Department of Surgery
Division of Chest Surgery, Breast and Endocrinology Surgery

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General Summary

The Divisions of Chest Surgery and of Breast and Endocrinology Surgery were established in June 2005. Since then, all staff members have been active in surgical practice, research, and education. Many studies are in progress.

Research Activities

Chest Surgery

Thoracoscopic surgery is the focus of our clinical activity. This minimally invasive surgery produces fewer postoperative complications and sequelae and is especially beneficial for elderly, high-risk patients. Thoracoscopic surgery requires advanced skills, and we have independently developed total thoracoscopic surgery, which uses only a thoracoscope and video monitors to provide intraoperative views. Our method of thoracoscopic surgery can be used to treat many chest conditions, such as juvenile pneumothorax, peripheral lung nodules, mediastinal tumors, and lung cancer.

Thoracoscopic surgery is also indicated for higher-risk patients who have such complications as advanced pulmonary emphysema, impaired pulmonary function, and extremely high age and are not candidates for conventional open surgery.

Operative procedures, including wedge resection, segmentectomy, lobectomy, and pneumonectomy of the lung, are all safely performed, in addition to resection of mediastinal tumors or the thymus. Surgery for lung cancer requires much more advanced skills and oncological considerations, which have also been independently developed. Of the mediastinal procedures, thymectomy is usually performed via thoracoscopy rather than via a conventional median sternotomy. In our department the percentage of chest operations performed via thoracoscopy is more than 90%, which we assume to be the highest rate in the world.

The minimally invasive thoracoscopic surgery is being investigated with prospective clinical studies. These studies include a comparative study of open surgery and video-assisted surgery for lung cancer and evaluations of video-assisted surgery for bullous lung diseases in elderly patients with impaired lung function, of video-assisted surgery for thymic tumors, and of video-assisted thymectomy for myasthenia gravis.

Our clinical studies are also evaluating new devices and methods, such as narrow-band

imaging for the thoracoscopic diagnosis of benign and malignant lung diseases, and LaparoSonic coagulating shears (Ethicon Endo-Surgery, Inc., Cincinnati, OH, USA) for small thoracotomy. Three-dimensional diagnosis with computed tomography is used to make thoracoscopic surgery safer. The diagnosis and treatment of ground glass opacity of the lung, which is considered to indicate early adenocarcinoma, are being evaluated.
Many basic research studies are also underway. In the morphological expression-related advancement of the molecular genetic analysis of lung cancer, we are investigating whether CA19-9 activity is an important marker of de novo carcinogenesis. The biological and genetic characteristics of peripheral adenocarcinoma of the lung are being investigated to establish the most appropriate surgical procedures. The correlation of the detection of blood circulating tumor cells and the prognosis of patients with lung cancer is being examined.
The oncogenes of lung cancer are being analyzed with a next-generation sequencer.
A system for viewing videos on the Internet is now being developed and will help improve surgical training and research.

Breast
1. Clinical study
1) The evaluation of sentinel node biopsy after neoadjuvant chemotherapy
The minimally invasive technique of sentinel lymph node biopsy produces less morbidity and allows accurate pathologic staging of the axilla. Experience with sentinel node biopsy after neoadjuvant chemotherapy is limited. The purpose of our clinical study is to evaluate the feasibility, accuracy, and safety of this procedure in patients with breast cancer after neoadjuvant chemotherapy.
2) Evaluation of the usefulness of Sonazoid for detecting breast cancer
We performed phase II and III studies of the ultrasonographic imaging of the breast with the microbubble contrast medium Sonazoid (Daiichi Sankyo Co., Ltd., Tokyo) in collaboration with the Department of Radiology.
3) Evaluation of the effectiveness of exercise for psychiatric illness in patients after surgery for breast cancer
Many women experience a psychiatric illness, such as emotional distress, depression, and anxiety, after breast cancer is diagnosed. We have prospectively investigated the effects of exercise on psychological health.
4) Evaluation of the beneficial effect of cryotherapy for small cancers of the breast (Kashiwa Hospital)
5) Therapeutic strategy for oligometastatic breast cancer
We have analyzed patients with metastatic breast cancer for 30 years. The analysis indicates that oligometastatic breast cancer is a distinct subgroup with a long-term prognosis superior to that of metastatic breast cancer. We are performing prospective studies to better characterize oligometastatic breast cancer and to improve the prognosis of metastatic breast cancer.
2. Basic research
1) Development of breast cancer
We have used immunohistochemical techniques to investigate biological factors involved

in the progression of carcinoma in situ to invasive breast cancer.
2) Clinically useful biomarkers for triple negative breast cancer
Triple-negative breast cancer is a heterogeneous disease. We have investigated prognostic and predictive biomarkers for triple-negative breast cancer.
3) Circulating tumor cells and disseminated tumor cells
Circulating tumor cells in the peripheral blood and disseminated tumor cells in the bone marrow of patients with breast cancer are strong prognostic factors. We have investigated their clinical values for patients with early breast cancers.
4) Cancer stem cells
We evaluated how cancer stem cells differed in presence between primary breast tumors and metastatic tumors and how they were correlated with prognosis.

Endocrine
1. Clinical usefulness of JT-95
A monoclonal antibody, designated JT-95, was made against a thyroid papillary carcinoma obtained by our Department of Breast and Endocrine Surgery. In collaboration with the Division of Molecular Cell Biology of The Jikei University, we have investigated the clinical usefulness of JT-95.
In a clinical study accepted by the Institutional Review Board of The Jikei University, we are examining the antigen detected by JT-95 in the serum of patients with thyroid papillary carcinoma and of patients with breast tumors but without a thyroid mass.
2. Association between JT-95 and cell-to-cell inhibition
We found that the adhesion between cells was inhibited in proportion to the quantity of JT-95 added in vitro. We have investigated the mechanism of cell-to-cell inhibition and association with lymph nodes metastases.
3. The structure of antigen of JT-95
By using messenger RNA sequences and protein assays we are investigating the structure of the antigen detected by JT-95. This antigen contains a type of fibronectin. We are now detecting binding sites for JT-95 in the antigen.

Publications

Odaka M, Shibasaki T, Asano H, Marushima H, Yamashita M, Morikawa T. Feasibility of thoracoscopic thymectomy for treatment of early-stage thymoma. *Asian J Endosc Surg.* 2015; **8:** 439-44.
Nogi H, Uchida K, Kamio M, Kato K, Toriumi Y, Akiba T, Morikawa T, Suzuki M, Kobayashi T, Takeyama H. Triple-negative breast cancer exhibits a favorable response to neoadjuvant chemotherapy independent of the expression of topoisomerase IIα. *Mol Clin Oncol.* 2016; **4:** 383-9.
Nakano S, Otsuka M, Mibu A, Oinuma T. Significance of fine needle aspiration cytology and vacuum-assisted core needle biopsy for small breast lesions. *Clin Breast Cancer.* 2015; **15:** e23-6.
Nakada T, Akiba T, Inagaki T, Morikawa T, Ohki T. Thymic cavernous hemangioma with a left innominate vein aneurysm. *Ann Thorac Surg.* 2015; **100:** 320-2.
Morikawa T. Heritage of the late Professor Tsuguo Naruke. *Journal of Visualized Surgery.* 2016; **2:** 86.