日本核医学会分科会
第 29 回　呼吸器核医学研究会

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会　場：福岡国際会議場　4F　411
会　長：徳島大学大学院　画像情報医学分野
大　塚　秀　樹

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文献レビュー

呼吸器核医学　文献レビュー　2013

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2012 年 10 月から 2013 年 9 月までの 12 か月間の呼吸器核医学に関連する論文を検索した．方法としては，PubMed にて Humans と English を選択し，以下のようなキーワードで検索した．lung scintigraphy, lung SPECT, lung positron emission tomography, pulmonary scintigraphy, pulmonary SPECT, pulmonary positron emission tomography, respiratory scintigraphy, respiratory SPECT, respiratory positron emission tomography．合計 1,772 の論文が該当した．10 年前の 2002 年 10 月から 2003 年 9 月までの 12 ヶ月間についても同様に検索したところ合計 1,261 であり，呼吸器核医学関連の文献の合計数として 4 割程度増加していた．内訳としては，scintigraphy，SPECT で検索される文献数は 998 編から 1,016 編とそれほど変化なく，PET で検索される文献数が 263 編から 756 編へと増加していた．

以下の 10 論文を紹介した．

1. Bajc M, et al. *Eur J Nucl Med Mol Imaging* 2013; 40: 1432–7.
   肺血流 SPECT 単独での肺血栓塞栓症の診断能について検討している．
2. Alhadad A, et al. *Thromb Res* 2012; 130: 877–81.
   肺血栓塞栓症のフォローアップおよび再発の予測に関する肺換気・血流 SPECT の有用性について検討している．
3. Dournes G, et al. *Eur Radiol* 2013 Aug 28.
   慢性血栓塞栓性肺高血圧症の患者の Dual-energy CT パーフュージョンおよび CT アンギオグラフィを肺換気・血流 SPECT と比較して，診断能や区域がどの程度一致するか等について検討している．
4. Mahdavi R, et al. *Ann Nucl Med* 2013 Aug 11.
   臨床的に肺血栓塞栓症が強く疑われている患者での，肺換気・血流 SPECT と CT アンギオグラフィの結果がどの程度一致するのかを検討している．
5. Roach PJ, et al. *J Nucl Med* 2013; 54: 1588–96.
   SPECT や SPECT/CT を用いた肺換気・血流機能画像について検討している．
6. Ohno Y, et al. *AJR Am J Roentgenol* 2012; 199: 794–802.
   肺容量減量手術の術前精査としての酸素造影 MRI と MDCT と SPECT/CT を比較検討している．
7. Sim YT, et al. *Lung* 2013 Sep 8.
   単発の肺結節の PET/CT による良悪の診断能を検討している．
8. Zhang J, et al. *Int J Cancer* 2013 Jul 24.
   肺悪性腫瘍の検出における 3 テスラの MRI の拡散強調画像と FDG-PET/CT を比較検討している．
9. Chandarana H, et al. *Radiology* 2013; 268: 874–81.
   担癌患者の肺結節について PET/MRI 複合機と PET/CT を比較検討している．
10. Kim JY, et al. *J Comput Assist Tomogr* 2013; 37: 596–601.
    侵襲性肺アスペルギルス症と非侵襲性肺アスペルギルス症の FDG-PET/CT による鑑別について検討している．

特　別　講　演

1. Technegas and V/P SPECT: Present and future

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Overview of Ventilation/Perfusion SPECT (V/P SPECT)
Ventilation/Perfusion SPECT (V/P SPECT) is the recommended scintigraphic technique for the diagnosis of *pulmonary embolism* (*PE*) and many other disorders that affect lung function. Moreover, according to *European Association of Nuclear Medicine* guidelines should be the preferred modality whenever possible. Recent studies showed that for the ventilation *Technegas* particles show advantages of over radiolabelled liquid aerosols and are not restricted to the presence of obstructive lung disease. Radiolabelled macroaggregated human albumin is the imaging agent of choice for perfusion scintigraphy. An optimal combination of nuclide activities and acquisition times for ventilation and perfusion, collimators and imaging matrix yields an adequate V/P SPECT study in approximately 20 minutes of imaging time. The recommended protocol based on the patient remaining in an unchanged position during the initial ventilation study and the perfusion study. Apart from pulmonary embolism, other pathologies should be identified and reported, such as broncho-obstructive disease, *left heart failure* (*LHF*), pneumonia and suspicion of other parenchymal process like tumors. Pitfalls exist both with respect to imaging technique and scan interpretation.

V/P SPECT and pulmonary embolism
Pulmonary embolism is a common disease with about 250,000 patients diagnosed each year in the American. In spite of advanced technology it remains a big diagnostic challenge because the clinical symptoms and signs which are frequently observed in pulmonary embolism, are also a feature of other conditions. Accordingly, the initial clinical suspicion needs to be confirmed or negated using a conclusive imaging test. Routinely *Multi-Detector Computed Tomography* (*MDCT*) is suggested as the initial imaging study. However, the latest evidence show that the optimal test is V/P SPECT interpreted with holistic principles according to European Guideline. Before performing imaging tests it is recommended to estimate the clinical probability for pulmonary embolism. Precise predictive model developed by Miniati et al. is recommended. Easy-to-use softwares are also available for computation (palm computer) (e.g. http://www.ifc.cnr.it/pisamodel).

Basic principles of pulmonary embolism diagnosis with V/P SPECT
The lung circulation has a distinct architecture where each broncho-pulmonary segment and sub-segment is supplied by a single end-artery. Emboli are usually multiple, occluding the arteries causing segmental or sub-segmental perfusion defects within still ventilated regions, causing so called mismatch. PE is often a recurring process giving rise to multiple emboli in various stages of resolution.

Reporting findings
Ventilation Perfusion patterns
Large V/P SPECT studies have shown that interpretation of all patterns representing ventilation together with perfusion achieves conclusive reports in 97 to 99% of cases.

An important step in the diagnostic procedure is to quantify the extent of embolism. V/P SPECT is particularly suitable for this because of its greater sensitivity compared to MDCT. The number of segments and sub-segments indicating PE typical mismatch are counted and expressed in percentage of the total lung parenchyma. Furthermore, areas with ventilation abnormalities were recognized and this allowed the degree of total lung malfunction to be estimated. The study showed that patients with up 40% pulmonary embolism could be safely treated at home if ventilation abnormalities engaged not more that 20% of the lung. Outpatient management in hemodynamically stable patients with pulmonary embolism is safe provided that the embolic burden, quantified using V/P SPECT is included in the treatment decision algorithm. In some settings the home treatment based on V/P SPECT has been implemented.

Chronic pulmonary embolism
Chronic pulmonary embolism is a progressive disease that develops in about 1% to 5% after an acute episode of PE, even in treated patients. It might lead to pulmonary hypertension, right heart failure, and arrhythmia, which are frequent causes of death. The value of V/P scintigraphy in this situation is well established. Among patients with pulmonary hypertension, scintigraphy had a sensitivity of 96% to 97% and specificity of 90%, whereas MDCT

had a sensitivity of 51%. All patients with pulmonary hypertension needs to be examined to exclude chronic PE as a cause.

Role of ventilation SPECT in diagnosis of other lung diseases

Chronic obstructive pulmonary disease (*COPD*)

A common alternative or additional diagnosis is COPD. The characteristic is a general unevenness of ventilation. Focal deposition may be observed in central or peripheral airways even when using *Technegas*. A very important fact is that COPD patients are at high risk of pulmonary embolism. The rate of PE in patients hospitalized for acute exacerbations of COPD may be as high as 25%. With V/P SPECT PE can be diagnosed even in the presence of COPD. Pulmonary embolism accounts for up to 10% of deaths in stable COPD patients. The degree of unevenness of aerosol distribution correlated with lung function tests. Significantly, as there are no contraindications to V/P SPECT, even very sick and breathless patients can be studied. It is the only physiological examination and V/P SPECT high sensitivity, was experimentally able to show an obstructive pattern in many apparently healthy smokers.

The method gives the possibility for physiological phenotyping having ability to localize ventilation and perfusion impairment and also estimate the total lung function.

Pneumonia

Pneumonia is also frequent in patients investigated for suspected pulmonary embolism. A typical finding is a ventilation defect in an area usually with better preserved perfusion, known as reverse mismatch. One of the typical patterns, which strongly support the diagnosis of pneumonia, is the “stripe sign”. This refers to maintained perfusion along the pleural surface.

Left Heart Failure

Left heart failure is another diagnosis that is often observed among patients suspected of pulmonary embolism. The typical pattern is anti-gravitational redistribution of perfusion. In consecutive patients with suspected pulmonary embolism, V/P SPECT showed anti-gravitational redistribution of perfusion from posterior to anterior region in 15% of the cases indicating left heart failure. The positive predictive value for heart failure in this study was at least 88%. As ventilation is usually less redistributed than perfusion, V/P mismatch may be observed in dorsal regions. This VP mismatch has a non-segmental pattern.

V/P SPECT versus MDCT

Diagnosis of pulmonary embolism

MDCT is often recommended as the first line test for pulmonary embolism diagnosis. However, the principal study evaluating the use of MDCT as an imaging tool for pulmonary embolism diagnosis shows that sensitivity is not more than 78% and that there are a high number of false positive results when clinical probability is not high.

Advocates for MDCT stress that this method has the advantage over V/P SPECT by allowing also alternative diagnoses. Nevertheless, V/P SPECT provides evidence about alternative diagnoses as well. Actually, a properly performed V/P SPECT interpreted on the basis of all patterns of ventilation and perfusion, frequently allows diagnosis of other pulmonary disease with or without pulmonary embolism and a comprehensive understanding of the patient’s symptoms. This added value of V/P SPECT appears at least as high as for additional diagnosis with MDCT. Further studies are needed in order to demonstrate the clinical impact of alternative diagnoses obtained by both methods.

The lack of a satisfactory gold standard for pulmonary embolism diagnosis poses difficulties for the assessment of sensitivity, specificity and accuracy of all diagnostic methods for pulmonary embolism. The best available point of reference is an adequate follow up of the patients. Moreover, results illustrate well the limited clinical utility of CTPA because of kidney failure, critical illness, recent myocardial infarction, ventilator support and allergy to the contrast agent. By contrast, V/P SPECT has no contraindications and suboptimal studies are very rare. Left heart failure and the degree of obstructivity is only possible so far to identify with V/P SPECT.

Radiation doses

Based upon data from ICRP reports the effective dose for V/P SPECT with the recommended protocol is about 35–40% of the dose from MDCT. The absorbed dose to the female breast for V/P SPECT is only 4% of the dose from MDCT with full dose saving means according to Hurwitz. This may have particular importance in pregnant women with proliferating breast tissue and in the whole generative period. The advantage of V/P SPECT increases after the 1st trimester.

Follow up

Follow up of pulmonary embolism using imaging is essential to assess: a) the effect of therapy, b) to be able to differentiate between new and old pulmonary embolism where there is a suspicion of pulmonary embolism recurrence and c) explain physical incapacity after pulmonary

embolism. These demands for follow up are only met with V/P SPECT. Obviously, the same method should be used for diagnosis and for follow up.

Research

The suitability of an imaging technique for research into pulmonary embolism and its treatment and clinical follow up are in principle the same. However, in research, there are even stronger, ethical, grounds for the use of non-traumatic procedures associated with lowest possible risks.

Hybrid V/P SPECT/CT

The dual modality, might have impact in some group of patients. SPECT/CT may provide a significant contribution to COPD patients where architecture of the lung is changed and remodeled. COPD patients are usually also more prone to complications, such as pulmonary embolism, pneumonia, left heart failure. Moreover, many of these patients have a tendency to develop tumors. These tumors are usually small and could only be visualized with CT. Correlation of perfusion defects on perfusion slices with specific pulmonary arterial branches seen on CT slices and heterogeneous defects on ventilation slices caused by airways changes could be easier to understand and interpret when applying both modalities.

Conclusions

V/P SPECT should be used as a primary tool for the diagnosis of PE because it has the highest sensitivity and accuracy and neither contraindications nor complications. In addition, it produces very few non-diagnostic reports. Furthermore, radiation doses are very low. This is particularly important for women in the reproductive period and during pregnancy. Quantification of V/P allows outpatient treatment.

V/P SPECT is the reference standard for chronic PE.

For COPD it is the only physiological method and is more sensitive for diagnosis than spirometry.

The left heart failure is another great possible indication.

The above mentioned advantages of V/P SPECT for studying pulmonary embolism and co-morbidities imply that it may be the most suitable technique both for follow up in patients with pulmonary embolism as well as for research regarding its treatment and pathophysiology.

2. Dual source dual energy CT の呼吸機能イメージングへの応用

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Dual Energy CT (DECT) とは，異なる管電圧を有する 2 種類の X 線を用いて同時に撮像された CT データから特定の組成を抽出あるいは抑制して画像化する技術である．撮像方法は装置により異なっており，2 管球が搭載された Dual source CT や 1 管球で管電圧を高速に切り替えながら曝射し撮像する装置などがある．当院には Dual source CT が導入されており，日常臨床や研究分野で用いている．

胸部領域における Dual source dual energy CT の応用としては，肺組織や腫瘍内部のヨード分布を表示し，肺野や肺結節の血液量分布を定性的あるいは半定量的に評価することなどが挙げられる．

肺血栓塞栓症診断においては，肺動脈内の塞栓子検出と同時に肺野の血液量分布も把握できるため，臨床的有用性が高い．肺野の血流評価には従来肺血流シンチが施行されてきたが，DECT では肺野の血液量分布をシンチとほぼ同等に評価できると報告されている．また，通常の造影 CT では同定不可能な肺動脈末梢の微細な塞栓子をも同定することが可能となり，肺塞栓の診断と病態把握における有用性が高いと考えられる．

そのほかにも，造影 CT から造影剤成分を除去した仮想非造影画像や，造影剤のみを抽出したヨードマップ，Xe gas を用いた換気 DECT の有用性も報告されている．

またわれわれは DECT を用いた臨床研究で肺血液量画像を半定量的に解析し，急性肺血栓塞栓症患者における右心負荷の評価が可能であることを示した．

本講演では，1) DECT の基礎的原理，2) DECT による肺血液量評価や肺腫瘤の造影効果の評価を始めとした臨床例の紹介，3) DECT 読影におけるピットフォールや被ばくに関しての説明に加えて，4) 研究面に関しても紹介した．