

## Conference Report

# The Sino-French 2012 Conference in Thoracic Oncology: an international academic platform for in-depth exchange on comprehensive research

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## Abstract

The Sino-French 2012 Conference in Thoracic Oncology, held November 17–18, 2012, was hosted by the Department of Thoracic Surgery at Sun Yat-sen University Cancer Center and organized in collaboration with two prestigious French hospitals: Institute Gustave Roussy and Marie Lannelongue Hospital. The conference was established by leading experts from China and France to serve as an international academic platform for sharing novel findings in basic research and valuable clinical practice experiences. Hot topics including innovation in surgical techniques, diagnosis and staging of early-stage lung cancer, minimally invasive surgery, multidisciplinary treatment of lung cancer, and progress in radiotherapy for lung cancer were explored. Highlights of the conference presentations are summarized in this report.

**Key words** Conference, thoracic oncology, thoracic surgery, targeted therapy, chemotherapy, radiotherapy

Cancer is still a major public health problem in both developed and developing countries<sup>[1]</sup>. Despite significant advances in surgery, medicine, and radiation therapy, thoracic neoplasms—especially lung cancer—remain the most fatal diseases worldwide. In the United States, lung cancer alone is expected to account for 26% of all female cancer deaths and 29% of all male cancer deaths in 2012, with a total of 160 340 deaths<sup>[1]</sup>. This situation is even worse in other parts of the world, with the morbidity and mortality ascending rapidly<sup>[2]</sup>. Because the outcome of prevention and treatment in thoracic oncology is far from satisfactory, international collaborations are indis-

pensable to make further progress in this area from both the basic and clinical research approaches.

French and Chinese experts in the field of thoracic oncology shared their research findings and clinical experience at the Sino-French 2012 Conference, held November 17–18, 2012 in Guangzhou, China. This international conference was hosted by the Department of Thoracic Surgery at Sun Yat-sen University Cancer Center (SYSUCC) and organized in collaboration with two French hospitals, namely, Institute Gustave Roussy (IGR) and Marie Lannelongue Hospital (CCML). The Guangdong Provincial Anti-Cancer Association and the *Chinese Journal of Cancer* also provided support to the organization of this forum. Speakers came from China (SYSUCC, The First Affiliated Hospital of Sun Yat-sen University, Fudan University Shanghai Cancer Center, Fudan University Zhongshan Hospital, Capital Medical University Beijing Lung Cancer Center, and Tianjin Medical University Cancer Center), France (IGR and CCML), and Poland (Jagiellonian University, John Paul II Hospital). The conference topics covered five aspects of thoracic oncology: innovation in surgical techniques, diagnosis and staging of early-stage lung cancer, minimally invasive surgery, multidisciplinary treatment in lung cancer, and progress in radiotherapy for lung

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cancer. In this article, we summarize the presentations on these topics.

## Innovation in Surgical Techniques

“The fact is that modern thoracic surgery is no longer restricted to conventional general thoracic surgery. It also involves the fields of cardiac, vascular, orthopedic, even plastic and reconstructive surgery,” Prof. Philippe Darteville (CCML) said in his opening speech. This point of view represents one trend in the future development of thoracic surgery, emphasizing the value of extensive surgery. In his presentation, Prof. Darteville demonstrated novel surgical techniques supported by convincing data, along with many successful clinical cases. The theoretical bases for extensive surgery in locally advanced non-small cell lung cancer (NSCLC) are as follows: (1) complete surgical resection is the best treatment for non-systemic lung cancer; (2) advantages of neoadjuvant therapy compared with adjuvant therapy have not been determined; (3) the development of modern thoracic surgery facilitates lung-sparing surgery; and (4) even N2 diseases, in some specific cases, can be candidates for surgery. Prof. Darteville reported a variety of major thoracic surgeries, including thoracic inlet tumor resection, carinal resection and reconstruction, superior vena cava resection and prosthetic replacement, aortic resection and reconstruction, and surgery for T4 NSCLC, which surprised conference participants. Admittedly, huge challenges exist for this kind of surgery, which is believed to be more risky but less effective, especially in the age of targeted therapy. However, Prof. Darteville addressed these challenges with convincing evidence. The 5-year survival rate for locally advanced NSCLC could be raised to 40%–50% if R0 resection could be achieved and regional lymph node status was confirmed to be N0/1. Even more impressively, the mean mortality rate for such major thoracic surgery could be controlled to as low as 4% via efficacious peri-operative care. At the end of his speech, Prof. Darteville emphasized that primary surgery for carefully selected patients with locally advanced NSCLC should be more frequently performed, as the benefit is worth the risk. However, “to fulfill this task,” he added, “modern thoracic surgeons are required to improve their clinical and surgical skills more comprehensively.”

Prof. Peng Lin from SYSUCC shared his experience and conveyed similar information for the treatment of malignant mesothelioma, for which he insisted that the role of extensive surgery was irreplaceable. Fourteen patients with pT1–3N0–1M0 disease who underwent en-bloc resection of pleura and lung plus diaphragm and pericardium were reported. The clinical and survival data were promising, with patients showing a median survival

of 31 months for stages I–II disease and 14 months for stage III disease. There was no postoperative death within 30 days; however, the relevant complication rate was relatively high (up to 60%). Most complications were atrial fibrillation, acute respiratory distress syndrome, and intrathoracic hemorrhage. Having performed careful analysis of current evidence from both clinical and pathologic points of view, Prof. Lin also made several recommendations on the preoperative work-up. He pointed out that because no consensus exists for specific diagnostic imaging criteria, pleural biopsy with video-assisted thoracic surgery was most accurate but more invasive. He also added that an accurate diagnosis depended on sufficient biopsied tissue and immunohistochemical examination to differentiate epithelioid/sarcomatoid/mixed subtypes. There are even fewer studies in the literature using a multidisciplinary approach to treat malignant mesothelioma in Chinese patients, according to Prof. Lin; after all, mesothelioma is a fairly rare disease in China. “It is just the beginning,” Prof. Lin said. “There is still a long way to go before we could obtain a clear picture.”

How to achieve radical resection is one aspect of extensive surgery, while how to repair and reconstruct the defect after resection is another. In his presentation, Prof. Lan-Jun Zhang (SYSUCC), the conference chair, provided an effective solution for reconstruction of bony chest wall defect. Prof. Zhang’s research team used novel biomaterial to invent artificial patches and ribs, which have been confirmed in both animal experiments and clinical applications to have good biocompatibility, plasticity, and adequate strength. Compared with the less availability and strength of autologous grafts, the foreign body reaction, and the increased risk of infection of synthetic materials, the new biomaterials achieve a balance between biocompatibility and flexibility. According to Prof. Zhang’s report, these biomaterial ribs and pleura have been successfully applied in 7 patients with T4 NSCLC and 6 patients with Ewing’s sarcoma for reconstruction of the bony chest wall. No thoracic deformity, chronic pain, or respiratory discomfort was observed 12 months after the operation<sup>[3]</sup>. “Since the experimental and clinical data are so impressive and promising,” Prof. Zhang said, “biomaterial ribs and pleura can be employed safely as an alternative to create an artificial chest wall to repair bony chest wall defects.”

Prof. Hai-Quan Chen from Fudan University Shanghai Cancer Center revealed the latest research findings from his surgical laboratory. By analyzing the genetic information in 936 surgically resected NSCLC specimens, he and colleagues pinpointed *RET* fusions that defined a unique molecular and clinicopathologic subtype of NSCLC<sup>[4]</sup>. Undoubtedly, from the unraveling mystery of *EGFR* gene mutation to the discovery of *ALK*

and *ROS1* fusion and the recently unveiled *RET* fusions, the management of lung cancer has entered the age of molecular classification and targeted therapy. Prof. Chen reported that the prevalence of *RET* fusions was 1.4% in NSCLC in a study by his group. He also discussed the characteristics of NSCLC with *RET* fusions, valid methods to screen *RET* fusions, and possible targeted therapies for *RET* fusions.

## Diagnosis and Staging of Early-Stage Lung Cancer

Accurate preoperative diagnosis and staging is of great value in the work-up for NSCLC. The strategy for this has continued to evolve over time—with the development of technology and clinical skills—from pure imaging study to endobronchial ultrasound plus biopsy. Two experts discussed their valuable clinical experience with participants in this part of the forum. Prof. Jaroslaw Kuzdzal, from John Paul II Hospital, Jagiellonian University, discussed the clinical application of transcervical extended mediastinal lymphadenectomy as a staging tool for NSCLC. This technique is unique and allows comprehensive and precise assessment of mediastinal status. However, estimates are as high as 11.3% for complication rate and 1.2% for mortality. “Provided that endobronchial ultrasound is less invasive and could also achieve similar accuracy,” Prof. Kuzdzal concluded, “transcervical extended mediastinal lymphadenectomy is unacceptable for a staging procedure, but it may have some place in the therapeutic effect of lymph node dissection.” On the other hand, Prof. Francois Le Roy Ladurie (CCML) re-emphasized the significance of endobronchial ultrasound for NSCLC staging, especially for N2 diseases, with his clinical experience accumulated at CCML.

Among all types of malignant diseases, lung cancer is definitely the number one killer for both men and women in China, according to Prof. Xiu-Yi Zhi (Director of Lung Cancer Expert Committee, Ministry of Health, China). Thus, a variety of organizations and networks, such as the Chinese Society for Cardiothoracic Surgery, Chinese Association for Thoracic Surgeons, and Chinese Anti-Cancer Association, were established for national collaboration and have contributed to cutting-edge research in lung cancer, particularly early diagnosis and staging for NSCLC.

Prof. Chang-Li Wang from Tianjin Medical University Cancer Center presented prognostic factors that influenced the survival of NSCLC patients after surgery. Prof. Wang emphasized that quality control of lymph node dissection could improve the overall survival for operable NSCLC because satisfactory lymph node dissection contributed to accurate staging. He also shared his valuable experience in personalized adjuvant therapy. Research from his laboratory revealed that

higher lymph node metastasis rate was closely related to poorer prognosis of NSCLC. More interestingly, only patients with higher lymph node metastasis rates benefited from adjuvant chemotherapy<sup>[6]</sup>. Initial results from his group’s study of adjuvant radiotherapy showed that patients with N2 disease might benefit from postoperative radiotherapy if tumor size is larger than 3 cm in diameter and the lymph node metastasis rate is higher than 33%. Prof. Wang commented at the end of his talk that adjuvant therapies should be administered wisely and tailored to the right subgroup of NSCLC patients.

## Minimally Invasive Surgery

Another trend in the future of thoracic surgery is, with no doubt, minimally invasive surgery performed with endoscopic techniques. For early-stage NSCLC, video-assisted thoracic surgery is now accepted as a reasonable alternative. Prof. Di Ge from Fudan University Zhongshan Hospital described the use of video-assisted thoracic surgery in 661 cases at his institution. In patients with stage I disease, the proportion of pulmonary resections using video-assisted thoracic surgery has been increasing steadily from 9.09% in 2005 to 77.9% in 2010. More impressively, the 5-year overall survival rate of for patients with stage I NSCLC was 84.6% in their group’s series, and this was accompanied by relatively low morbidity and mortality. These convincing data helped to convince thoracic surgeons in China to employ this novel surgical technique with confidence.

Promising results in the literature confirm that radical resection of pulmonary metastases is a safe and potentially curative procedure<sup>[6]</sup>. However, the ideal surgical approach for lung metastasectomy remains controversial. Prof. Hao Long from SYSUCC introduced hand-assisted thoracic surgery as “an ideal technique” for bilateral lung metastasectomy and explained, “it should strike a balance among lesion identification, simple resection and re-resection, minimal morbidity and lung sparing.” According to his report, the hand-assisted thoracic surgery approach could avoid the excessive invasiveness in thoracotomy or sternotomy and allow palpation with a hand within the pleural cavity. The preliminary outcome of 55 cases in Prof. Long’s study seemed promising, with a 5-year overall survival rate of 47.2% and a minimal complication rate of 3.6%.

Prof. Jian-Hua Fu (SYSUCC) discussed the present and future of minimally invasive esophagectomy. Based on experience at SYSUCC, a thoracoscopic plus laparoscopic approach could safely replace open esophagectomy in the majority of cases, but after a long learning curve. Prof. Fu reported that there was no difference between minimally invasive esophagectomy

and open esophagectomy regarding survival rate or overall morbidity and mortality. Furthermore, shorter intrathoracic operative time, less blood loss, more lymph node yield, and shorter length of stay in the minimally invasive esophagectomy group were observed in his and other similar studies. Interestingly, in the evaluation of its impact on quality of life, minimally invasive esophagectomy tended to improve the short-term but not long-term quality of life. "Preliminary results of minimally invasive esophagectomy seem to be encouraging," but Prof. Fu concluded, "randomized control trials are warranted to verify this trend."

## Multidisciplinary Treatment in Lung Cancer

For patients with early-stage NSCLC, surgery offers the best hope for cure. However, despite complete resection, survival rates are disappointing. The 5-year survival rates range from 67% for patients with T1N0 disease to 23% for those with T1-3N2<sup>[7,8]</sup>. Therefore, to further improve the overall survival for patients with lung cancer, more attention has been given to the multidisciplinary approach. Prof. Thierry Le Chevalier (IGR and CCML) summarized the status quo of adjuvant/neoadjuvant chemotherapy for operable NSCLC. According to his point of view, both adjuvant and neoadjuvant chemotherapy could contribute to a better overall survival for patients with operable NSCLC with an absolute 5-year benefit of 4%; however, induction chemotherapy is preferred to postoperative chemotherapy for the following reasons: (1) a total of 90% of patients will receive the planned dosage; (2) preoperative downstaging may allow a complete resection; (3) micrometastases are attacked at the front line; (4) it provides insight into the sensitivity of agents used in induction and adjuvant settings; and (5) it offers time to identify patients with unsuspected metastases and/or unrecognized comorbidities before giving local therapy. Prof. Le Chevalier also announced findings from studies of other adjuvant treatments including tailored chemotherapy, targeted therapy (RADIANT and E1505 trials), and vaccination (MAGRIT), though the results are still preliminary.

Prof. Si-Yu Wang from SYSUCC discussed anti-angiogenic therapy for early-stage NSCLC and shared preliminary results of a trial by his group in which the anti-angiogenic agent bevacizumab was added in the neoadjuvant setting. Patients in this pilot study showed a higher objective response rate before surgery and no increased complication rate after surgery. Therefore, further randomized controlled trials are warranted to confirm the value of this approach.

Advanced NSCLC is consistently the most active domain for both basic and clinical research. Prof. Li

Zhang (SYSUCC) described the current status of treatment for advanced NSCLC in China. He noted that targeted therapy, represented by tyrosine kinase inhibitors (TKIs), is replacing chemotherapy as the first-line treatment in the proper molecular subgroup of patients. More importantly, the evolving gene landscape in NSCLC and the discovery of novel targets have shifted treatment patterns from indiscriminate to personalization. Prof. Zhang also reviewed evidence that favored the application of maintenance therapy<sup>[9-13]</sup> and lastly concluded that for patients with stable disease or response after 4 cycles of first-line chemotherapy, immediate treatment with alternative, single-agent chemotherapy (such as pemetrexed in patients with non-squamous histology, docetaxel in unselected patients, or erlotinib in unselected patients) may be considered.

Only 20%–25% of patients with NSCLC present with early-stage disease that can be surgically resected, and a substantial number of these patients are considered unable to tolerate surgery because of comorbidities. For this latter cohort, radiotherapy should be the standard treatment. In addition, for NSCLC patients with advanced disease, multimodal treatment is required and usually includes radiotherapy. Prof. Cécile Le Péchoux (IGR) discussed clinical trials reported in the literature and evaluated the role of postoperative radiotherapy in NSCLC. Early data regarding postoperative radiotherapy failed to show any benefit for NSCLC patients, and therefore this approach was not recommended<sup>[14]</sup>. However, Prof. Le Péchoux suggested, "These results should be interpreted with caution." According to today's state-of-the-art, previous studies were limited by challenges in patient selection and quality control that might have influenced outcome. "What should be learned from those lessons is that the benefit of postoperative radiotherapy could only be achieved by good quality of surgery, proper selection of patients, and advanced technique of radiotherapy," she explained. At the end of her presentation, Prof. Le Péchoux stated her expectation that technical advances could enhance the ability of postoperative radiotherapy to improve local relapse-free survival and possibly overall survival. However, this concept must be proven in further randomized controlled trials.

Prof. Min Fan from Fudan University Shanghai Cancer Center discussed methods by which to optimize radiotherapy for locally advanced NSCLC, including improved radiation technology, concurrent chemoradiotherapy, dosage modification, non-conventional fractionation, and prophylactic cranial irradiation. The existing evidence only confirms the benefit of advanced radiation delivery, radiochemotherapy, and non-conventional fractionation. Interestingly, in a study of prophylactic cranial irradiation<sup>[15]</sup>, the incidence of brain



metastasis was reduced. Unfortunately, this benefit has not been translated to a better overall survival or disease-free survival.

As discussed above, in the new era of targeted therapy, TKIs tend to alter the treatment patterns for NSCLC in almost every aspect, including the management for brain metastasis. Prof. Ling Cai from SYSUCC reported her group's promising findings in a comparative study of brain metastasis from NSCLC treated with TKIs. A cohort of 282 NSCLC patients with brain metastases who underwent whole brain radiotherapy/stereotactic radiosurgery/surgery at SYSUCC were reviewed and analyzed. The patients were categorized into two groups depending on whether TKIs were administered—TKI group and non-TKI group. Prof. Cai and colleagues found that the median overall survival and intracranial and extracranial progression-free survival were better for the TKI group. Also, these positive results were highly related to the EGFR mutation status of primary tumors and brain metastases. Although it was only a retrospective study, Prof. Cai commented that the promising outcome of their preliminary study encouraged further clinical trials to verify the value of targeted therapy in this area.

Radiotherapy is still only reserved for patients with inoperable early-stage NSCLC. However, recent convincing data about stereotactic ablative radiotherapy may justifiably open investigation into the current role of surgery. Prof. Hui Liu from SYSUCC gave an update on stereotactic ablative radiotherapy and discussed surprising but exciting findings. The local control rate by stereotactic ablative radiotherapy has been raised to 98%, similar to that by surgical resection. Only the lack of lymph node staging and lack of data from randomized control trials made stereotactic ablative radiotherapy a lower priority choice to surgery. Prof. Liu expects results from several ongoing trials (ROSEL, Accuray STARS, RTOG 0618, JCOG, and RTOG 1021/ACOSOG Z4099) comparing stereotactic ablative radiotherapy and surgery will prompt a change in treatment options. Another issue that needs resolution is the proper prescription dose for

stereotactic ablative radiotherapy. As both local recurrence rate and radiation toxicity are directly related to dosage, a phase I/II dose escalation study (RTOG 0813) has been initiated to define the suitable prescription dose for stereotactic ablative radiotherapy. Another challenge in stereotactic ablative radiotherapy is identifying high-risk patients. Prof. Liu reported the disseminated failure rate of stereotactic ablative radiotherapy was 22%. This figure was even higher when the tumor size was larger than 3 cm. Because there is no accurate method/model to find high-risk patients with stage I NSCLC, this field of study needs to be further explored in the future.

## Prospective

The Sino-French 2012 Conference in Thoracic Oncology is an academic platform where leading international experts share their research findings and clinical experience, while young physicians and researchers gain broad and cutting-edge knowledge. The complexity of histogenesis, invasion, and metastasis of malignancies is far beyond what we have imagined. Conquering cancer is a task that can never be fulfilled by a single research center. To make cancer go away from us, international collaboration is indispensable. With the aid of this academic platform, medical resources can be integrated and optimized to facilitate international studies and clinical trials. Only in this way can we accelerate the discovery of vulnerable spots in cancer and turn them into weapons against it.

Cancer is a global health issue that threatens many lives each year. We hope this international platform contributes to the global community by providing health education for cancer prevention and early detection and delivering accurate information for treatment. The continued goal of the Sino-French Conference is to maintain international collaboration sustainably and effectively and to ultimately eliminate the fear of cancer.

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## References

- [1] Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J Clin*, 2012,62:10–29.
- [2] Long N, Moore MA, Chen W, et al. Cancer epidemiology and control in North-East Asia—past, present and future. *Asian Pac J Cancer Prev*, 2010,11 Suppl 2:107–148.
- [3] Zhang LJ, Wang WP, Li WY, et al. A new alternative for bony chest wall reconstruction using biomaterial artificial rib and pleura: animal experiment and clinical application. *Eur J Cardiothorac Surg*, 2011,40:939–947.
- [4] Wang R, Hu H, Pan Y, et al. Ret fusions define a unique molecular and clinicopathologic subtype of non-small-cell lung cancer. *J Clin Oncol*, 2012,30:4352–4359.
- [5] Wang CL, Li Y, Yue DS, et al. Value of the metastatic lymph node ratio for predicting the prognosis of non-small-cell lung cancer patients. *World J Surg*, 2012,36:455–462.
- [6] Long-term results of lung metastasectomy: prognostic analyses based on 5206 cases. *The International Registry of Lung Metastases. J Thorac Cardiovasc Surg*, 1997,113:37–49.
- [7] Zell JA, Ignatius Ou SH, Ziogas A, et al. Validation of the proposed international association for the study of lung cancer non-small cell lung cancer staging system revisions for advanced bronchioloalveolar carcinoma using data from the California cancer registry. *J Thorac Oncol*, 2007,2:1078–1085.
- [8] Mountain CF. Revisions in the international system for staging

- lung cancer. *Chest*, 1997,111:1710–1717.
- [9] Perol M, Chouaid C, Perol D, et al. Randomized, phase III study of gemcitabine or erlotinib maintenance therapy versus observation, with predefined second-line treatment, after cisplatin-gemcitabine induction chemotherapy in advanced non-small-cell lung cancer. *J Clin Oncol*, 2012,30:3516–3524.
- [10] Belani CP, Brodowicz T, Ciuleanu TE, et al. Quality of life in patients with advanced non-small-cell lung cancer given maintenance treatment with pemetrexed versus placebo (H3E-MC-JMEN): results from a randomised, double-blind, phase 3 study. *Lancet Oncol*, 2012,13:292–299.
- [11] Gridelli C, de Marinis F, Di Maio M, et al. Maintenance treatment of advanced non-small-cell lung cancer: results of an international expert panel meeting of the Italian Association of Thoracic Oncology. *Lung Cancer*, 2012,76:269–279.
- [12] Cappuzzo F, Ciuleanu T, Stelmakh L, et al. Erlotinib as maintenance treatment in advanced non-small-cell lung cancer: a multicentre, randomised, placebo-controlled phase 3 study. *Lancet Oncol*, 2010,11:521–529.
- [13] Zhang L, Ma S, Song X, et al. Gefitinib versus placebo as maintenance therapy in patients with locally advanced or metastatic non-small-cell lung cancer (INFORM; C-TONG 0804): a multicentre, double-blind randomised phase 3 trial. *Lancet Oncol*, 2012,13:466–475.
- [14] Kal HB, El Sharouni SY, Struikmans H. Postoperative radiotherapy in non-small-cell lung cancer. *Lancet*, 1998,352:1385–1386.
- [15] Gore EM, Bae K, Wong SJ, et al. Phase III comparison of prophylactic cranial irradiation versus observation in patients with locally advanced non-small-cell lung cancer: primary analysis of radiation therapy oncology group study RTOG 0214. *J Clin Oncol*, 2011,29:272–278.