임상의과학 석사학위논문

Utility of Simultaneous Respiratory Gated ^{18}F-FDG PET/CT Acquisition with Continuous Bed Flow Technology in Lung Cancer and Non-Lung Cancer Lesions

폐암 및 양성 폐 병변에서 Continuous Bed Flow 기술을 이용한 동시 호흡 게이트 ^{18}F-FDG PET / CT 의 유용성

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Abstract

Utility of Simultaneous Respiratory Gated ^{18}F-FDG PET/CT Acquisition with Continuous Bed Motion Technology in Lung Cancer and Non-Lung Cancer Lesions

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Purpose:

This study aimed to evaluate the usefulness of simultaneous respiratory gating in evaluating lung cancer and benign lesion by investigating the metabolic parameters of lung lesions, both lung cancer and benign lesions, in non-gated positron emission tomographic (PET) images and concurrently acquired with respiratory gated PET data.

Methods:

The records of 121 patients who were treated at the hospital from April 2015 to April 2016 were retrospectively examined. PET images were acquired before treatments and all PET data were concurrently obtained in non-gated and simultaneous amplitude-based respiratory gated mode. Metabolic parameters; standardized uptake value (SUV)max, SUVmean, and metabolic tumor volume (MTV) of each lesion were analyzed.

Results:

Gated mode yielded a greater SUVmax and SUVmean, and smaller MTV than non-gated mode in both lung cancers (n = 108) and benign lesions (n=15). Lung cancers showed Higher SUVmax and SUVmean than benign lesions. For the lung cancers based on the location, and their T stage of TNM staging (AJCC 8^{th}) indicated equivalent results. Additionally, comparing the pathologic volume and MTV in 46 of the resected cancers showed small distinctions in gated mode. Finally, the change rates of SUVmax, SUVmean, and MTV from non-gated to gated mode in 3-5cm sized benign lesions were significantly higher than those in lung cancers.

Conclusions:

PET image acquisition using an amplitude-based simultaneous respiratory gating algorithm improves staging and treatment planning as it provides more accurate quantification and enables more precise measurement of SUV and MTV. Moreover, it has a potential of defining cancer from benign lesions.

Keywords: Simultaneous respiratory gating, ^{18}F-FDG-PET/CT,

Standardized uptake value (SUV), Metabolic tumor volume

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Introduction

With the use of 18fluorodeoxyglucose (^{18}F-FDG) positron emission tomographic/computed tomography (PET/CT) imaging, great improvements in diagnosis, treatment planning, and the monitoring of various cancers have been facilitated [1], especially for lung cancer, which is one of the most fatal cancers in the world. Several studies demonstrated the significant clinical impact of ^{18}F-FDG PET/CT imaging, which fuses anatomic and functional data in a single image [2]. ^{18}F-FDG PET/CT has greater sensitivity compared with chest CT, especially for the detection of small pulmonary nodules (SPN) [1, 3]. It is well-known that the higher metabolic activity of standard uptake value (SUV) represents a greater likelihood of malignancy. SUV has accordingly been studied as a prognostic factor in lung cancer, especially non-small cell lung cancer (NSCLC) [4]. Thus, accurate measurement of lesion metabolism is important for the diagnosis of malignancy [5]. However, because PET acquisition takes a longer time compared with CT, there are several challenging issues associated with lung imaging, especially the motion artifacts introduced by respiration. Motion can cause blurring and affects the clinician's ability to evaluate the lesion's metabolic activity. This, in turn, reduces the accuracy of quantification and impairs clinicians' management of their patients.

A number of studies have attempted to compensate for respiratory motion artifacts. One of the protocols intended to reduce respiratory motion errors in PET data is respiratory gated PET (or 4D-PET). It reduces blurring, which results in smaller target volumes, and the accurate target volumes is critical for the planning of effective radiotherapy [6]. The SUV of most malignancies increase until 2 hours, meanwhile the benign lesions show less

of an increase or a decrease in the delayed phase [7]. However, those studies require additional PET/CT acquisition, which can cause the change of SUV at each time point and have more radiation exposure [8]. Therefore, comparing the SUV of respiratory gated images with the whole-body image is able to be impractical and imprecise. Thus, the study applied simultaneous respiratory gated PET/CT acquisition, which can remove the problem of different time points between the respiratory gated image and whole-body image. The goal of this study was to evaluate the effect of simultaneous respiratory gating during PET/CT acquisition on the metabolic parameters of lung lesions, both lung cancer and benign lesion.

Materials and Methods

Patients

Between April 2015 to April 2016, 121 patients (male, n = 83; female, n = 38; mean age 63.81 ± 10.6 years) who underwent ^{18}FDG-PET/CT at our hospital for staging of lung lesion, with subsequent histopathological diagnosis, were retrospectively discerned. Patients' characteristics are summarized in Table 1. This retrospective study was approved by internal institutional review board and the informed consent was exempted.

PET Acquisition and Respiratory Gating

All patients underwent whole body FDG-PET/CT imaging after the administration of 18F-FDG according to patient weight (5.18 MBq kg-1, maximum 518 MBq), by a Biography 40 mCT Flow PET/CT scanner (Siemens Medical Solutions USA, Inc.). PET image acquisition was achieved by an optimised, amplitude-based respiratory gating algorithm (HD·Chest, Siemens Medical Solutions USA, Inc.) with continuous bed motion acquisition techniques, integrated in the Syngo CT & PET Oncology Software (Siemens Medical Solutions USA, Inc.). The respiratory gating covered from lung apex to base on supine position. When gating was applied from lung apex to lung base, the table speed was slowed to 1.0 mm/s (Figure 1). A scan speed of 1.5 mm/s was used in area without integrated respiratory gated motion management acquisition. An AX-733V respiratory gating system (Anzai Medical Co, Ltd., Japan) acquired the respiratory amplitude signal. An elastic belt placed around the patient's abdomen sensed the pressure signal.

Respiratory gating was performed with a duty cycle of 35% which provided a good balance between image quality and motion rejection.

CT acquisition was performed after 18F-FDG injection. The helical non-contrast CT was acquired with a free breathing protocol to define the image range, which was from the skull base to the inguinal area with the following parameters: Caredose 4D/CareKv 120 with quality reference of 100 mAs, tube rotation time of 0.5 sec, and pitch of 1.0mm. CT images were reconstructed using iterative technique (SAFIRE, Siemens).

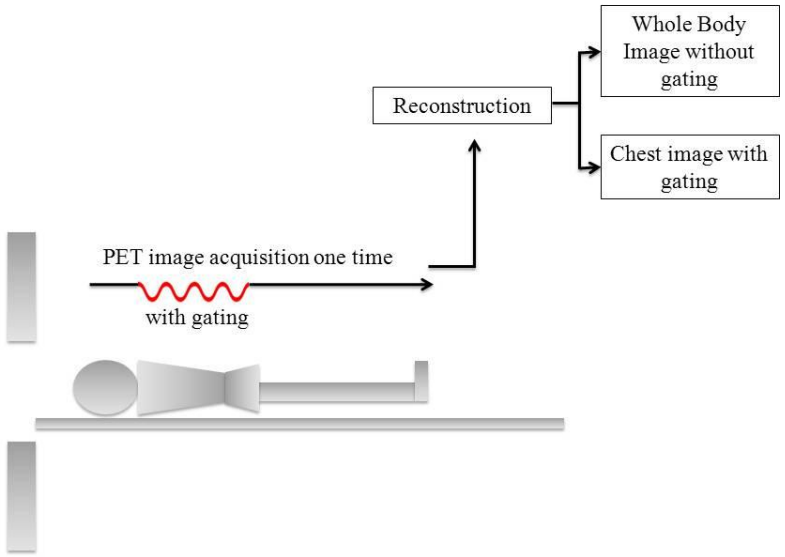


Figure 1. Diagram of image acquisition and simultaneous respiratory gating through Biography 40 mCT Flow

PET Reconstruction

The PET images from the scanner were reconstructed by TrueX algorithm incorporating time-of-flight (TOF) information (Ture X + TOF, UltraHD PET, Siemens). The reconstruction was done with 2 iterations, 21 subsets, and a matrix size of 400 x 400 for gated acquisition and 256 x 256 for rest of the region. The slice thickness of the PET reconstructions was matched with the attenuation correction CT with image thickness of 3.0 mm and increment of 2.0 mm with Gaussian filter with full width at half maximum (FWHM) of 5.0 mm.

Image Interpretation and Analysis

We evaluated the lesions with the following metabolic parameters: maximum Standardized uptake value (SUVmax), minimum SUV(SUVmean), and metabolic tumor volume (MTV), provided by Syngo.via software (Siemens Medical Solutions USA, Inc.). Lean body mass was used for SUV (g/ml) and MTV (cm3) calculation. This was accomplished by delineating the lesion on the PET images using a threshold of 40% SUVmax segmentation. Differences in lesions' SUVs between non-gated and gated were measured in PET images using same contour. All evaluated cancerous lesions in non-gated and gated modes were analysed according to the locations and sizes. We also determined whether there were significant differences in benign lesions in non-gated vs. gated mode.

Standard Pathologic Volume Reference

Pathologic tumor volumes were calculated from the three-dimensional

(d1, d2, and d3) diameters of the resected cancers from pathologic report. The tumor was measured before fixation if its size was ≤ 1 cm. Tumors > 1 cm were measured immediately after fixation. The ellipsoidal volume was calculated by following equation:

$$\text{Pathologic volume} = \pi/6 \times (d1 \times d2 \times d3)$$

Statistical Analysis

All metabolic parameters were reported as mean ± standard deviation (SD). Differences in SUVs and MTV between non-gated and gated mode were analysed using Wilcoxon Signed Ranks test and paired T-test from a commercial statistics software package (SPSS version 21.0, IBM Software, Chicago, IL, USA). We regarded as statistically significant when p values were less than 0.05.

Results

Patient Characteristics and Metabolic Parameters of Lung cancer and Benign Lesions

One hundred six patients were diagnosed with lung cancer, including 8 with small cell lung cancer (SCLC) and 98 with non-small cell lung cancer (NSCLC). Of the 98 with NSCLC, 69 were diagnosed as adenocarcinoma, and 21 were diagnosed as squamous cell carcinoma. The 8 lesions were diagnosed as NSCLC without subtyping due to the lack of additional immunohistological differentiation. Staging of NSCLCs was based on the American Joint Committtee on Cancer (AJCC), 8^{th} edition. Two patients were diagnosed with double primary lung cancer: One patient with NSCLC at right middle lobe (RML) and left upper lobe (LUL), and the other patient with adenocarcinoma at same location. There were 15 patients diagnosed as benign lesions (Table 1).

All 123 of both lung cancer and benign lesions showed significant increases of SUVmax and SUVmean and a decrease of MTV in gated mode compared to those in non-gated mode ($p<0.05$, according to Paired *t*-test). Moreover, SUVmax and SUVmean were significantly higher in lung cancers than those in benign lesions regardless of respiratory gating ($p<0.05$, t-test)(Table 2).

Table 1. Characteristics of patients

		Lung cancer (n=106)	Benign lesion (n=15)
Sex (Male: Female)		74: 32	9: 6
Age (years)		65.04 ± 1.0	55.63 ± 1.9
Histologic type			
	Small cell lung cancer	8	
	Non-small cell lung cancer	98	
	Adenocarcinoma	69	
	Squamous cell carcinoma	21	
	*NSCLC**	8	
	Benign nodule		1
	Abscess		4
	Harmatoma		2
	Inflammation		4
	Sarcoidosis		2
	Tuberculosis		2
Disease Staging [a]	*NSCLC (n=98)*		
	IA	18	
	IB	8	
	IIA	8	
	IIB	2	
	IIIA	14	
	IIIB	4	
	IV	44	
T-staging [b]			
	T1	27	
	T2	62	
	Over T3	20	
Location			
	RUL	20	2
	RML	11 [c]	0
	RLL	28 [c]	3
	Right hilum	1	1
	LUL	30 [c]	5
	LLL	18	4

[a, b] Disease staging and T-staging based on AJCC 8th

[c] There were 2 patients diagnosed with double primary lesions: One patient diagnosed NSCLC at RML and LUL, and the other with Squamous cell carcinoma at same lobes.

* Specimens from 8 patients with NSCLC did not undergo further immunohistological differentiation due to the limited quality of the specimen.

NSCLC, Non-small cell lung cancer; RUL, Right upper lobe; RML, Right middle lobe; RLL, Right lower lobe; LUL, Left upper lobe; LLL, Left lower lobe; PET, Positron emission tomography

Table 2. Comparison of the metabolic parameters (SUVmax, SUVmean, and MTV) of non-gated and gate mode in lung cancer and benign lesion

	Lung cancer (n=108)			Benign lesion (n=15)		
	Non-gate	Gated	p value	Non-gate	Gated	p value
SUVmax	10.55 ± 6.0*	11.27 ± 6.1[a]	<0.001	6.96 ± 4.3*	7.82 ± 4.9 [a]	0.001
SUVmean	6.22 ± 3.6[b]	6.54 ±3.5[c]	<0.001	4.05 ± 2.6 [b]	4.45 ± 2.8 [c]	0.001
MTV	33.29 ± 51.1	28.99 ± 45.2	<0.001	21.23 ± 21.2	16.04 ± 18.0	0.023

*, [a], [b], and [c] Comparing the lung cancer and benign lesion in each non-gated and gated mode, SUVmax and SUVmean of lung cancer were significantly higher than benign lesion.

Effect of Respiratory Gating on Metabolic Parameters by Location and Size of Lung Cancer

The effect of respiratory gating on metabolic parameters based on the location of the lesions was analyzed. In gated mode, SUVmax and SUVmean significantly increased while MTV decreased at RML, RLL, LUL and LLL (Table 3).

Further analysis of the 19 lesions in RUL and 31 LUL lung cancers was performed (Table 4). RUL lung cancers showed no difference of SUVmax, SUVmean, and MTV in gated and non-gated mode regardless of location (p>0.05). In LUL lung cancers, on the other hand, there were 16 lesions located in upper portion and 14 lesions of lower portion based on pulmonary hilar level. Significant difference of SUVmax, SUVmean, and MTV between gated and non-gated mode was identified in lower portion (p<0.05) (Table 4). Figure 2. represents the effects of respiratory gating of the lung cancer.

To investigate the effect of respiratory gating on metabolic parameters based on the size of the lesions, all the lung cancers were categorized into 3 groups (T1: 3cm or smaller, T2: 3-5cm, and T3: more than 5cm), based on their T-staging (AJCC 8^{th}) from contrast CT. All the groups showed significant increase of SUVmax, SUVmean, and decrease of MTV in gated mode (Figure 3). The results of SUV and MTV of the lung cancers from non-gated within the three subgroups, based on their location were additionally compared. 20 of lung cancers in RUL did not showed significant difference between non-gated and gated mode regardless of size. In RML, 7 of 3-5cm-sized lesions showed significant difference of SUV and MTV between non-gated and gated mode (p<0.01). All 28 of RLL lung cancer showed significant difference (p<0.01), regardless of their sizes. For LLL, lung cancers more than 5cm showed significant increase of SUVmax and decrease of MTV in gated mode

compared with non-gated mode ($p< 0.01$). In LLL lung cancer, 10 of lesions within 3cm showed significant change of SUVs, and MTV, while 6 of 3-5cm lesions showed significant change in SUVmean ($p<0.01$). Table 5 summarized the results of SUVs and MTV comparison between non-gated and gated mode according to the size and location

The lung cancers volume resected by surgery into 3 groups based on their T staging (AJCC 8^{th}) as above were analyzed (Figure 4). In the resected lesions, there were significant increase of gated SUVs and decrease of gated MTV within 3cm (SUVmax: non-gated: gated =7.11±5.1: 7.86±5.5, SUVmean = 4.24±3.2: 4.68±3.4, MTV = 5.94±5.2: 4.17±2.8, all $p<0.01$). Gated SUVmean was significantly increased (non-gated: gated =6.54±4.7: 6.92±4.4, $p=0.04$) in 3-5cm sized lesions. Furthermore, the difference between MTV and pathologic volume of 46 resected cancers were compared in gated and non-gated mode. Cancers measured in gated mode were significantly smaller (non-gated: gated = -1.73: -0.056, $p<0.001$).

Table 3. Comparison of the metabolic parameters gated, and non-gated modes based on lung cancer location

	RUL (n=20)		RML (n=10)		RLL (n=28)		LUL (n=31)		LLL (n=18)	
	Non-Gated	Gated	Non-Gated	Gated	Non-Gated	Gated	Non-Gated	Gated	Non-Gated	Gated
SUVmax	11.74 ± 5.0	12.03 ± 5.2	12.51 ± 7.9*	13.80 ± 7.7*	9.28 ± 5.5*	10.4 ± 5.6*	10.95 ± 6.6*	11.35 ± 6.7*	9.29 ± 5.6*	10.10 ± 5.9*
SUVmean	6.90 ± 3.0	6.99 ± 3.0	7.31 ± 4.8*	7.85 ± 4.7*	5.61 ± 3.5*	6.15 ± 3.5*	6.41 ± 4.0*	6.54 ± 4.0*	5.39 ± 3.3*	5.85 ± 3.5*
MTV	24.57 ± 30.8	25.00 ± 31.1	26.16 ± 24.5*	22.3.0 ± 24.8*	38.56 ± 65.9*	31.01 ± 58.2*	38.96 ± 54.9*	34.24 ± 45.6*	27.97 ± 50.8*	24.15 ± 47.3*

*The differences of SUVmax,SUVmean and MTV were significant between non-gated and gated mode in RML, RLL, LUL, and LLL ($p< 0.05$).

The analysis was performed excluding the one lesion located at pulmonary hilum.

Table 4. Further comparison of the metabolic parameters between gated and non-gated modes based on the location in RUL and LUL

	RUL (n=20)						LUL(n=31)					
	Upper(n=13)			Lower(n=7)			Upper(n=16)			Lower(n=15)		
	Non-gated	Gated	p value	Non-gated	Gated	p value	Non-gated	Gated	p value	Non-gated	Gated	p value
SUVmax	12.40± 4.6	12.62±4.9	0.21	10.52±5.8	10.93±6.1	0.24	11.93±8.0	12.33 ± 8.1	0.16	9.89±4.8	10.30±5.1	0.02
SUVmean	7.27±2.7	7.28±2.7	0.81	6.23±3.7	6.45±3.7	0.05	7.01±4.8	7.1±4.8	0.57	5.77±2.9	5.94±3.0	0.02
MTV	17.57±18.0	18.14±18.3	0.26	26.50±3.4	23.65±4.2	0.50	45.14±59.3	39.33±48.8	0.13	32.38±51.0	28.81±43.1	0.03

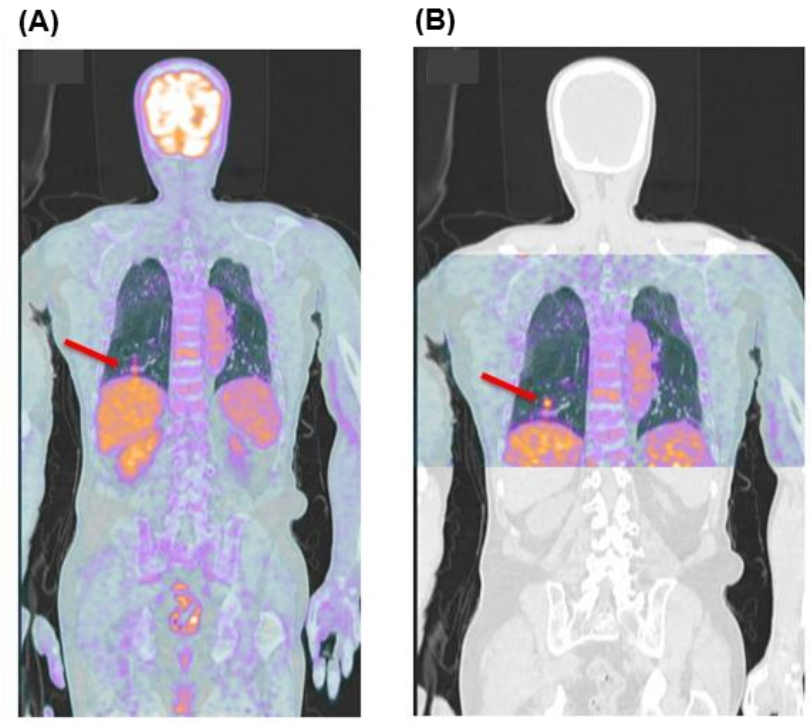
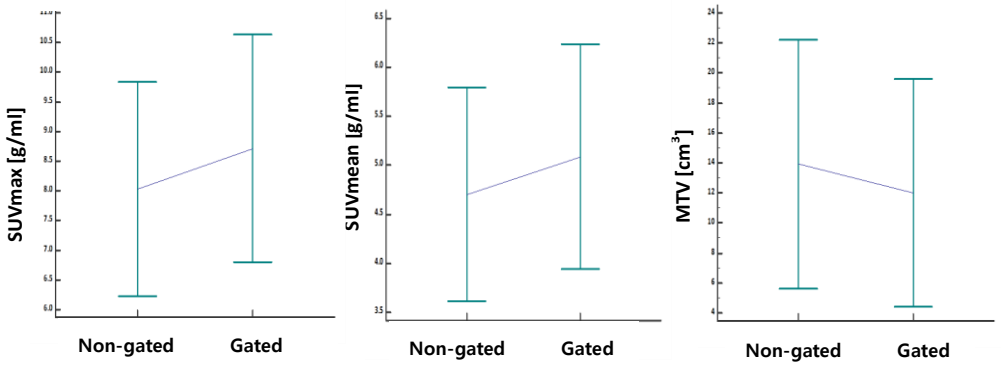


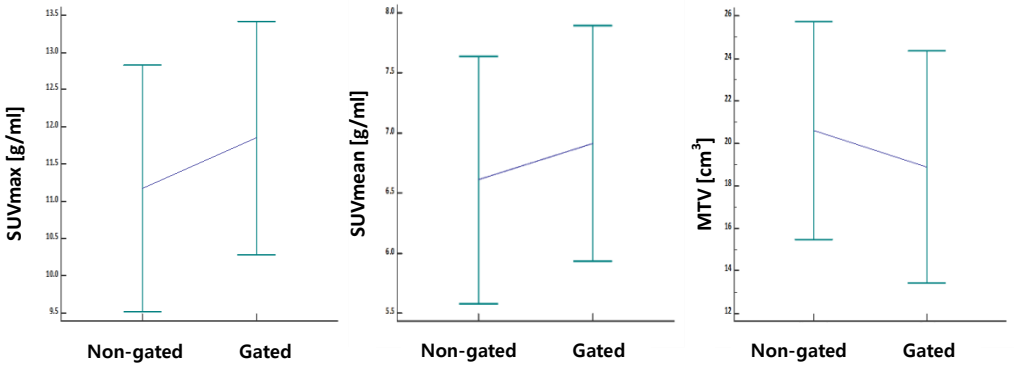
Figure 2. Representative case

A 77-year-old male patient with RLL pulmonary nodule underwent ^{18}F-FDG PET/CT. Data were simultaneously acquired using non-gating (a) and respiratory gating (b) through Biography 40mCT Flow. The nodule (red arrow) was diagnosed as squamous cell carcinoma. The cancer's SUVmax, SUVmean, and MTV in non-gated mode were 2.51, 1.53, and 3.58. In gated mode, SUVmax and SUVmean increased to 4.99 (49.70%) and 2.79 (45.16%), and MTV decreased to 1.82 (-96.70%). The patient went under RLL lobectomy through video-assisted thoracoscopic surgery. In the pathologic report, the measured volume of the tumor was 1.8 x 1.2 x 0.8 cm^3, and final stage was diagnosed as IA (T1aN0M0).

(A)


SUVmax [g/ml]
Non-gated
Gated
SUVmean [g/ml]
Non-gated
Gated
MTV [cm3]
Non-gated
Gated

(B)


SUVmax [g/ml]
Non-gated
Gated
SUVmean [g/ml]
Non-gated
Gated
MTV [cm3]
Non-gated
Gated

(C)

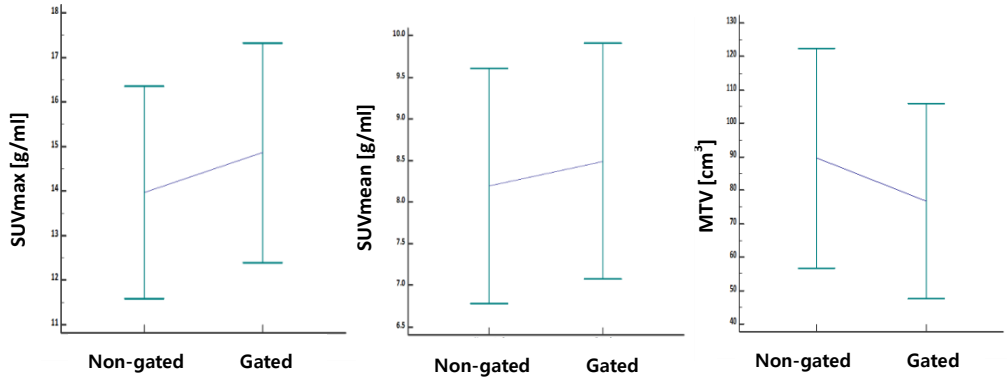


Figure 3. Respiratory gating effect of metabolic parameters of lung cancer

SUVmax, SUVmean, and MTV in 43 of T1 (A), 40 of T2 (B), and 25 of over T3 (C) in non-gated and gated mode. The lesions in all stages showed significant increase of SUVmax, SUVmean, and decrease of MTV in gated mode ($p \leq 0.01$)

Table 5. Comparing SUV and MTV of lung cancers between non-gated and gated mode, considering both size and location

		≤3cm				3-5cm				>5cm			
		N	NG	G	p	N	NG	G	p	N	NG	G	p
RUL		8				10				2			
	SUVmax		9.45 ±6.2	9.81±6.5	0.12		13.31± 3.8	13.41± 4.1	0.39		13.10± 1.6	14.0± 3.6	0.66
	SUVmean		5.57 ±3.8	5.73±3.8	0.09		7.78± 2.2	7.78± 2.8	0.95		7.84± 1.7	8.09± 2.6	0.66
	MTV		19.27 ±40. 8	17.56± 37.4	0.07		29.60± 25.5	32.19± 29.0	0.65		20.66± 4.9	18.80± 2.6	0.18
RML		2				7				1			
	SUVmax		18.29 ±16. 8	18.64± 17.8	0.66		10.11± 5.0	11.53± 4.1	0.02		17.83	20.38	NS
	SUVmean		10.88 ±10. 3	11.05± 10.8	0.66		5.81± 2.8	6.40± 2.3	0.05		10.84	11.61	NS
	MTV		49.50 ±57. 9	49.56± 57.2	0.66		18.64± 9.2	13.60± 5.7	0.03		32.16	28.73	NS
RLL		12				8				8			
	SUVmax		6.66 ±4.2	7.72±4.7	<0.01		9.70±3. 9	11.22± 3.8	0.01		12.81± 6.8	13.60± 6.8	0.01
	SUVmean		4.00 ±2.5	4.56±2.8	<0.01		5.81± 2.7	6.59± 2.6	0.01		7.73± 4.3	8.08± 4.3	0.01
	MTV		8.12 ±6.6	6.01±4.3	<0.01		19.68± 14.3	14.51± 9.2	0.01		103.10 ±98.7	85.02± 90.6	0.02
LUL		11				9				11			
	SUVmax		7.91 ±4.8	8.22±5.1	0.11		11.58± 7.8	11.71± 7.7	0.59		13.46± 6.5	14.19± 6.7	0.03*
	SUVmean		4.51 ±2.7	4.70±2.9	0.11		7.03±5. 1	7.04±5 .0	0.89		7.8.0± 3.6	7.97± 3.6	0.23
	MTV		14.01 ±33.	12.58± 28.5	0.18		19.99± 11.4	19.11± 9.7	0.44		79.45± 70.6	68.28± 58.0	0.01*

		9									
LLL	10				6			2			
	SUVmax	6.63 ±4.6	7.59±5.7	0.03	11.09± 4.9	11.66± 4.4	0.12	17.19± 0.5	18.00± 1.9	0.66
	SUVmean	3.89 ±3.0	4.46±3.6	0.03	6.54± 3.0	6.86± 2.9	0.05	9.39± 0.1	9.79± 0.5	0.18
	MTV	9.43 ±0.2	6.63±5.2	<0.0.1	12.74± 7.9	10.68± 5.4	0.12	166.39 ±8.2	152.18 ±27.9	0.18

*9 of 11 lesions were located at superior to pulmonary hilar level.

N: Number, NG: Non-gated, G: Gated, p: p value

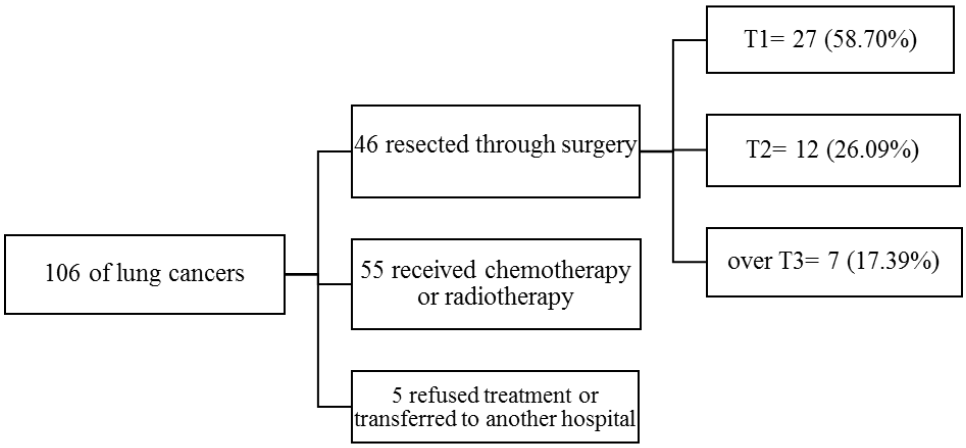


Figure 4. Classification of 106 lung cancer lesions in their T-staging (AJCC 8th)

Three patients considered to have double primary lesions underwent chemotherapy.

Effect of Respiratory Gating on Metabolic Parameters by Location and Size of Benign Lesions

According to the location of 15 benign lesions, there were 2 of RUL, 3 of RLL, 5 of LUL, 4 of LLL, and one at pulmonary hilum. Only significant differences of SUVmax and SUVmean presented in lesions in LUL (SUVmax; non-gated: gated =7.76 ± 4.1: 8.80 ± 4.4, SUVmean; non-gated: gated =4.55 ±2.5: 5.03 ±2.6, all p=0.02). Additional analysis of SUV and MTV change from non-gated to gated mode based on the size was performed as in lung cancer lesion. SUVmax and SUVmean of lesions with 5cm or smaller (≤3cm and 3-5cm) in gated mode were significantly increased, and gated MTV was significantly decreased in 3-5cm-sized lesions (Table 6.).

Table 6. Comparison of the metabolic parameters of non-gated and gate mode in benign lesions, based on the size

	≤3cm (n=7)			**3-5cm (n=5)**			**>5cm (n=3)**		
	Non-gated	Gated	p-value	Non-gated	Gated	p-value	Non-gated	Gated	p-value
SUVmax	5.46±3.1	5.88±3.4	0.03	8.94±2.7	10.37±2.3	0.04	10.88±3.5	12.00±5.0	0.11
SUVmean	3.05±1.7	3.26±1.9	0.02	5.13±1.7	5.82±1.5	0.04	6.38±2.4	6.88±3.1	0.11
MTV	29.64±27.6	25.53±24.0	0.30	15.41±9.8	8.60±4.2	0.04	46.41±17.1	37.15±21.2	0.29

Comparing Lung Cancer and Benign Lesions through Respiratory Gating

The lung cancer lesions and benign lesion in three groups by size (≤3cm, 3-5cm, and >5cm) were categorized. In 3-5 cm sized lesion, SUVmax and SUVmean change rates (%) from non-gated mode to gated mode was bigger in benign lesions with marginal significance (SUVmax (%); Lung cancer: Benign lesion= 6.71±11.0: 14.50±6.9, p=0.03, SUVmean (%)= 5.55±9.9: 12.21±5.3, p=0.02). Moreover, decreased MTV variation rate (%) of benign lesions was significantly larger in benign lesions with 3-5 cm (Lung cancer: Benign lesion= -15.33±31.9: -72.86±59.0, p<0.01)). However, considering their location, there was no significant difference between the lung cancer and benign lesions (all p>0.05).

Discussion

Accurate evaluation of the lesions in lung cancer through PET/CT is required for disease staging and radiotherapy treatment planning. Staging lung cancer, especially NSCLC, was one of the first approved indications for used of PET in late 20th century [9], and PET/CT has arisen as an important diagnostic method for NSCLC [10]. While the patient is undergoing PET/CT examination, however, respiration often causes inaccurate estimates of FDG uptake and size of the lesion [11, 12]. Due to the longer image acquisition time of PET compared to CT, PET images are more affected by respiration. Gouping C. et al. reported that using amplitude-based gating resulted in significant improvements in estimates of SUVmax and SUVmean in lung cancer [13]. In the results, regardless of whether the lesion is cancerous or benign, respiratory gating resulted in a significant increase of SUVmax and SUVmean and a reduction of MTV, compared with the non-gated mode.

Considering lung cancers, the results showed significant changes from non-gated to gated mode, depending on their locations and sizes. Willem G. et al. reported that respiratory gating increased the SUVmean and decreased the volume of lesions in the middle and lower lobes [14]. In the study, SUVmax, SUVmean, and MTV showed significant differences between the two modes for lesions located in middle and lower lobes of both lungs including LUL. It is well known that the extent of the motion artifact varies by location within the lung [15]. As the lesion is located closer to the diaphragm, respiratory gating provides a better estimate, while the effect of gating decreases at locations contiguous to the apex [6]. The results indicated that the cancers closer to the diaphragm are more affected by lung respiratory motion. Indeed, comparable number of lesions in LUL (16 superior lesions and 15 inferior

lesions based on pulmonary hilar level) could have brought about the expectation.

Regardless of the T-stage (AJCC 8th) from contrast CT, all gated SUVmax, SUVmean, and MTV showed significant difference between non-gated and gated mode. Small lesions, 5cm or smaller ones presented significant increase of SUV in gated mode based on their pathologic sizes. Several phantom studies reported that SUV measurements are underestimated by respiratory motion effects, depending on the size [16]. The results suggest that the smaller the lesion, the more accurate information may be provided through the respiratory gating. Moreover, the difference between the pathologic volume and MTV was smaller in gated mode. Lesions ≤ 1cm were measured before being fixed, whereas those > 1 cm were measured immediately after fixation. In the study, only 5 of 47 cancers were measured before fixation. Thus, pathologic cancer volumes of the study, even though they may have shrunk from fixation, were large enough to evaluate. As MTV does not represent only volume but also an in vivo surrogate marker for metabolic activity, it provides as a prognostic factor for survival in several solid tumors [17]. Wijsman R. et al. reported that there was significantly less organ damage in lung cancers with gated tumor volumes after radiotherapy [18]. Thus, the study asserted that accurate measurement of MTV by simultaneous respiratory gating system will give us better information in treatment planning and better outcome. Additionally, the results may potentially improve the clinical evaluation by reducing the errors in volume and FDG uptake of cancers. This in turn may improve the disease management in staging and treatment planning.

By continuous bed motion acquisition techniques, it could shorten the setup and acquisition times, reduce axial noise variance from respiratory

motion, and improve the image quality by controlling the table speed. Amplitude-based respiratory gating based on HD·Chest technology calculates the optimal amplitude and range by searching throughout the entire respiratory signal of the gated bed positions and without dividing a number of intervals. The image data are acquired when the waveform value is within upper threshold (U) and lower threshold (L). For each value of L, the results of U are enforced. In the study, the value of U was modified until it included 35% of the acquired data [19]. Therefore, by finding optimal amplitude range of the specific duty cycle, respiratory signal, or variable breathing patterns, image quality can be improved.

There are several limitations in the studies. The results of comparing SUV and MTV from non-gated to gated mode considering the location within the T-stage were far from the data which consider only the lesion size (Table 5.). Further supplement study with enough data is required. The threshold used in the study was 40% of SUVmax which was automatically set by the program. When it comes to volume, there are some research that fixed threshold of 36-44% provides a volume of interest (VOI) of true lesion volume larger than 4mL precisely, if PET is the only data to estimate [20]. Thus, there might have some error of calculating MTV of the lesion by using specific threshold. However, the results of the study could be interpreted as a tendency of change of SUV and MTV from non-gated to gated mode. Moreover, there were relatively few cases of benign lesions, which limited comparisons of the metabolic parameters with lung cancers. The results demonstrated a significant larger change rate of SUVmax%, SUVmean% and MTV% in benign lesions from non-gated to gated mode in 3-5cm sized ones. When it comes to supplement location, there was no difference between lung cancer and benign lesions according to the size. With more detailed

elaboration comparison between lung cancer and benign lesions, respiratory gating will be more objective and improve accurate quantification parameters and help clinicians distinguish lung cancer from benign ones. Although CT acquisition with normal expiration achieves the best match between PET and CT images [21], a free breathing protocol can be a second-best alternative to reduce error [21]. Indeed, in the study, metabolic parameters in both gated and non-gated mode were examined in only PET data to avoid selective bias and CT data were acquired from free breathing protocol.

Conclusion

Simultaneous respiratory gating improves the accuracy of metabolic parameters evaluation in lung cancers without additional image acquisition and radiation exposure. These methods will improve clinical practice such as diagnosis, staging, and treatment planning of lung cancers by more accurate quantification, as well as enshrining the potential of defining cancer from benign lesions. More studies are required to understand how improved PET data achieved through respiratory gating provide advantages in treatment response and the follow-up process.

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요약 (국문초록)

폐암 및 양성 폐 병변에서

Continuous Bed Flow 기술을 이용한

동시 호흡 게이트 ^{18}F-FDG PET / CT의 유용성

김지현

의과대학 임상의과학과

서울대학교

목적:

본 연구에서는 폐암과 양성 병변의 대사적 매개변수를 호흡게이트 또는 게이트 없이 (non-gated mode) 진행한 양전자 방출단층 촬영 (PET/CT)을 동시에 함께 얻음으로써 동시 호흡게이팅의 유용성을 평가하고자 하였다.

방법:

2015년 4월부터 2016년 4월까지 본 병원에서 치료받은 121명의 환자를 휴향적으로 조사하였다. 게이트없이 그리고 진폭 기반 호흡 게이팅 모드 PET/CT 데이터를 동시에 획득하였다. 이에 얻은

데이터로 병변의 대사 매개변수; 표준 섭취값(SUV)max, SUVmean, 및 종양의 대사성 부피(MTV)를 분석하였다.

결과:

호흡 게이트 모드에서의 폐암(n=108) 과 양성 폐 병변(n=15)모두에서 non-gated 모드보다 SUVmax와 SUVmean이 더 크고 MTV가 더 유의학게 작았다. 폐암은 양성 폐 병변보다 높은 SUVmax와 SUVmean을 보였다. AJCC 8판을 바탕으로 위치 와 T병기에 따른 폐암의 호흡 게이트 모드와 non-gated 모드에서의 대사 매개 변수는 앞서 같은 결과를 나타났다. 또한 절제된 46개의 암에서 병리학적 부피와 MTV를 비교하였고 호흡게이트 모드에서 유의하게 적은 차이를 보였다. 마지막으로 양성 폐 병변의 non-gated모드에서 게이트모드로의 대사 매개 변수 (SUVmax, SUVmean, 그리고 MTV)변화율은 폐암에서의 변화율보다 유의하게 높았다.

결론:

진폭 기반 동시 호흡 게이팅 알고리즘을 사용하는 PET 이미지 획득은 보다 정확한 정량화를 제공하고 SUV및 MTV의 정확한 측정을 가능하게 하므로 폐암의 병기설정 또는 치료계획에 있어 도움을 줄 수 있다. 또한 위 결과는 양성 폐 병변에서 암을 구분하는 가능성이 있다.

Keywords: 동시 호흡 게이팅 ^{18}F-FDG PET/CT, 표준 섭취값 (SUV), 대사성 종양 부피 (MTV)