

# Can calcified pulmonary metastases detected by $^{18}\text{F}$ -FDG PET/CT suggest the primary tumor?

Chae Moon Hong, MD, Byeong-Cheol Ahn, MD, PhD

Department of Nuclear Medicine, Kyungpook National University School of Medicine and Hospital, Daegu, Republic of Korea

Byeong-Cheol Ahn, MD, PhD, Professor, Director of Department of Nuclear Medicine, Kyungpook National University School of Medicine and Hospital 50, Samduk 2-ga, Jung Gu, Daegu, 700-721, Republic of Korea. abc2000@knu.ac.kr

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## Abstract

Many calcified nodules are encountered on the  $^{18}\text{F}$ -FDG PET/CT scan and even though most of them are benign, the possibility of calcified pulmonary metastases (CPM) should be considered. The CT portion can often differentiate benign diseases due to their morphology. Measuring SUVmax is very important. Understanding the mechanism of calcification in malignant metastatic pulmonary lesions may be useful to suggest their origin.

Recently, fluorin-18-fluorodeoxyglucose positron emission tomography/computerized tomography ( $^{18}\text{F}$ -FDG PET/CT) has been widely used to detect metastatic lesions in various cancers, and the lungs are a common site for metastasis. Typical findings of pulmonary metastases are many like, variable-sized round nodules located in the peripheral portion of the lungs indicating haematogenous metastases, or diffuse thickening of the interstitium indicating lymphangiitic carcinomatosis [1]. The avidity of the tracer in these metastases is variable according to the biologic characteristics of the primary cancer. Diffuse, lobar, or segmental  $^{18}\text{F}$ -FDG uptake in the lungs is seen in the extensive type of lymphangiitic carcinomatosis, while there is a linear or hazy area of  $^{18}\text{F}$ -FDG uptake in the limited type [2].

Unusual types of lung metastases, such as calcified pulmonary metastases (CPM), are not infrequently encountered in patients with advanced stages of malignancy. Computerized tomography is the best way to detect calcification, and many typical CT findings are suggested to differentiate benign pulmonary nodules from CPM [1,3]. However, calcification or ossification can also occur in metastatic nodules. Most CPM originate from primary sarcomas, such as osteosarcoma, chondrosarcoma, synovial sarcoma, giant cell tumor of the bone, malignant mesenchymoma, fibrosarcoma of the breast, mucinous adenocarcinoma of the gastrointestinal tract and breast, cystadenocarcinoma of the ovaries, papillary thyroid carcinoma, and medullary thyroid carcinoma [1, 4].

Several mechanisms are suggested for the calcification of metastatic pulmonary nodules, including: a) Bone formation like in osteosarcoma or chondrosarcoma, b) Dystrophic calcification as in papillary thyroid carcinoma, in giant cell tumor of the bone, in synovial sarcoma, or in treated metastatic tumors and c) Mucoïd calcification in mucinous adenocarcinoma of the gastrointestinal tract and breast [1, 5].

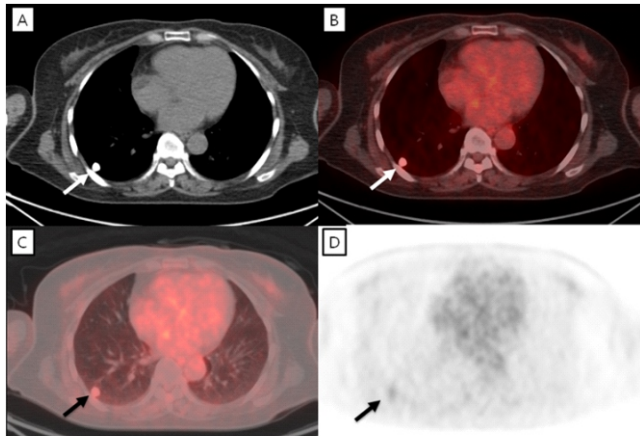
Radiographic features of CPM in CT have been previously described [1, 4, 5], but there were few published data of  $^{18}\text{F}$ -FDG uptake patterns of CPM. In this review, we will approach the patterns of  $^{18}\text{F}$ -FDG uptake according to the pathophysiologic mechanisms of CPM.

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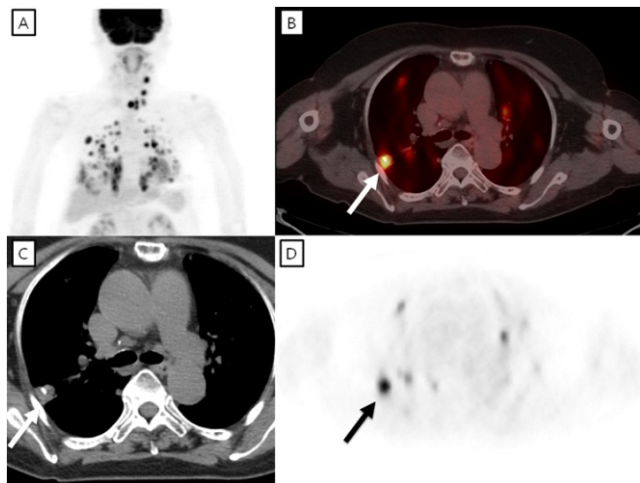
Bony formation produced by osteosarcoma or chondrosarcoma is the most common type of CPM. Calcification is the result of bone formation in the osteoid matrix produced by malignant osteosarcoma cells. In chondrosarcoma tumor cartilage is converted to bone [5]. In a recent systemic review and meta-analysis of bone sarcoma (including osteosarcoma, chondrosarcoma and others) [6],  $^{18}\text{F}$ -FDG PET/CT showed high sensitivity (88%) and higher specificity (98%) in detecting lung metastases caused by bone sarcoma. In osteosarcoma, maximum standardized uptake value (SUVmax) of lung metastases has been reported to be 0.4-6.3 [7]. The value of SUVmax of lung metastases in chondrosarcoma was reported to be from background level to 7.3 [8]. Although these studies did not perform a subgroup analysis of CPM from bone sarcoma,  $^{18}\text{F}$ -FDG PET/CT seems to be helpful for the diagnosis of bone sarcoma-related CPM. Figure 1 shows a focal hypermetabolic CPM from osteosarcoma.

Dystrophic calcification occurs in papillary thyroid carcinoma, medullary thyroid carcinoma, giant cell tumors, and synovial sarcoma. There is deposition of calcium in areas of necrosis and degeneration. Sometimes, dystrophic calcification can progress to heterotopic bone formation [5]. In lung metastases of papillary thyroid carcinoma, the range of SUVmax is from background to 28.3 [9]. Figure 2 shows multiple metastatic lesions of papillary thyroid carcinoma. One of the metastatic nodules contains calcium deposition, which might be associated with dystrophic calcification due to presence of the cancer

for a long period of time.



**Figure 1.** A 57 years old female patient with osteosarcoma in the left limb underwent tumor excision and limb salvage operation, followed by chemotherapy. <sup>18</sup>F-FDG PET/CT showed calcified pulmonary metastases (CPM). A) Non-enhanced CT of PET/CT showed a dense, calcified nodule in the peripheral portion of the right lower lung field. B), C) Fusion <sup>18</sup>F-FDG PET/CT showed <sup>18</sup>F-FDG avidity the CPM. D) <sup>18</sup>F-FDG PET image showed focal <sup>18</sup>F-FDG uptake in the CPM with SUVmax 2.5.



**Figure 2.** A 70 years old female patient with papillary thyroid carcinoma and multiple lung and lymph node metastases who 7 years prior, underwent total thyroidectomy with lymph node dissection and multiple rounds of high-dose radioiodine therapy (total 25.9GBq). Unfortunately, there was no radioiodine uptake in metastatic lesions. However, A) a maximal intensity projection image of <sup>18</sup>F-FDG PET/CT showed multiple hypermetabolic lesions in the cervical and lung areas, suggesting lymph node and lung metastases. B) Multiple hypermetabolic lung nodules are visualized in fusion <sup>18</sup>F-FDG PET/CT. C) Non-enhanced CT showed a metastatic nodule with calcification in the right upper lobe. D) <sup>18</sup>F-FDG PET showed focal <sup>18</sup>F-FDG uptake (SUVmax 9.5) by the calcified pulmonary metastases.

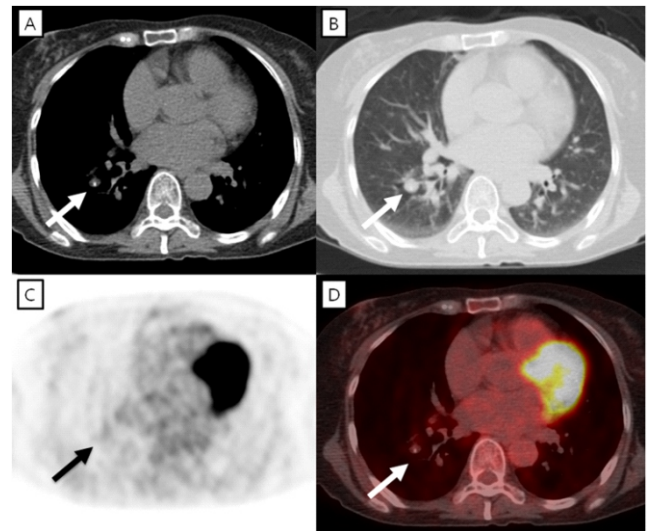
Mechanism about CPM from medullary thyroid carcinoma is also considered as dystrophic calcification [10]. Figure 3 shows CPM with SUVmax of 1.6 from medullary thyroid carcinoma. Calcification of the metastatic lesion might be associated with previous chemotherapy, with iodine 131-metaiodobenzylguanidine (<sup>131</sup>I-MIBG) and long standing of the cancer (for more than 10 years).

As the <sup>18</sup>F-FDG uptake of giant cell tumors is variable, it is

difficult to distinguish whether the tumor is benign or malignant. Several case reports of lung metastases from giant cell tumors showed that SUVmax was between 2.9-4.9 [11, 12].

**Table 1.** Mechanism, origin and <sup>18</sup>F-FDG uptake of the calcified pulmonary metastases

Mechanism	Origin	<sup>18</sup> F-FDG uptake
Bone formation	Osteosarcoma, chondrosarcoma	Variable (no uptake to SUVmax 7.4)
Dystrophic calcification	Papillary thyroid carcinoma, medullary thyroid carcinoma, giant cell tumor, synovial sarcoma, treated metastatic tumor	Variable (no uptake to SUVmax 28.3)
Mucoid calcification	Mucinous adenocarcinoma	Relatively low (no uptake to SUVmax 3.1)



**Figure 3.** A 61 years old female patient diagnosed as medullary thyroid carcinoma with multiple lung and lymph node metastases 10 years ago, underwent chemotherapy and <sup>131</sup>I-MIBG treatment (7.4GBq) due to far advanced inoperable state. However, the disease was progressed and calcitonin level was elevated to 46,217ng/L. She underwent <sup>18</sup>F-FDG PET/CT. A) and B) show a metastatic nodule with calcium deposition in CT scan. C) and D) show mild <sup>18</sup>F-FDG uptake at the CPM (SUVmax 1.6).

As for the primary synovial sarcoma SUVmax is variable (range, 0.8-25.0) [13] and as for its lung metastases the <sup>18</sup>F-FDG uptake is variable.

In dystrophic calcification, although there are no published data about the <sup>18</sup>F-FDG uptake of CPM, we assume that it is variable.

Mucoid calcification occurs in mucus produced by mucinous adenocarcinoma, and calcium deposition is promoted

by glycoprotein released during mucus degeneration [5]. The  $^{18}\text{F}$ -FDG uptake value of lung metastases of mucinous adenocarcinoma showed SUVmax from background level to 3.1 [14].

Many calcified nodules are encountered on the  $^{18}\text{F}$ -FDG PET/CT scan and even though most of them are benign, the possibility of CPM should be considered. In these studies, the CT portion can differentiate benign diseases due to their morphology. Multiple parenchymal nodules, with smooth edges, endovascular and peripherally in lower and middle lung, with cavitation, calcification or micronodular lesion are considered as typical feature of multiple metastases [15]. Calcification with central, diffuse, popcorn type, and laminate type are regarded as benign features, such as hamartoma or haemangioma [4].

*In conclusion*, CPM due to bony formation and dystrophic calcification shows variable  $^{18}\text{F}$ -FDG uptake and SUVmax values. When CPM is associated with mucoid calcification they have relatively low  $^{18}\text{F}$ -FDG uptake. As  $^{18}\text{F}$ -FDG PET/CT is usually performed in torso or in whole body scans, careful description of the morphology and the SUVmax of the CPM can suggest the primary tumor.

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