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Medical economics of whole-body FDG PET in patients suspected of having non-small cell lung carcinoma—Reassessment based on the revised Japanese national insurance reimbursement system

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Focusing on the savings expected from the revised Japanese national insurance reimbursement system in the management of patients suspected of having non-small cell lung carcinoma (NSCLC), cost-effectiveness was assessed using decision tree sensitivity analysis on the basis of the 2 competing strategies of whole-body FDG PET (WB-PET) and conventional imaging (CI). ***Methods:*** A WB-PET strategy that models dependence upon chest FDG PET scan, WB-PET scan, and brain MR imaging with contrast was designed. The cost of a FDG PET examination was updated and determined to be US$625.00. The CI strategy involves a combination of conventional examinations, such as abdominal CT with contrast, brain MR imaging with contrast, and a whole-body bone scan. A simulation of 1,000 patients suspected of having NSCLC (Stages I to IV) was created for each strategy using a decision tree and baselines of other relevant variables cited from published data. ***Results:*** By using the WB-PET strategy in place of the CI strategy for the management of patients suspected of having NSCLC in hospitals with an NSCLC prevalence of 75%, the cost saving (CS) for each patient would be US$697.69 for an M1 prevalence of 20% and US$683.52 for an M1 prevalence of 40%, but the CS gradually decreases as the NSCLC prevalence increases. The break-even point requires less than an 80% prevalence in order for the WB-PET strategy to gain life expectancy (LE) per patient. By using the WB-PET strategy in place of the CI strategy for the management of patients suspected of having NSCLC in hospitals with an NSCLC prevalence of 75%, the gain in LE for each patient would be 0.04 years (11.06 vs. 11.02 years) for an M1 prevalence of 20% and 0.10 years (10.13 vs. 10.03 years) for an M1 prevalence of 40%. The maximum cost of a PET study without losing LE would be US$1322.68 per patient for prevalences of 75% NSCLC and 20% M1 disease. ***Conclusions:*** The present study quantitatively showed WB-PET, employed in place of CI for managing NSCLC patients, to be cost-effective in the Japanese revised insurance reimbursement system. However, the present cost is very low from the industrial viewpoint.

Key words: cost-benefit, ^{18}F-FDG, lung cancer, staging

INTRODUCTION

A LARGE NUMBER of PET systems have been introduced in hospitals and nuclear medicine facilities around the world. Recently, approximately 50 PET systems have been installed in Japan despite the enormous capital allocation necessary for its installation. However, national insurance reimbursement of PET studies was not approved yet, except for PET examination with ^{15}O gas, by the Japanese Ministry of Health, Labor and Work. The principal reason for the Ministry not approving insurance reimbursement of costly PET studies is probably that it accelerates the serious economic problem of rising health-care costs in Japan. Thus, the harsh medical environment has hindered the wide spread usage and development of clinical

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PET studies.

Many Japanese nuclear medicine specialists have expected for a long time that the Japanese Ministry would allow cost reimbursement at approximately 130,000 yen (US$1,083.00) for a 2-[^{18}F]fluoro-2-deoxy-D-glucose (FDG) PET examination. Unexpectedly, the Japanese Ministry decided the reimbursement cost at 75,000 yen (US$625.00) for a FDG PET examination for differential diagnosis and staging of ten forms of malignant neoplasmas, localization of an epileptic focus, and assessment of myocardial viability. PET was added to the list of the national insurance reimbursement system on April 1, 2002.[1] This reimbursement cost is very low as compared to costs in the United States and the European countries. We already published the documentation, which concluded that the introduction of a whole-body FDG PET (WB-PET) strategy in place of a conventional imaging (CI) strategy for managing non-small cell lung carcinoma (NSCLC) patients is potentially cost-effective in Japan.[2] It is important to reassess to what extent the low cost of a FDG PET examination is cost-effective, macroeconomically.

Focusing on the savings expected from introduction of this national insurance reimbursement system in the management of patients suspected of having NSCLC, the cost-effectiveness of this new system was assessed using decision tree sensitivity analysis on the basis of the 2 competing strategies of WB-PET and CI. In addition, we also evaluated to what extent the framework mandated by the revised reimbursement system would allow us to raise a FDG PET study cost without losing life expectancy (LE) of patients with NSCLC.

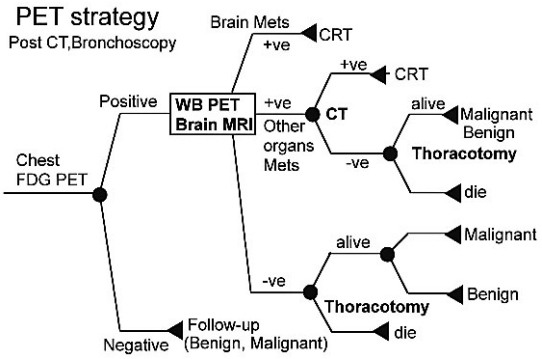

Fig. 1 Decision-tree for the WB PET (whole-body FDG PET) strategy in a simulation of 1,000 patients suspected of having NSCLC. CRT = chemoradiotherapy. +ve = positive. –ve = negative. Mets = metastasis.

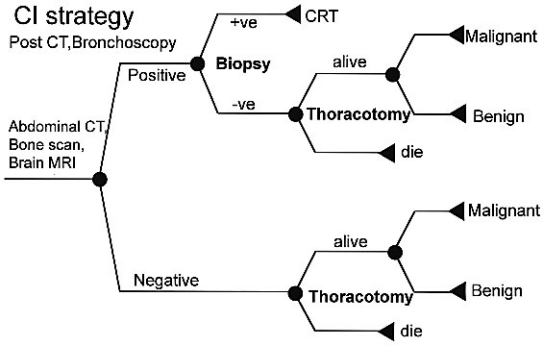

Fig. 2 Decision-tree for the CI (conventional imaging) strategy in a simulation of 1,000 patients suspected of having NSCLC. CRT = chemoradiotherapy. +ve = positive. –ve = negative. Mets = metastasis.

MATERIALS AND METHODS

The current study was built upon and revised by the analysis performed in our previously published report on the cost-effectiveness of FDG PET in the management of patients suspected of having NSCLC.[2–4] To determine the expected cost savings (CS) and expected gain in LE, a decision tree analysis was redesigned on the basis of the 2 competing strategies of conventional imaging (CI) and WB-PET for selection of potential surgical candidates. A WB-PET strategy that models dependence upon chest FDG PET scan using a three-dimensional acquisition mode, WB-PET scan using a two-dimensional acquisition mode, and brain MR imaging (MRI) with contrast was designed (Fig. 1). The cost of a FDG PET examination, which includes both chest PET and WB-PET, was updated and determined to be 75,000 yen (US$625.00). The decision tree for the WB-PET strategy does not encompass certain examinations, i.e. chest CT scan, transbronchial lung biopsy and transcutaneous needle biopsy of the lung, because the insurance reimbursement of PET studies is strictly limited to patients suspected of having lung cancer who have already undergone such examinations but whose diseases have not yet been pathologically proven. Chest PET is usually performed when differential diagnosis is required and WB-PET and brain MRI are for preoperative staging in patients suspected of having NSCLC. Thus, all patients who are only positive on chest FDG PET, eventually receive both a WB-PET and a brain MRI examination as part of the WB-PET strategy, which has recently been introduced in hospitals throughout Japan. Every patient whose WB-PET examination is positive for distant metastasis (M1 disease), receives a CT study to confirm the metastasis.

The CI strategy for preoperative staging in patients suspected of having NSCLC means a combination of conventional examinations: abdominal CT with contrast, brain MRI with contrast, and whole-body skeletal scintigraphy.[4–6] This combination of examinations has been performed nationwide for the initial staging for NSCLC patients. The CI strategy is also adopted for patients suspected of having NSCLC and whose diseases have not yet been pathologically proven, except NSCLC patients with definite N3 and/or M1 on chest CT. All of the patients whose CI studies are positive for M1 disease, receive biopsy to confirm metastasis (Fig. 2).

Table 1 Baseline of all relevant variables used in the decision tree

CI strategy		
Prevalence of lung cancer: 75%		
Prevalence of metastasis: 20%, 40%		
Sensitivity for detecting metastasis in CI: 90%		
Specificity for detecting metastasis in CI: 90%		
PET strategy		
Prevalence of lung cancer: 75%		
Prevalence of metastasis: 20%, 40%		
Sensitivity for detecting lung cancer in chest PET: 96.3%		
Specificity for detecting lung cancer in chest PET: 78.6%		
Sensitivity for detecting metastasis in WB PET and brain MRI: 90%		
Specificity for detecting metastasis in WB PET and brain MRI: 90%		
Mortality (%)		
PET	0	
CT	0.0025	
Thoracotomy	3.0	
Life Expectancy (yr)		
NSCLC		
Surgical cure		7.0
Follow-up in pts with surgically curable disease		1.0
Follow-up/Chemoradiotherapy/thoracotomy in pts with M		0.5
Benign disease		28.2
Cost (yen)		
Bone scan	41,490	
Brain MRI with contrast	30,670	
Abdominal CT with contrast	33,540	
FDG PET	75,000	
Thoracotomy	331,450	
Excisional biopsy	32,450	

A simulation of 1,000 patients suspected of having NSCLC (Stages I to IV) was created for each strategy using a decision tree and baselines of other relevant variables (Table 1). Mediastinoscopy was not incorporated into each of these strategies. In general, pulmonologists and thoracic surgeons in Japanese hospitals do not perform mediastinoscopy, or perform it less often in patients with NSCLC.

Sensitivities and specificities of CI, chest PET, WB-PET, mortalities, and LE were cited from published data[2] (Table 1). The LE of the patients with benign disease, who were expected to achieve their full LE, was based on our published data.[2,3] The prevalence (pretest likelihood) of M1 disease was assumed to be 20% or 40%, so that there might be a wide difference of the results. Biopsy was assumed to have a 100% accuracy rate. The prevalence of NSCLC varied within a reasonable range, but the prevalence of distant diseases was fixed for both decision tree analyses. The exact probability of each outcome in the decision trees was calculated using Bayesian theory.[7]

The medical examination costs in Japanese yen were based on the revised established insurance reimbursement system bills. A hospital charge and extra costs related to examinations and surgical procedures were not included in the current study. The cost in U.S. dollars was calculated at a yen-to-dollar conversion rate of ¥120 to $1.

Sensitivity analysis

The accuracies of CI and WB-PET in detecting distant metastatic foci (M1 disease) have not been well documented, even though these values may have a great influence in the clinical setting and vary among institutions.[8–11] The prevalence of NSCLC can also vary according to the institution. Therefore, one-way sensitivity analyses to determine the influence of NSCLC prevalence values on the CS and gain in LE were performed for the CI strategy versus the WB-PET strategy. Referring to the published literature,[8–11] WB-PET and CI were each assumed to have a 90% sensitivity and a 90% specificity for detecting M1 disease on a patient-by-patient basis (not a focus-by-focus basis). In these analyses, an NSCLC prevalence of 75% was highlighted because our hospital has a prevalence of approximately this value. We calculated the net costs minus the costs of hospitalization, radiotherapy and chemotherapy. In general, we do not hospitalize patients for imaging studies and/or chemoradiotherapy.

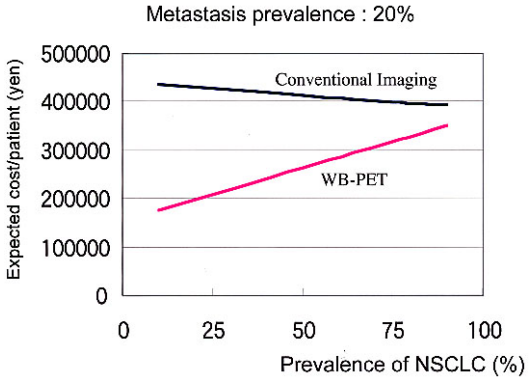

Fig. 3 Results of the one-way sensitivity analysis for NSCLC prevalence values ranging from 10% to 90% on the expected cost per patient enabled in the CI strategy vs. the WB-PET strategy, when a prevalence of M1 disease is 20%.

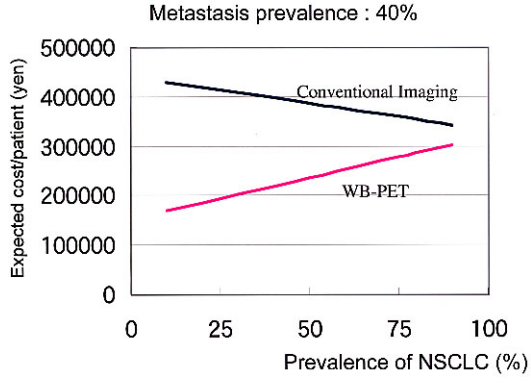

Fig. 4 Results of the one-way sensitivity analysis for NSCLC prevalence values ranging from 10% to 90% on the expected cost per patient enabled in the CI strategy vs. the WB-PET strategy, when a prevalence of M1 disease is 40%.

The maximum cost without loss of LE

We evaluated to what extent the framework mandated by the revised reimbursement system would allow us to raise a FDG PET study cost without losing LE of patients with NSCLC.

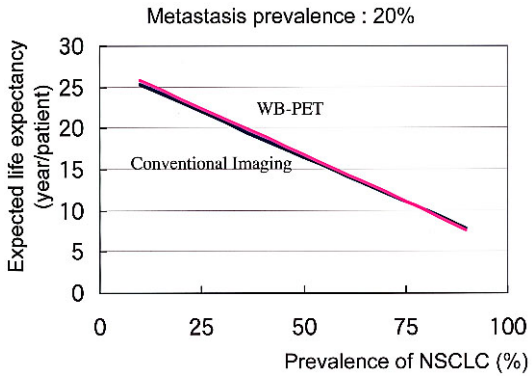

Fig. 5 Results of the one-way sensitivity analysis for NSCLC prevalence values ranging from 10% to 90% on the expected LE per patient for the CI strategy vs. the WB PET strategy, when a prevalence of M1 disease is 20%.

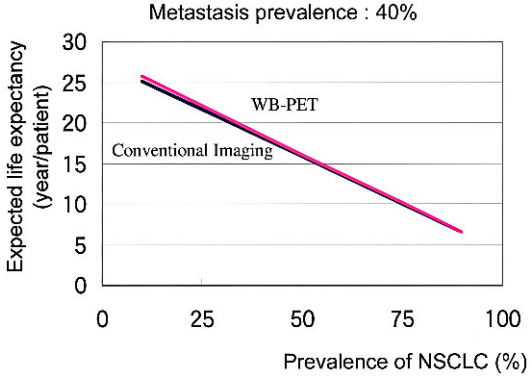

Fig. 6 Results of the one-way sensitivity analysis for NSCLC prevalence values ranging from 10% to 90% on the expected LE per patient for the CI strategy vs. the WB PET strategy, when a prevalence of M1 disease is 40%.

RESULTS

Figures 3 and 4 show the one-way sensitivity analysis for NSCLC prevalences, ranging from 10% to 90% for the expected costs per patient for the CI strategy versus the WB-PET strategy. The prevalence of M1 disease is 20% in Figure 3 and 40% in Figure 4. The expected costs per patient in the WB-PET strategy increase as the NSCLC prevalence increases, because the numbers of thoracotomies for curable disease and the numbers of MRI and CT studies increase as the NSCLC prevalence increases. On the other hand, the expected costs per patient with the CI strategy slightly decrease as the NSCLC prevalence increases, because the numbers of unnecessary thoracotomies for benign disease decrease, though the numbers of less costly biopsies increase, as the NSCLC prevalence increases.

As a matter of course, the number of thoracotomies for benign disease increased as the NSCLC prevalence value decreased. The CI strategy had 900 thoracotomies for benign disease at prevalences of 10% NSCLC and 20% M1 disease, and 100 at prevalences of 90% NSCLC and 20% M1 disease. On the other hand, the WB-PET strategy had 188 thoracotomies for benign disease at prevalences of 10% NSCLC and 20% M1 disease, and 21 at prevalences of 90% NSCLC and 20% M1 disease. As for unnecessary thoracotomy for M1 disease, there was little or no difference between the two strategies. Both the CI strategy and the WB PET strategy had 2 thoracotomies for M1 disease at prevalences of 10% NSCLC and 20% M1 disease. The CI strategy had 18 unnecessary thoracotomies for M1 disease and the WB PET strategy had 17 at prevalences of 90% NSCLC and 20% M1 disease.

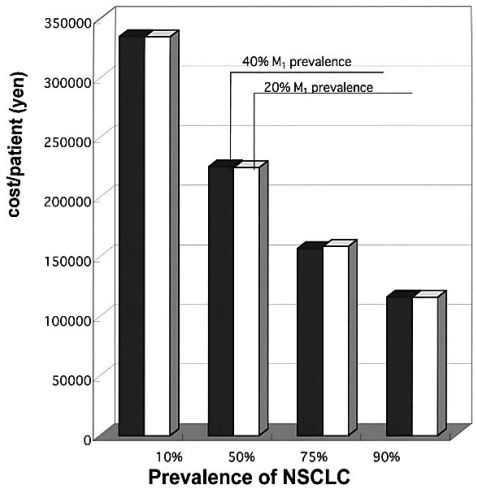

Fig. 7 The maximum costs of a FDG PET study without losing life expectancy for NSCLC prevalences of 10%, 50%, 75%, and 90%, on the basis of the framework mandated by the revised insurance reimbursement system.

Using the WB-PET strategy in place of the CI strategy for the management of patients suspected of having NSCLC in hospitals with an NSCLC prevalence of 75%, the CS for each patient would be ¥83,723 (US$697.69) for an M1 prevalence of 20% and ¥82,022 (US$683.52) for an M1 prevalence of 40%, but the CS gradually decreases as the NSCLC prevalence increases.

Figures 5 and 6 show the one-way sensitivity analysis for NSCLC prevalences, ranging from 10% to 90% for the expected LE per patient for the CI strategy versus the WB-PET strategy. The prevalence of M1 disease is 20% in Figure 5 and 40% in Figure 6. The expected LE per patient with both strategies decreases as NSCLC prevalence increases. This is as expected because the number of NSCLC patients increases and the number of benign disease patients decreases as the NSCLC prevalence increases. The two lines cross each other at an NSCLC prevalence of approximately 80% (break-even point) with an M1 disease prevalence of 20% and 40% each. The break-even point requires less than an 80% prevalence in order for the WB-PET strategy to gain LE per patient. Using the WB-PET strategy in place of the CI strategy for the management of patients suspected of having NSCLC

in hospitals with an NSCLC prevalence of 75%, the gain in LE for each patient would be 0.04 years (11.06 vs. 11.02 years) for an M1 prevalence of 20% and 0.10 years (10.13 vs. 10.03 years) for an M1 prevalence of 40%.

The maximum cost of a FDG PET study without losing LE on the basis of the framework mandated by the revised insurance reimbursement system would be ¥334,689 (US$2,789.07) per patient for prevalences of 10% NSCLC and 20% M1 disease, ¥334,940 (US$2,791.16) per patient for prevalences of 10% NSCLC and 40% M1 disease, each (Fig. 7). The maximum cost would decline as a prevalence of NSCLC decreases, and be ¥158,772 (US$1,322.68) per patient for prevalences of 75% NSCLC and 20% M1 disease.

DISCUSSION

Early detection of remote metastasis is crucial for patients with lung cancer since those with M1 disease are not candidates for curative thoracotomy. M1 disease detection is an important role of WB-PET. CI, i.e., a combination of skeletal scintigraphy, abdominal CT with contrast, and brain MR imaging with contrast, for staging of lung cancer has been performed widely in Japan. It is cumbersome, time-consuming, and costly for patients suspected of having lung cancer to undergo this combined study. Furthermore, the patients may suffer from significant morbidities associated with contrast materials.

Cost-effectiveness analyses may only be valid temporarily, principally because reimbursement costs can be changed at any time and the prices of medical equipment including computer hardware should decrease with advances in technology. This is why cost-benefit analyses should be updated whenever medical costs or insurance reimbursement systems change. Consistent and ongoing assessment of the appropriate balance between medical cost and patient outcome is one of the central issues of medical economic analysis.

Our newly devised WB-PET strategy is based on the regulations, indications, and cost for FDG PET examinations, which the Japanese Ministry of Health, Labor, and Work introduced for national insurance reimbursement. The Ministry revised and newly stipulated ten forms of malignant neoplasms (lung cancer, cerebral tumor, head and neck cancer, breast cancer, pancreatic cancer, intrahepatic metastasis, malignant lymphoma, melanoma, colorectal cancer, and primary unknown cancer), as well as the indications and cost for FDG PET examinations.[1] The cost of a FDG PET examination was set at 75,000 yen (US$625.00), which is the lowest worldwide and is approximately one third or a half of the cost in the Unites States and European countries. While a patient with lung cancer is a suitable candidate, the insurance reimbursement of PET studies is strictly limited to patients suspected of having lung cancer, who have already undergone chest CT and/or MRI examinations, transbronchial lung biopsy or transcutaneous needle biopsy of the lung but whose diseases have not yet been pathologically confirmed, or to patients with pathologically confirmed lung cancer, whose staging has not yet been established by morphological imaging.

The use of a single WB-PET study for the staging of NSCLC is expected to be somewhat limited. FDG PET has been documented to be inferior to brain MRI in detecting cerebral metastases.[8–12] Because of the high glucose uptake by the normal brain and small cerebral metastases in general, the sensitivity of WB-PET for detecting brain metastasis is not particularly high. In our series, therefore, brain MRI was incorporated into one arm of the WB-PET strategy tree. FDG uptake is generally low in mucinous or bronchioloalveolar cell carcinoma.[13] Patients with a pulmonary nodule, which exhibits little or no uptake, should be placed on a regular recall schedule and be more judiciously followed up. It is uncertain whether all skeletal metastases can be seen in a WB-PET study. Whether bone scan can be totally omitted is controversial.[14,15] Patients with bone pain, who have negative finding in a PET study, may undergo bone scan.

As for unnecessary thoracotomy for M1 disease, there was little or no difference between the two strategies. However, the number of thoracotomies for benign disease increased as the NSCLC prevalence decreased. The CI strategy had 900 thoracotomies for benign disease at prevalences of 10% NSCLC and 20% M1 disease, and 100 at prevalences of 90% NSCLC and 20% M1 disease. On the other hand, the WB-PET strategy had 188 thoracotomies for benign disease at prevalences of 10% NSCLC and 20% M1 disease, and 21 at prevalences of 90% NSCLC and 20% M1 disease.

In the CI strategy, low NSCLC prevalences resulted in high cost expectations because all patients with benign disease ended up undergoing unnecessary thoracotomies. The WB-PET strategy reduced the number of benign disease thoracotomies to approximately 20%, accruing CS. There was little or no difference between the two strategies in unnecessary thoracotomy for M1 disease. Thus, the introduction of WB PET in place of the combined studies of CI would allow unnecessary thoracotomies and surgical deaths to be avoided, thereby lowering the prevalence.

A gain in the expected LE was observed with the introduction of WB-PET in place of the CI strategy, but with a break-even point at an NSCLC prevalence of approximately 80%. The break-even point requires less than 80% prevalence in order for the WB-PET strategy to gain LE. In other words, life loss would hinder hospitals with NSCLC prevalences greater than 80% performing FDG PET studies, despite the CS.

Our results, derived from the revised insurance reimbursement system with a low cost for a PET study, are focused on improving the situation of patients suspected of having NSCLC. Generally speaking, macroeconomists

who are interested in the development of medical policy may recommend in favor of cutting examination costs. By contrast, microeconomists recommend against cutting examination costs, simply because they are interested in industrial policy rather than medical policy. Examination cost cutting would worsen the conditions of hospital and pharmaceutical managers, possibly abolishing increased incentives to install a PET system. The examination cost increase is thus reversed. At any rate, the most important point, we believe, is the patient outcome resulting from the introduction of a new strategy, if the cost is within a reasonable range.

The maximum cost of a FDG PET study without losing LE on the basis of the framework mandated by the revised insurance reimbursement system would be ¥158,772 (US$1,322.68) per patient for prevalences of 75% NSCLC and 20% M1 disease. The cost is perhaps reasonable from the industrial viewpoint, though the cost is twice as much as the present cost.

Last but not least, the use of WB-PET for the staging of NSCLC remains economically variable, differing among countries where there are many options to choose from. The savings we calculated from the decision tree sensitivity analysis were not as great as those in published data.[4,16,17] The strategies, costs, and variables, which have been described herein, are regulated by the Japanese Ministry. However, we believe that a newly introduced WB-PET strategy would be cost-effective even in other countries, given that some morphological imaging studies for staging could be replaced by a single WB PET study. To determine how society's resources are allocated within the scientific realm of medical economics, we highly recommend that cost-effectiveness of the WB-PET strategy be assessed in each country for the management of patients suspected of having NSCLC because lung cancer is a leading cause of cancer death worldwide.

In conclusion, the present study, designed from the viewpoint of "positive economics," quantitatively showed WB-PET in place of CI for managing NSCLC patients to be cost-effective in the Japanese revised insurance reimbursement system. However, the present cost is very low from the industrial viewpoint.

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This article principally describes the cost-effectiveness of whole-body PET, in the management of patients with non-small cell lung carcinoma (NSCLC), focusing on the savings expected from the revised Japanese national insurance reimbursement (RJNIR) system. We also evaluated to what extent the framework mandated by the RJNIR system would allow us to raise a FDG PET study cost without losing life expectancy of patients with NSCLC.

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