European Journal of Radiology xxx (2011) xxx-xxx



Contents lists available at ScienceDirect

### European Journal of Radiology



journal homepage: www.elsevier.com/locate/ejrad

# Clinically unrecognized pulmonary aspiration during gastrointestinal endoscopy with sedation: A potential pitfall interfering the performance of <sup>18</sup>F-FDG PET for cancer screening

Te-Chun Hsieh<sup>a,b,1</sup>, Yu-Chin Wu<sup>a,1</sup>, Hueisch-Jy Ding<sup>c,2</sup>, Chih-Hsiu Wang<sup>a,1</sup>, Kuo-Yang Yen<sup>a,b,1</sup>, Shung-Shung Sun<sup>a,b,1</sup>, Jun-Jun Yeh<sup>d,\*</sup>, Chia-Hung Kao<sup>a,e,\*\*</sup>

<sup>a</sup> Department of Nuclear Medicine and PET Center, China Medical University and Hospital, No. 2, Yuh-Der Road, Taichung 404, Taiwan

<sup>b</sup> Department of Biomedical Imaging and Radiological Science, China Medical University and Hospital, No. 2, Yuh-Der Road, Taichung 404, Taiwan

<sup>c</sup> Department of Medical Imaging and Radiological Sciences, I-Shou University, No. 1, Sec. 1, Syuecheng Road, Dashu Township, Kaohsiung County 840, Taiwan

<sup>d</sup> Department of Chest Medicine, Pingtung Christian Hospital, No. 60, Ta-Lian Road, Pingtung 90059, Taiwan

<sup>e</sup> School of Medicine, China Medical University and Hospital, No. 2, Yuh-Der Road, Taichung 404, Taiwan

### ARTICLE INFO

Article history: Received 27 July 2010 Received in revised form 7 September 2010 Accepted 20 October 2010

Keywords: Gastrointestinal endoscopy Sedation Pulmonary aspiration <sup>18</sup>F-FDG PET Cancer screening

### ABSTRACT

*Purpose:* We found several cases with unexpected pulmonary abnormalities on the <sup>18</sup>F-FDG PET scan after the gastrointestinal endoscopy with sedation during a compact health check-up course, interfering the interpretations of <sup>18</sup>F-FDG PET scan for cancer screening. The current studies aimed to analyze the incidence and the clinical relevance of this pulmonary finding.

*Materials and methods:* From June to December 2009, 127 subjects undergoing the sequential gastrointestinal endoscopy with sedation and <sup>18</sup>F-FDG PET scan within 48 h as part of routine health check-up were retrospectively enrolled in this study. The incidence of abnormal pulmonary findings and their  $SUV_{max}$  of FDG were calculated and correlated with the clinical manifestations.

*Results:* Five subjects had abnormal <sup>18</sup>F-FDG PET findings but pulmonary symptoms were only found in 2. The SUV<sub>max</sub> did not seem to reflect the severity of pulmonary symptoms or the need of intervention. Although the incidence of unrecognized pulmonary aspiration featuring inflammation detected by the <sup>18</sup>F-FDG PET scan was high (3.94%, 5/127), the incidence of events needed intervention remained low (0.79%, 1/127), similar to those previously reported literatures.

*Conclusions:* Although higher incidence of pulmonary aspiration in this study, it probably reflects the better sensitivity of <sup>18</sup>F-FDG PET for inflammation. The low incidence of clinical events needed intervention may still reflect the safety of sedation used for gastrointestinal endoscopy. Proper arrangement of the sequential examinations if subjects need both gastrointestinal endoscopy with sedation and <sup>18</sup>F-FDG PET is important to reduce the interference degrading the performance of <sup>18</sup>F-FDG PET in cancer screening, diagnosis or staging.

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### 1. Introduction

\* Corresponding author at: Department of Chest Medicine, Pingtung Christian Hospital, No. 60, Ta-Lian Road, Pingtung 90059, Taiwan. Tel.: +886 8 7368686; fax: +886 8 7360534.

\*\* Corresponding author at: Department of Nuclear Medicine and PET Center, China Medical University and Hospital, No. 2, Yuh-Der Road, Taichung 404, Taiwan. Tel.: +886 4 22052121x7412; fax: +886 4 22336174.

*E-mail addresses*: rancholosamigos@yahoo.com.tw (T.-C. Hsieh), kubler0514@pchome.com.tw (Y.-C. Wu), hujydi@isu.edu.tw (H.-J. Ding), shelleyw@ms64.hinet.net (C.-H. Wang), yen.kuoyan@msa.hinet.net (K.-Y. Yen), sunss0715@yahoo.com.tw (S.-S. Sun), anvin.funlan@msa.hinet.net, jj.yehevs@yahoo.com.tw (J.-J. Yeh), d10040@mail.cmuh.org.tw (C.-H. Kao).

<sup>1</sup> Tel.: +886 4 22052121x7401; fax: +886 4 22336174.

<sup>2</sup> Tel.: +886 7 6151100x7801; fax: +886 7 6155150.

0720-048X/\$ - see front matter © 2011 Published by Elsevier Ireland Ltd. doi:10.1016/j.ejrad.2010.10.030

With more and more quality demands of prevention medicine for early detection of potentially life-threatening diseases, increasing modern techniques have been used for traditional examinations, such as so-called "painless" enteroscopy. Nevertheless, more and more high technology equipments have also been used for routine health check-up, for example: magnetic resonance imaging, computed tomography (CT), 2-[<sup>18</sup>F]fluoro-2deoxy-D-glucose positron emission tomography (<sup>18</sup>F-FDG PET) and so forth. In a modern busy society, many subjects usually request a compact course of examinations within 1–2 days to save the time and reduce the repeated preparation for examination. However, we recently encountered some unexpected findings on <sup>18</sup>F-FDG PET soon after the prior gastrointestinal endoscopic examination with sedation during this kind of compact course. We reviewed all cases

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### Table 1 Demographic data of all non-diabetic subjects.

Sex	Number (persons)	Age (years old)	p value	Serum glucose concentration (mg/dL)	p value
Male Female	74 53	$\begin{array}{l} 52.91 \pm 10.99  (2880)^a \\ 52.74 \pm 10.52  (3479)^a \end{array}$	<i>p</i> = 0.93 <sup>b</sup>	$\begin{array}{l}92.91\pm10.47(60119)^a\\90.00\pm10.60(72118)^a\end{array}$	<i>p</i> = 0.12 <sup>b</sup>

<sup>a</sup> Mean  $\pm$  standard deviation (range).

<sup>b</sup> Student's *t* test.

in the same period and tried to find the incidence, clinical relevance and possible cause of these findings.

### 2. Materials and methods

### 2.1. Subjects

From June to December 2009, consecutive 367 subjects underwent <sup>18</sup>F-FDG PET scans as part of the self-paid health check-up in our hospital. Among these 367 subjects, 143 underwent gastrointestinal endoscopy with sedation within 48h before their <sup>18</sup>F-FDG PET scans. Sixteen subjects were excluded for further analysis because of diabetes mellitus (12 subjects), hyperglycemia (1 subject) and no available data of pre-injection serum glucose concentration (3 subjects). All the subjects did not have known history of malignancy. Recent medical records of these subjects were reviewed and none of them had pulmonary symptoms before the <sup>18</sup>F-FDG PET scan. Among the remaining 127 non-diabetic subjects (74 males and 53 females; Table 1), 7 underwent esophagogastroduodenoscopy only, 9 underwent colonoscopy only and 111 underwent both esophagogastroduodenoscopy and colonoscopy. All 127 subjects received gastrointestinal endoscopic examinations with left decubitus position. Before the serial examinations, all 127 non-diabetic subjects did not have known gastroesophageal reflux disease, asthma, neurological disease, or gastroparesis as well as diabetes mellitus, which might contribute to the development of pulmonary aspiration during the sedation. The anesthesiologists conducted all the sedation or anesthesia with single or combined use of propofol, midazolam and narcotics. All the recruited subjects were inducted to the level of moderate sedation (conscious sedation) without documenting use of endotracheal intubation or airway masking throughout the course of gastrointestinal endoscopic examinations with sedation. This study was approved by the Institutional Review Board of China Medical University Hospital and given exempt status from the informed consent requirement.

### 2.2. <sup>18</sup>F-FDG PET

The subjects were asked to fast at least 4h before scanning. Each of them was injected intravenously with 370 MBq of <sup>18</sup>F-FDG and rested supine in a quiet, dimly lit room. The whole body images from the head to the upper thighs were performed with a GE Advance NXi PET scanner (General Electric Medical Systems, Milwaukee, WI, USA) with an axial field of view (AFOV) of 15 cm (35 slices per field of view with a slice thickness of 4.30 mm) 40 min after injection of <sup>18</sup>F-FDG. Scanning consisted of an 18-min 2-dimensional emission scan ensued by a 3-min 2dimensional transmission scan. Transmission scans were acquired with Ge-68 rod sources for attenuation correction. Images were reconstructed by FORE-OSEM (Fourier rebinning ordered subsets expectation maximization) algorithm into  $128 \times 128 \times 35$  image matrices (voxel size  $1.95 \text{ mm} \times 1.95 \text{ mm} \times 4.25 \text{ mm}$ ), using segmented attenuation correction. The images were reconstructed and displayed in a 3-dimensional fashion as well as transaxial, sagittal, and coronal sections for interpretation. If there was any suspicious <sup>18</sup>F-FDG-avid lesion detected, a delayed scan for the region of the lesion was performed in 1 h after the whole body scan for assistance of differentiating between the benignity and malignancy [1,2]. A semiquantitative parameter, standardized uptake value (SUV), was defined as:

 $SUV = \frac{\text{tracer activity in the tumor per unit mass}}{\text{amount of injected radioactivity per unit body mass}}$ 

and calculated from each region of interest with increased <sup>18</sup>F-FDG radioactivity in the pulmonary region. The maximum standardized uptake value (SUV<sub>max</sub>) of each <sup>18</sup>F-FDG-avid lesion was used for further comparison. An additional parameter, called retention index (RI), was included for supplementary analysis. The definition of RI was:

 $RI = \frac{SUV_{max} \text{ on delayed images} - SUV_{max} \text{ on early images}}{SUV_{max} \text{ on early images}}\%$ 

A persistent <sup>18</sup>F-FDG-avid abnormal finding on both the initial whole body scan and delayed scan would be routinely requested an additional immediate <sup>18</sup>F-FDG PET/CT scan, using a PET/CT scanner (Discovery STE, General Electric Medical Systems, Milwaukee, WI, USA) that was designated for survey of patients with known malignancies in our hospital, covered the region of aforementioned <sup>18</sup>F-FDG-avid abnormal finding on the same day to obtain a better correlation of metabolic and anatomic characters for diagnosis without additional dose of <sup>18</sup>F-FDG [3]. The additional <sup>18</sup>F-FDG PET/CT scan was acquired with a spiral non-contrastenhanced low-radiation-dose CT scan (0.8-s rotation time, 120 kVp, variable mA with AutomA technique, 3.75-mm slice thickness and 1.75: 1 pitch) first for anatomical references and attenuation correction (converted to 511-keV-equivalent attenuation factors) of the following PET emission images. Then, the PET emission scan was performed as 2-min 3-dimensional scan per AFOV and reconstructed to attenuation-corrected, 3.27-mm transaxial slice thickness covering the chest region for further interpretation [4]. Four of these 5 subjects received the additional PET/CT scan but 1 declined. At least 2 experienced nuclear medicine physicians reviewed the <sup>18</sup>F-FDG PET images and interpreted the results with consensus. Student's t test and descriptive statistics were used for analysis. A *p* value < 0.05 was thought to be statistically significant.

### 3. Results

### 3.1. Demographic data

Abnormal pulmonary findings on the <sup>18</sup>F-FDG PET scans were noted in 5 subjects. The average time interval between the initial and delayed scans was 34 min (range: 28–40 min). None of the 5 subjects had abnormal extrapulmonary findings and the other 122 subjects did not have any abnormal findings either in the pulmonary or extrapulmonary regions on the <sup>18</sup>F-FDG PET scans. The average age and serum glucose concentration of the 5 subjects with positive <sup>18</sup>F-FDG PET findings and other 122 subjects were listed in Table 2. They were not statistically different between each other. The incidence of pulmonary abnormalities on the <sup>18</sup>F-FDG PET scans after the gastrointestinal endoscopy with sedation is 3.94% (5/127). The SUV<sub>max</sub> in symptomatic subjects were higher than that in asymptomatic subjects in both early-phase (5.935 and

Please cite this article in press as: Hsieh T-C, et al. Clinically unrecognized pulmonary aspiration during gastrointestinal endoscopy with sedation: A potential pitfall interfering the performance of <sup>18</sup>F-FDG PET for cancer screening. Eur J Radiol (2011), doi:10.1016/j.ejrad.2010.10.030

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### Table 2

Demographic data of subjects with and without abnormal pulmonary findings on <sup>18</sup>F-FDG PET scans.

	Age (years old)	p value	Serum glucose concentration (mg/dL)	p value
Subjects with positive pulmonary findings on <sup>18</sup> F-FDG PET Subjects without abnormal pulmonary findings on <sup>18</sup> F-FDG PET	55.60 ± 11.17 (47- 52.72 ± 10.77 (28-	$(71)^{a}$ $(80)^{a}$ $p = 0.56^{b}$	$\begin{array}{l} 93.60\pm12.46(73104)^a\\ 91.61\pm10.55(60119)^a \end{array}$	<i>p</i> = 0.68 <sup>b</sup>

<sup>a</sup> Mean  $\pm$  standard deviation (range).

<sup>b</sup> Student's *t* test.

3.249 versus 1.316, 1.115 and 1.260) and delayed-phase (6.904 and 5.017 versus 1.998, 1.466 and 1.536) images (Table 3). However, there was no such observation between RI and development of symptoms. Besides, the severity of symptoms seemed irrelevant to  $SUV_{max}$ . The relevant brief clinical and radiological data of these 5 subjects with positive findings were described respectively in the figure legends (Figs. 1–5).

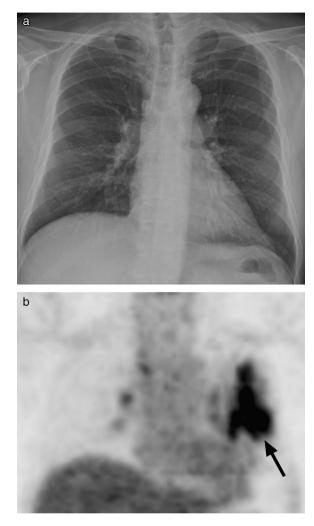
### 4. Discussions

For many reasons, such as to ease the procedure and to decrease the discomfort of the subjects, many gastroenterologists now consider sedation and analgesia more frequently as routine use for the endoscopic examination. In one recent study, more than 98% of endoscopists in the United States routinely administer sedation during upper and lower gastrointestinal endoscopies [5]. However, whether anesthesiologists or non-anesthesiologists direct the sedation or anesthesia remains controversial [6]. In addition, the expected depth of sedation varies and usually depends on the clinical need and physicians' preferences. Despite these considerations, most reviews and reports in the literature support the current consensus of safety and convenience to perform the endoscopic examination with sedation [7-10]. Pulmonary aspiration during the anesthesia is thought to be a rare complication with the modern anesthesia techniques and knowledge, and the resultant lethal pulmonary complication is even rarer [11–13]. The incidence of pulmonary aspiration during the anesthesia is more frequent especially in emergent operations, subjects with depressed consciousness, elders and children [11,12]. However, for the gastrointestinal endoscopic examination, it seldom needs deep sedation or anesthesia to facilitate the procedure. Therefore, the reported incidence of complications related to anesthesia, such as pulmonary aspiration and so forth, in the endoscopic examination is seldom (less than 1% mostly) [6,14]. Moreover, if this procedure is for health check-up, the incidence is even less because of the general conditions of these subjects are usually good without distress.

Because the <sup>18</sup>F-FDG PET scan is getting more easily available worldwidely and more affordable for its cheaper cost as well as the increase of the need for early detection of the occult malignancy for more effective anticancer strategies, it is now more frequently requested for a cancer screening test as part of the routine self-paid health check-up [15–21] although most health insurances, especially the government-directed ones, do not provide the reimbursement so far. For the purpose of cancer screening, a test with higher sensitivity to detect the malignancy is usually

### Table 3 SUV<sub>max</sub> and RI of the 5 subjects with positive pulmonary <sup>18</sup>F-FDG PET findings.

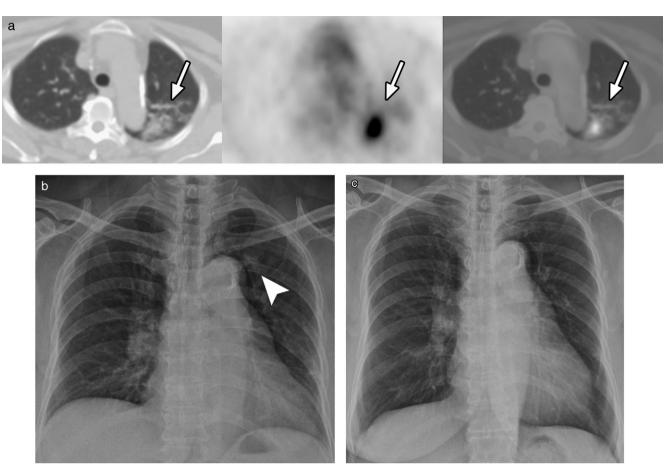
Subject	Sex	Age (years old)	Early-phase SUV <sub>max</sub>	Delayed-phase SUV <sub>max</sub>	RI	Existence of pulmonary symptoms
1	Male	64	5.935	6.904	16.33%	Yes
2	Female	71	3.249	5.017	54.41%	Yes
3	Male	47	1.316	1.998	51.82%	No
4	Female	49	1.115	1.466	31.53%	No
5	Female	47	1.260	1.536	21.90%	No



**Fig. 1.** Subject 1's serial radiographic studies. (a) Chest plain radiograph (CXR) before gastrointestinal endoscopy (Glscope) with sedation and (b) maximum intensity projection of <sup>18</sup>F-FDG PET after Glscope. There was a lobar <sup>18</sup>F-FDG-avid abnormality in the left lung field (arrow) but no active lung lesion in the CXR. Severe chills occurred during the PET examination and later, high fever on the night of the examination day. However, the symptoms resolved spontaneously on the next day without any medical treatment. He declined any further laboratory and radiological examinations for follow-up but remained no sequel clinically thereafter.

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**Fig. 2.** Subject 2's serial radiographic studies. (a) A prominent <sup>18</sup>F-FDG-avid focus (white arrows) on the representative transaxial slices of CT, PET and fused PET/CT (left to right) after Glscope correlated with (b) the faint infiltration on the CXR immediately after Glscope (arrowhead). However, there was no obvious abnormality on the CXR immediately before Glscope (not shown). The subject complained of severe cough with sputum after Glscope. Aspiration pneumonia was suspected and empirical antibiotic treatment was prescribed by the consultant pulmonologist. (c) The faint infiltration resolved on the follow-up CXR 1 week after Glscope.

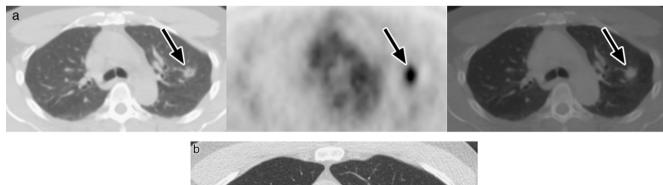
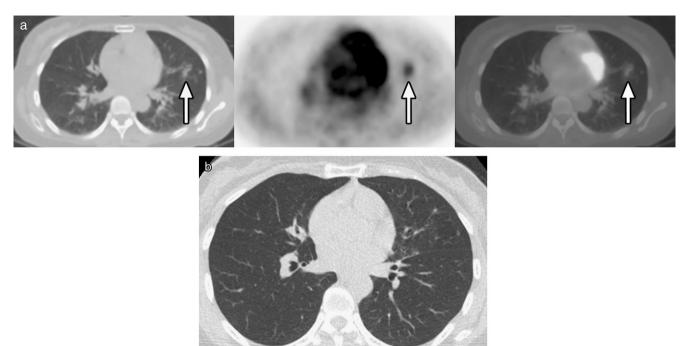




Fig. 3. Subject 3's serial radiographic studies. (a) There was faint, tiny <sup>18</sup>F-FDG-avid focus (black arrows) with corresponding CT ground-glass opacity in the left upper lung field on the representative transaxial slices of CT, PET and fused PET/CT after GIscope. The subject did not experience any pulmonary symptom before and after GIscope and there was no CXR abnormality before GIscope (not shown). (b) Resolution of the prior ground-glass opacity was observed on the follow-up chest CT 3 weeks after GIscope.

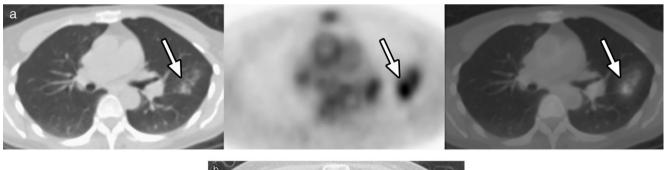
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**Fig. 4.** Subject 4's serial radiographic studies. (a) There was focal prominent <sup>18</sup>F-FDG-avid area (white arrows) with corresponding CT opacity in the upper lobe of left lung on the representative transaxial slices of CT, PET and fused PET/CT after Glscope after Glscope. The subject did not experience any pulmonary symptom before and after Glscope and there was no CXR abnormality before Glscope (not shown). (b) Resolution of the prior opacity was observed on the follow-up chest CT 6 weeks after Glscope.

more desirable. However, a false positive result may initiate subsequent unnecessary and possibly harmful examinations to verify the suspected lesion. Traditionally, a pulmonary lesion with an SUV<sub>max</sub> of <sup>18</sup>F-FDG more than 2.5 is thought to be of high possibility for malignancy [22]. However, high <sup>18</sup>F-FDG uptake may also appear in various inflammatory processes [23], leading a false positive result for malignancy (but a true positive result for inflammation). The increased pulmonary <sup>18</sup>F-FDG uptake of the 5 subjects, whether symptomatic or not, may be considered as the result of inflammation. Because of the observable radiological change closely before and after the gastrointestinal endoscopic examinations with sedation and the common location of findings in the left upper lobe of lungs since all our subjects undergoing the gastrointestinal endoscopic examination with a left decubitus position, we think that the sedation-related pulmonary aspiration would be

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**Fig. 5.** Subject 5's serial radiographic studies. (a) There was prominent <sup>18</sup>F-FDG-avid finding (white arrows) with corresponding CT ground-glass opacity in the upper lobe of left lung on the representative transaxial slices of CT, PET and fused PET/CT after GIscope after GIscope. The subject did not experience any pulmonary symptom before and after GIscope and there was no CXR abnormality before GIscope (not shown). (b) Resolution of the prior opacity was observed on the follow-up chest CT 1 week after GIscope.

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explainable as the most possible cause. Although the incidence of pulmonary aspiration is much higher than those reported in the literature, some of our cases are asymptomatic and may not be noticed or even further evaluated if these subjects do not undergo a subsequent <sup>18</sup>F-FDG PET scan. Three of our cases do not develop pulmonary symptoms and the SUV<sub>max</sub> of their pulmonary findings is below 2.5. The SUV<sub>max</sub> of the two symptomatic subjects is above 2.5 but the value does not reflect the severity of their symptoms. Hence, a cutoff of SUV<sub>max</sub> = 2.5 may serve as a predictor of development of pulmonary symptom in such cases. The possibility of malignancy is much less likely because of the unusual fast progression and spontaneous resolution of pulmonary lesion. Nevertheless, only 1 subject in our study needs further medical treatment, and the incidence (1/127 = 0.79%) is more close to those ever-reported sedation-/anesthesia-related complications in the literature. Therefore, the much higher incidence of pulmonary aspiration in our study may only reflect the better sensitivity of <sup>18</sup>F-FDG PET to detect the consequent inflammation rather than an increase of adverse effects of the gastrointestinal endoscopy with sedation. These findings may also suggest that the silent pulmonary aspirations occur more frequently than expected. They may less influence the subsequent management on the health subjects for screening but greatly interfere the diagnostic and staging ability of <sup>18</sup>F-FDG PET for those who need both gastrointestinal endoscopy and <sup>18</sup>F-FDG PET for their illness, such as esophageal, gastric and colon cancer. Hence, a proper arrangement of the sequential examinations, whether an order of <sup>18</sup>F-FDG PET and then endoscopy, or certain delay of <sup>18</sup>F-FDG PET if endoscopy has been done, is mandatory to reduce the undesirable interaction or interference that degrade the performance of <sup>18</sup>F-FDG PET in cancer screening, diagnosis or staging.

### 5. Conclusions

Our current study discloses more than expected incidence of the pulmonary aspiration during the gastrointestinal endoscopic examination with sedation in comparison with those ever reported in the literature according to the incidental findings on the <sup>18</sup>F-FDG PET scans. However, these findings may well be considered as subclinical signs of silent aspiration that do not necessarily became clinical evident events since most of the subjects in our study remain asymptomatic whether during the initial or further follow-up period. Hence, the incidence of the complications need to intervene is close to those reported in the literature, suggesting the still reliable safety of the current technique of sedation/anesthesia used for the gastrointestinal endoscopic examination. On the other hand, proper arrangement of the sequence of the examinations if subjects need both gastrointestinal endoscopy with sedation and <sup>18</sup>F-FDG PET is important to reduce the undesirable interaction or interference that degrade the performance of <sup>18</sup>F-FDG PET in cancer screening, diagnosis or staging.

### **Conflict of interest**

We declare that we have no conflict of interest.

#### Acknowledgements

We want to thank the grant support of the study project (DMR-96-066 and 97-104) in our hospital, Taiwan Department of Health Clinical Trial and Research Center and for Excellence (DOH100-TD-B-111-004), and Taiwan Department of Health Cancer Research Center for Excellence (DOH100-TD-C-111-005).

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