흉부 영상 의학의 최신 지견 2007

□종설□

건국대학교 의과대학 영상의학과
이 정 근

What's New 2007 in Thoracic Radiology?

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Introduction

In diagnostic radiology, as in many other medical fields, there has been many cutting-edge technology and new informations added with fast step in recent years. Among them, thoracic radiology is the one of the most brilliant fields walked in step with pulmonology. Rapid development of medical imaging machines, introduction of fusion technology, and most of all, the computer technology which supports all these cutting-edge technique development have provided us better system for visual diagnosis and monitoring of the thoracic patients. It is generally agreed that the one of the most important developments in medical science in recent twenty years is, the radiologic imaging, such as digital radiology, computed tomogram (CT), magnetic resonance (MR) imaging and PET (positron emission tomogram)-CT, etc.

Soon after the introduction of spiral/helical CT (1 detector system) in early 90's, there have been huge advancement in multidetector CT from 4, to 8, to 16, and to 64 detector systems and we now have 256 detectors (Toshiba), dual source tube CT system (Siemens, Definition) and one tube with two energy CT (General Electric, XT system). With these developments, we have better temporal resolution (faster image scanning), more spatial resolution (less than 1 mm thickness), also much better, faster multidimensional viewing with support of computer technique. Virtual bronchoscopy is easily demonstrated with one breath hold in a few seconds, pulmonary CT angiograms also show the pulmonary embolisms in up to subsegmental artery levels vividly in 3 dimensional images and even small coronary arteries of the pumping heart are vividly displayed[1].

PET-CT has expanded its role, not only in differentiation of malignancy from benign lesion in thorax, but also for, staging of lung cancer, re-staging, therapy planning and treatment monitoring. We need the help of PET-CT in everyday practice of evaluation of solitary pulmonary nodule, lung cancer, esophageal cancer and malignant lymphoma patients[2].

Early detection of lung cancer has long been regarded as the one of the goals of lung cancer management since the poor prognosis of lung cancer. And many trials are now on going with some results. CT features of the 61 lung cancers, discovered during low dose CT screening for 5 years, emphasizing the ground glass opacity of low grade malignancy such as bronchioloalveolar cell carcinoma and adenocarcinoma, especially in women will be shown[3].

The classic X-ray films are now almost all gone in most radiology department of many big hospitals in Korea and digital imaging systems are on its

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way with PACS (Picture Archiving Communication System). Digital image systems have made us easily detect lung nodules and other chest diseases. Dual energy radiography, temporal subtraction radiography, tomosynthesis are a few examples of digital techniques which made lung lesion detection easier without much radiation exposure compared with CT. And CAD (computer aided detection), CADx (computer aided diagnosis) are also helpful in lesion detection and diagnosis of several chest diseases, if only we understand the capabilities and limitations[4].

With diffusion-weighted ^{3}He MR imaging, the potential for detection of early emphysema of healthy smokers is demonstrated. This technique could become an important tool for understanding the pulmonary processes in emphysema, and for implementing treatment before clinical symptoms, and for monitoring the effect of treatment[5].

Several new articles about new information in thoracic radiology will be introduced briefly.

Blodgett TM, Meltzer CC, Townsend DW. PET/CT : Form and Function. Radiology 2007;242:360-85.

ABSTRACT: Functional imaging with PET is playing an increasingly important role in the diagnosis and staging of malignant disease, image-guided therapy planning, and treatment monitoring. PET with the labeled glucose analogue fluorine 18 fluorodeoxyglucose (FDG) is a relatively recent addition to the medical technology for imaging of cancer, and FDG PET complements the more conventional anatomic imaging modalities of CT and MRI. CT is complementary in the sense that it provides accurate localization of organs and lesions, while PET maps both normal and abnormal tissue function. When combined, the two modalities can help both identify and localize functional abnormalities. Attempts to align CT and PET data sets with fusion software are generally successful in the brain; other areas of the body is more challenging, owing to the increased number of degrees of freedom between the two data sets. These challenges have recently been addressed by the introduction of the combined PET/CT scanner, a hardware-oriented approach to image fusion. With such a device, accurately registered anatomic and functional images can be acquired for each patient in a single scanning session. Currently, over 800 combined PET/CT scanners are installed in medical institutions worldwide, many of them for the diagnosis and staging of malignant disease and increasingly for monitoring of the response to therapy. This review will describe some of the most recent technologic developments in PET/CT instrumentation and the clinical indications for which combined PET/CT has been shown to be more useful than PET and CT performed separately.

LUNG CANCER

Initial Diagnosis: SPN Evaluation

The utility of PET in the evaluation of pulmonary nodules has been the subject of several studies, many of which have shown the sensitivity and specificity of FDG PET to be approximately 90%. In most evaluations, the sensitivity tends to be higher than the specificity, which is due to the lack of specificity of FDG, and when fungal infections or other infectious or inflammatory processes are prevalent, the specificity tends to be even lower. It is likely that the additional information garnered from the CT portion of a combined PET/CT scan will help improve the specificity over that of PET

alone. However, to our knowledge, no studies have yet directly compared the performance of PET with that of PET/CT for the evaluation of pulmonary nodules.

A meta-analysis summarized the data for 1,474 nodules from 40 studies and showed that the overall combined sensitivity and specificity of FDG PET was 91.2%, although a sensitivity of 96.8% and a specificity of 77.8% were more reflective of the findings in clinical practice.

Although several studies have shown the utility of FDG PET and PET/CT in the evaluation of solitary pulmonary nodules (PET and PET/CT are not generally indicated for multiple pulmonary nodules), there are several potential limitations in clinical practice that need to be considered. For instance, several nonmalignant inflammatory and infectious processes, such as tuberculosis and fungal infections, can take up FDG and mimic the appearance of a malignant nodule on PET or PET/CT images. Sarcoidosis, silicosis, and other granulomatous processes can also appear similar to malignant nodules. Therefore, it is necessary to know details about the patient regarding exposure, as well as pertinent medical history. In addition, the CT portion of a combined PET/CT scan can often provide additional information for further characterization of pulmonary nodules.

There is some evidence to suggest that "dual-time-point" imaging may also be helpful in differentiating malignant versus inflammatory and infectious processes. This involves performing the first PET or PET/CT examination at the usual time after FDG injection (approximately 1 hour) and then performing another examination at a later time (average of 2 - 4 hours after FDG injection). The reasoning behind this delayed second examination is that malignant nodules generally tend to continue to accumulate FDG over time, whereas inflammatory and infectious processes tend to show less FDG uptake over time. By obtaining images at more than one time point, it is possible to determine the trend of FDG uptake.

Although newer PET scanners capable of higher resolution have an intrinsic spatial resolution close to 4 mm, most scanners in use today can, in general, depict 6 - 12-mm lesions as long as they are relatively metabolically active. However, false-negative scans can be seen in primary or metastatic nodules that are less metabolically active, such as bronchioalveolar cell carcinoma (BAC). Even a 3-cm BAC may not be detected on FDG PET or PET/CT images owing to the lack of FDG uptake; in fact, BAC may be undetectable on FDG PET images up to 57% of the time. Another primary tumor with reportedly low relative FDG uptake is carcinoid tumor, which like BAC, can be a cause of false-negative PET images. However, FDG PET has a very high negative predictive value for solitary pulmonary nodules, so a patient who may not tolerate an invasive procedure can be followed up with serial CT to help assess stability or resolution of disease.

Standardized uptake values (SUVs) with PET alone have been used to help differentiate a benign from a malignant lesion, with an SUV of 2.5 often being cited as a guideline for the cutoff between uptake in benign (SUV$<$2.5) and that in malignant (SUV$\geq$2.5) processes. Where SUVs are used to help evaluate a response to therapy, it is important to use the same scanner, since SUVs can differ markedly between scanners that are not cross calibrated. Most physicians who are experienced at interpreting PET images advocate the use of SUVs for therapy purposes rather than for the differentiation of benign from malignant processes, where qualitative assessment is usually more important.

PET/CT can often be helpful in the precise localization of pulmonary lesions, particularly when there are lesions adjacent to structures with physiologic FDG activity, such as the heart. With nodules more centrally located in the lung parenchyma, this benefit is less noticeable because there is little background FDG activity. However, when there is more than one nodule in the same region, the increased localization information becomes much more apparent. In addition, results of a recent study suggest that accurate retrospective coregistration of PET and CT data sets is possible in the thorax, as long as the anatomic positioning of the patient and respiratory instructions are carefully matched.

Several other tracers have been and continue to be developed, and these show promise either as alternatives or as a complement to FDG. The one that has seen the most use so far is a thymidine analog, ^{18}F-3′-fluoro-3′-deoxy-L-thymidine (FLT). As a marker of cellular proliferation, this tracer should theoretically be more specific for neoplasms, particularly for tumors that have a high rate of cellular proliferation. However, preliminary results have been mixed with regard to the ability of FLT to enable distinction between tumor and infection and inflammation. Most of these studies have reported some false-positive and some false-negative images. In addition, there is also intense background physiologic FLT uptake in both the liver and the bone marrow, making FLT less appealing as a single tracer.

Although few data exist demonstrating the utility of PET/CT for directing biopsy, this is certainly a potentially useful application that is underutilized. The added localization information that is available on fused PET/CT images is useful in determining which nodule or portion of the nodule should be subjected to biopsy.

Staging

Lung cancer is typically divided into small cell and non-small cell subtypes. Most patients with small cell lung cancer are thought to have systemic disease at diagnosis and are typically not considered to be surgical candidates, with rare exceptions. This review will be limited to a discussion of non-small cell lung carcinoma.

Non-small Cell Lung Cancer

PET alone has not been shown to be particularly useful in determining the T status of the primary lesion and is generally not helpful for determining chest wall involvement. However, because CT is better at predicting chest wall involvement, PET/CT would intuitively seem to be the preferred modality. A recent study by Cerfolio et al showed that PET/CT more accurately predicted T status (70% of cases) than did PET alone (47%).

In the more important role of assessing the mediastinum, several studies have shown FDG PET to be more accurate than CT. In one of the largest studies in which PET was compared with CT for evaluation of the mediastinum, PET was shown to have a sensitivity and specificity, respectively, of 91% and 86%, compared with 75% and 66% for CT. Although size criteria are often helpful for the radiologist in determining whether a node is malignant, there is poor correlation between nodal size and the presence of metastatic disease in the mediastinum, with metastatic disease present in 21% of normal-sized nodes, while up to 40% of enlarged nodes are free of malignancy. In addition, evaluation with PET has been shown to reduce the number of futile thoracotomies by up to 41%, relative to the rate from conventional work-up,

usually by showing the presence of unsuspected contralateral mediastinal involvement or distant metastases. Several other studies have shown that PET imaging is more sensitive and specific than CT and can change patient care up to 67% of the time.

Lardinois et al showed that integrated PET/CT provided additional information in 20 (41%) of 49 patients, beyond that provided by conventional visual correlation of PET and CT images. Antoch and colleagues compared PET, CT, and PET/CT for staging in 27 patients with non-small cell lung cancer and found that PET/CT had a higher sensitivity, specificity, and accuracy (89%, 94%, and 93%, respectively) than did PET (89%, 89%, and 89%, respectively) or CT (70%, 59%, and 63%, respectively). PET/CT was also shown to be significantly more sensitive for evaluating the American Thoracic Society nodal stations 4R, 5, 7, 10L, and 11 and was more accurate than PET for evaluating stations 7 and 11.

In addition, PET/CT has been shown to depict more distant metastatic lesions than do other imaging modalities at the time of staging. The presence and precise localization of extrathoracic metastases are better evaluated with PET/CT because of its ability to depict small lesions that may not show mass effect, enhancement, or necrosis.

In recent years, many of the radiation therapy planning systems have been upgraded to be able to incorporate both CT and PET data sets. Many also have the ability to fuse the two data sets by using the planning software. Some preliminary studies have shown that radiation portals and tumor volumes change up to 50% of the time when both PET and CT data sets are considered, compared with the traditional CT planning method. This anatomic and functional plan has the biggest effect when there are portions of a tumor that may not be visible or are not included on CT images alone. With both the anatomic and metabolic data, radiation oncologists are able to define viable tumor volume more accurately, as well as minimize the amount of exposure to normal tissue.

Restaging

Following extensive surgery or radiation, it is fairly common to have some degree of scarring within the remaining lung parenchyma. Serial CT to identify areas of growth or change is typically used to follow these patients up. With PET and PET/CT, most of these patients can be evaluated more accurately and earlier than with other imaging modalities. Much of the FDG uptake due to inflammation from surgery resolves relatively quickly (typically within 6 weeks), and these patients can be reevaluated at this time for residual or recurrent tumor, particularly patients in whom the margins may not have been clear. In the restaging evaluation of patients with lung cancer, one of the most challenging aspects is differentiating recurrent or residual tumor from posttherapy changes. Both processes can appear identical on CT images, which presents a challenge to the use of this modality in the posttreatment patient with lung cancer. Conversely scar and fibrosis are, by definition, dead tissue and should not result in any FDG uptake, which makes PET or PET/CT ideal for this indication. PET has been shown to have a sensitivity of 98-100% for the differentiation of tumor from posttreatment changes in the lung.

Radiation pneumonitis is a cause of false-positive FDG PET images. In addition, evaluation of the primary tumor is generally not possible in the setting of radiation pneumonitis. Because of the

radiosensitivity of the lung, patients who have undergone irradiation to the lungs are not typically reevaluated for 2-4 months after their last treatment. However, the inflammatory effects of radiation can last more than a year.

Lindell RM, Hartman TE, Swensen SJ, Jett JR, Midthun DE, Tazelaar HD, Mandrekar JN. Five-year Lung Cancer Screening Experience: CT Appearance, Growth Rate, Location, and Histologic Features of 61 Lung Cancers. Radiology 2007;242:555-62.

Purpose: To retrospectively evaluate the computed tomography (CT)-determined size, morphology, location, morphologic change, and growth rate of incidence and prevalence lung cancers detected in high-risk individuals who underwent annual chest CT screening for 5 years and to evaluate the histologic features and stages of these cancers.

Materials and Methods: The study was institutional review board approved and HIPAA compliant. Informed consent was waived. CT scans of 61 cancers (24 in men, 37 in women; age range, 53-79 years; mean, 65 years) were retrospectively reviewed for cancer size, morphology, and location. Forty-eight cancers were assessed for morphologic change and volume doubling time (VDT), which was calculated by using a modified Schwartz equation. Histologic sections were retrospectively reviewed.

Results: Mean tumor size was 16.4 mm (range, 5.5-52.5 mm). Most common CT morphologic features were as follows: for bronchioloalveolar carcinoma (BAC) (n = 9), ground-glass attenuation (n = 6, 67%) and smooth (n = 3, 33%), irregular (n = 3, 33%), or spiculated (n = 3, 33%) margin; for non-BAC adenocarcinomas (n = 25), semisolid (n = 11, 44%) or solid (n = 12, 48%) attenuation and irregular margin (n = 14, 56%); for squamous cell carcinoma (n = 14), solid attenuation (n = 12, 86%) and irregular margin (n = 10, 71%); for small cell or mixed small and large cell neuroendocrine carcinoma (n = 7), solid attenuation (n = 6, 86%) and irregular margin (n = 5, 71%); for non-small cell carcinoma not otherwise specified (n = 5), solid attenuation (n = 4, 80%) and irregular margin (n = 3, 60%); and for large cell carcinoma (n = 1), solid attenuation and spiculated shape (n = 1, 100%). Attenuation most often (in 12 of 21 cases) increased. Margins most often (in 16 of 20 cases) became more irregular or spiculated. Mean VDT was 518 days. Thirteen of 48 cancers had a VDT longer than 400 days; 11 of these 13 cancers were in women.

Conclusion: Overdiagnosis, especially in women, may be a substantial concern in lung cancer screening.

McAdams HP, Samei E, Dobbins J 3rd, Tourassi GD, Ravin CE. Recent Advances in Chest Radiography. Radiology 2006;241:663-83.

There have been many remarkable advances in conventional thoracic imaging over the past decade. Perhaps the most remarkable is the rapid conversion from film-based to digital radiographic (DR) systems. Computed radiography is now the preferred imaging modality for bedside chest imaging. Direct radiography is rapidly replacing film-based chest units for in-department PA and lateral examinations. An exciting aspect of the conversion to DR is the ability to enhance the diagnostic capabilities and influence of chest radiography. Opportunities for direct computer-aided detection (CAD) of various lesions may enhance the radiologist's accuracy and improve

efficiency. Newer techniques such as dual-energy and temporal subtraction radiography show promise for improved detection of subtle and often obscured or overlooked lung lesions. Digital tomosynthesis is a particularly promising technique that allows reconstruction of multisection images from a short acquisition at very low patient dose. Preliminary data suggest that, compared with conventional radiography, tomosynthesis may also improve detection of subtle lung lesions. The ultimate influence of these new technologies will, of course, depend on the outcome of rigorous scientific validation.

1. new digital detector
2. image display technologies
3. image-processing techniques
4. CAD and CADx applications
5. dual-energy and temporal subtraction radiography
6. chest tomosynthesis

Fain SB, Panth SR, Evans MD, Wentland AL, Holmes JH, Korosec FR, O'Brien MJ, Fountaine H, Grist TM. Early Emphysematous Changes in Asymptomatic Smokers: detection with 3He MR Imaging. Radiology 2006;239:875-83.

Purpose: To prospectively compare apparent diffusion coefficient (ADC) measurements derived from diffusion-weighted hyperpolarized helium 3 (^{3}He) MRimaging with functional and structural findings using spirometric tests and thin-section CT of the lungs in asymptomatic smokers and healthy nonsmokers of similar age.

Materials and Methods: All studies were HIPAA compliant and were approved by the institutional review board. Informed consent was obtained. Ventilation and diffusion-weighted ^{3}He MR images were obtained in healthy subjects: 11 smokers (five women, six men; mean age, 47 years ± 18 [standard deviation]; range, 23 - 73 years) and eight nonsmokers (<100 cigarettes in lifetime) (four women, four men; mean age, 46 years ± 16; range, 23 - 69 years). Mean ADC values for smokers and nonsmokers were compared with spirometric values, diffusing capacity of the lung for carbon monoxide (DLCO), age, and pack-years with Spearman rank correlation coefficient (r_s) and multiple linear regression analysis. Mean ADC value and thin-section CT emphysema index of relative area less than -950 HU (RA_{950}) were compared on a regional basis by using linear mixed-effect models.

Results: Mean ADC values and number of pack-years were significantly correlated (r_s = 0.60; 95% confidence interval (CI): 0.21, 1.00; p = .007); relationship remained significant after adjustment for age (p = .003). DLCO was strongly correlated with pack-years (r_s = -0.63; 95% CI: -0.97, -0.29; p = .004). Negative correlations between mean ADC values and percentage predicted DLCO (r_s = -0.79; 95% CI: -0.93, -0.64; p < .001) and the ratio of forced expiratory volume in 1 second to forced vital capacity (r_s = -0.72; 95% CI: -0.92, -0.52; p = .001) were statistically significant. Correlations between spirometric values or RA_{950} and number of pack-years were not significant (.05 level).

Conclusion: Correlations between mean ADC values and pulmonary function test measurements for diagnosing emphysema, especially DLCO, were statistically significant.

References

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