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Original Article

FDG-PET/CT imaging in lung malignancy: the effect of respiratory gating on the standardised uptake values of lung lesions

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Abstract

Background

FDG-PET/CT has gained widespread acceptance as an invaluable tool in the management of oncology patients, in which, the standardised uptake values (SUV) are used to provide a simplistic measure of the metabolic activity of the lesion. However, in the evaluation of lung malignancy, respiratory motion results in a smearing (partial volume) artefact, that leads to underestimation of the lesion SUV. Respiratory gating has been employed as a potential solution. However, literature regarding the effect of respiratory gating on SUVs in lung malignancy is mostly limited to pilot studies with small sample sizes.

Objective

To assess the effect of respiratory gating on the SUV of lung lesions in the FDG-PET/CT evaluation of lung malignancy in the clinical setting. Thereby, to provide proof of principle of the effectiveness of respiratory gating in reducing the smearing (partial volume) artefact created by respiratory motion and to determine its ability to provide a more accurate estimation of SUVs in the evaluation of patients with lung malignancy.

Method

A retrospective cohort study was conducted on 49 consecutive patients with biopsy proven lung malignancy who underwent both conventional (non-gated) and respiratory gated FDG-PET/CT imaging between December 2018 to June 2019. The maximum SUV, SUVmax, of the lung lesions was recorded from both sets of images. A paired-samples t-test was performed to compare the SUVmax values between the two groups.

Results

There was a statistically significant difference in the SUVmax value between the non-gated (M=9.6284, SD=5.13304) and the gated (M =10.4651, SD=5.51711) series; t(48)= -3.755, p = 0.000. These results suggest that respiratory gating does influence the SUVmax of lung lesions. Specifically, our results suggest that when respiratory gating is employed, the SUVmax of lung lesions increases compared to the non-gated value.

Conclusion

Respiratory gating is effective in reducing the smearing (partial volume) artefact created by respiratory motion and provides a more accurate estimation of the SUV for lung lesions in the PET/CT evaluation of lung malignancy.

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Introduction

Positron emission tomography (PET) imaging is a functional nuclear medicine technique that is used to assess the metabolic uptake within tissues of the body.

It involves detection of gamma rays emitted by a positron emitting radiopharmaceutical administered to the body, the most frequent being Fluorine-18 Fluorodeoxyglucose (F18- FDG), a glucose analogue. The value of FDG PET imaging in the field of oncology is based on the observation that malignant cells have an increased glycolytic rate and an increased cellular glucose uptake [1].

However, FDG-PET cannot be used as an independent imaging modality in oncology, the primary limitation being the poor depiction of anatomic structures on PET imaging. Subsequently, FDG-PET/CT was developed, where PET imaging was integrated with computerized tomography (CT) offering a combination of both morphological and functional detail [1]. FDG-PET/CT has since gained widespread acceptance as an invaluable tool in the care of oncology patients which includes diagnosis, staging, treatment-effectiveness monitoring and radiotherapeutic planning [1].

The standardised uptake value (SUV) is a semi-quantitative measure of the radiopharmaceutical uptake in a region of interest that normalises the lesion activity to the injected activity and the volume of distribution (usually the total body weight or lean body mass). There are many different formulae for SUV, depending on how the SUV is normalised (e.g. with regard to total body weight, lean body mass or body surface area) and how the region of interest (ROI) is analysed (e.g. SUVmax or SUVmean). Most commonly, SUVmax is utilised as it is highly reproducible and easy to calculate and it is the most commonly used measure of FDG avidity in current clinical practice. SUVmax is calculated using the formula SUVmax = tracer uptake in ROI / (injected activity / patient weight).

The SUVmax is useful in differentiating benign from malignant lesions with a higher SUVmax associated with more malignant lesions [2]. A SUVmax cutoff of 2.5 or greater is associated with malignancy for large pulmonary nodules (greater than 1.0 cm) but there is no such cut off in the assessment of smaller pulmonary nodules (less than 1.0 cm) [2]. The SUVmax also provides important information regarding prognosis. The SUVmax is known to be inversely related to prognosis with a low SUVmax associated with low-grade histology and higher overall survival compared to higher SUVmax lesions [3]. Therefore, the SUVmax has many implications in modern medicine including in the initial assessment of lesions, formulation of treatment plans and in assessing the metabolic response following treatment.

Of all malignancies, lung cancer is the most common worldwide, with 2.1 million new cases detected in 2018. It also continues to be the leading cause of cancer death with 1.8 million deaths in 2018, accounting for approximately 18% of all cancer deaths [4]. Lung cancer poses a unique challenge in PET imaging due to respiratory motion. The movement of the lesion with respiration results in image blurring and misidentification of the lesion including its FDG uptake. This results in a reduced target to background ratio of FDG uptake as well as an overestimation of the lesion size due to the smearing (partial volume) artefact created by the respiratory motion. The number of counts acquired during a given period of time, whether the lesion is static or moving, is the same. Therefore, any increase in the apparent lesion size due to the smearing (partial volume) artefact will

underestimate the SUVmax or glucose concentration within the tumours, thereby downgrading its malignant potential [5].

Respiratory gating has been employed to reduce the partial volume artefact created by respiratory motion and provide a more accurate estimation of SUV in lung lesions. However, literature regarding the effect of respiratory gating on SUV values in lung cancer are limited to a very small number of patients, usually in pilot studies.

Objective

To assess the effect of respiratory gating on the SUV of lung lesions in the FDG-PET/CT evaluation of lung malignancy in the clinical setting. Thereby, to provide proof of principle of the effectiveness of respiratory gating in reducing the smearing (partial volume) artefact created by respiratory motion and to determine its ability to provide a more accurate estimation of SUVs in the evaluation of lung malignancy.

Materials and Methods

Study Design

A retrospective cohort study was conducted at the Department of Nuclear Medicine, Westmead Hospital, Westmead, Australia on 49 consecutive patients that underwent both respiratory gated and conventional whole body FDG-PET/CT for lung malignancy over a 6-month period from 1st December 2018 to 1st June 2019.

Inclusion Criteria

Patients with biopsy-proven lung malignancy.

Exclusion Criteria

Patients with lesions less than 1.0 cm in diameter were excluded from the study cohort due to the limited spatial resolution of PET imaging in assessing the metabolic activity of lesions less than 1.0cm in size [6].

Instrumentation and Data Acquisition

Images were acquired using a Siemens Biograph128 PET-CT scanner. An initial low dose CT was performed for attenuation correction followed by a conventional whole body PET/CT after injection of the radiopharmaceutical. Conventional PET images were acquired approximately one hour after the injection. Subsequently the respiratory gated images were obtained. The respiratory gating system used was the Anzai respiratory gating system which uses a patient contact load cell sensor. This sensor which is in contact with the patient's upper abdomen detects abdominal wall motion and integrates this information with the PET camera to acquire images during the same phase of respiration to minimise motion related artefacts.

Image Analysis and Measurements

Each study was read retrospectively and measurements obtained using the Siemens molecular imaging software "Syngo-Via". The low dose CT images were first analysed to calculate the maximum diameter of each lung lesion. In the presence of more than one lesion the largest lesion was selected. Subsequently,

the SUVmax values for the lung lesions were obtained by placing the region of interest (ROI) over the selected lesion. The SUVmax measurements of each selected lesion were recorded twice, first from the conventional (non-gated) PET/CT images and secondly from the respiratory gated images. The histological subtype of lung malignancy was also recorded from the biopsy results available on the patient electronic medical records.

Statistical analysis

Continuous variables were presented as mean values with standard deviations (SD) and categorical variables were presented as percentages. A paired-samples t-test was conducted to compare the SUVmax values of lung lesions in the conventional (non-gated) and gated series. Differences were considered statistically significant when the p value was less than 0.05. The Statistical Package for Social Sciences version 23 was used for all calculations and statistical analysis.

Ethics clearance

Ethics clearance was obtained from the Research and Ethics Committee of the Western Sydney Local Health District.

Results

The percentages of patients belonging to the different histological subtypes are represented in Figure 1. The most common histological subtype was adenocarcinomas accounting for 57.1% of all lesions. This was followed by squamous cell carcinoma (20.4%), small cell carcinoma (14.3 %), metastatic lesions (6.1%) and spindle cell carcinoma (2.0%).

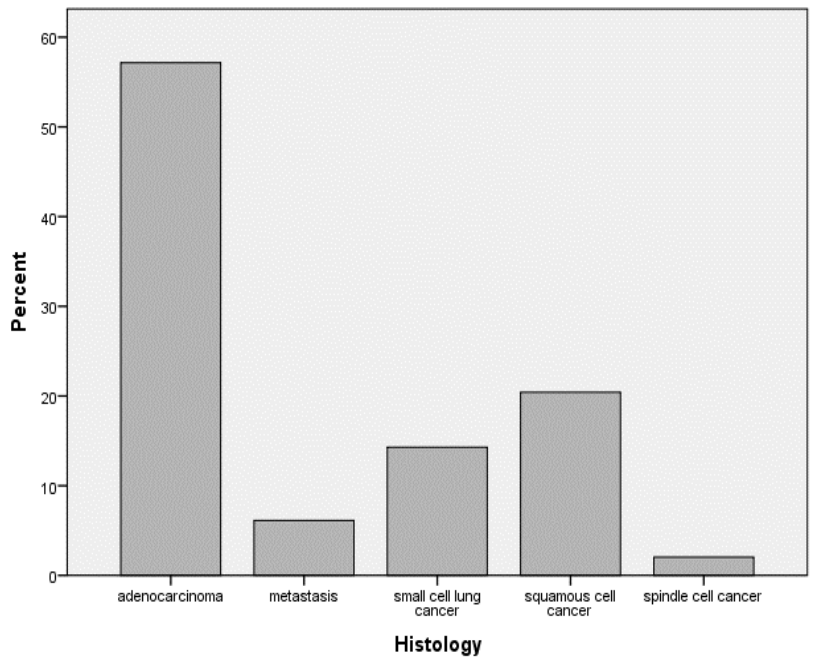

Figure 1: Histological subtypes of lung malignancy

The maximum diameter of the largest lesion in each patient is represented in Figure 2. The lesion sizes ranged from 1.0 cm to 7.5 cm with a mean of 2.8 cm and a standard deviation of 1.5 cm.

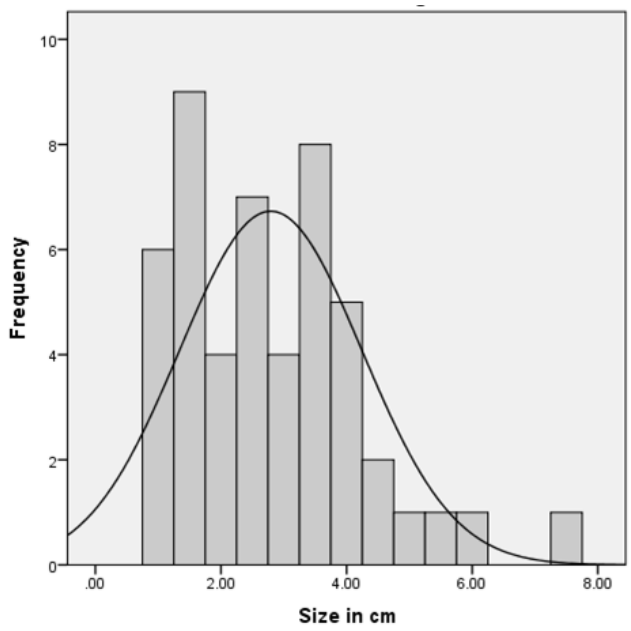

Figure 2 : Size of lung lesions

There was a significant difference in the SUVmax value between the non-gated (*M*=9.6284, *SD*=5.13304) and gated (*M* =10.4651, *SD*=5.51711) series; t(48)= -3.755, p = 0.000 (table 1). (*M*= mean, *SD*= standard deviation) series (Table 1).

Table 1: Summarised paired sample t test

Paired non-gated and gated series	Mean difference	t	df	Sig.
	-.83673	-3.755	48	0.000

(t = t statistic, df= degrees of freedom, Sig.=significance 2-tailed)

These results suggest that respiratory gating affects SUVmax values of lung lesions. Specifically, our results suggest that when respiratory gating is employed the SUVmax of lung lesions increases.

Discussion

The SUV was designed as a simple method to quantify uptake of radiopharmaceuticals in PET imaging. However, they have a number of limitations. SUV is dependent on many patient-related factors including the defined region of interest (ROI), the activity injected, plasma glucose levels, competition with endogenous glucose, rate of phosphorylation, body size and body composition as well as tumour type. Technically, SUV values will vary depending on the PET scanner's signal-to-noise properties, the accuracy of the image reconstruction

algorithm as well as corrections algorithms and the time between injection and image acquisition [7].

One of the problems with existing SUV measurements in lung cancer is that there is potential for underestimation of the actual metabolic activity because of smearing of the lesion size due to respiratory motion. Respiratory gating was designed to provide a more accurate estimation of the SUV by reducing the partial volume artefacts created by respiration motion and thereby prevent overestimation of the lesion size. Thus, respiratory gating was found to increase the SUV values of lesions compared to non-gated images. The findings in this study also confirm an increase in the SUV of lung lesions on respiratory gated imaging compared to non-gated PET imaging by reduction of the motion related partial volume artifact [5].

The SUVmax helps in differentiating benign from malignant lesions and also provides information regarding the prognosis. Therefore, respiratory gating has a role in providing a more accurate estimation of SUVmax which, in turn, helps in the differentiation between benign and malignant lesions and improves the prognostication of lesions.

The ability to gate PET scans should also have a major impact on radiotherapy planning by providing improved definition of the tumour during radiation treatment. This should enable a greater radiation dose to be delivered directly to the lesion while sparing more of the normal surrounding tissues from the harmful effects of radiation.

The current field standard in respiratory gating involves the use of specific hardware such as belts and motion sensors attached to the patient and integrated with the PET scanner. The disadvantage of using this method includes the need for further training of technologists, potential discomfort to patients and longer setup and scanning times [8].

Recent advances in respiratory gating involves the development of data-driven gating or software gating as an alternative gating approach. With software gating, motion information is extracted from raw PET data to provide motion characterisation analogous to that of hardware. Software gating requires no additional time or effort from technologists or patients and overcomes the limitations associated with hardware gating [8]. However, further research is required to determine the optimum technology for respiratory gating to be applied across the field.

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