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Improved staging using intraoperative ultrasound for mediastinal lymphadenectomy in NSCLC surgery

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**Objectives:** The extend of lymph node involvement in patients with non-small cell lung cancer (NSCLC) is the cornerstone of staging and influences both multimodality treatment and final outcome. We studied safety, accuracy and characteristics of intraoperative ultrasound (US) guided systematic mediastinal nodal dissection in patients with resected NSCLC.

**Methods:** Intraoperative hand held ultrasound probe was used in systematic mediastinal nodal dissection in 84 patients after radical surgery for NSCLC. Mapping of the lymph nodes by their number and station followed by histopathologic evaluation was performed. Data were compared with 86 patients who underwent lung resections and standard systematic mediastinal nodal dissection for NSCLC within the same time period at our institution. Statistical analysis was carried out.

Results: The surgical procedure used depended on the extent of the disease, as well as the cardiopulmonary reserve of the patients and was comparable in both groups of patients. Operating time was prolonged for 12 (6–20) minutes in patients with US guided mediastinal nodal dissection, but number and stations of evaluated lymph nodes was significantly higher (p>0.001) at the same group of patients. Skip nodal metastases were found in 24% of patients without N1 nodal involvement. We upstaged 12 (10%) patients using US guided mediastinal lymphadenectomy. Standard staging system seemed to be improved in US guided mediastinal lymphadenectomy patients. Complications rate showed no difference between analyzed groups of patients.

Conclusion: Higher number and location of analyzed mediastinal nodal stations in patients with resected NSCLC using hand held ultrasound probe suggested to be of great oncology significance. Procedure showed absolute safety and high accuracy. Our results indicate that intraoperative US may have important staging implication. Further clinical studies should be carried out in order to improve intraoperative staging in NSCLC patients.

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The benefits of PCR-Invader method for analysis of EGFR gene

mutation in the primary non-small-cell lung cancer

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Background: In late years, reports about Epidermal Growth Factor Receptor (EGFR)-Tyrosine Kinase Inhibitors (TKIs) in the non-small cell ung cancer (NSCLC) and the EGFR-mutation have increased. The theory that existence of somaticmutations in the EGFR kinase domain is corresponded with therapeutic sensitivity of TKIs in patients with NSCLC, has been recognized widespread, andEGFR mutation becomes one of the effect-prediction-factors of EGFR-TKIs. TheDirect Sequencing method is used commonly for analysis of their EGFR gene, there are few reports about PCR-Invader method for analysis of the EGFR gene.

**Material and Methods:** We intended 100 cases of lung specimen in the NSCLC, which were stored both as fresh-frozen tissues at  $-80^{\circ}\text{C}$  and formalin-fixedparaffin-embedding tissues for this study. We analyzed retrospectively whether EGFR mutations could be detected by both the PCR-Invader and the DirectSequence method in each case.

Results: The EGFR mutations were found in 38% of cases by PCR-Invader method, and found in 32% by Direct Sequencing method. These mutations were recognized 18% in Exon21, 19% in Exon19 and 3% in Exon20. EGFR mutations were detected in the following characteristics: histological types were 37 adenocarcinomaand one adenosquamous carcinoma, the genders were 10 male and 28 female, and 31 cases were never smoker. By the PCR-Invader method using fresh-frozentissues, the mutation of Exon19 or Exon21 could be detected in 37 cases, although their mutations could be measured by Direct Sequence method in 32cases. Four cases of L858R in Exon21 and one case of E746-A750 deletion in Exon19 were detectable only by PCR-Invader method. In the formalin-fixedparaffinembedding tissues, 22 cases of the EGFR mutations were found in Exon19 or Exon21 by PCR-Invader method and 20 cases of the mutations were detected by Direct Sequence method. Two cases of E746-A750 deletion in Exon19 were only detected by PCR-Invader method.

Conclusions: The PCR-Invader method for analysis of the EGFR mutation in the NSCLCmight be superior to the Direct Sequence method, as the

ability of detection of Exon21 and Exon19-mutations was higher. Besides, the EGFR mutation measurement by the PCR- Invader method was reliable even if the formalin-fixedparaffin-embedding tissues were used.

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Utilization of traditional chinese medicine for lung cancer in Taiwan: a population-based study

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Background: Complementary/alternative medicine (CAM) used in lung cancer has increased. Traditional Chinese medicine (TCM) is an important category of CAM and is popular in Taiwan. The National Health Insurance covered 99% of the inhabitants and 91% of the medical institutes in Taiwan, including TCM and Western medicine. Basing on the National Health Insurance Research Database (NHIRD), a nationwide survey was conducted. This study aimed to investigate the utilization of TCM for lung cancer in Taiwan.

Material and Methods: Only TCM outpatient service was covered by National Health Insurance. TCM outpatient reimbursement claims from NHIRD of 2007 were analyzed. The data of registry for catastrophic illness patients was used to analyze the prevelance of lung cancer. Patients with lung cancer were identified by ICD-9 Code of 162, and 162.0–162.9.

Results: In 2007, a total 1202 (6.3%) lung cancer patients used 7990 TCM outpatient visits. Female patients (50.3%) were a little more than male ones (49.7%). Median age was 62. Hospitals provided more TCM service (67.5%) than TCM clinic (32.5%). The most frequently used therapies were traditional Chinese herbs/medicine (97.1%), following by acupuncture and traumatology manipulative therapies (2.9%). For TCM users of lung cancer, 27.3% patients had one visit, 39.7% had 2–6 visits, and 33.0% had more than 6 visits of TCM outpatient service in 2007. The cost of per visit was NTD 626.57(USD 18.51/ EUD 14.27).

Conclusions: Our results revealed that a small portion of lung cancer patients use TCM in Taiwan. The cost of TCM is low. Further research is needed to investigate the efficiency of TCM and interaction of TCM and Western medicine.

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Preliminary results of MAGE-A3 expression and baseline demographic data from MAGRIT, a large phase III trial of MAGE-A3 ASCI (Antigen-Specific Cancer Immunotherapeutic) in adjuvant NSCI C

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Background: The MAGE-A3 gene is a tumor-specific gene expressed in Non-Small Cell Lung Cancer. The MAGRIT Phase III trial evaluates the potential efficacy of the MAGE-A3 ASCI in resected stage IB, II and IIIA MAGE-A3(+) NSCLC patients. We report here the frequency of MAGE-A3 gene expression according to stage, histology and tumor size. Demographics of the first randomized patients are reported.

Methods: MAGE-A3 expression was tested by quantitative Reverse Transcription Polymerase Chain Reaction (RT-PCR) on Formalin Fixed Paraffin-Embedded (FFPE) tumor tissue from surgical samples. Baseline patient and tumor characteristics were collected and associated with the expression of MAGE-A3.

Results: Tumor samples from 2690 operable NSCLC patients were screened for MAGE-A3 expression between Oct 4, 2007 and April 14, 2009 and 32.9% found positive. The number of invalid samples is low (2.3%). The expression of the MAGE-A3 gene is 34% in stage IB, 34.9% in stage III. 31.3% in stage IIIA. It is 47.2% in squamous cell carcinoma and 24.3% in adenocarcinoma. Irrespective from stage and histopathology, expression increased with primary tumor size: 23.7% for tumors <2cm to