,952	135,723

List of papers published in 2015

Journal

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Clinical Laboratories

Atsushi Ochiai, Takeshi Kuwata, Genichiro Ishii, Satoshi Fujii, Motohiro Kojima, Masato Sugano, Chisako Yamauchi, Eiichi Yoshikawa, Shigehisa Yoshida, Masahiro Inoue, Masahiro Karibe, Seiji Iwasaki, Miki Goto, Masaki Takeda, Satoru Sunohara, Hiromi Kimura, Yasuharu Hashimoto, Yukihiro Okano, Akiko Yamada, Mari Hisano, Mika Sasanuma, Aya Koike, Takuya Yamaguchi, Takuya Aiba, Keiko Nakai, Ayumi Setsuta, Mayumi Motohashi, Ayumi Nakanishi, Sayuri Shibayama, Izumi Suzuki, Yasuko Yoshihara, Kazumi Yamaguchi, Rie Taniguchi, Kumiko Sudo, Saki Nakamura, Kazuki Motohashi, Atsushi Watanabe, Eriko Iwamoto, Yasuteru Yamagishi, Kazumi Tamura, Asami Sekine, Nagisa Bouno, Rie Kuroiwa, Masayuki Ito, Michiko Iida, Yuki Soeda, Megumi Michikawa, Tomoko Seto, Emiko Yoshikawa, Yoshiko Ohtake, Miwa Yamada, Megumi Yamaguchi

Introduction

The Department of Pathology and Clinical Laboratories (DPCL) has two divisions: Pathology Division (PD) and Clinical Laboratory Division (CLD). Both divisions play a fundamental role in routine hospital service and support research activities at the National Cancer Center Hospital East (NCCHE).

DPCL received ISO15189:2007 accreditation in 2012, and successfully transited to the newest version (ISO15189:2012) in 2014, ensuring quality control and quality assurance of testing, including the one for clinical trials, performed in the departments. In 2015, two sections, Physiology and Supporting laboratory testing in clinical studies, received ISO15189:2012, ensuring the quality control and quality assurance of the testing, including the ones for clinical trials, performed in the departments with global standards.

Routine activities

Primarily, the routine activity at the PD is surgical pathology. The Number of samples examined in the department in 2015 is listed in Table 1.

The CLD consists of seven sections: i) general laboratory medicine, ii) hematology, iii) biochemistry/serology, iv) Physiology, v) Bacteriology, vi) Blood transfusion and vii) Supporting laboratory tests in clinical studies. The numbers of tests performed in each division are listed in Table 2 and 3. The total number of tests performed in the DPCL in 2015 increased to 7.5% compared with the previous year; including a 94.4% and a 12.9% increase in the Blood transfusion and Serology sections, respectively.

Research activities

All of the pathologists were involved in research activities at RCIO (Research Center for Innovative Oncology). All the technologists working in the department are also highly motivated to develop advanced diagnostic technologies and various results are presented in several meetings.

Clinical trials

Practically, the CLD participated in all of the clinical trials operated at the NCCHE by providing laboratory data. The section for supporting laboratory testing in clinical studies was transferred to the DPCL in June 2014. The section, coordinating with the pathology and physiology sections, reinforces quality control and quality assurance for clinical tests performed in clinical trials at the NCCHE.

Education

Clinicopathological conferences are held regularly with each clinical department/section. In the PD, conference-style training sessions are open weekly for the residents.

Future prospects

Pathological diagnosis and laboratory tests

play a fundamental role not only in routine hospital work but also in medical research. As an ISO15189-certified clinical laboratory, the DPCL will be continuously involved in investigating new diagnostic technologies, developing new drugs and conducting translational/clinical research in the NCCHE.

Table 1. Number of pathology and cytology samples examined in Pathology Division in 2015

Department	Biopsy	Surgical	Cytology	Autopsy
Digestive Endoscopy	4,951	0	4	0
Gastrointestinal Oncology	154	0	74	0
Breast Surgery	593	358	132	0
Head and Neck Surgery	621	391	388	0
Thoracic Surgery	433	531	530	1
Thoracic Oncology	784	3	907	1
Hematology and medical oncology	545	3	209	2
Hepatobiliary and Pancreatic Oncology	489	1	450	0
Urology	264	103	736	0
Upper Abdominal Surgery	186	473	226	1
Radiation Oncology	149	3	4	0
Lower Abdominal Surgery	83	398	19	0
Orthopedics	43	16	1	0
Esophageal Surgery	8	182	19	0
Head and Neck Oncology	34	1	11	0
Obstetrics and Gynecology	18	0	199	0
Dental division	10	0	0	0
Anesthesiology	3	0	2	0
Dermatology	16	0	0	0
Plastic Surgery	2	5	2	0
Palliative medicine	1	1	4	0
Others	24	1	7	0
Total	9,411	2,469	3,924	5

Table 2. Number of laboratory tests examined in Clinical Laboratory Division in 2014 and 2015

	2014	2015
General laboratory medicine	48,199	48,199
Hematology	302,752	302,752
Biochemistry	1,970,515	1,970,515
Serology	164,382	270,112
Blood transfusion	10,720	11,438
Bacteriology	26,870	29,917
Physiology	22,730	24,703
Total	2,383,461	2,846,826

Table 3. Number of cases and samples prepared in Clinical Laboratory Division for clinical trials in 2015

	Cases	Samples
General laboratory test	3,204	5,972
Electrocardiogram (ECG)	998	1,397
Pathology	864	4,273

Surgical Center

Masaru Konishi, Hiroyuki Yamamoto, Emiko Kanazawa

Introduction

The Surgical Center performs function-preserving operations for ordinary cancer patients as much as possible in consideration of patient quality of life (QOL), but depending on the case, the extended surgery is done to cure localized highly progressive cancers. Thoracoscopic and laparoscopic surgery are routinely indicated for the treatment of various cancer patients.

Routine activities

In 2015, 3,115 cases underwent surgical treatment including 2,834 general anesthesia cases. This total was an increase of 210 over 2014.

To preserve organ functions, limited resection or reconstructive operation is indicated in our hospital. These procedures include vertical partial laryngectomy for voice preservation, breast-conserving surgery, total mastectomy with breast reconstruction, pancreas-sparing duodenectomy, partial anal sphincter preserving surgery and bladder-sparing surgery.

With the refinements in laparoscopic instruments and advances in surgical experience, laparoscopic surgery is a safe alternative for selected patients with malignant neoplasms, and has fulfilled its indications. In our hospital, laparoscopic surgery has been introduced in the esophageal, thoracic, gastric, colorectal, hepatobiliary, pancreatic, and urology divisions. A robotic surgical system had been used to provide less invasive surgery since 2014. The system was indicated for prostate, rectal and gastric cancer.

Education

We place importance on the education of young surgeons. All surgical groups have their own training programs for resident surgeons. Many surgeons from domestic or foreign hospitals have visited our center to learn surgical techniques.

Table 1. Total number of operations

Anesthesia	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
General	119	141	145	143	127	163	162	171	153	160	148	158	1,790
General and epidural	92	83	105	105	76	99	85	79	70	93	82	75	1,044
Lumbar	4	9	8	6	10	7	5	2	6	10	12	8	87
Local	14	18	16	11	22	13	11	17	17	13	22	20	194
Total	229	251	274	265	235	282	263	269	246	276	264	261	3,115

Supportive Care Center

Koichi Goto

Introduction

Our Department was established as an organization to provide, in addition to conventional consultation support, positive and comprehensive support from a variety of professional occupations for actual or potential, physical, mental, and social problems that cancer patients and their families have to confront. The main activities are establishment of a continuous support system for patients and families, enhancement of a home care support system, and promotion of community cooperation for establishing early palliative care.

Routine activities

1) Consultation support/community medicine cooperation

In 2015, we received 5,179 new consultations. Among them, 4,151 (80.2%) were from patients who had received medical treatment from our hospital, or their families, and 1,028 (20.6%) were from patients who had received medical treatment at other medical institutions, or their families, or local medical welfare workers (Table 1).

In this year, to improve QOL during cancer treatment, we started new educational services for cancer patients such as an oral care program, a skin and nail care program, and a physical rehabilitation program. We provide these new additional services taking into account the difficulties faced by patients.

The new building, which is named NEXT, for enlarged operating and endoscopic rooms is under construction in our hospital. Therefore, to acquire more new patients, we have started new case conferences held in communities in order to build face-to-face relationships between the physicians of our hospital and local physicians.

2) Continuous nursing support

For outpatients, we provide continuous nursing support. In 2015, we provided continuous support and consultation services to about 2,600 patients, mainly in the areas of thoracic and gastrointestinal oncology.

In order to promote self-care by inpatients and/or their families, as well as to secure appropriate social resources, we provide medical and social support with a view to home care even from an early time of hospitalization. We carried out a screening program for about 2,250 patients who needed social support and provided them with appropriate support.

In order to sustain seamless medical and social support, we strengthen cooperation with home-visit nursing stations to deal with the problems faced by home care patients and/or their families, mainly related to medical management. In 2015, we carried out interventions such as approximately 1,030 phone-calls and face-to-face consultations.

Table 1. Details of the consultation support provided in 2015

	Number	%
New consultations	5,179	
Total number	16,843	
Purpose of new support request		
Support for nursing hospital selection	3,030	58.5
Consultation about treatment and diagnosis	670	12.9
Consultation about social problems	584	11.3
Consultation about physical symptoms	46	0.9
Consultation for caregivers	44	0.8
Mental problems	37	0.7
Others	768	14.8
Responsible hospital		
Our hospital	4,151	80.2
Other hospitals	831	16.0
Others	197	3.8
Treatment state		
Before diagnosis	209	4.0
Before first treatment	1,029	19.9
During chemotherapy	1,450	28.0
After treatment/during follow-up	930	18.0
Only palliative care	1,401	27.1
Dead (Bereaved family)	10	0.2
Others	150	2.9

Section of Radiation Safety and Quality Assurance

Tetsuo Akimoto, Hidenobu Tachibana, Kenji Hotta, Hiromi Baba, Koichi Nemoto

Introduction

Radiation therapy technologies have improved recently and will continue to progress. However, while advanced technology has provided higher accuracy and precision in radiotherapy, it has introduced more complex situations and difficulties in performing the treatment adequately. Radiotherapy errors can occur at several time points from planning through treatment. The accuracy and precision of dose delivery in radiation therapy is important because there is evidence that a 7-10% change in the dose to the target volume may result in a significant change in tumor control probability. "Quality assurance in radiotherapy" is for all procedures that ensure consistency of the medical prescription, and safe fulfillment of that prescription, as regards the dose to the target volume, together with the minimal dose to normal tissue, minimal exposure of personnel and adequate patient monitoring aimed at determining the end result of the treatment.

The primary aim of the Section of Radiation Safety and Quality Assurance is to develop quality assurance programs for photon and proton therapy machines as well as to check that quality requirements in photon and proton therapy products are met and to adjust and correct performance if the requirements are found not to have been met. The second aim is to install and establish advanced technologies in clinical practices in the radiation oncology department. Other goals are to develop high-precision radiotherapy as intensity modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), respiratory-gating radiation therapy, marker-tracking radiation therapy, image-guided radiation therapy (IGRT), stereotactic RT and proton beam therapy (PBT) in cancer treatment.

Routine activities

At present, the staff of the Section of Radiation Safety and Quality Assurance consists of one radiation oncologists, three medical physicists and one radiological technologist. We have more than 1,000 new patients for photon and proton therapy every year. The section is responsible for four linear accelerators, two CT simulators and four different treatment planning systems in photon/electron therapy. In proton therapy, one accelerator, two treatment units, and one planning system are managed.

Quality assurance programs have been established for photon and proton therapy by the medical physicists. The daily, monthly and annual programs are performed by the medical physicists and radiological technologists. In addition, the medical physicists perform radiotherapy planning for IMRT/VMAT in prostate and head and neck sites, stereotactic RT in the liver and lungs, and proton therapy in the head and neck, esophagus, lung, liver, prostate and infants. The medical physicists support conventional radiotherapy planning and also check the quality and safety for all treatment plans.

Research activities

In the Radiation Safety and Quality Assurance Section, the following research activities are on-going:

1) Design and development of new proton beam irradiation system
2) Design and development of monitor unit calculation for proton therapy
3) Design and development of a Monte Carlo-based dose calculation algorithm for proton therapy
4) Design and development of a CT-based image guided and adaptive proton therapy system.

5) Design and development of four-dimensional planning for motion synchronized dose delivery for photon therapy.
6) Design and development of CT-pulmonary ventilation imaging
7) Design and development of quality assurance system for gated radiotherapy
8) Multi-institutional study of independent MU/Dose verification for conventional, stereotactic RT, IMRT, VMAT as well as for Vero, CyberKnife and Tomotherapy in photon therapy

Clinical trials

The following multi-institutional clinical trials are ongoing:

1) Establishment of safety for radiotherapy planning of photon therapy

Education

We established an on-the job-training program for quality assurance programs for a photon linear accelerator and over 100 medical physicists and radiological technologists have taken the educational program. We held a meeting for independent MU/dose verification and over 180 medical physicists and radiological technologists participated in the meeting. We trained graduated students from Tsukuba University and Komazawa University for a quality assurance program in photon therapy.

Future prospects

We maintain the quality of photon/electron and proton therapy machines and also establish new technologies to improve patient outcomes. In addition, we will work on radiotherapy as well as radiology including establishment of a quality assurance program for diagnostic instruments and management of radioactive materials.

List of papers published in 2015

Journal

1. Kohno R, Yamaguchi H, Motegi K, Tanaka F, Akita T, Nagata Y, Hotta K, Miyagishi T, Nishioka S, Dohmae T, Akimoto T. Position verification of the RADPOS 4-D *in-vivo* dosimetry system. Int J Med Phys Clin Eng Radiat Oncol, 4:318-325, 2015
2. Hotta K, Kohno R, Nagafuchi K, Yamaguchi H, Tansho R, Takada Y, Akimoto T. Evaluation of monitor unit calculation based on measurement and calculation with a simplified Monte Carlo method for passive beam delivery system in proton beam therapy. J Appl Clin Med Phys, 16:228-238, 2015

Nutrition Management Office

Haruka Citose, Yumi Ochiai, Takako Kuroda, Marie Ohishi, Kana Shiraiwa, Taichi Watanabe, Keiko Asano, Rumi Noda, Ayuko Umezawa, Yoshio Shimokawa, Hideki Takano, Koichi Abe, Takahiro Takahashi, Tatsuya Hirakawa, Satoshi Watanabe, Hideki Ogiwara, Akio Sairennji

Introduction

In 2015, we focused on the activities of the NST (nutrition support team). Increasing the number of consultations was an effort to improve quality. We received an increase in health care fees.

Routine activities

Dietary meals totaled 327,706 in 2015, and we gave nutrition-related dietary advice to 2,612 persons. There have been 1,577 new requests for consultations with the NST, an average of 131 per month (Table 1). The total number of consultations in 2015 was 2,094. 2015 saw 50% growth against the previous year.

Cooking classes for cancer prevention were held three times as planned.

Cooking classes to cope with cancer symptoms have been held 167 times since the beginning of the program.

Research activities

We are doing a "study on the effectiveness of rehabilitation and nutrition therapy in perioperative hepatobiliary surgery". The "Impact on the development and postoperative complications of obesity in colon cancer patients of a preoperative weight loss program" is also carried out. These studies were to verify the effect of preoperative nutritional guidance. And, through team medical practices, we are aiming to participate in a total treatment plan.

In other research, there is a diet support research for cancer survivors.

Table 1. Number of NST Collsultaticns in 2015 (New request number)

Clinical Departments	Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sept	Oct	Nov	Dec	Total
Head and Neck Surgery	6	5	7	10	5	6	5	3	4	7	8	10	76
Head and Neck Medical Oncology	7	11	14	13	10	13	11	7	10	9	9	10	124
Gastrointestinal Oncology	4	4	5	1	3	4	1	2	1	3	3	4	35
Colorectal Surgery	4	2	1	0	2	0	3	4	2	4	2	4	28
Gastrointestinal Oncology	27	25	28	29	29	34	35	34	32	37	28	30	368
Hepatobiliary and Pancreatic Surgery	0	0	1	6	2	3	1	1	2	0	0	2	18
Hepatobiliary & Pancreatic Oncology	9	16	15	5	14	18	23	23	18	18	21	21	201
Thoracic Surgery	0	1	2	5	5	2	1	2	5	2	2	1	28
Thoracic Oncology	26	28	33	33	32	25	21	25	23	21	26	21	314
Urology	1	1	0	0	0	2	1	0	1	0	0	0	6
Hematology	9	14	14	15	19	22	20	18	25	23	21	21	221
Breast and Medical Oncology	7	7	11	9	7	10	12	13	11	15	7	17	126
Palliative Medicine	1	1	5	2	0	0	0	0	1	0	0	0	10
Other departments	2	2	2	2	1	2	2	3	4	1	1	0	22
Total	103	117	138	130	129	141	136	135	139	140	128	141	1,577

Education

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

Future prospects

Regarding the cooking classes that we have worked on over many years, we will consider a better plan to offer the classes in a way to meet the needs of patients and their families, and locals. In addition, we plan to hold numerous lectures for local residents. We will plan these together with the government. We want to disseminate information and understanding of said information about diets that influence cancer therapy and cancer prevention among a lot of people .

Office of Cancer Registry

Hironobu Ohmatsu, Takashi Kojima, Tokiko Inagaki, Yumi Ishii, Maiko Miura, Yayoi Ohtsuka

Introduction

In September 2014, the "Health Information Management Office" was separated into the Medical Information Management Office and the Office of Cancer Registry. The Office of Cancer Registry is a department for executing a hospital-based cancer registry.

Routine activities

Diagnostic cases registered in 2014 in the hospital cancer registry (the first visit of cancer patients diagnosed from January to December in our hospital) were 5,796 (of which, initial treatment conducted in our hospital: 3,833 cases: in our hospital diagnosis only: 150 cases; after the start of treatment in another hospital: 941 cases; and diagnosis and treatment in another hospital (including a second opinion): 872 cases). The number of new registrations shows that the number of female patients has been consistently less over time than male patients due to irregular situations according to department (see Table 1).

Table 1. The number of cancer registrations of NCCH-East

Year	Male	Female	Total
2000	3,054	1,625	4,679
2011	3,145	1,733	4,878
2012	3,435	1,749	5,184
2013	3,996	2,043	6,039
2014	3,753	2,043	5,796

The number of new registrations according to the place of residence was 786 in Kashiwa City, 461 in Matsudo City, 353 in Nagareyama City ... (see Table 2)

Table 2. The number of new registrations according to the place of residence

	Residence (city)	No. of registrations
1	Kashiwa	786
2	Matsudo	461
3	Nagareyama	353
4	Noda	343
5	Abiko	257

Last year, for the first time, the hospital cancer registry aggregate results (2014 cases) were published in the internal server of the hospital because it is seen as basic data that can help in medical care, research and the management analysis. In the future, we aim to publish these results every year.

Medical Information Management Office

Hironobu Ohmatsu, Tokiko Inagaki

Introduction

The Medical Information Management Office is a department for managing the medical records of hospitals by professional medical information management officers.

Routine activities

- Auditing Discharge Summary (quantitative inspection)
  Data on discharge summaries should be entered and approved by the attending physician (Table 1). We inspected and checked the summaries and, where required, gave some advice for correct input.
- Maintenance of disease codes based on ICD-10
- Analysis of medical contents on DPC (Diagnostic Procedure Combination) and recommendation for efficiency.

Table 1. Submitting rate of dischatge summary

2012	2013	2014	2015*
79%	81%	98%	91%

* Definition was changed from "entered" to "entered and approved" from May 2015.

Future prospects

We would like to make recommendations and proposals of good and effective medical care based on DPC data. Each department has held the "DPC round".

Department of Pharmacy

Shinichiro Saito, Kunio Takahashi, Toshikatsu Kawasaki, Yasuhiko Ichida, Tomoyuki Akimoto, Reiko Matsui, Hisanaga Nomura, Yasuaki Ryushima, Naoko Yoshino, Minako Yoshida, Hideki Funasaki, Yoshiki Kojima, Daisuke Kanou, Yousuke Maki, Nobuo Mochizuki, Kenji Kawasumi, Tomoka Okano, Shinya Motonaga, Ryoko Udagawa, Hiroko Ouchi, Tomoko Morita, Mai Itagaki, Shinya Suzuki, Takeshi Koike, Misaki Kobayashi, Motoko Kaneko, Akira Shinohara, Takahiro Outa, Daisuke Hisamatsu, Ayumi Yamaguchi, Takayuki Sano

Introduction

The main objectives of our Department of Pharmacy are: 1) To promote clinical studies to create new evidence-based data; 2) To provide chemotherapy based on the most updated evidence-based data; and 3) To pursue patient-centered pharmaceutical care.

Our residents' training program started in 2006. In 2015, five residents joined our Department. Presently, we have a total of 24 residents. In addition, our Department has accepted seven trainees from other institutions for our oncology pharmacist training programs. Through 2015, which is two terms of the training courses, we have educated eight pharmacy students and two advanced-training pharmacy students.

The Department of Pharmacy provides various important services: controlling inventory; dispensing medications; preparing i.v. solutions for chemotherapy, which include the aseptic mixing of antineoplastic agents; collecting and providing drug information; managing therapeutic drug monitoring; checking treatment regimens for each patient's chemotherapy; and providing pharmaceutical management and counseling.

Our Department reviews the drugs taken by patients before and during their hospitalization. In inpatient care, the Department assigns pharmacists to provide medication counseling and drug information for healthcare providers and patients, to pursue effective pharmaceutical care. In outpatient care, the Department provides a pharmacy outpatient service in which pharmacists check patients for adverse reactions and doses of antineoplastic agents, especially in the case of oral anticancer medications. We then assess the necessity of supportive-care medications and suggest them to physicians. The pharmacy outpatient service also reviews the drugs taken by all patients to evaluate when patients have to stop their anticoagulants before their operation or when they have to stop to take metformin before examinations with iodinated-contrast material. Pharmacists are on duty at the Outpatient Chemotherapy Center as dedicated staff members. The pharmacists provide a Chemotherapy Hotline Service, which is a direct line for our outpatients who have any problems concerning their chemotherapy treatment. In the Outpatient Chemotherapy Center, pharmacists are always available to provide drug information for healthcare providers and patients. We also manage investigational drugs.

New developments

Checking home medication, that is, medication reconciliation, is one of the core services in the pharmacy division. At the National Cancer Center Hospital East, pharmacists used to perform the service from a dispensing room window. However, the working place has changed from the dispensing room window to hospital wards, because patients had a long waiting time and underwent the burden of having their brought-in medicine checked. According to the change of working place, ward pharmacists have checked brought-in home medication in the ward since February 5th, 2015. The change of service location does not only reduce the burden of patients having to wait, but also reduces the nurses' work burden. In addition, the number of brought-in medicine checks has increased, and this enhances the clinical pharmacy service in the inpatient division.

Table 1. Pharmacy Achievement

	2012	2013	2014	2015
Number of Prescriptions				
Prepared in hospital pharmacy				
Total	90,392	97,444	105,477	102,757
Inpatients	84,800	91,549	99,367	99,390
Outpatients	5,592	5,895	6,110	3,367
Taken to outside pharmacies	59,722	64,123	70,879	77,546
(% of prescriptions filled outside)	(91.4%)	(91.6%)	(92.1%)	(95.8%)
Injections				
Total	160,105	158,557	164,485	167,973
Inpatients	126,428	125,106	131,278	132,252
Outpatients	33,677	33,451	33,207	35,721
Number of Prescriptions				
(Investigational new drugs)	4,584	5,110	6,792	6,308
Aseptic Preparation of Injection Mixture				
Anticancer drugs	38,663	42,735	47,362	55,049
Others	3,994	4,204	5,633	5,145
Number of medication counseling sessions (for inpatients)				
Patient	6,418	7,248	7,512	5,232
counseling sessions that earned a counseling fee	7,139	5,005	7,916	6,860
Number of medication counseling sessions (for outpatients)				
in the Outpatient Chemotherapy Center	8,965	10,073	9,765	12,651
in the pharmacy outpatient service	1,782	2,375	3,493	4,621
in the 'Nexavar' outpatient service	381	202	270	241
Number of calls on the Chemotherapy Hotline	1,665	2,087	2,258	2,399
Number of checking home medications	6,017	6,506	7,087	9,524
Number of insurance-reimbursement claims for dedicated clinical-pharmacist services		8,094	25,592	26,479

List of papers published in 2015

Journal

1. Shinohara A, Ikeda M, Okuyama H, Kobayashi M, Funazaki H, Mitsunaga S, Shimizu S, Ohno I, Takahashi H, Ichida Y, Takahashi K, Okusaka T, Saitoh S. Efficacy of prophylactic minocycline treatment for skin toxicities induced by erlotinib plus gemcitabine in patients with advanced pancreatic cancer: a retrospective study. Am J Clin Dermatol, 16:221-229, 2015

Department of Nursing

Chie Asanuma

Introduction

Guided by the principle that nurses are active team members in state-of-the-art cancer treatment and participate in the development of cancer nursing at the core hospital providing cancer nursing care in Japan, the Department of Nursing of the National Cancer Center Hospital East works based on the following basic policies:

1) To provide nursing care founded on trust and reassurance, respecting the dignity of life and the rights of patients;
2) To pursue the essential values of nursing and practice scientific and creative nursing;
3) To facilitate clinical studies and disseminate new information concerning cancer nursing; and
4) To promote development of leadership skills.

In addition, the Department of Nursing is involved in and contributing to hospital management, working to help find a better balance between the provision of quality medical and nursing services and the efficiency of business.

Routine activities

1) Nursing Activities

Backed by the consciousness and a sense of responsibility of the nurses at the Hospital East, the Department of Nursing has been striving to support the progress of medicine and to provide safe and reliable nursing care meeting the needs of patients and their families in the best possible way. To this end, the Department has been making efforts to develop institutional systems, improve work practice, promote team medicine, promote regional healthcare collaboration, and develop and recruit human resources, so that it can actively be involved in hospital management and provide quality medical and nursing services through linkage, cooperation, and collaboration, across the borders of different vocations.

The average number of inpatients, bed utilization rate, bed availability, average length of stay, number of outpatients, number of chemotherapy patients at the Outpatient Treatment Center, number of operations, and other performance indicators all exceeded the records in the previous year.

The increase in the number of patients saw a response in the increase in nurses, outpatient and ward clerks, and nursing assistants, as well as delegation of work responsibilities among different vocations, sharing of work responsibilities, and improvement of work practice, which resulted in remarkable improvements in efficiency, safety, and cost performance.

2) Educational Activities

The in-house education program of our hospital is characterized by the two-tier structure consisting of "basic education" providing basic knowledge and skills in nursing and "specialist education in cancer nursing" for the practice of cancer nursing. On the foundation of the basic knowledge and skills in nursing, the in-house education program trains nurses who can deliver "nursing offering peace of mind," where patients and their families may choose treatment and care through their own decisions, while nurses use their excellent expertise and skills to alleviate pain. The nurses trained in this way are sent to work in clinical settings.

In addition, in-house programs for nurse administrators, researchers, and educators are also offered, as well as active support got the participation in overseas training and outside training for the nurses who want further advancement.

Training programs are also offered to the nurses from other organizations, such as "Delirium Program Training," "Communication Training," and

"Cancer Nursing Training," achieving qualitative improvement and career advancement of nurses both in and outside of the hospital.

3) Certified Nurse Specialists and Certified Nurses

One certified nurse specialist in cancer, one certified nurse in skin and excretory care, and one certified nurse in palliative care were newly qualified in 2015. At present, there are eight certified nurse specialists in two areas and 31 certified nurses in eight areas working in various nursing units, serving as role models in nursing practice in respective specialties. They are also working in cross-organizational roles as the members of medical teams, such as infection control, palliative care, and nutrition support teams.

The scheme for in-house certified nurses in anticancer IV was created to enhance the specialty of nurses and expand their work responsibilities for the purpose of reducing the workload of physicians so that they could concentrate on their work. In the third year of implementation, this scheme has qualified 55 in-house certified nurses. The scheme for in-house certified nurses in radiotherapy intravenous injection, launched last year, qualified four in-house certified nurses, who are working actively in clinical practice.

"Delirium Program Training," "Communication Training," "Cancer Nursing Training," and other training programs were offered to nurses from other organizations, and were attended by many nurses from across the country. The in-house education programs of our hospital are also made available to the nurses from five national hospitals in Chiba Prefecture and other hospitals in the country. These have been attended by 244 nurses in total, achieving qualitative improvement and career advancement of nurses both in and outside of the hospital.

4) Operation of Certified Nurse Education Courses and Training of Certified Nurses

The training course for certification in palliative care, established in 2013 after obtaining facility accreditation as an educational institution for certified nurses from the Japanese Nursing Association, has seen successful graduation of 11 trainees in the first batch and 18 in the second. At present, it is attended by 22 trainees in the third batch.

The 29 trainees in the first and second graduating classes passed the examination for certified nurses in palliative care, and are working as role models in palliative care at various medical institutions.

Following the training course for certification in palliative care, the certified nurse training course in chemotherapy is in the process of preparation, scheduled for opening in July 2016.

Research activities

Including three presentations at overseas venues, 30 presentations were made at academic conferences. Three of these studies were supported by subsidies from outside organizations. The increase in the number of presentations in nursing study, the acquisition of study funds from outside sources, and the improvement of the quality of study owe a lot to the support of the clinical trial support team consisting of physicians and other members from the Hospital East, as well as the nursing study support team consisting of certified nurse specialists and certified nurses. These support teams are providing assistance and stimulating the inquiring minds of nurses, who are courageously tackling the clinical problems.

The publication of 26 articles in journals and the issuance of the book "Communication Skills Using NURSE," edited by the Department of Nursing of the Hospital East, were the products of our research activities in clinical practice.

We strive for further improvement of the quality of our nursing study, so that we can create and disseminate new approaches to evidence-based cancer nursing at the National Cancer Center Hospital East.

Future prospects

Our tasks for 2016 include making a further leap forward as a research core hospital and obtaining the accreditation as a specific function hospital providing advanced, pioneering medical care. In conjunction with the construction of the NEXT building, we also expect the addition of more

operating rooms and endoscopy rooms and the construction of ICUs. The Department of Nursing of the Hospital East, as a component in team medicine, plans to provide advanced, pioneering medical care expected of a research core hospital/specific function hospital; to promote clinical study and trials; and to reinforce the system for patient safety. At the same time, we strive for appropriate training, recruitment, and placement of nurses, which are the basis for the improvement of the quality of nursing and the innovations in nursing in response to the progress of medicine.

As we understand the critical importance of stable business operations in realizing the ideals and missions of the National Cancer Center, the Department of Nursing of the Hospital East works in cooperation and collaboration with other departments to facilitate management improvements.

Clinical Research Support office

Akihiro Sato, Miki Fukutani, Sakiko Kuroda, Takako Tomizawa, Kayo Toyosaki, Masako Nakamoto, Kana Fukui, Masato Yonemura, Hiromi Hasegawa, Yoshihiro Aoyagi, Seiko Matsuda, Kaori Tobayama, Ayako Sugama, Tsukiko Higuchi, Wataru Okamoto, Akiko Nakayama, Izumi Miki, Tomohisa Sudo, Yuuko Tagami

Introduction

The Research Management and Data Management Section supports the investigator-initiated clinical trial program in the NCCHE though the clinical datacenter, study management, site visit monitoring, safety information management, and bio statistics.

The Bio Bank and TR Support Section supports Translational Research including a genome-wide screening network program through study management and data management.

Routine activities

Data Management Section
-Database and CRF form design
-Registration
-Data management
-System administration
-Bio statistics
Research Management Section
-Study management
-Site visit monitoring
-Safety information management
-Medical writing
Bio Bank and TR Support Section
-Study management for TR
-Data management for TR
-Research concierges for Bio Bank

Clinical trials

Data Management and Research Management sections
- In 2015, five IND trials started enrollment.
- A total of 86 patients were enrolled

Bio Bank and TR Support Section
- In 2015, five TR trials were conducted.
- A total of 1,783 patients were enrolled

Education

On-the-job-training for new staff.

Support the education program for clinical trial methodology and GCP in the NCC.

Co-host the GCP training seminar with other ARO.

Future prospects

Preparation for conducting global IIT IND trials.

Certified nurse curriculum

Toshirou Nishida, Asuko Sekimoto

Curriculum for certified nurses

In March 2015, 18 students of the second-generation class completed the accredited curriculum (palliative care), and 16 students passed the certified nurse qualification examination sponsored by the Japanese Nursing Association. Consequently, 27 students, including the students of the inaugural class, registered as palliative care certified nurses in July 2015.

In July 2015, 22 students entered our nursing institute, and are presently in the third-generation class.

In October 2015, 22 students of the fourth-generation class passed the entrance examination at the competition ratio of 1.5 (compared to 1.2 last year).

Since April, 2015, our institute has improved as a means of education that aims toward the practice of well-grounded cancer chemotherapy nursing and as a point of feedback to a system in cutting-edge fields in cancer medical research. On November 10, 2015, we were authorized by the Japanese Nursing Association as a certified nurse educational institution (cancer chemotherapy nursing), and thereafter, started admitting trainees to our institute in December. Eleven applied for the entrance exam, which has a quota of 15, and eight applicants passed.

In February 2015, the follow-up training for the first graduating class was held, and 80 people, including certified nurses of the hospital, participated.

Image for the future

Through our curricula, we shall improve on the latest and professional knowledge, as well as improve skills for cancer medical care and cancer nursing and provide further contributions to reflect our in-service education, its procedure, and the system concerned. We shall introduce our current certified nurse curriculum to society to help secure staff resources as well as support for future career development.