immune-oncology clinic has been established. Objective: The objective of this initiative is to generate a standardized, reproducible, and safe implementation immunotherapy program that could be easily recreated at any community cancer center. This presentation will discuss the clinic design, immunotherapy teaching class, logistics and standardized ICI delivery, care monitoring, and follow-up. Keywords: Elderly with comorbidities, Immunotherapy clinic

MTE14.01
Nodule Management (Pro Con Debate and Case Presentations)

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A recent observation study on the management of lung nodules 8 mm to 20 mm by community pulmonologists in the US showed a high benign biopsy rate of 62% and benign surgical resection rate of 35%. Furthermore, the surgical resection rates were similar irrespective of the pre-test probability of malignancy risk.1 The study suggested there is a lack of adherence to nodule management guidelines. However, there are a number of lung nodule management guidelines and lung nodule malignancy risk prediction tools.2-5 Some are based on 2D diameter size measurement while others used volumetric measurement or a combination of both. New nodules with a prior negative CT have a higher probability of malignancy even at a smaller size. 7-9 Comparing to baseline screen, the malignancy risk of new nodules is higher for nodules <8mm.9 Computer assisted diagnostic (CAD) tools facilitates volume measurement and reduce inter-observer variability but they may not be generally available. Volumetric measurement is particularly useful for comparison of serial scans for evidence of growth. Growth independent nodule characteristics such as right upper lung and central distribution may further improve volume based new nodule malignancy prediction. Nodule size and growth are the most important parameters for malignancy. To measure size accurately especially to determine changes in volume, it is necessary to address standardization of technical requirements related to the scanners and image acquisition protocols.10 The action thresholds for early recall CT imaging study, PET/CT or biopsy vary in different guidelines with major differences for non-solid nodules making it difficult for clinicians to remember or apply. Therefore, a lack of adherence to guideline recommendations could be related to a lack of clarity of guidelines. To facilitate implementation, there is a need to have an integrated nodule malignancy risk tool that takes into account prior LDCT history when there is more than a baseline LDCT. In this session, the important issues regarding which model should be applied and which nodule management approach should be used (e.g. diameter or volume) for baseline and new nodules will be discussed through case presentations.

References:

MTE15.01

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Thoracoscope is, by its original meaning, defined as an endoscope to observe intrathoracic space, just like a bronchoscope for bronchial lumen. But today this endoscope has been widely accepted as a surgical instrument to perform various kinds of intrathoracic procedures which had been otherwise done with open thoracotomy. Video-assisted thoracic surgery (VATS) has been expected to reduce the surgical burden, and already applied for the complex surgeries such as those for lung cancer. It is now a part of our routine procedures. However, despite the minimally invasiveness of the procedure, VATS may become a risky surgery in several special situations. Not only the surgeons, but also pulmonologist, medical oncologist, or radiation oncologist should know the nature of the surgery, and the situations in which VATS should be rather avoided. In this MTE sessions, I would like to present the special situations in which the VATS procedures are at too high risk, and therefore, and are not considered to be performed. High Risk Surgery: When dose the surgery become at high risk? In what situation, we should think the surgery is at high risk? Generally, there must be two kinds of situations each alone or both combined, which make the surgery at high risk. One is the patients at high risk for surgery even for a routine lobectomy, with a limited pulmonary reserve. The other is the difficult, complex surgery such as the extended pulmonary resection. Technical limitations of a VATS procedure are generally related to several different situations, which are described below. In this MTE session, I would like to focus upon the surgical, technical risks for the VATS procedures. VATS Lung Resections at Technically High Risk: 2-1. Difficult one lung ventilation. One-lung ventilation, collapsing the one entire lung of the operative side, is an indispensable part of the stable VATS procedure. Thoracic cavity is usually filled with expanded lung, and only very limited space is left when the lungs are aired. To make VATS procedures possible, deflation (collapse) of the lung on affected side is indispensable, which provides the space for observation and working of surgical instruments. Therefore, for patients who do not tolerate to the one-lung ventilation because of the limited pulmonary reserve or previous history of lung resection, VATS is generally not indicated. For these patients, we consider routine open thoracotomy with intermittent collapse of the operative side of the lung. 2-2. Tight Adhesions. Tight adhesions might exist within the thoracic cavity, especially for patients with the history of pleurisy or surgery. As seen previously, the working pleural space is an indispensable element of a VATS procedure. Surgeons are concerned about such history in case
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MTE16.02

The Management of Small Cell Lung Cancer following First Line Treatment Failure

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SCLC remains a clinical challenge that has not benefited from the same medical advances in recent years as non-small cell lung cancer (NSCLC). Beyond first line chemotherapy, there are few approved therapies for recurrent small cell lung cancer (SCLC). A multitude of agents have been tested over the past decades, yet little improvement has been made in survival rates. This talk will review previous efforts in treating SCLC upon progression after first-line therapy, the current science that is changing our understanding of the biology of SCLC and will discuss the evidence for new agents in this indication, by reviewing recent and current clinical trials. The addition of platinum agents to first-line chemotherapy regimens in the 1980’s improved overall response (OR) and complete response (CR) rates, and thus platinum doublet chemotherapy, most commonly in combination with etoposide, is the current standard of care. SCLC is initially very chemosensitive, OR rates to platinum-etoposide chemotherapy in the first line setting for limited disease (LD) are between 60-90% with CR rates of 40-70%, and one third of patients will survive 5 years and be considered cured. The prognosis is far less optimistic for the two thirds of patients with SCLC who are diagnosed with extensive-stage (ES) disease. OR rates for ES SCLC are 40-70%, and CR rates are 10-20%. The median progression-free survival (PFS) in the first-line setting is in the order of 15 months for LD and 6 months for ES. Unfortunately, the high response rate seen in the first line setting is not maintained when patients are retreated. Patients can be classified into three groups based on their response to initial chemotherapy: sensitive (tumor response > 90 days), resistant (recurrence within 90 days of completing primary therapy) and refractory (non-responders and progression on treatment). Therapeutic options therefore include re-challenge for those patients with sensitive disease or a change of regimen. Topotecan has been approved by the FDA since 1996 for the second-line treatment of SCLC following first-line relapse. There are additionally several guideline-recommended therapies that are not FDA/EMA approved, such as cyclophosphamide/doxorubicin/vincristine (CAV), irinotecan (Japan), docetaxel, paclitaxel, gemcitabine, temozolomide and nivolumab with ipilimumab. Response rates to second line therapy are 27% at best and less than 15% in chemo-refractory cases, with a median time to progression of only 13 weeks. Despite decades of testing with multiple agents, there have been no new drug approvals in over 20 years and improved therapy is urgently needed. With the advent of targeted therapies over the past decades, there has been no shortage of early phase clinical trials in SCLC. However, these agents have yet to demonstrate success in phase II-III evaluation. The lack of progress in improving survival rates for SCLC led to its inclusion in the U.S. Congress’ Recalcitrant Cancer Research Act in 2012. Subsequent comprehensive molecular characterization of the disease has led to a better understanding of known molecular vulnerabilities and has pointed to new areas requiring therapeutic interrogation. Examples include developmental regulatory pathway abnormalities, DNA damage repair aberrations, and the manipulation of the immune response. Fundamental to further therapeutic progress remains the challenge of understanding the mechanisms that underlie the rapid emergence of chemo-resistance in SCLC. Recent reports of early phase clinical trials with immune checkpoint inhibitors documenting important response and survival rates, provide tangible hope for the approval of new treatment options. However, immune strategies should exclude the empiric testing of new monotherapies and combinations in the absence of strong pre-clinical science. This will necessitate the development of next generation pre-clinical models, that are biologically representative of the human immune system and disease. Finally, improved translational research will inform more rational clinical trial design, and concentrate

VATS resection is indicated. There are several types of adhesions which make VATS procedure difficult. Examples for these conditions are as follows: 1) Previous pleurisy. If intrathoracic adhesion, mostly due to the previous pleurisy, is extensive, it is impossible to have an enough working space. In fact, lysis under thoracoscopy can be done, but it is usually time-consuming with significant amount of blood loss. There might be even a higher risk of damaging the visceral pleura and lung parenchyma, which may cause prolonged air leakage especially in the elderly with bullous lung. Therefore, except for a localized one, the extensive synphysis of pleura should be respected as a contraindication and a case which should be converted to the open thoracotomy. 2) Adhesions at pulmonary hilum (“Frozen hilum”). In some cases with past history of infection such as tuberculosis, the hilar nodes are tightly adhesive to the bronchovascular structures. This is extremely difficult situation even for routine lobectomy. VATS resection for such cases are hardly considered. 3) Previous thoracotomy. Major lung resection after previous lung resection involving the hilum (for example, a completion right lower lobectomy after middle lobectomy) is one of the most challenging surgery even by open thoracotomy. Also, for these operations, VATS resection is rarely indicated. 2-3. Complex Procedures. Among various procedures in thoracic surgery, complex procedures are thought to be done safely by open thoracotomy, and not by VATS. These might include the following: such as bronchovascular plasty, combined resection with neighboring structures, pneumonectomy, and pleuro-pneumonectomy. 2-4. Other Situations Which Make VATS Procedure at High Risk: 1) Complex anatomical variation. When complex anatomical variations are found during the surgery, the procedure should be converted to open thoracotomy without hesitation. 2) Large lesions. Any large intrathoracic mass, wherever it is located, have a trouble in being retrieved from the thoracic cavity. Not only they inevitably require enough extension of the trocar port or access thoracotomy, but also, they might be crushed during being extracted, which may result in tumor dissemination. 3) Special locations. In the intrapulmonary and mediastinal lesions, there are special locations where the thoracoscopic instrumentation is quite difficult: Lesions located at mediastinal aspect of the lung, and those close to hilum. Mediastinal mass (swollen lymph nodes) adjacent to the vital structures such as great vessels is also least suitable for this technique because of danger of massive bleeding. Keywords: Surgery, VATS, Risk

MTE16.01

Proper Treatment of LCNEC; Chemotherapy or Targeted Therapy

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Neuroendocrine Tumors of the Lung consisted of two subtypes which is small cell lung cancer (SCLC) and large cell neuroendocrine carcinoma (LCNEC). Both subtypes represent around 15% of all Lung Cancer. The incidence of LCNEC was quite low as compare to SCLC. However both are aggressive and poor prognosis. The treatment of LCNEC was usually followed the SCLC. In early stages (I-II-III), surgery is recommended but does not seem to be sufficient. Platinum-based adjuvant chemotherapy may be useful while the role of neoadjuvant chemotherapy is still not well defined. In patients with advanced stage LCNEC, the chemotherapy regimens used in SCLC which is cisplatin plus etoposide remain the standard of treatment, but results are not satisfactory. Due to their peculiar clinical and biological features and the lack of literature data, there is an emerging need for a consensus on the best treatment strategy for LCNEC and for the identification of new therapeutic options. In this review, we will discuss the key aspects of LCNEC management and the possibility of using the gene sequencing to clarify the selection of chemotherapy regimen. Keywords: large cell neuroendocrine carcinoma, lung

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