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Alternative imaging strategy of solitary pulmonary nodule by FDG PET/CT
Can be imagined a tailored PET?

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ABSTRACT

Objective: Patients with solitary pulmonary nodule (SPN) are usually sent to total-body positron emission tomography/computed tomography (PET/CT) examination with 18F-fluorodeoxyglucose (FDG). However, a segmental scan strategy may improve cost/effectiveness in this category of patients.
Conclusion: A segmental PET/CT scan only at the chest level could be performed in patients with indeterminate SPN. Limiting the PET/CT field to the thoracic region would greatly affect on radiobiology, department organization and health-care costs.

1. Introduction

The characterization of solitary pulmonary nodules (SPN) detected incidentally represents an important public health issue. Management of these nodules is described in many International guidelines, providing different invasive and non-invasive approaches in accordance with the risk of an underlying lung cancer. Thoracic computed tomography (CT) is the most common recommended imaging modality when screening for lung cancer in high-risk populations [1]. Hybrid positron emission tomography (PET)/CT combines the two imaging modalities to acquire fundamentally anatomic and morphological information (CT) together with metabolic and molecular features consistent with the increasing demands for personalization of healthcare (PET). Although PET/CT is fully integrated into the clinical guidelines [2,3] and represents an advantageous modality of diagnostic imaging, its role in the algorithm of SPN is influenced by different parameters, such as the exposure to ionizing radiation, the risk of over-diagnosis and over-treatment and cost/effective ratio, which is directly related to the appropriateness and justification. The editorial has been conceived to address the opportunity to perform a segmental PET/CT acquisition in patients with SPN. The discussion is based on the assumption that a segmental PET/CT scan might have valuable effects on radiobiology, health economy and hospital organization.

2. Patient selection criteria (pre-test probability of malignancy)

The pre-test likelihood of lung nodule malignancy can be determined based on the clinical (age, smoker status, familiarity, and history of cancer) and CT (nodule diameter, shape, and location) characteristics of the patients. Thus, the probability of cancer can be evaluated based on statistical models that include clinical and instrumental data, such as the nodule malignancy prediction calculator by Brock University (available at link: https://brocku.ca/lung-cancer-risk-calculator). Numerous algorithms have been created for the definition of malignancy likelihood (Table 1). As shown, the most common definition is: very low likelihood (<5%), low to moderate or intermediate likelihood (5–65%) and high likelihood (>65%) of malignancy. The estimated probability of malignancy represents a useful tool for evaluating how to manage patients with indeterminate lung nodules. The latest recommendations from the American College of Chest Physicians suggest employing different clinical and instrumental approaches in accordance with the size of lung nodules [2]. For example, individuals with solid nodules measuring

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Table 1
Definition of lung malignancy likelihood.

Authors	Year	Classification	Categories
MacMahon et al. [4]	2005	Fleischer Society	- Low (minimal or absent history of smoking and other known risk factors) - High (history of smoking or of other known risk factors)
Gould et al. [5]	2007	ACCP 2nd ed.[a]	- Low (<5%) - Intermediate (5–60%) - High (>60%)
Gould et al. [2]	2013	ACCP 3rd ed.[b]	- Low (<5%) - Intermediate (5–65%) - High (>65%)
Callister et al. [3]	2015	British Thoracic Society[c]	- <10% - >10%
Walter et al. [6]	2016	Nelson trial[d]	- Low (<3.7 mm) - Intermediate (<8.2 mm) - High (≥8.2 mm)

ACCP = American College of Chest Physicians.
[a] Based on clinical data.
[b] Based on clinical factors, FDG PET results, non-surgical biopsy results and CT scan surveillance.
[c] Morphological nodule characteristics and Brock model, only for lung nodules with a diameter ranging between 8 and 30 mm.
[d] Based on the axial diameter of the lung nodule.

between 8 and 30 mm and with a low/moderate or a high likelihood of malignancy should be managed by performing imaging tests, such as PET/CT with 18F-fluorodeoxyglucose (FDG) to better characterize the nodule, nonsurgical biopsy or surgical diagnosis. The imaging and invasive indications should be evaluated with respect to the clinical history of the patients.

3. Current guidelines

Clinical guidelines are considered useful recommendations for the management of patients. Several National and International guidelines are available. The management of patients with lung nodules is very difficult, due to heterogeneity of clinical conditions and the nature of lung lesions. One of the most important considerations is the different approaches in the management of lung nodules in patients with a previous malignancy and those without. Usually, these latter subsets of patients are considered at lower risk of lung malignancy, although the size and other morphological characteristics of pulmonary nodule can significantly affect the diagnosis. PET/CT is usually recommended in some categories of patients, based on the pre-test likelihood of malignancy (see the previous paragraph). Table 2 reports the recommendations for PET/CT in accordance with the most useful guidelines for the management of lung nodules. PET/CT is mainly recommended to characterize SPN >8 mm in diameter in patients with low to moderate pretest probability of malignancy [2–4]. However, the British Thoracic Society guidelines recommend PET/CT in young patients, also in the case of low risk of malignancy [3]. Conversely, neither the European Association of Nuclear Medicine (EANM) nor the Society of Nuclear Medicine and Molecular Imaging (SNMMI) guidelines provide a recommendation for the execution of PET/CT in patients with SPN [7,8].

Table 2
International guidelines for the recommendation of PET/CT in the management of lung nodules.

Guidelines	PET/CT recommendations
Fleischer Society [4]	In patients with a lung nodule >8 mm in diameter, PET/CT should be performed both in patients with low and high risk of malignancy
ACCP [2]	In patients with new, solid, indeterminate nodule on chest CT, 8–30 mm, and with low/moderate or high probability of cancer, PET/CT is recommended
British Thoracic Society [3]	If risk of malignancy is <10%, PET/CT should be performed for larger nodules in young patients. In patients with >10% risk of malignancy, PET/CT is recommended for staging only in patients with a high pretest probability of malignancy
SNMMI [7]	No specific indications
EANM [8]	No specific indications

SNMMI = American Society of Nuclear Medicine and Molecular Imaging; EANM = European Association of Nuclear Medicine.

4. Radiobiological considerations

In recent years, medical exposure to ionizing radiation has rapidly increased due to the growth in procedure volumes and the high radiation doses of some more complex procedures, such as PET/CT. The effective dose from PET/CT ranges from 10 mSv to 32 mSv, with CT contributing for a percentage between 54% and 81% of the total [9,10]. An effective dose of 14 mSv produced from FDG-PET/CT is associated with an excess radiogenic cancer death risk of 0.07% up to 0.62% [11]. In PET/CT, the radiation dose depends on several issues, such as dose of the injected radiotracer, X-ray energy and the extension of CT scanned area. A reduction of both FDG administered dose and X-ray exposure may have important implications with respect to the basic pillars of radiation protection (ALARA criteria): radiation doses should be kept as low as reasonably achievable.

5. Economic analysis

In recent years, serious concerns have emerged over the rising health care costs, particularly for sophisticated imaging techniques [12], whose cost growth is at a higher rate than overall health care costs [13]. All innovative imaging modalities require more expensive equipment, contrast media or radiopharmaceuticals, and longer acquisition time, particularly when additional procedures other than the standard ones are clinically valuable [14,15]. In case of PET/CT, radiotracers are expensive and the rapid physical time